Research Article

Oxidation of 4-[(4-Methylphenyl) Amino]-4-Oxo Butanoic Acid by Ceric Ammonium Sulphate (IV) in Aqueous Perchloric Acid Medium: A Kinetic and Mechanistic Study

SATEESH B C[a], DR.VIDYAVATI SHASTRY[b*], SHASHIDHAR S[c], RAVINDRA K S[d]

[a] *Department of chemistry, Shri Pillappa College of engineering, Bangalore-560089, India.*

[b,c&d] *Department of chemistry, SEA College of engineering and technology, Bangalore-560049, India.*

www.ijppr.humanjournals.com

ABSTRACT

The kinetics of oxidation of 4-oxo-4(p-tolylamino) butanoic acid by ceric ammonium sulphate (IV) in perchloric acid medium has been studied spectrophotometrically at constant ionic strength 0.01 mol dm^{-3}. The reaction exhibits first order kinetics with respect to [Ce (IV)], [4-oxo acid] and inverse first order dependence with [H$^+$]. Ionic strength variation has no momentous effect on the reaction rate. The reaction constants concerned with different steps of mechanism are computed and a suitable mechanism has been proposed. Under different experimental conditions we can observe good concurrence between observed and calculated rate constants. Inverse first order dependence on [H$^+$] is verified by linearity of plots kobs versus 1 / [H$^+$] and log kobs versus log [H$^+$]. Polymerization study is done by adding acrylonitrile followed by methanol dilution and rate law is derived as follows, Rate = kobs = kK$_2$ / 1+K$_1$ [H$^+$].

1. INTRODUCTION

Cerium belongs to the group of inner transition elements with incompletely filled 4f levels. Ce (IV) and Ce (III) are the two important oxidation states of cerium. Ce (IV) compounds are more acidic, more easily hydrolysed and more susceptible for complexation than Ce (III). Salts of Ce (IV) are better oxidants which are useful for the oxidation of organic substrates in general and particularly alcohols [1-4] and a complex of cerium (IV) - substrate develops during the oxidation of organic substrate in various acidic medium. The complex developed further unimolecularly dissociates in rate determining step. In acidic medium, Ce (IV) posses oxidation potential which varies from 1.28 – 1.87 volts depending on the nature and concentration of acid used. In present study, enolization is greater than oxidation (measured by bromination method) and the enolization step can be visualized as proceeding via the enol form of keto group of 4-[(4-methylphenyl) amino]-4-oxobutanoic acid (4-Oxo butanoic acid).
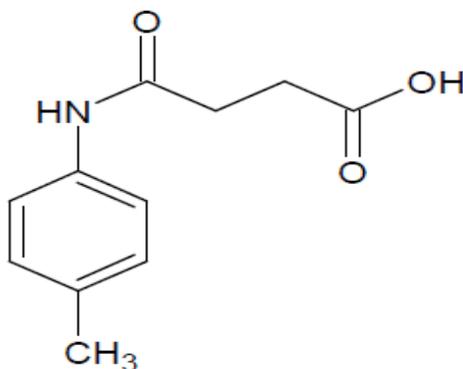
Figure 1: Structure of 4-[(4-methylphenyl) amino]-4-oxobutanoic acid

Synthesis of 4-[(4-methylphenyl) amino]-4-oxobutanoic acid:

Succinic anhydride (0.01 M) was taken in toluene and heated to get clear solution, to this solution para-toluidine in toluene (0.01 M) was added drop wise and heating was continued for one hour. The reaction completion is monitored by thin layer chromatography, obtained precipitate was filtered under vacuum, dried to get title compound as white solid which was recrystallized by using aqueous ethanol and determined by its melting point [5].

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

115
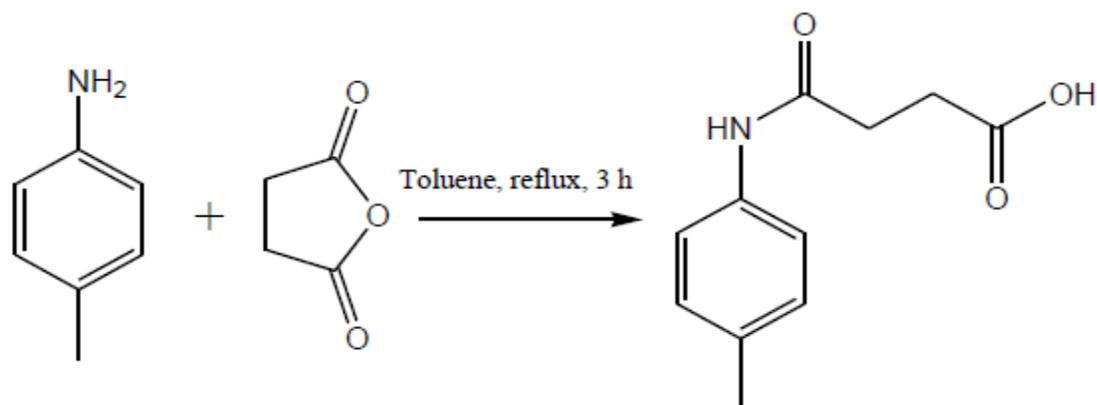
2. Kinetic measurements:

Pseudo first order conditions were maintained for the oxidation of 4-[(4-methylphenyl) amino]-4-oxobutanoic acid by cerium (IV) in acidic medium at fixed ionic strength 0.01mol dm^{-3}.

