

Oxidation of threonine by Corey's reagent: A kinetic study

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Abstract

Oxidation of Threonine by pyridinium chlorochromate in DMF-water medium has been studied. The rate of reaction was found to be of first order dependence on [PCC], [Threonine] and [H⁺]. The Michaelis–Menten type kinetics is observed with respect to Threonine. The increase in the rate of oxidation with increase in acidity indicates the involvement of a protonated chromium (VI) species in the rate-determining step. The product of oxidation has been identified as an aldehyde. The rate of reaction decreased with increase in the polarity of medium indicates that there is involvement of an ion-dipole type of interaction in the rate-determining step.

Keywords: Kinetics; oxidation; Corey's Reagent (Pyridinium chlorochromate); Threonine; DMF (N, N-Dimethylformamide)

1. Introduction

A large variety of compounds containing chromium (VI) have proved to be versatile reagent capable of oxidising almost every oxidisable functional group [1,2]. Pyridinium chlorochromate (PCC) is one of the most versatile available oxidising agents [3]. A number of reports on the oxidation of several substrates by pyridinium chlorochromate are available in literature [4-8].

The study on kinetics of oxidation of amino acids is an area of active experimentation due to their biological importance. Amino acids perform a multitude of structural, hormonal and catalytic functions essential to life. They represent organism forerunners of essential biomolecules such as proteins, hormones, enzymes. Thus, the mechanism of analogous non-enzymatic chemical processes in the oxidation of amino acids is a potential area for intensive investigations. We report herein the kinetics of oxidation of Threonine by PCC in the DMF-H₂O acidic media.

2. Experimental method

Pyridinium chlorochromate was prepared by the method of E. J. Corey and W.T. Suggs [9], and its purity was checked iodometrically and by the UV-vis spectra. Threonine Analar grade (SRL) was used as supplied, purity was checked by its melting point 233°C and all other reagents were of Analar 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 Threonine 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 thermostated compartment of JASCO model 7800 UV/vis. spectrophotometer.

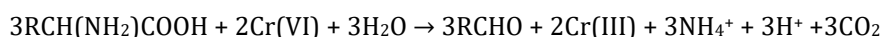
The kinetic runs were followed for more than 70% completion of reaction and good first order kinetics was observed. Pseudo-first order rate constants, k_{obs} , were obtained from the slope of the plot of lg (absorbance) versus time

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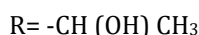
3. Results and discussion

3.1. Stoichiometry and product analysis

Reaction mixture containing known slight excess of PCC over Threonine containing 0.3 mol/dm³ [HClO₄] in 70 vol. % DMF, 30 vol. % water mixture (v/v), were allowed to stand at 40°C. When the reaction was completed, the PCC concentration was assayed by measuring the absorbance at 354 nm. The results indicated that 2 mol of PCC react with 3 mol of Threonine. The qualitative product study was made under kinetic conditions. The main reaction product was identified as aldehyde by its 2,4-D.N.P. derivative. The Nessler reagent test and lime water test were used to detect the ammonium ion and carbon dioxide, respectively, and Cr(III) was confirmed by the visible spectra of the reaction solution after completion of the reaction. The observed stoichiometry may be represented as follows:



Where



3.2. Effect of PCC

The observed rate constant k was not affected by the change in PCC initial concentration Table 1.

Table 1 Variation of rate with PCC, Threonine, perchloric acid concentrations, DMF : H₂O and temperature

