CHAPTER III

Kinetic, Mechanistic and Spectral Investigation of Oxidative Degradation and Deamination of Atenolol by Cerium(IV) in Aqueous Perchloric acid Medium

Cerium(IV) has been used as an oxidising agent and an analytical reagent, especially in acid medium. Kinetic studies on the oxidation of different substrates using cerium(IV) as an oxidant in perchloric acid medium have been reported. In sulphuric acid medium, cerium (IV) forms several sulphate complexes, but their role has not received much attention so far. Thus the reaction rate increases with increase in acid concentration and this effect is not understood. The 4-(2-hydroxy-3-isopropylaminopropoxy) phenylacetamide, commercially known as atenolol (ATN), a β-adrenoreceptor blocking agent is used as antihypertensive drug. It is also used for anti-angina treatment to relieve symptoms, improve tolerance and as an anti-arrhythmic to help regulate heartbeat and infections. It is also used in management of alcohol withdrawal, in anxiety states, migraine prophylaxis, hyperthyroidism and tremor.

A literature survey reveals that there are no reports on the kinetics of oxidation of atenolol(ATN) by any oxidants, except with two oxidants. Oxidation of atenolol by cerium(IV) is fast which is controlled by decreasing the acid concentration and ionic strength. In continuation of work in our laboratory on cerium(IV) oxidation, and in order to explore the mechanism of oxidation by cerium(IV) in aqueous acidic medium, we have selected atenolol as a substrate for oxidation. This chapter deals
with the title reaction to investigate the redox chemistry of cerium(IV) and to arrive at a plausible mechanism and to know the active form of cerium(IV) in aqueous perchloric acid medium.

**EXPERIMENTAL**

**Materials**

A Stock solution of ATN (M/s. S.S. Antibiotics Pvt. Ltd, Aurangabad, India) was prepared by dissolving the appropriate amount of sample in double distilled water. The purity of the sample was checked by TLC and its m.p. 152 °C. The cerium(IV) solution was prepared by dissolving ceric ammonium sulphate (Trizma chemicals Co., India) in double distilled water in presence of 0.50 mol dm$^{-3}$ H$_2$SO$_4$. The stock solution of cerium(IV) was standardized by known method$^7$. The cerium(III) solution was prepared by dissolving Ce(OAc)$_3$ (BDH Mumbai, India) in water and the concentration of cerium(III) was ascertained by a standard procedure$^8$. All other reagents were of analytical grade and their solutions were prepared by dissolving required amounts of the samples in double distilled water. Perchloric acid and sodium perchlorate were used to provide the required acidity and to maintain the ionic strength respectively.

**Kinetic procedure**

All kinetic measurements were performed under pseudo-first order conditions where [ATN] was in excess over [Ce(IV)] at a constant ionic strength of 0.50 mol dm$^{-3}$. The reaction was initiated by mixing previously thermostatted solutions of cerium(IV) and atenolol which also contained the necessary quantities of perchloric acid and
sodium perchlorate to maintain the required acidity and ionic strength respectively. The temperature was maintained at 25 ± 0.1°C. The course of reaction was followed by monitoring the decrease in absorbance of cerium(IV) in a 1cm quartz cell of a Hitachi model 150-20 spectrophotometer at 360 nm as a function of time. Earlier it was verified that there is negligible interference from the other reagents at this wavelength. The application of Beer’s law to cerium(IV) at 360 nm had been verified earlier, giving ε = 3100 ± 150 dm³ mol⁻¹ cm⁻¹ (Fig. III(i)(p68)). An example run is shown in Table III(i)(p.69). The first order rate constants, k_{obs} were obtained from the slope of log (Abs) versus time. The first order plots in almost all cases were linear up to 80% completion of the reaction and the k_{obs} values were reproducible within ± 5%.

RESULTS
Stoichiometry and product analysis
The reaction mixture containing the excess [Ce(IV)] over [ATN] was mixed in the presence of 0.05 mol dm⁻³ HClO₄ at a constant ionic strength of 0.50 mol dm⁻³ and allowed to react for about 2 hours at 25 ± 1.0 °C. The remaining [cerium(IV)] was then analyzed spectrophotometrically. The results indicated that two moles of Ce(IV) consumed by one mole of atenolol, (i.e. 2:1) according to equation (1)(Table III(ii)(p.70)).

