

**MECHANISM OF Ru(III)-CATALYZED OXIDATION OF L-CYSTINE BY Ce(IV) IONS IN SULPHURIC ACID MEDIUM**

\*<sup>1</sup>Owalude, S.O., <sup>1</sup>Odebunmi, E.O., <sup>2</sup>Bamigboye, C.A. and <sup>2</sup>Adebayo, A.B.

<sup>1</sup>Department of Chemistry, University of Ilorin, P. M. B. 1515, Ilorin, Nigeria

<sup>2</sup>Department of Industrial Chemistry, University of Ilorin, P. M. B. 1515, Ilorin, Nigeria.

\***Correspondence:** sowalude@gmail.com; owalude@unilorin.edu.ng

**ABSTRACT**

Mechanism of oxidation of L-cystine by acidic solution of Ce(IV) ions in the presence of Ru(III) ions as homogeneous catalyst was studied using kinetic approach. A first-order dependence of the reaction rate on [cystine] and [Ce(IV)] was observed. The rate is inversely proportional to  $[H^+]$  and decreased with increasing ionic strength of the medium. The active species of the oxidant in sulphuric acid medium and that of the catalyst were  $Ce(SO_4)_2$  and  $[RuCl_2(H_2O)_4]^+$  respectively. A suitable mechanism based on the kinetic data is proposed. The activation parameters and the thermodynamic quantities were also evaluated which supported the proposed mechanisms.

**Keywords:** Activation parameters, cerium(IV) ions, kinetics, L-cystine, ruthenium(III) chloride.

**INTRODUCTION**

The study of mechanism of oxidation of amino acids is of immense biochemical importance and helps greatly in the understanding of their reducing properties in solutions [1]. L-cystine is sulphur-containing amino acid dimer that aids in the healing of burns and wounds. It also helps in breaking down mucus deposits in patients suffering from bronchitis and cystic fibrosis [2]. The reducing ability of L-cystine also functions as a scavenger to oxidants and free radicals. Review of literature revealed that kinetic studies on the oxidation of L-cystine were limited [3]. The toxic effects of metals and synthesis of reaction products can therefore be achieved by clear understanding of the mechanism of such biological redox reactions such as those of L-cystine. Oxidation reactions of Ce(IV) in aqueous sulfuric acid media has been reported to be ineffective but can be effectively catalyzed by metal ions even at low concentration [4]. Ruthenium(III) and iridium(III) ions are the most efficient among these metal ions [5]. Cerium(IV) ions is an electron oxidant with reduction potential of the couple Ce(IV)/Ce(III) of -1.70 V which has been widely applied as oxidant for various organic and inorganic molecules [6]. It exists in sulphuric

acid medium as several sulphate complexes such as  $\text{Ce}(\text{OH})^{3+}$ ,  $\text{Ce}(\text{SO})_4^{2+}$ ,  $\text{Ce}(\text{SO}_4)_2$ ,  $\text{Ce}(\text{SO}_4)_2(\text{HSO}_4^-)$  and  $\text{H}_3\text{Ce}(\text{SO}_4)_4^-$  [7]. These different complexes of Ce(IV) ions can act as the active species during reactions. The mechanism is therefore expected to be quite complicated [6]. The role of these complexes in the oxidation mechanism has not been well understood. Oxidation reactions using Ru(III) as catalyst involves several active species of ruthenium depending on the reaction media and oxidation states of ruthenium [8].

To the best of our knowledge, report on the mechanism of Ru(III) catalyzed oxidation of L-cystine by Ce(IV) ions has not been well documented. We have therefore investigated the kinetics and mechanism of Ru(III) catalyzed oxidation of L-cystine by cerium(IV) in aqueous sulphuric acid medium in order to clarify the mechanism by identifying the active forms of Ru(III), cerium(IV) and cystine. This report is hereby presented to provide further insight into the mechanism of oxidation of L-cystine by Ce(IV) ions in sulphuric acid medium and to provide further insight on the behavior of ruthenium (III) as a catalyst in the oxidation of amino acids.