Ce (IV) X 10^4 mol dm^{-3}
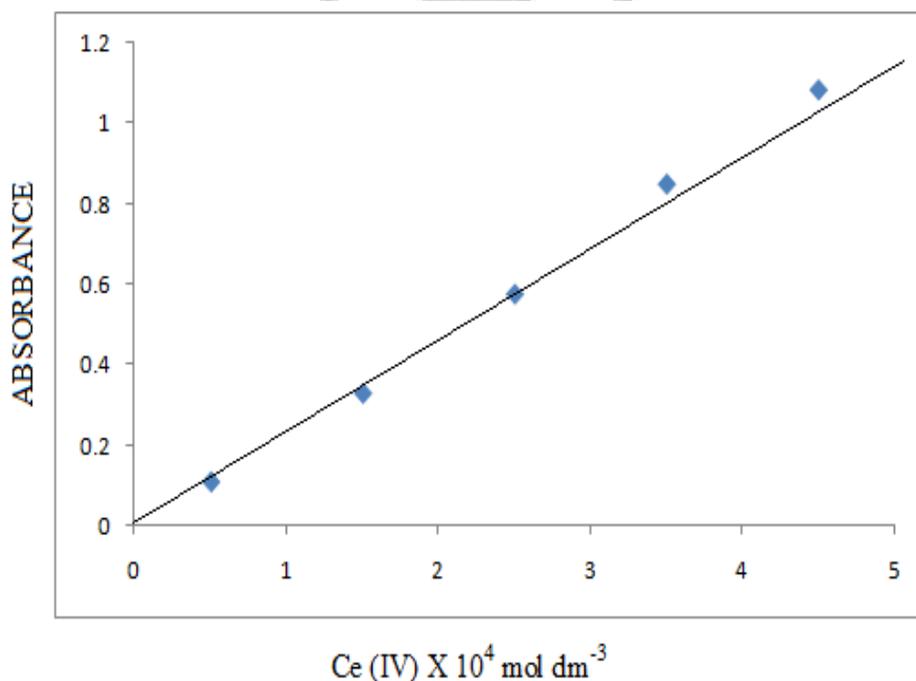
Figure 2: Verification of Beer's law for cerium at 360 nm in 0.01 mol dm^{-3} HClO$_4$.

The reaction is initiated by adding required quantities of thermally equilibrated solutions of [Ce (IV)] and [4-oxo butanoic acid] which also posses necessary quantities of HClO$_4$ (1.0×10^{-2} mol dm^{-3}) and KNO$_3$ (1.0×10^{-2} mol dm^{-3}). The reaction progress is monitored by measuring decrease in absorbance due to cerium (IV) using spectrophotometer at 360 nm. The kinetic runs were

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

116

followed to more than 95% completion of reaction and from the plot of [Ce (IV)] against time, the rate constants (k) for pseudo first order reaction were measured. The values are reproducible within ±4%. The Beer's law obedience of Cerium (IV) solution at 360 nm in the concentration range 0.5×10^{-4} to 4.5×10^{-4} mol dm^{-3} has been tested under reaction conditions in perchloric acid solution, as shown in Fig.2. The sample run for oxidation 4-[(4-methylphenyl) amino]-4-oxobutanoic acid by cerium (IV) in acidic medium at standard condition is as shown in Table 1.

3. Stoichiometry and Product analysis:

The reaction stoichiometry was determined by equilibrating reaction mixture of various [Ce (IV)] and [4-oxo butanoic acid] ratios at 25°C for 24 hours, maintaining fixed concentration of HClO$_4$ (1.0×10^{-2} mol dm^{-3}) and KNO$_3$ (1.0×10^{-2} mol dm^{-3}). The unreacted cerium was estimated iodometrically [6] and it reveals that two moles of cerium has been consumed by one mole of 4-oxo butanoic acid. The products of oxidation may be 4-methyl phenyl carbamic acid and prop-2-enoic acid respectively [7].

Table 1: Sample run for oxidation of 4-[(4-methylphenyl) amino]-4-oxobutanoic acid by Ce (IV) in acidic medium at 4-Oxo butanoic acid (2.5×10^{-3} mol dm^{-3}), Ce (IV) (2.5×10^{-4} mol dm^{-3}), HClO$_4$ (1.0×10^{-2} mol dm^{-3}) and KNO$_3$ (1.0×10^{-2} mol dm^{-3}).