\[
\text{OH}
\begin{align*}
\text{O-CH}_2\text{-CH-CH}_2\text{-NH-CH-(CH}_3)_2 \\
\text{CH}_2\text{C-} \\
\end{align*}
\begin{align*}
+ 2\text{Ce(IV)} + 2\text{H}_2\text{O} & \rightarrow \\
\text{O-CH}_2\text{-C-OH} \\
\text{CH}_2\text{C-} \\
\text{NH}_2
\end{align*}
+ \text{NH}_3 + 2\text{Ce(III)} + 2\text{H}^+ \\
+ \text{CH}_2\text{-NH-CH-(CH}_3)_2
\]

(1)
Figure III(i)

Verification of Beer's law for [Ce(IV)] at 360 nm in 0.05 mol dm$^{-3}$ perchloric acid at 25 °C (* $1.0 \times 10^{-2}$ sulphuric acid is also present)
Table III(i)

Example run for the oxidation of atenolol by cerium(IV) in aqueous perchloric acid medium at 25 °C.

\[ [ATN] = 2.0 \times 10^{-3}; \]
\[ [Ce(IV)] = 2.0 \times 10^{-4}; \]
\[ [H^+] = 0.05, \]
\[ I = 0.50 \text{ /mol dm}^3. \]

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Optical density (360 nm)</th>
<th>[Ce(IV)] \times 10^4 (mol dm(^{-3}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.613</td>
<td>1.97</td>
</tr>
<tr>
<td>1.0</td>
<td>0.462</td>
<td>1.49</td>
</tr>
<tr>
<td>2.0</td>
<td>0.359</td>
<td>1.16</td>
</tr>
<tr>
<td>3.0</td>
<td>0.287</td>
<td>0.92</td>
</tr>
<tr>
<td>4.0</td>
<td>0.232</td>
<td>0.75</td>
</tr>
<tr>
<td>5.0</td>
<td>0.182</td>
<td>0.58</td>
</tr>
<tr>
<td>6.0</td>
<td>0.147</td>
<td>0.47</td>
</tr>
<tr>
<td>7.0</td>
<td>0.119</td>
<td>0.38</td>
</tr>
<tr>
<td>8.0</td>
<td>0.094</td>
<td>0.30</td>
</tr>
<tr>
<td>9.0</td>
<td>0.076</td>
<td>0.24</td>
</tr>
<tr>
<td>10.0</td>
<td>0.060</td>
<td>0.19</td>
</tr>
</tbody>
</table>
Table III(ii)

Stoichiometry of atenolol oxidation by cerium(IV) in aqueous perchloric acid medium at 25 °C.

\[ [H^+] = 0.05; \quad I = 0.50 \text{ /mol dm}^3. \]

<table>
<thead>
<tr>
<th>[Ce(IV)] ( \times 10^4 ) (mol dm(^{-3}))</th>
<th>[ATN] ( \times 10^4 ) (mol dm(^{-3}))</th>
<th>[Ce(IV)] ( \times 10^4 ) (mol dm(^{-3}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taken</td>
<td>Taken</td>
<td>Found</td>
</tr>
<tr>
<td>3.0</td>
<td>1.0</td>
<td>1.03</td>
</tr>
<tr>
<td>6.0</td>
<td>3.0</td>
<td>0.02</td>
</tr>
<tr>
<td>4.0</td>
<td>2.0</td>
<td>0.04</td>
</tr>
<tr>
<td>8.0</td>
<td>3.0</td>
<td>2.05</td>
</tr>
<tr>
<td>5.0</td>
<td>2.0</td>
<td>0.98</td>
</tr>
</tbody>
</table>
The main reaction product, 4-Hydroxycarboxymethoxy phenyl acetic acid was extracted with ether and recrystallised from aqueous alcohol and the purity was checked by HPLC. This is identified as 4-Hydroxycarboxy methoxy phenyl acetic acid by its I.R. spectrum, which showed a band at (ν) 1690 cm\(^{-1}\) due to >C=O stretching of acid and a broad band at 2845 cm\(^{-1}\) due to O-H stretching. 4-Hydroxycarboxy methoxy phenyl acetic acid was further characterized by \(^1\)HNMR spectrum (DMSO), showed a shifts (δ) at 10 ppm (br, due to two carboxylic OH, 2H), 7.7 ppm (d due to aromatic, 2Ha), 6.9 ppm (d, due to aromatic, 2Hb), 4.6 ppm (s, due to methylene, 2Hc), 3.5 ppm (s, due to methylene, 2Hd) respectively and Mass spectra ESI technique (solvents: Acetonitrile + water + ammonium acetate) (M^+17) (ammoniated) 228 and (M^+) m/z 211. Ammonia was identified by using Nessler’s reagent. Another product, N-isopropylmethylamine, which is highly soluble in water, was identified by spot test. It was observed that the 4-Hydroxycarboxy methoxy phenyl acetic acid and N-isopropyl methylamine do not undergo further oxidation under the present kinetic conditions.