| [PCC] × 10 ³ (mol dm ⁻³) | [Threonine] × 10 ² (mol dm ⁻³) | [H ⁺] × 10 (mol dm ⁻³) | Temp. (K) | DMF: H ₂ O (%) | $k_{obs} \times 10^5$ (s ⁻¹) |
|--|--|---|--------------|------------------------------|---|
| 2.5 | 2.0 | 3.0 | 313 | 70:30 | 42.75 |
| 2.25 | 2.0 | 3.0 | 313 | 70:30 | 43.10 |
| 2.0 | 2.0 | 3.0 | 313 | 70:30 | 42.80 |
| 1.75 | 2.0 | 3.0 | 313 | 70:30 | 42.65 |
| 1.5 | 2.0 | 3.0 | 313 | 70:30 | 42.90 |
| 1.0 | 2.0 | 3.0 | 313 | 70:30 | 43.15 |
| 2.0 | 1.2 | 3.0 | 313 | 70:30 | 19.20 |
| 2.0 | 1.43 | 3.0 | 313 | 70:30 | 22.50 |
| 2.0 | 1.6 | 3.0 | 313 | 70:30 | 32.60 |
| 2.0 | 2.0 | 3.0 | 313 | 70:30 | 42.10 |
| 2.0 | 2.4 | 3.0 | 313 | 70:30 | 48.65 |
| 2.0 | 2.8 | 3.0 | 313 | 70:30 | 52.20 |
| 2.0 | 3.66 | 3.0 | 313 | 70:30 | 60.90 |
| 2.0 | 5.0 | 3.0 | 313 | 70:30 | 69.90 |
| 2.0 | 2.0 | 1 | 313 | 70:30 | 14.20 |
| 2.0 | 2.0 | 2.5 | 313 | 70:30 | 27.80 |
| 2.0 | 2.0 | 3.0 | 313 | 70:30 | 38.10 |
| 2.0 | 2.0 | 3.5 | 313 | 70:30 | 52.15 |
| 2.0 | 2.0 | 5.0 | 313 | 70:30 | 65.50 |
| 2.0 | 2.0 | 7.0 | 313 | 70:30 | 97.90 |
| 2.0 | 2.0 | 3.0 | 298 | 70:30 | 12.00 |

| | | | | | |
|-----|-----|-----|-----|-------|-------|
| 2.0 | 2.0 | 3.0 | 303 | 70:30 | 18.10 |
| 2.0 | 2.0 | 3.0 | 308 | 70:30 | 23.25 |
| 2.0 | 2.0 | 3.0 | 313 | 70:30 | 42.20 |
| 2.0 | 2.0 | 3.0 | 318 | 70:30 | 53.40 |
| 2.0 | 2.0 | 3.0 | 323 | 70:30 | 75.90 |
| 2.0 | 2.0 | 3.0 | 313 | 70:30 | 42.50 |
| 2.0 | 2.0 | 3.0 | 313 | 60:40 | 32.45 |
| 2.0 | 2.0 | 3.0 | 313 | 55:45 | 24.70 |
| 2.0 | 2.0 | 3.0 | 313 | 50:50 | 15.60 |
| 2.0 | 2.0 | 3.0 | 313 | 40:60 | 12.30 |
| 2.0 | 2.0 | 3.0 | 313 | 30:70 | 10.10 |

3.3. Effect of substrate

The reaction rate increased with an increase in the concentration of Threonine (Table 1). The plot of $\lg k_{\text{obs}}$ versus $\lg[\text{Threonine}]$ (Figure-1) was linear with positive slope indicating first order dependence of the rate on $[\text{Threonine}]$. The plot of $1/k_{\text{obs}}$ versus $1/[\text{Threonine}]$ (Figure-2) is a straight line with positive intercept, which indicates that the Michaelis–Menten type kinetics is followed with respect to Threonine. A similar phenomenon has been observed in the oxidation of α -amino acid by Cr(VI) [10,11].