Time in Seconds	Absorbance at 360 nm	Time in Seconds	Absorbance at 360 nm
0	0.363	80	0.067
10	0.297	90	0.053
20	0.243	100	0.042
30	0.198	110	0.033
40	0.161	120	0.025
50	0.131	130	0.019
60	0.105	140	0.013
70	0.085	150	0.009

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

117
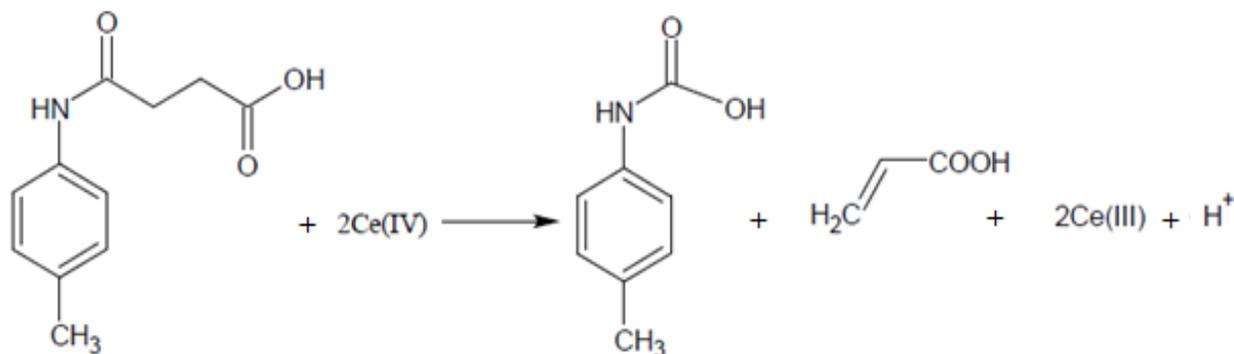
4. Reaction order:

4.1 Cerium (IV) Dependence:

The concentration of Cerium (IV) in reaction is varied from 0.5×10^{-4} to 4.5×10^{-4} mol dm^{-3} keeping concentration of 4-Oxo butanoic acid (2.5×10^{-3} mol dm^{-3}), HClO$_4$ (1.0×10^{-2} mol dm^{-3}) and KNO$_3$ (1.0×10^{-2} mol dm^{-3}) as constant. By plotting graph of logk versus time, straight line is obtained which is linear up to 90% reaction completion (Fig.3), which clearly indicates unit order dependence in oxidant.

Table 2: Effect of Variation of [Ce (IV)] (2.5×10^{-4} mol dm^{-3}), [4-Oxo butanoic acid] (2.5×10^{-3} mol dm^{-3}), [HClO$_4$] (1.0×10^{-2} mol dm^{-3}) and [KNO$_3$] (1.0×10^{-2} mol dm^{-3}) on 4-[(4-methylphenyl) amino]-4-oxobutanoic acid oxidation by Cerium (IV) at constant ionic strength 0.01mol dm^{-3} at 25^{0}C in aqueous acidic medium.

[Ce(IV)] X 10^{-4}(mol dm^{-3})	[4-Oxo butanoic acid] X 10^{-3} (mol dm^{-3})	[HClO$_4$] X 10^{-2}(mol dm^{-3})	[KNO$_3$] X 10^{-2}(mol dm^{-3})	kobs X 10^{-2} Exp	kobs X 10^{-2} Cal
0.5	2.5	1.0	1.0	2.549	2.610
1.5	2.5	1.0	1.0	2.672	2.610
2.5	2.5	1.0	1.0	2.581	2.610
3.5	2.5	1.0	1.0	2.713	2.610
4.5	2.5	1.0	1.0	2.771	2.610
2.5	0.5	1.0	1.0	2.544	2.610
2.5	1.5	1.0	1.0	2.572	2.610

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

118

2.5	2.5	1.0.	1.0	2.581	2.610
2.5	3.5	1.0	1.0	2.619	2.610
2.5	4.5	1.0	1.0	2.672	2.610
2.5	2.5	0.25	1.0	6.372	6.432
2.5	2.5	0.5	1.0	3.891	3.990
2.5	2.5	1.0	1.0	2.587	2.610
2.5	2.5	2.0	1.0	1.174	1.213
2.5	2.5	3.0	1.0	0.809	0.831
2.5	2.5	1.0	0.25	2.501	2.610
2.5	2.5	1.0	0.5	2.587	2.610
2.5	2.5	1.0	1.0	2.581	2.610
2.5	2.5	1.0	2.0	2.383	2.610
2.5	2.5	1.0	3.0	2.474	2.610

4.2 4-[(4-methylphenyl) amino]-4-oxobutanoic acid dependence:

The concentration of 4-Oxo butanoic acid in reaction is varied from 0.5×10^{-3} to 4.5×10^{-3} mol dm^{-3} keeping concentration of Ce (IV) (2.5×10^{-4} mol dm^{-3}), HClO$_4$ (1.0×10^{-2} mol dm^{-3}) and KNO$_3$ (1.0×10^{-2} mol dm^{-3}) as constant. Log-log plot shows unit order dependence in 4-oxo butanoic acid.