Spectrofluorimetric studies

The fluorescence study was carried out (Hitachi F 2000 spectrofluorimeter) in methanol solvent for good dissolution of pure and the product, of present study. There was no interference of the solvent methanol seen in the fluorescent study. We have taken the fluorescence study of pure compound, atenolol and also for the product of the reaction of atenolol with alkaline permanganate. The excitation for the atenolol
was observed at 370 nm and the emission was found at 411 nm with intensity 106. The excitation of the product was observed at 370 nm and the emission was found at 416 nm with the considerable decrease in the fluorescent intensity to 36.62, which is due to quenching.

Regression analysis of experimental data to obtain the correlation coefficient, r and the standard deviation, S of points from the regression line was performed using a Pentium III personnel computer.

**Reaction orders**

The reaction orders were determined from the slopes of log.k.obs versus log (concentration) plots by varying the concentration of reductant and acid in turn, while keeping other factors constant.

**Effect of [Cerium(IV)]**

The cerium(IV) concentration was varied in the 5.0 x 10^{-5} to 5.0 x 10^{-4} mol dm^{-3} range and the linearity of plots of log(Abs) versus time (Fig. III(ii)(p.74);(r> 0.979, S ≤ 0.0045)) indicated a reaction order in [Ce(IV)] as unity. This was also confirmed by varying the [Ce(IV)], which did not show any change in pseudo-first order rate constants k.obs values(Table III(iii)(p.73)).

**Effect of [Atenolol]**

The substrate, atenolol was varied in the of 5.0 x 10^{-4} to 5.0 x 10^{-3} mol dm^{-3} range at 25 °C keeping all other reactant concentrations and conditions constant (Table(III)(iii)(p73)). The apparent reaction order in [ATN] was found to be less than unity as shown in Fig. III(iii)(p.76).
Table III(iii)

Effect of \([\text{Ce(IV)}]\) and \([\text{ATN}]\) on the oxidation of atenolol by cerium(IV) in aqueous acidic medium at 25 °C

\([\text{H}^+] = 0.05; \quad I = 0.50/\text{mol dm}^3.\)

<table>
<thead>
<tr>
<th>([\text{Ce(IV)}] \times 10^4) (mol dm(^{-3}))</th>
<th>([\text{ATN}] \times 10^3) (mol dm(^{-3}))</th>
<th>(k_{\text{obs}} \times 10^3) (s(^{-1}))</th>
<th>Found.</th>
<th>Calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>2.0</td>
<td>3.78</td>
<td>3.87</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>3.78</td>
<td>3.87</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>2.0</td>
<td>3.80</td>
<td>3.87</td>
<td></td>
</tr>
<tr>
<td>4.0</td>
<td>2.0</td>
<td>3.81</td>
<td>3.87</td>
<td></td>
</tr>
<tr>
<td>5.0</td>
<td>2.0</td>
<td>3.82</td>
<td>3.87</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>0.5</td>
<td>2.19</td>
<td>2.25</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>1.0</td>
<td>2.90</td>
<td>3.12</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>2.0</td>
<td>3.80</td>
<td>3.87</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>4.0</td>
<td>4.40</td>
<td>4.39</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>5.0</td>
<td>4.60</td>
<td>4.53</td>
<td></td>
</tr>
</tbody>
</table>
Figure III(ii)

First order plots of oxidation of atenolol by cerium(IV) in aqueous acid medium at 25 °C

\([\text{Ce(IV)}] \times 10^4 \text{ mol dm}^{-3}: (1) 0.5, (2) 1.0, (3) 2.0, (4) 4.0, (5) 5.0\)