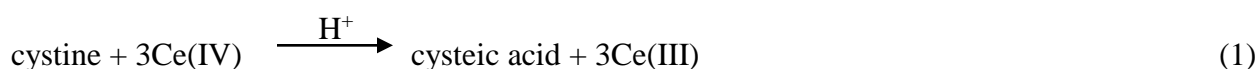
## EXPERIMENTAL

All chemicals were commercially sourced from BDH and Sigma Aldrich. They were used directly as received. Ce(IV) solution was prepared by dissolving cerium(IV) ammonium sulphate in  $0.1 \text{ mol dm}^{-3}$  sulphuric acid and was standardized with iron(II) ammonium sulphate solution [9].  $0.1 \text{ mol dm}^{-3}$  L-cystine stock solution was prepared freshly before use by dissolving 2.403 g in 100 mL of dilute sulphuric acid. Stock solution of Ru(III) ( $0.01 \text{ mol dm}^{-3}$ ) was prepared by dissolving 0.2074 g  $\text{RuCl}_3$  in 100 mL of  $0.20 \text{ mol dm}^{-3}$  HCl and the concentration was always checked using ethylenediaminetetraacetic acid (EDTA) titration [10].

*Kinetic measurements:* The kinetic measurements were carried out at  $35 \pm 0.5 \text{ }^\circ\text{C}$  in  $0.10 \text{ mol dm}^{-3}$  sulphuric acid medium under the pseudo-first-order conditions such that  $[\text{H}^+] \gg [\text{cystine}] \gg [\text{Ce(IV)}]$ . The reaction was initiated by mixing appropriate quantities of previously thermostated solutions of Ce(IV) and cystine which also contained the required amounts of  $\text{H}_2\text{SO}_4$  and  $\text{NaSO}_4$ . The progress of the reaction was monitored by estimating the decrease in the absorbance of Ce(IV) ions at time intervals at a wavelength of 395 nm using a Beckman Coulter DU 730 UV-Vis spectrometer. Kinetic runs were followed for more than 80 % completion of the reaction and the observed first-order rate constants,  $k_{\text{obs}}$ , were calculated from the slopes of the

plots of  $\log[\text{Cerium(IV)}]$  versus time. The calculated rate constants were averages of at least three measurements and were reproducible to within  $\pm 5\%$ .

*Stoichiometry:* The reaction mixture containing the excess of Ce(IV) concentration over cystine with both solutions prepared in  $0.10 \text{ mol dm}^{-3} \text{ H}_2\text{SO}_4$  at a constant ionic strength of  $0.20 \text{ mol dm}^{-3}$ , maintained by  $\text{NaSO}_4$ , was kept at  $25 \pm 2^\circ \text{C}$  for 48 h. The unreacted Ce(IV) was then analyzed spectrophotometrically. The results indicated that 3 mol of Ce(IV) were consumed by 1 mol of cystine.



*Polymerization study:* Formation of free radicals in the reaction was investigated by the addition of a known quantity of aqueous 20 % acrylamide into the reaction mixture at the initial stage and the mixture was kept in an inert atmosphere for 24 hours. No gel formation was noticed. Control experiments from which either Ce(IV) or cystine were excluded also produced no gel formation. On further diluting the reaction mixture with methanol, no precipitate was formed thus confirming the absence of free radicals in the reaction.

## RESULTS AND DISCUSSION

*Variation of  $k_{\text{obs}}$  with reactants concentration:* The values of the observed rate constants ( $k_{\text{obs}}$ ) as presented in Table 1 are almost constant with increasing initial concentrations of Ce(IV), an indication that the order with respect to Ce(IV) concentration is unity [11]. In another set of experiments, the  $k_{\text{obs}}$  were evaluated at different initial concentrations of the cystine keeping all other parameters constant. The values of  $k_{\text{obs}}$  increased with increase in concentration of cystine almost in direct proportion such that when divided by the corresponding cystine concentration a fairly constant value was obtained. This suggests that the reactions are first-order with respect to cystine. Plot of  $k_{\text{obs}}$  against [cystine] was linear passing through the origin (Fig. 1) which confirms that the reactions are first-order with respect to cystine [12].