4.3 Perchloric acid Dependence:

The concentration of [HClO$_4$] in reaction is varied from 0.25×10^{-2} to 3.0×10^{-2} mol dm^{-3} maintaining fixed concentration of 4-Oxo butanoic acid (2.5×10^{-3} mol dm^{-3}), Ce (IV) (2.5×10^{-4} mol dm^{-3}) and KNO$_3$ (1.0×10^{-2} mol dm^{-3}). The rate constant decreases with increase in [HClO$_4$] (Table 2). The graph of kobs against 1 / [H$^+$] and log kobs against log [H$^+$] were found to be linear (Fig.4 and Fig.5) which indicates inverse first order with respect to hydrogen ion concentration.

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

119

Time (sec)
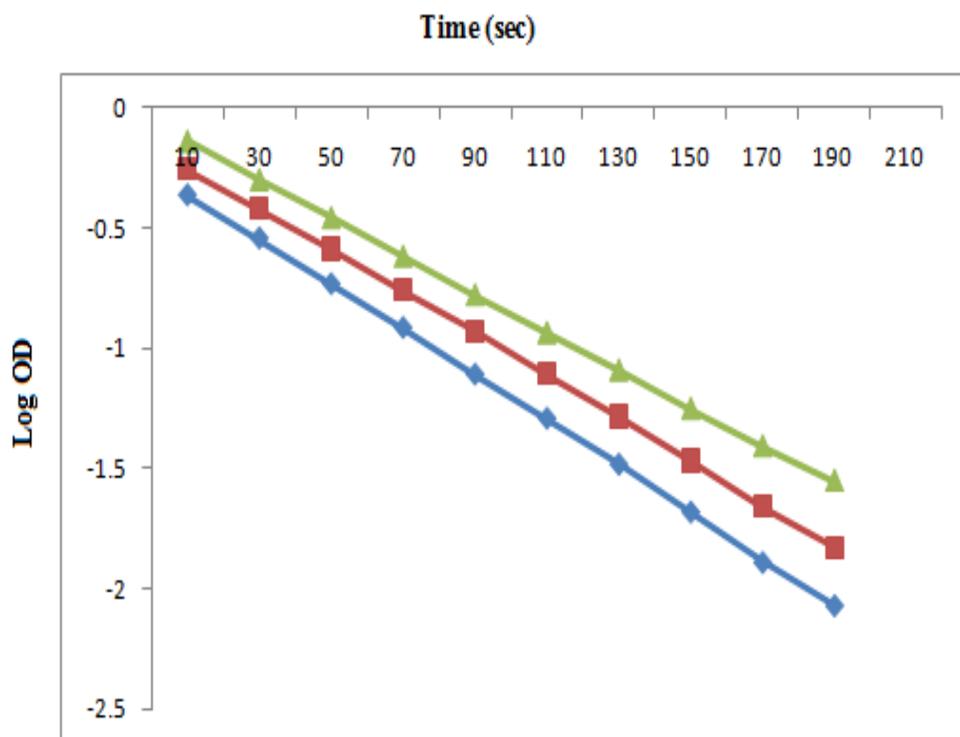
Figure 3: A graph of log OD versus time shows first order behavior in Cerium (IV).

$1 / [H^+]$
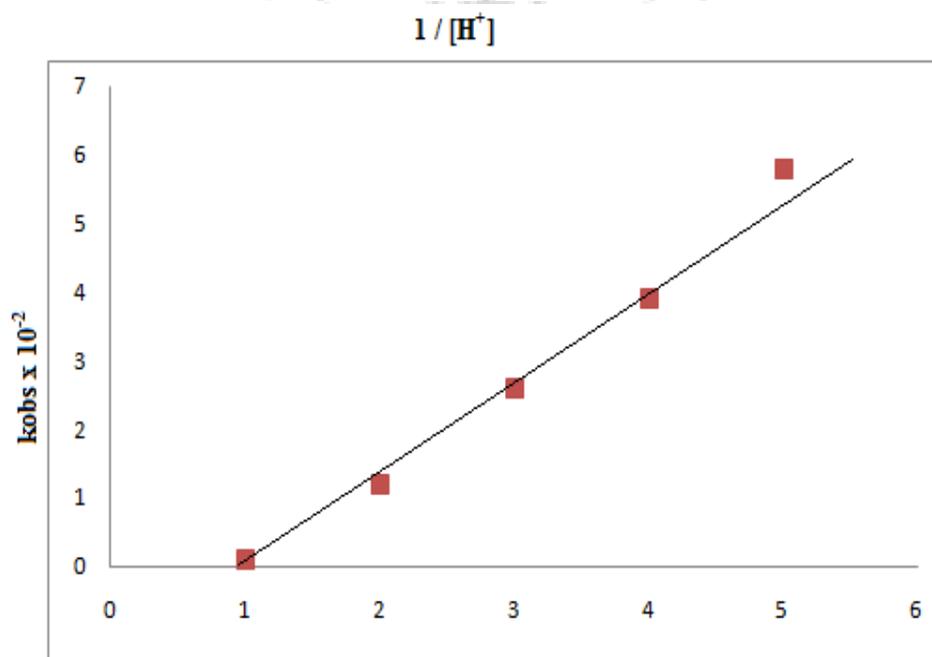
Figure 4: Plot of kobs v/s $1 / [H^+]$ for verification of linearity with respect to $[H^+]$.