(Conditions as in Table III(iii)(p.73))
Effect of varying acidity

The effect of acid on the reaction was studied by using perchloric acid at constant concentrations of atenolol and cerium(IV) and keeping a constant ionic strength of 0.1 mol dm$^{-3}$ at 25 °C. A constant amount of sulphuric acid coming from the stock solution of cerium(IV) is also present in all cases. The rate constants increased with increase in [acid] (Table III(iv)(p79)). The in situ $[H^+]$ concentration in the sulphuric acid-sulphate media was calculated using the known ionization constant$^{11}$ of acid sulphate as in an earlier study$^{12}$. An example calculation of $[H^+]$ is given below. From the knowledge of sulphate and acidity, the concentration of $\text{HSO}_4^-$ was calculated from the quadratic equation applicable to this case and the actual $[H^+]$ in solution. Thus in the case of 0.1 mol dm$^{-3}$ perchloric acid, the total $[H^+] = 0.1 + 0.028 = 0.128$ and $[\text{SO}_4^{2-}] = 0.014$ (from $\text{H}_2\text{SO}_4$ present in Ce(IV) stock solution).

$$K = \frac{[\text{HSO}_4^-]}{[H^+][\text{SO}_4^{2-}]}$$

Where 'a' and 'b' are the concentration of acid 0.128 mol dm$^{-3}$ and sulphate (0.014 mol dm$^{-3}$) respectively and 'x' that of bisulphate,

$$x = 0.128 - 0.014 = 0.114$$

or $8.3 x^2 - 4.569x + 0.03486 = 0$ and $[\text{HSO}_4^-] = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$

Thus, $[H^+] = (a-x) = 0.42 - 7.71 \times 10^{-3}$

$= 0.41229$
Order with respect to \([\text{ATN}]\) and \([\text{HClO}_4]\) on the oxidation of atenolol by cerium(IV) in aqueous perchloric acid medium at 25 °C.

Figure III(iii)
and \([\text{SO}_4^{2-}] = (b-x) = 0.01 - 7.71 \times 10^{-3}\)

\[= 2.29 \times 10^{-3}\]

The order in \([\text{H}^+]\) was fractional as found from a plot of \(\log k_{\text{obs}}\) versus \(\log [\text{H}^+]\)
(Fig. III(iv)(p.80)\((r>0.991, S<0.005)\)). Cerium(IV) is known to form several complexes\(^3\) in acid sulphate media, such as \(\text{Ce(OH)}^{3+}, \text{Ce(SO}_4^{2+}, \text{Ce(SO}_4^2, \text{Ce(SO}_4)_2, \text{Ce(SO}_4)_2(\text{HSO}_4)^- \text{and H}_3\text{Ce(SO}_4)_4^-\) as shown in equilibria (2) to (6).

\[
\text{Ce}^{4+} + \text{H}_2\text{O} \rightleftharpoons \text{Ce(OH)}^{3+} + \text{H}^+ \quad \text{K}_{\text{OH}} \quad (2)
\]

\[
\text{Ce}^{4+} + \text{SO}_4^{2-} \rightleftharpoons \text{Ce(SO}_4)^{2+} \quad \text{K}_1 \quad (3)
\]

\[
\text{Ce(SO}_4^2 + \text{SO}_4^{2-} \rightleftharpoons \text{Ce(SO}_4)_2 \quad \text{K}_2 \quad (4)
\]

\[
\text{Ce(SO}_4)_2 + \text{HSO}_4^- \rightleftharpoons \text{Ce(SO}_4)_2(\text{HSO}_4)^- \quad \text{K}_3 \quad (5)
\]

\[
\text{Ce(SO}_4)_2 \text{HSO}_4^- + \text{H}_2\text{SO}_4^- + \text{H}^+ \rightleftharpoons \text{H}_3\text{Ce(SO}_4)_4^- \quad \text{K}_4 \quad (6)
\]

Since the total cerium(IV) is distributed between different species with the equilibrium constants, \(\text{K}_{\text{OH}} = 15, \beta_1 = \text{K}_1 = 384.62, \beta_2 = \text{K}_1\text{K}_2 = 169.49, \beta_3 = \text{K}_1\text{K}_2\text{K}_3 = 101.17 \text{ and } \beta_4 = \text{K}_1\text{K}_2\text{K}_3\text{K}_4 = 203.4\) characterizing such equilibria, the approximate concentration of such species may be calculated from equation (7) from the concentration of the dissolved cerium(IV) and acid sulphate, as also the competing equilibria and their constants.

\[
[\text{Ce(IV)}]_h = [\text{Ce(IV)}]_0 \{(1+ \frac{\text{K}_{\text{OH}}}{[\text{H}^+]}) + \beta_1[\text{SO}_4^{2-}] + \beta_2[\text{SO}_4^{2-}]^2 + \beta_3[\text{SO}_4^{2-}]^2[\text{HSO}_4^-] + \beta_4[\text{SO}_4^{2-}]^2[\text{HSO}_4^-][\text{H}^+])\}
\]