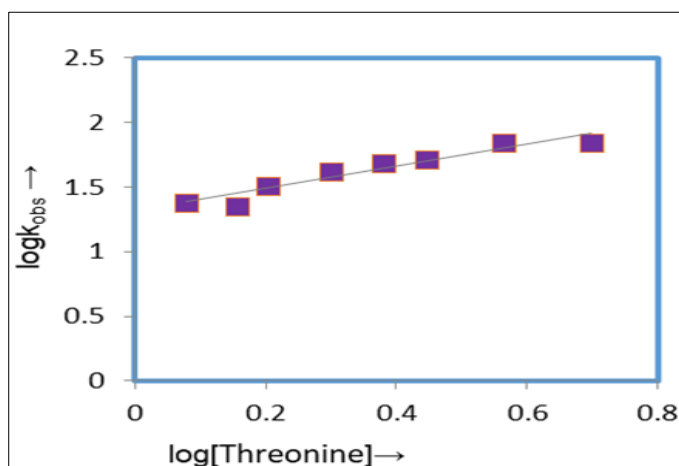


Figure 1 Variation Of Rate With Substrate Concentration $\log k_{\text{obs}}$ versus $\log[\text{Threonine}]$

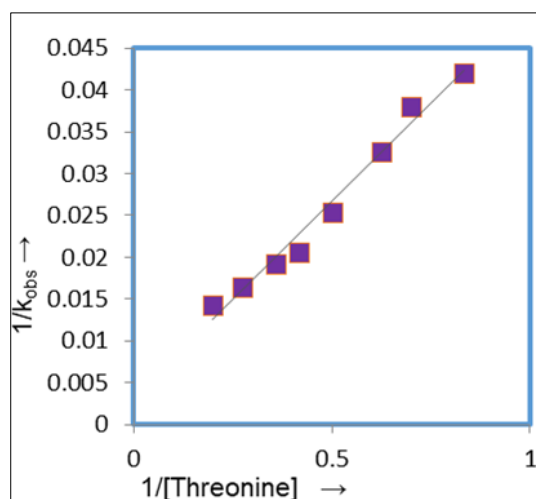


Figure 2 Variation Of Rate With Substrate Concentration $1/k_{obs}$ versus $1/[\text{Threonine}]$

3.4. Effect of ionic strength

The effect of ionic strength was studied by varying sodium sulphate concentration in the range of Debye-Huckel limiting law. 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 iron and a neutral molecule or between neutral molecules [12].

Table 2 Variation of rate with sodium sulphate concentration

$[\text{Threonine}] = 2.0 \times 10^{-2} \text{ mol dm}^{-3}$; $[\text{HClO}_4] = 0.3 \text{ mol dm}^{-3}$; $[\text{PCC}] = 2.0 \times 10^{-3} \text{ mol dm}^{-3}$; $\text{DMF} = 70 \%$ (v/v)

| $[\text{Na}_2\text{SO}_4] \times 10^3 \text{ (mol dm}^{-3}\text{)}$ | 1.0 | 3.0 | 5.0 | 7.0 | 11.0 |
|---|-------|-------|-------|-------|-------|
| $k_{obs} \times 10^5 \text{ (s}^{-1}\text{)}$ | 42.20 | 42.50 | 42.90 | 43.10 | 42.25 |

3.5. Effect of solvent composition

It was observed that the change in solvent composition by varying DMF (% v/v) in the reaction mixture. The rate of reaction increased with an increase in volume percentage of DMF [Table 1]. Many theories have been put forward to give a quantitative explanation [13,14] for the effect of dielectric constant 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 [15] had shown that in the linear plot of $\lg k_{obs}$ versus $1/D$ a positive slope indicates a positive ion-dipole reaction, while a negative one indicates the involvement of two dipoles or a negative ion-dipole reaction. In the present investigation a plot of $\lg k_{obs}$ versus $1/D$ (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.