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

120
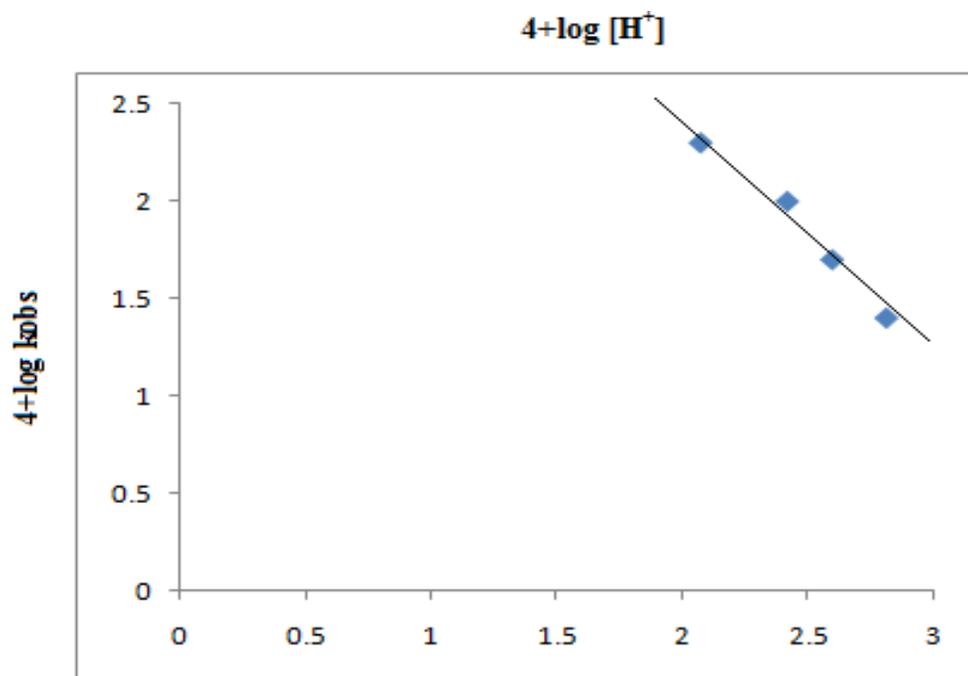
Figure 5: Graph of log kobs against log [H$^+$] for verification of linearity with respect to [H$^+$].

4.4 Potassium nitrate Dependence (Salt effect):

The concentration of KNO_3 in reaction is varied from 0.25×10^{-2} to 3.0×10^{-2} mol dm^{-3} and maintaining the concentration of 4-Oxo butanoic acid (2.5×10^{-3} mol dm^{-3}), Ce (IV) (2.5×10^{-4} mol dm^{-3}) and $HClO_4$ (1.0×10^{-2} mol dm^{-3}) as constant. Variation of nitrate has no vital effect on reaction rate (Table 2).

5. Test for free radicals:

Free radical involvement in oxidation of 4-[(4-methylphenyl)amino]-4-oxobutanoic acid by Cerium (IV) was studied by adding acrylonitrile followed by methyl alcohol dilution which involves precipitate formation indicating that reaction path involves free radical mechanism.

6. Effect of temperature:

Effect of temperature on reaction rate was measured at temperature ranging from 298K-318K maintaining fixed concentration of 4-Oxo butanoic acid (2.5×10^{-3} mol dm^{-3}), Ce (IV) (2.5×10^{-4} mol dm^{-3}) $HClO_4$ (1.0×10^{-2} mol dm^{-3}) and KNO_3 (1.0×10^{-2} mol dm^{-3}) (Fig.6). The reaction rate

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

121

enhances with increase in temperature (Table 3). The graph of logk versus 1/T (Arrhenius plot) gives straight line and the experimental energy of activation Ea and the frequency factor $\log_{10}A$ were calculated from the slope and the intercept. The Eyrings parameters $\Delta H^{\#}$, $\Delta S^{\#}$, $\Delta G^{\#}$ were calculated and tabulated (Table 4).

Table 3: Effect of Temperature on the Rate of Oxidation of 4-[(4-methylphenyl) amino]-4-oxo butanoic acid by Cerium (IV) in perchloric acid medium.