*Variation of  $k_{\text{obs}}$  with ionic strength:* The effect of ionic strength was studied by varying the  $\text{Na}_2\text{SO}_4$  concentration in the reaction medium from  $0.05$  to  $0.35 \text{ mol dm}^{-3}$  while maintaining constant the other parameters. The results as shown in Table 1 revealed a marginal decrease in

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CATALYZED OXIDATION OF L-CYSTINE BY Ce(IV) IONS IN SULPHURIC ACID MEDIUM**

rate constants with increase in ionic strength. This suggests that the rate determining steps of reaction occurred between a positive and neutral species as shown in the mechanism [7].

Table 1: Effect of various parameters on the observed first-order rate constants  $k_{obs}$  for Ru(III) catalyzed oxidation of L-cystine by Ce(IV) at 35 °C.

[H <sup>+</sup> ] (mol dm <sup>-3</sup> )	[Cystine] (mol dm <sup>-3</sup> )	[RuCl <sub>3</sub> ] × 10 <sup>7</sup> (mol dm <sup>-3</sup> )	μ (mol dm <sup>-3</sup> )	[Ce(IV)] × 10 <sup>3</sup> (mol dm <sup>-3</sup> )	$k_{obs}$ × 10 <sup>4</sup> (s <sup>-1</sup> )
0.10	0.015	5.0	0.20	1.0	11.70
0.20	0.015	5.0	0.20	1.0	10.00
0.30	0.015	5.0	0.20	1.0	8.54
0.40	0.015	5.0	0.20	1.0	7.68
0.60	0.015	5.0	0.20	1.0	6.73
0.70	0.015	5.0	0.20	1.0	4.77
0.35	0.015	5.0	0.20	1.0	0.93
0.10	0.035	5.0	0.20	1.0	3.40
0.10	0.055	5.0	0.20	1.0	5.60
0.10	0.075	5.0	0.20	1.0	7.43
0.10	0.095	5.0	0.20	1.0	9.4
0.10	0.115	5.0	0.20	1.0	12.02
0.10	0.015	1.0	0.20	1.0	0.46
0.10	0.015	3.0	0.20	1.0	0.58
0.10	0.015	5.0	0.20	1.0	0.63
0.10	0.015	7.0	0.20	1.0	0.74
0.10	0.015	9.0	0.20	1.0	0.82
0.10	0.015	11.0	0.20	1.0	0.96
0.10	0.015	5.0	0.20	2.0	7.70
0.10	0.015	5.0	0.20	3.0	7.54
0.10	0.015	5.0	0.20	4.0	7.68
0.10	0.015	5.0	0.20	6.0	7.64
0.10	0.015	5.0	0.20	7.0	6.73
0.10	0.015	5.0	0.05	1.0	8.55
0.10	0.015	5.0	0.30	1.0	7.64
0.10	0.015	5.0	0.40	1.0	6.44
0.10	0.015	5.0	0.50	1.0	6.17
0.10	0.015	5.0	0.60	1.0	5.94
0.10	0.015	5.0	0.70	1.0	4.66