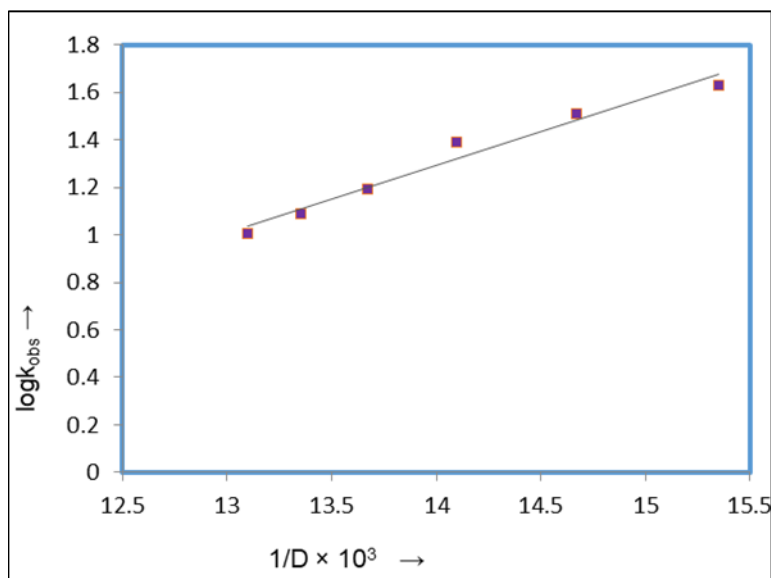


Figure 3 Variation Of Rate With Solvent Composition $\log k_{obs}$ versus $1/D$

3.6. Effect of temperature

The rate constant of the reaction was found to increase with an increase in temperature [Table 1]. The energy of activation was obtained by the plot of $\lg k$ versus $1/T$ (Figure- 4). 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 [16]. The complex formation is proved by the plot of inverse of rate constant against inverse of substrate concentration. It has been pointed out [17] that if entropy of activation is negative and small the reaction will be slow.

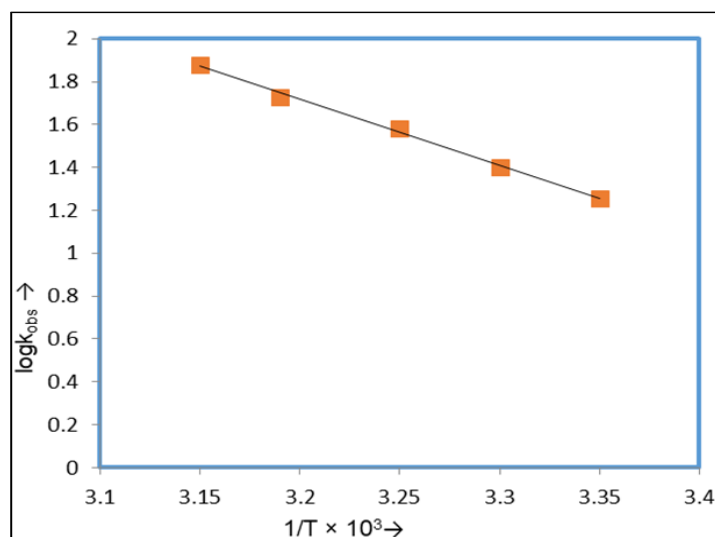


Figure 4 Variation Of Rate With Temperature $\log k_{obs}$ versus $1/T$

3.7. Effect of perchloric acid

The rate was found to increase with an increase in the perchloric acid concentration [Table1]. A plot of $\lg k_{obs}$ versus $\log[HClO_4]$ (Figure-5) is a straight line with a positive slope ≈ 1 . This shows that reaction is of first order with respect to the hydrogen ion concentration.

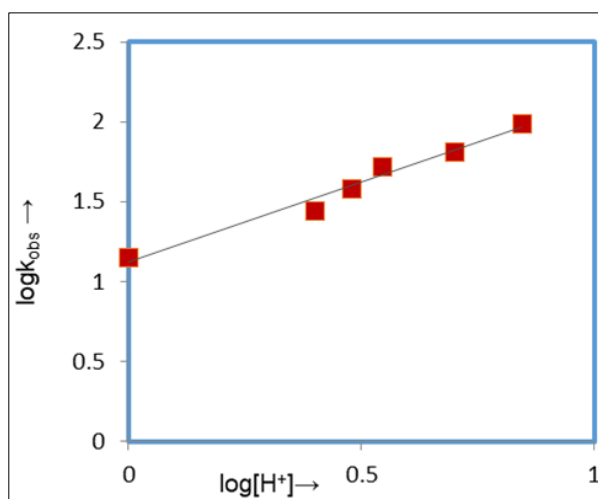


Figure 5 Variation Of Rate With H⁺ Ion Concentration log k_{obs} versus log[H⁺]

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 Threonine or zwitterion. 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 Threonine is not involved in the reaction sequence and the zwitterion is the active species in this reaction.