Temp. (K)	Kobs x 10^{-2}
298	2.581
303	3.813
308	5.032
313	6.316
318	7.452

7. RESULTS AND DISCUSSION

The ceric salts exist as different ionic species in different acid media which depends on pH of solution. In perchloric acid medium, ceric salt exist as $Ce(OH)^{3+}$ and $Ce(OH)_2^{2+}$ as given by Rajesh Shukla et al [8]. In sulphuric acid medium it exist as $Ce(SO_4)_2^{2+}$, $Ce(SO_4)_2$ and $Ce(SO_4)_3^{2-}$ as given by Fandis G Anand etal [9].

SCHEME-1

$$Substrate(S) + Ce(IV) \underset{K_2}{\rightleftharpoons} Complex(C)$$

$$Complex(C) \xrightarrow{k} R^{\cdot} + Ce(III) + H^{+}$$

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

122
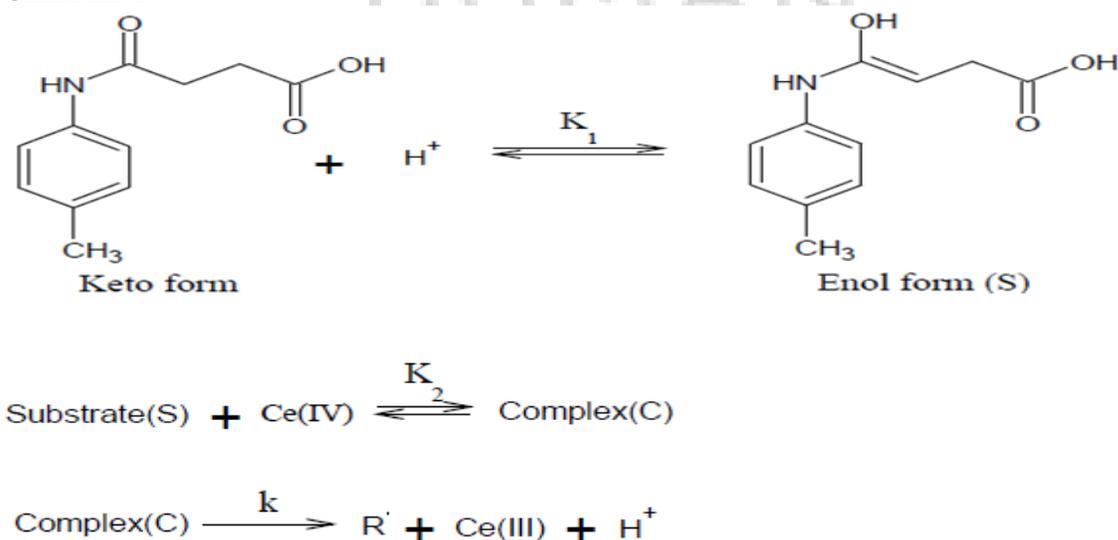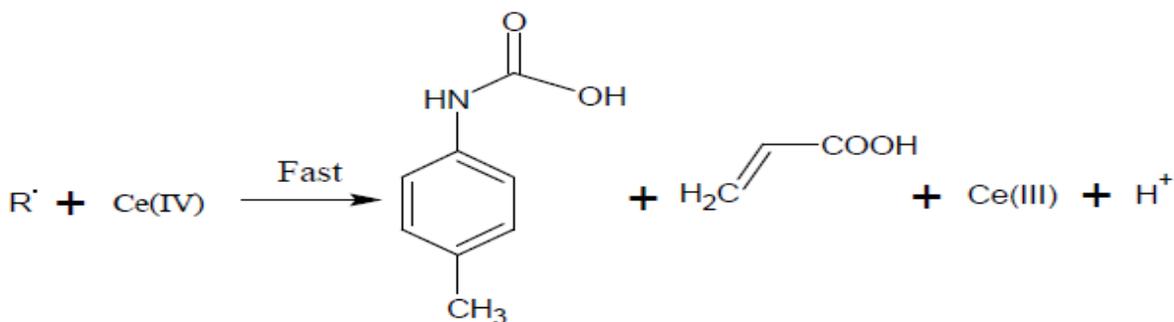
Rate law can be proposed by considering scheme-1 as follows,

Rate = -d [Ce (IV)] / dt = k [C]

Rate = kK_2 [Ce (IV)]$_f$ [4-Oxo butanoic acid]$_f$ ....(1)

[4-Oxo butanoic acid]$_T$ = [4-Oxo butanoic acid]$_f$ + K_1 [4-Oxo butanoic acid]$_f$ [H$^+$]

[4-Oxo butanoic acid]$_T$ = [4-Oxo butanoic acid]$_f$ (1 + K_1[H$^+$])

[4-Oxo butanoic acid]$_f$ = [4-Oxo butanoic acid]$_T$ / (1 + K_1[H$^+$]) ....(2)

[Ce]$_T$ = [Ce]$_f$ + K_2 [4-Oxo butanoic acid] [Ce]$_f$

[Ce]$_T$ = [Ce]$_f$ (1+K_2 [4-Oxo butanoic acid])

[Ce]$_f$ = [Ce]$_T$ / (1+K_2 [4-Oxo butanoic acid]) ....(3)