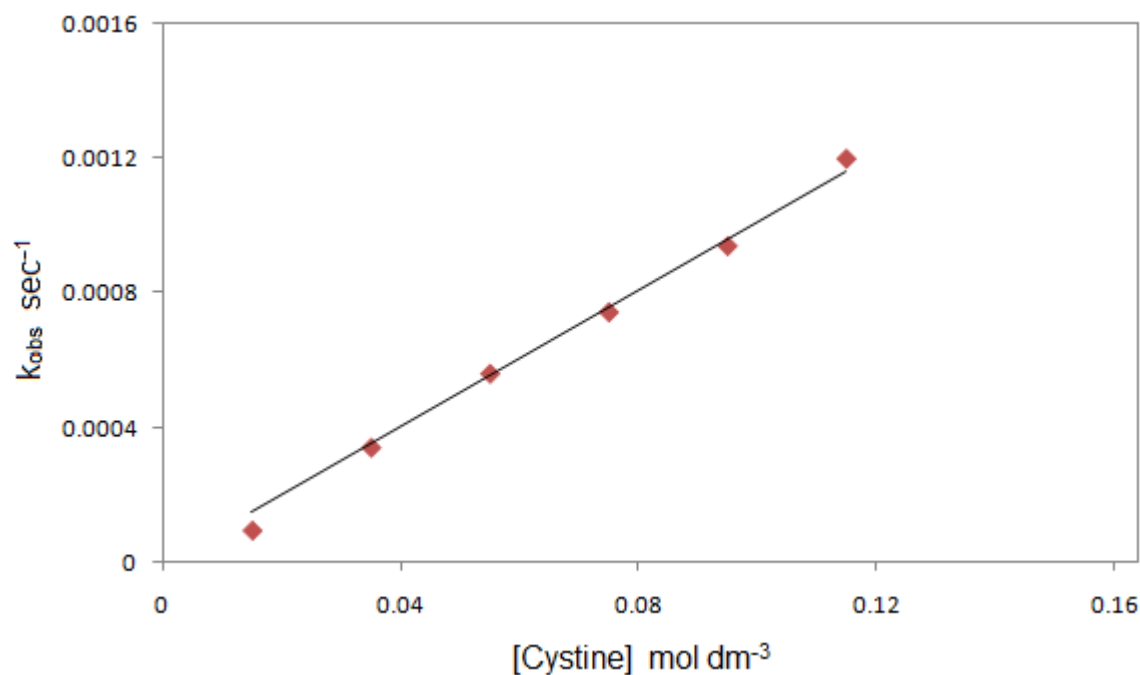


Fig. 1: Plots of  $k_{obs}$  versus [cystine] at 35 °C.  $[\text{Ce(IV)}] = 0.001 \text{ mol dm}^{-3}$ ,  $[\text{H}^+] = 0.1 \text{ mol dm}^{-3}$ ,  $[\text{Na}_2\text{SO}_4] = 0.2 \text{ mol dm}^{-3}$ ,  $[\text{RuCl}_3] = 5 \times 10^{-7} \text{ mol dm}^{-3}$ .

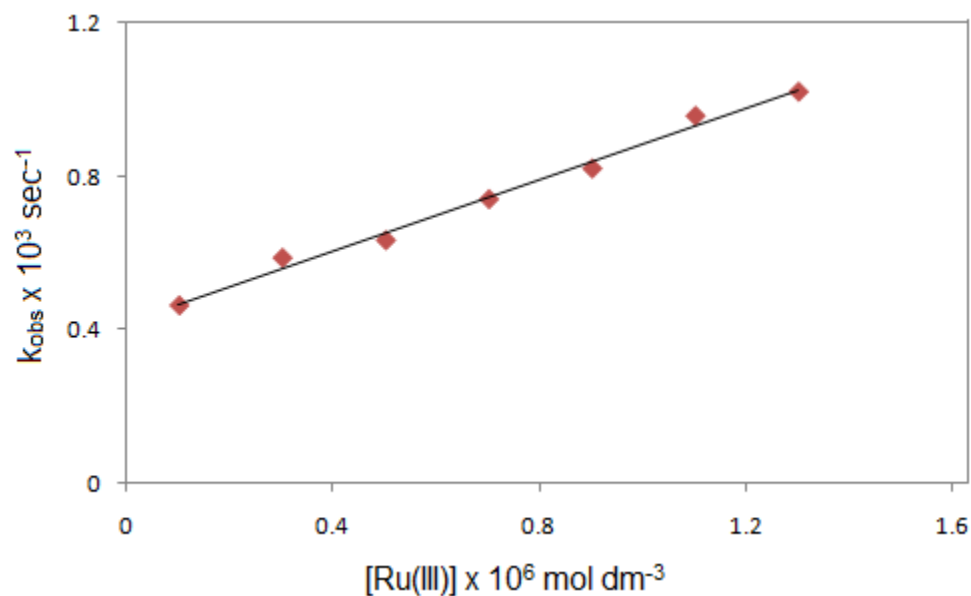


Fig 2:  $k_{obs}$  versus  $[\text{Ru(III)}]$  at 35 °C,  $[\text{Ce(IV)}] = 0.001 \text{ mol dm}^{-3}$ ,  $[\text{H}^+] = 0.1 \text{ mol dm}^{-3}$ ,  $[\text{Na}_2\text{SO}_4] = 0.2 \text{ mol dm}^{-3}$ ,  $[\text{Cystine}] = 0.015 \text{ mol dm}^{-3}$ .