The acid catalysis may well be attributed to a protonation of PCC (equation-2) to yield a stronger oxidant and an electrophile both with the protonated and unprotonated forms being reactive. The formation of a protonated species of PCC has been also reported [18-20].

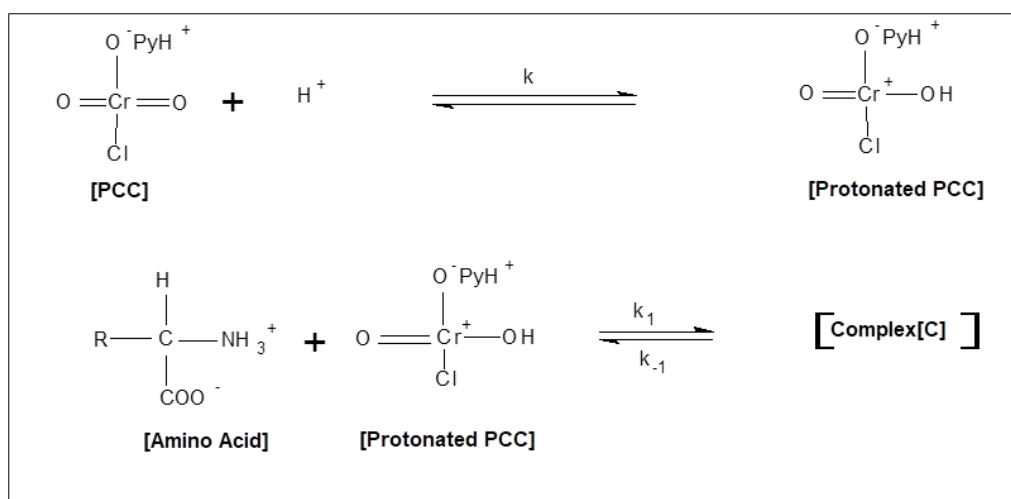


3.8. Effect of acrylonitrile

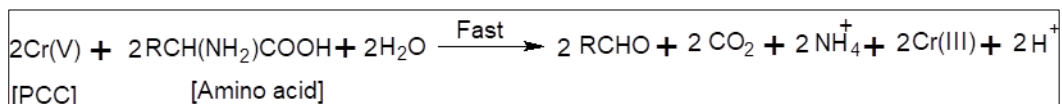
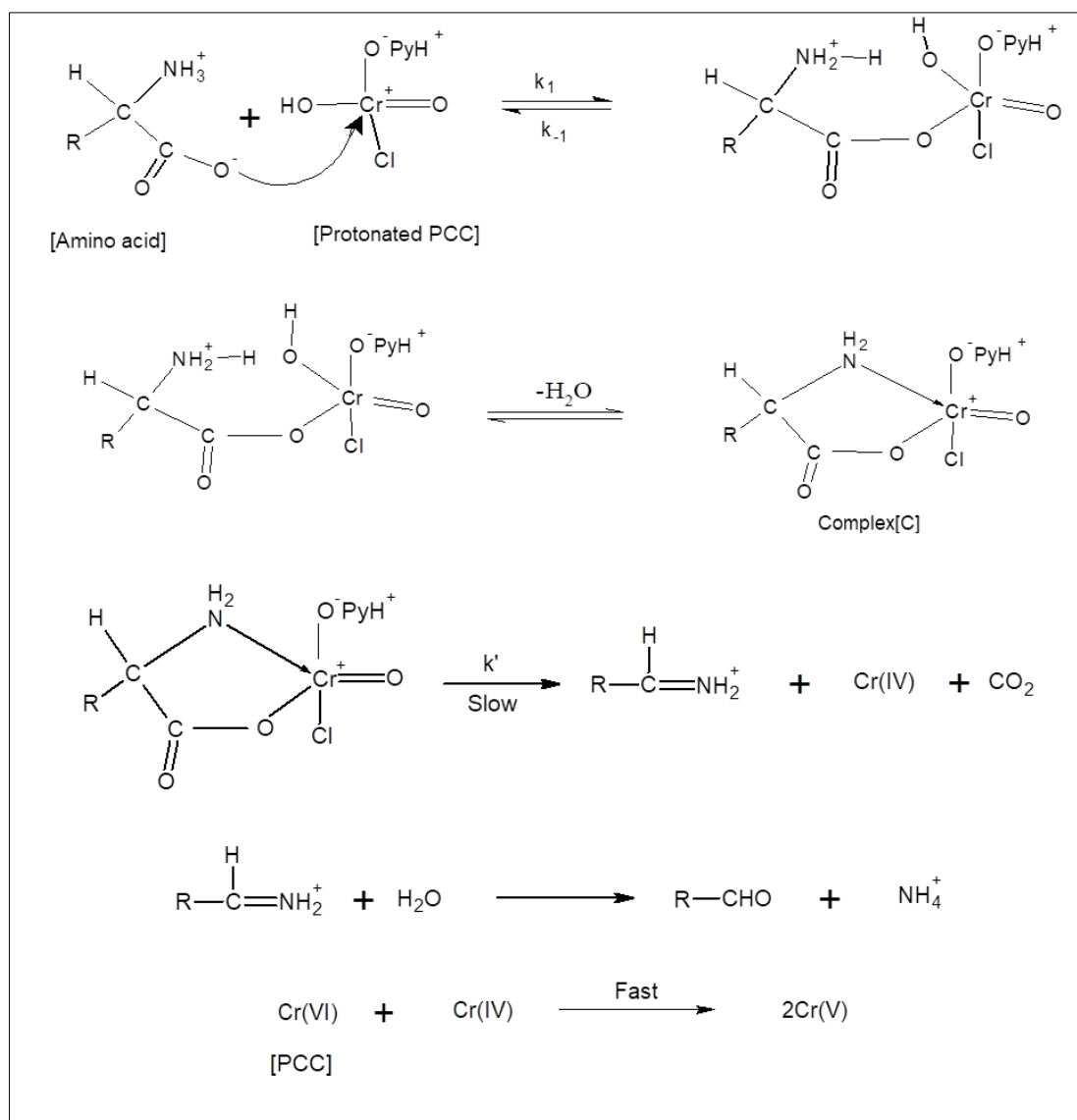
Involvement of radical mechanism is ruled out, as there is neither any decrease in rate in the presence of stabilizer free acrylonitrile nor milky appearance under kinetic conditions.

3.9. Mechanism

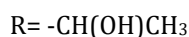
On the basis of the above experimental results, a suitable mechanism is given below:



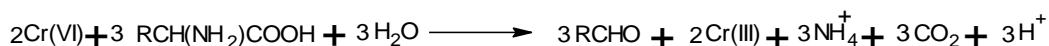
The formation of a complex between Threonine and protonated PCC may be represented as:



Where



The overall reaction may be represented as follows:



4. Conclusion

The study on the oxidation of Threonine by pyridinium chlorochromate in DMF-water medium in the presence of perchloric acid reveals that the neutral amino acid takes part in the reaction, and the protonated amino acid is not involved in the reaction. The Michaelis-Menten type kinetics is observed with respect to Threonine. Although the intercept value is very small, it indicates that the formation of a complex which may be highly reactive so concentration

will be very small at any time. The reaction was carried out at different temperatures. In the temperature range of 298-323 K, the Arrhenius equation is valid.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in this manuscript.

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