Substitute equation (2) and (3) in equation (1)
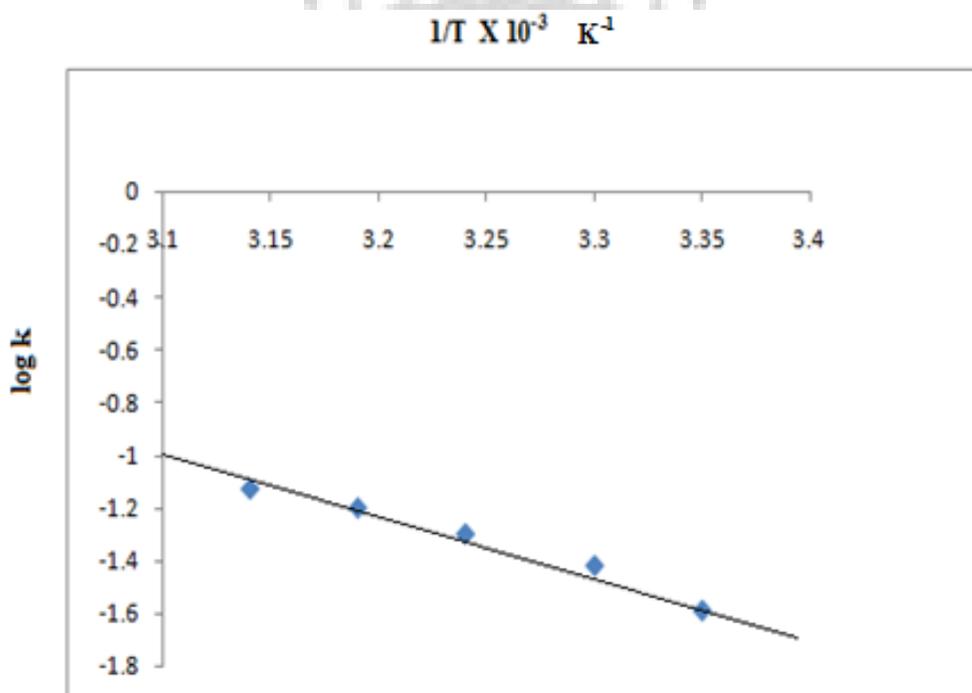
Figure 6: Arrhenius plot for variation of temperature for oxidation of 4-[(4-methylphenyl) amino]-4-oxobutanoic acid by Cerium (IV) in perchloric acid medium.

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

123

Rate = k K_2 [Ce]$_T$ [4-Oxo butanoic acid]$_T$ / 1+ K_2 [4-Oxo butanoic acid] (1+ K_1 [H$^+$]) ……….(4)

[Ce (IV)] <<<< [H$^+$], hence 1+ K_2[4-Oxo butanoic acid] will be neglected, than equation (4) can be written as,

Rate = k K_2 [Ce]$_T$ [4-Oxo butanoic acid]$_T$ / (1+ K_1 [H$^+$])

Rate / [Ce (IV)] [4-Oxo butanoic acid] = kK_2 / 1+K_1 [H$^+$]

Rate / [Ce (IV)] [4-Oxo butanoic acid] = kobs = kK_2 / 1+K_1 [H$^+$]

1 / kobs = 1 + K_1 [H$^+$] / kK_2

1 / kobs = 1/ kK_2 + K_1 [H$^+$] / kK_2

Plot the graph of 1/ kobs against [H$^+$] which is linear [Fig.7], the slope is equal to K_1/ kK_2 and the intercept is 1 / kK_2. From the above plot K_1, kK_2 were obtained and the values are found to be 636.37 and 0.166 respectively. These values in addition useful to calculate experimental rate constants. Rate constants calculated were in good concordance with experimental results.

Table 4: Activation Parameters for 4-[(4-methylphenyl) amino]-4-oxobutanoic acid oxidation by Cerium (IV) in aqueous perchloric acid medium.

Activation Parameters	Values
Ea (kJ/mol)	36.87
$\Delta H^{\#}$ (kJ/K/mol)	34.39
$\Delta S^{\#}$ (J/K/mol)	-159.92
$\Delta G^{\#}$ (kJ/K/mol)	82.04
Log$_{10}$A	1.0

8. CONCLUSION

The kinetic data and product obtained in the present investigation demonstrated that the mechanistic pathway for the oxidation of 4-[(4-methylphenyl) amino]-4-oxobutanoic acid proceeds via free radical mechanism. The above study reveals that the Cerium (IV) reacts with 4-oxo acid (enol form) result in intermediate complex which on decomposition results in cleavage of carbon-carbon bond yielding 4-methyl phenyl carbamic acid and prop-2-enoic acid. The free energy of activation is 83 kJ/mol indicating a unified mechanism in oxidation of 4-oxo butanoic acid which is similar with other oxo acid studies [9]. The higher negative value of entropy of activation supports the formation of complex in reaction. The above experimental procedure