*Variation of  $k_{\text{obs}}$  with Ru(III) ion concentration:* The oxidation reaction was carried out in the presence of different initial concentrations of ruthenium trichloride. The rate constant increased with increase in the concentration of the Ru(III) ion. The plot of  $k_{\text{obs}}$  versus [Ru(III)] (Fig. 2) was linear with an intercept indicating that the reaction rate is proportional to [Ru(III)] and that the rate of uncatalyzed path is not negligible [13].

*Variation of  $k_{\text{obs}}$  with temperature:* The oxidation reactions in the presence of the catalyst, Ru(III) chloride and without the catalyst were carried out at four different temperatures between 35 °C and 65 °C while maintaining the other parameters constant. The observed first-order rate constants in both cases increased with increase in temperature. The plots of  $\log k_2$  against  $1/T$  were linear for both the catalyzed and un-catalyzed oxidation reaction (Fig. 3). The Arrhenius activation energy  $E_a$  for the un-catalyzed and the catalyzed oxidation of L-cystine were 18.92 and 16.05 kJ mol<sup>-1</sup>, respectively. The entropy of activation for the un-catalyzed and the catalyzed oxidation reaction were -136.74 and -148.47 kJ mol<sup>-1</sup> K<sup>-1</sup> respectively. The negative value of entropy of activation in each case suggests the compactness of the transition state as compared to the ground state. The most effective form of Ru(III) ions as catalyst, [Ru(H<sub>2</sub>O)<sub>6</sub>]<sup>3+</sup>, could only be obtained in media other than acidic solutions. Ru(III) has been reported to be very ineffective in sulphuric acid medium [14]. This is supported by little difference obtained between the activation energy values for the un-catalyzed and the catalyzed reaction in the present study [15]. Although its activity may be slow in this medium, ruthenium(III) and iridium(III) have been found to catalyze even at trace amounts [16]