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

124

shows a regioselective route for carboxylic acids synthesis, especially carbamic acids. 4-phenyl 4-oxo acids derivatives are generally used in the therapy: particularly as Kynurenine-3-hydroxylase inhibitors, in the prevention and / or treatment of a neurodegenerative diseases like Huntingston's chorea, Acquire immune deficiency syndrome (AIDS), Cerebral ischemia, Cerebral hypoxia, Parkinson's disease, Head and spinal card injury and Amyotrophic lateral sclerosis etc., wherein the inhibition of such an enzyme is needed. The above method gives simple routine for determination of 4-Phenyl 4-oxo derivatives in bulk and pharmaceutical dosage forms.
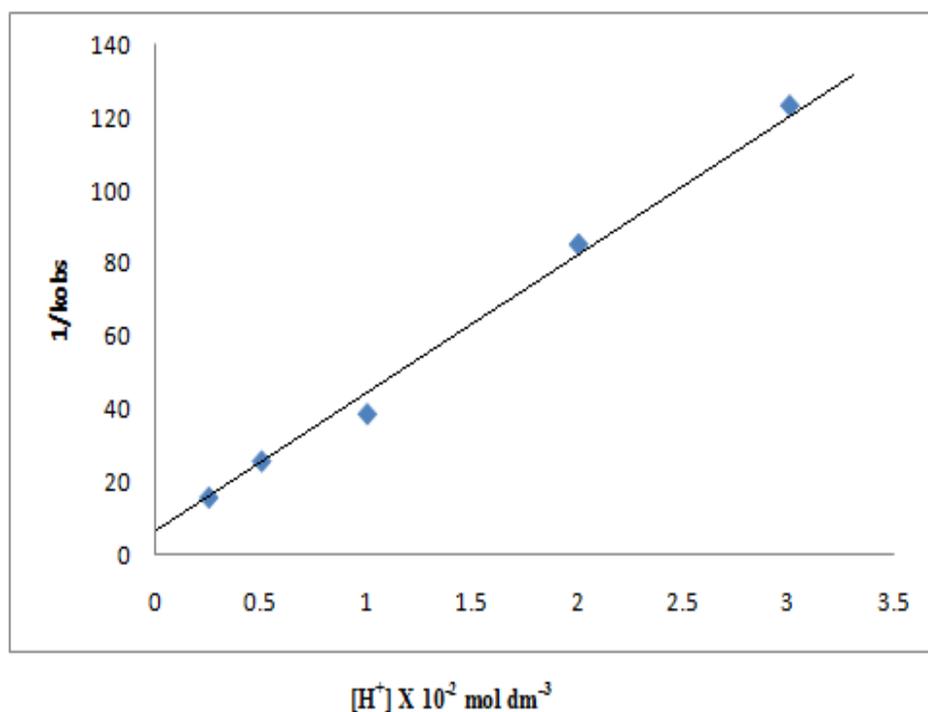
Figure 7: Plot of 1/ kobs against [H$^+$] for rate law verification.

REFERENCES

1) Young, Lewis Brewster, "Cerium (IV) oxidation of organic compounds. I.Benzyl and related alcohols. II.Cycloheptatriene", University microfilms.Inc., Ann Arbor, Michiagan, 68(10), 1943, 491.

2) S.S.Muhammad and K.Vijaychander Rao, "Oxidation of alcohols by Cerium (IV) and Oxidation of methanol by ceric sulfate", 36(8), 1963, 949-952.

3) Nave, Paul Michael, "Oxidative cleavage of alcohols by cerium (IV) and chromic acid", University microfilms.Inc., Ann Arbor, Michiagan, 70(13), 1969, 615.

4) Praveen K.Tandon, Alok K Singh, Sumita sahgal and Santosh kumar, "Oxidation of cyclic alcohols by cerium (IV) in acidic medium in the presence of iridium (III) chloride", Journal of molecular catalysis A chemical, 282(1), 2008, 136-143.

5) F. Feigl and V. Anger, "Spot Test in Organic Analysis", Elsevier, Amsterdam 1975. 459.

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

125

6) G.Svehla "Vogel's Quantitative Inorganic Analysis" Seventh Edn. 1996, 197–199.

7) E.B.Reid, "A text book of macro and semimicro qualitative inorganic analysis"; Arthur I.Vogel, Longmans, Green, New York – London edition.4 (1954).

8) Rajesh shukla, Sushma rani and Tewari.I.C, "Oxidation of crotonic acid with Ce (IV) perchlorate", International Journal of Chemical Research, 4(1), 2012, 122-125.

9) Fandis G Anand and Agarwal Rashmi, "Kinetics and mechanistic study of oxidation of atenolol by cerium (IV) in sulphuric acid medium", International research journal of Phramacy, 3(3), 2012, 268-270.

Citation: DR.VIDYAVATI SHASTRY et al. Ijppr.Human, 2015; Vol. 5 (1): 114-126.

126