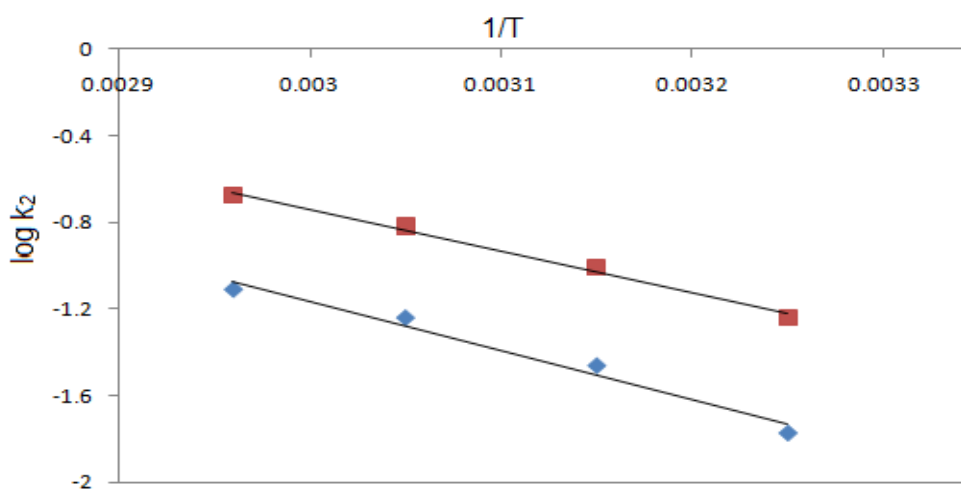


Fig. 3: Plots of  $\log k_2$  versus  $1/T$  for the Ru(III)-catalyzed (■) and uncatalyzed (◆) oxidation of cystine by Ce(IV) ions in acidic medium.  $[\text{Cystine}] = 0.015 \text{ mol dm}^{-3}$ ,  $[\text{Na}_2\text{SO}_4] = 0.20 \text{ mol dm}^{-3}$ ,  $[\text{Ce(IV)}] = 0.001 \text{ mol dm}^{-3}$ ,  $[\text{H}^+] = 0.1 \text{ mol dm}^{-3}$ ,  $[\text{RuCl}_3] = 5 \times 10^{-7} \text{ mol dm}^{-3}$ .

*Variation of  $k_{\text{obs}}$  with  $[\text{H}^+]$ :* The effect of increased acidity of the reaction medium on the rate of reaction was investigated at 308 K using perchloric acid in the range  $0.1 \leq 0.7 \text{ mol dm}^{-3}$ . The results presented in Table 1 shows that pseudo-first-order rate constants decreased with increase in hydrogen ion concentration. The decrease in rate with increase in  $[\text{H}^+]$  may be attributed to the conversion of cystine<sup>+</sup> to cystine<sup>2+</sup> [17].

*Reactive species of cystine, Ru(III) chloride and Ce(IV) ions*

In strongly acidic media, L-cystine exists in two protonated forms,  $^-\text{OOC}(\text{NH}_3^+)\text{CH}-\text{CH}_2-\text{S}-\text{S}-\text{CH}_2-\text{CH}(\text{NH}_3^+)\text{COOH}$  [cystine<sup>+</sup>] and  $\text{HOOC}(\text{NH}_3^+)\text{CH}-\text{CH}_2-\text{S}-\text{S}-\text{CH}_2-\text{CH}(\text{NH}_3^+)\text{COOH}$  [cystine<sup>2+</sup>]. The acidic strength was maintained constant at  $[\text{H}^+] = 1.0 \text{ mol dm}^{-3}$  throughout the experiment. These two forms exist and the predominant species [cystine<sup>+</sup>] is presumed to be the active species [2,17]. As recently reported by our research group, the active species of Ce(IV) ions among other several possible forms is  $\text{Ce}(\text{SO}_4)_2$  while that of Ru(III) chloride is  $[\text{RuCl}_2(\text{H}_2\text{O})_4]^+$  which is always in equilibrium with its hydrolyzed form  $[\text{RuCl}_3(\text{H}_2\text{O})_3\text{OH}]$  [15]. In strong acidic medium as obtained in this present work, the following equilibrium reaction has been reported:

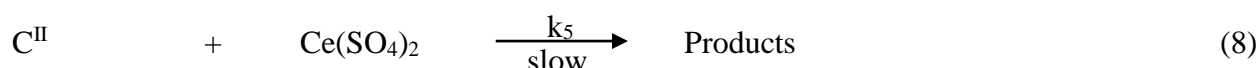
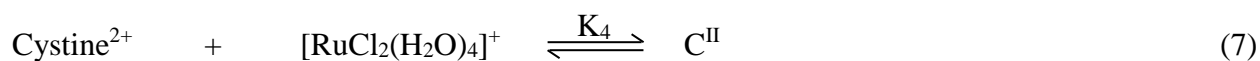
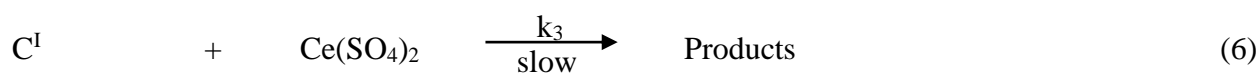
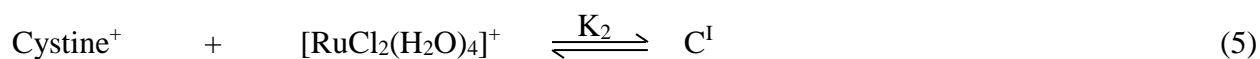
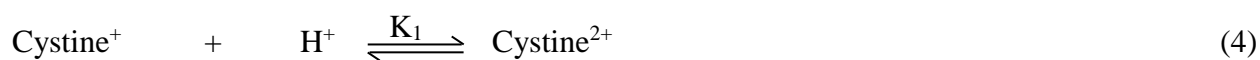


The negative effect of  $[\text{H}^+]$  observed in this experiment can therefore be explained in terms of formation of  $[\text{RuCl}_2(\text{H}_2\text{O})_4]^+$  according to the equilibrium expressed in equation 3 [15].

*Reaction mechanism:* The kinetic data revealed a first-order dependence in Ce(IV), cystine and Ru(III) chloride, an inverse dependence on  $\text{H}^+$  ion concentration.

The following mechanism is proposed for the reactions:

**Owalude, S.O., Odebunmi, E.O., Bamigboye, C.A. and Adebayo, A.B: MECHANISM OF Ru(III)-  
CATALYZED OXIDATION OF L-CYSTINE BY Ce(IV) IONS IN SULPHURIC ACID MEDIUM**



Literature evidence have shown that L-cystine exist in two active forms,  $^-\text{OOC}(\text{NH}_3)\text{CH}-\text{CH}_2-\text{S}-\text{S}-\text{CH}_2-\text{CH}(\text{NH}_3^+)\text{COOH}$  (cystine<sup>+</sup>); 93%) and  $\text{HOOC}(\text{NH}_3)\text{CH}-\text{CH}_2-\text{S}-\text{S}-\text{CH}_2-\text{CH}(\text{NH}_3^+)\text{COOH}$  (cystine<sup>2+</sup>); 6%) [17]. The first step of the mechanism is therefore proposed to involve the equilibrium between the predominant species of L-cystine (cystine<sup>+</sup>) and the protonated form (cystine<sup>2+</sup>). The cystine<sup>+</sup> reacts with the active form of the catalyst,  $[\text{RuCl}_2(\text{H}_2\text{O})_4]^+$  in the next step to form an intermediate complex C<sup>I</sup> which is subsequently oxidized by  $\text{Ce}(\text{SO}_4)_2$  to yield the products. The oxidation product of L-cystine has been reported as cysteic acid [17]. The mechanism continues with reaction of the protonated L-cystine molecule and  $[\text{RuCl}_2(\text{H}_2\text{O})_4]^+$  to form another intermediate complex C<sup>II</sup>. Oxidation of C<sup>II</sup> by  $\text{Ce}(\text{SO}_4)_2$  in a slow step yields the products. The rate law derived from the proposed mechanism is:

$$\text{Rate} = \frac{K_2 k_3 [\text{cystine}]_{\text{T}} [\text{Ru(III)}] [\text{Ce(IV)}]}{\{1 + K_1 [\text{H}^+] + K_2 [\text{Ru(III)}]\}} \quad (9)$$

Equation 9 shows a first-order dependence of the reaction rate on both the cystine and cerium(IV) concentrations that was experimentally observed in this study. Also at very low concentration of Ru(III) chloride such as the condition throughout the present study, the  $K_2[\text{Ru(III)}]$  term in the denominator of equation 12 becomes negligible and the rate law thus tend towards a first-order dependence on Ru(III) chloride concentration.

## CONCLUSION

Kinetics of oxidation of L-cystine by Ce(IV) ions in the presence of ruthenium(III) chloride as homogeneous catalyst has been studied in aqueous sulphuric acid medium. The oxidation reaction was shown to be effectively enhanced by ruthenium(III) ions. The main active species of cerium(IV) and



ruthenium(III) are considered to be  $\text{Ce}(\text{SO}_4)_2$  and  $[\text{RuCl}_2(\text{H}_2\text{O})_4]^+$  respectively. The average value of the second-order-rate constant ( $k_2$ ) for the oxidation reaction of L-cystine is  $0.01 \text{ mol dm}^{-3} \text{ s}^{-1}$ . The proposed mechanism is consistent with the obtained experimental data.

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