A sample calculation of different cerium (IV) species in 0.10 mol dm\(^{-3}\) HClO\(_4\) is given below.
\[ [H^+] = 0.121; \quad [SO_4^{2-}] = 0.698 \times 10^{-2}; \quad [HSO_4^-] = 7.012 \times 10^{-3} \text{ mol dm}^{-3} \]

\[ [\text{Ce(IV)}] = 2 \times 10^4 = [\text{Ce}^{4+}] \left\{ 1 + \frac{15}{0.121} + 384.62 (0.698 \times 10^{-2}) \right. \]
\[ + 169.49 (0.698 \times 10^{-2})^2 + 101.7 (0.698 \times 10^{-2}) (7.012 \times 10^{-3}) \]
\[ + 203.4 (0.698 \times 10^{-2})^2 (7.012 \times 10^{-3})^2 (0.121) \right\} \]

\[ = [\text{Ce(IV)}] \left\{ 1 + 123.967 + 2.684 + 8.258 \times 10^{-3} + 3.456 \times 10^{-5} + 5.896 \times 10^{-8} \right\} \]

Therefore

\[ [\text{Ce}^{4+}] = \frac{2.0 \times 10^{-4}}{127.659} = 15.667 \times 10^{-7}; \quad \alpha_0 = \frac{15.667 \times 10^{-7}}{2 \times 10^{-4}} = 7.830 \]

Similarly,

\[ [\text{Ce(OH)}^{3+}] = 123.967 \times 15.667 \times 10^{-7} = 1.942 \times 10^{-4}; \quad \alpha_1 = 0.971 \]
\[ [\text{CeSO}_4^{2-}] = 2.6846 \times 15.667 \times 10^{-7} = 4.206 \times 10^{-6}; \quad \alpha_2 = 21.03 \times 10^{-3} \]
\[ [\text{Ce(SO}_4)] = 8.258 \times 10^{-3} \times 15.667 \times 10^{-7} = 12.938 \times 10^{-9}; \quad \alpha_3 = 6.469 \times 10^{-5} \]
\[ [\text{HCE(SO}_4)] = 3.456 \times 10^{-3} \times 15.667 \times 10^{-7} = 5.215 \times 10^{-11}; \quad \alpha_4 = 2.30 \times 10^{-7} \]
\[ [\text{H}_3\text{Ce(SO}_4)] = 5.896 \times 10^{-8} \times 15.667 \times 10^{-7} = 9.237 \times 10^{-14}; \quad \alpha_5 = 4.618 \times 10^{-10} \]

Where \( \alpha_0, \alpha_1, \alpha_2, \alpha_3, \alpha_4 \) and \( \alpha_5 \) are the fractions of the total Ce(IV) species, \( \text{Ce}^{4+}, \text{Ce(OH)}^{3+}, \text{CeSO}_4^{2-}, \text{Ce(SO}_4), \text{HCE(SO}_4), \) and \( \text{H}_3\text{Ce(SO}_4) \) respectively. The results of such calculations are given in Table III(iv) p.79 and are used to draw Fig. III(iv)(p.80). It is seen that, of the concentrations of different species, the variation of only \( [\text{Ce(SO}_4)]_2 (\text{HSO}_4)^- \) with acidity shows any parallelism with the variation of rate with acidity. The UV-Vis spectrum of cerium(IV) with different hydrogen ion concentrations is shown in Fig. III(v)(p.81). The absorbance of cerium(IV) increases with an increase in hydrogen ion concentration and finally remains constant. This
Table III(iv)

Variation of different cerium(IV) species* with [H\(^+\)] on the oxidation of atenolol by cerium(IV) in acid medium at 25 °C

\[
[\text{ATN}] = 2 \times 10^{-3}; \quad [\text{Ce(IV)}] = 2 \times 10^{-4};
\]

\[I = 0.50 \text{ /mol dm}^{-3}.\]

<table>
<thead>
<tr>
<th>([\text{HClO}_4]^b) (x 10^2)</th>
<th>([\text{H}^+])</th>
<th>([\text{SO}_4^{2-}]) (x 10^3)</th>
<th>([\text{HSO}_4^-]) (x 10^3)</th>
<th>(\alpha_0) (x 10^3)</th>
<th>(\alpha_1) (x 10^3)</th>
<th>(\alpha_2) (x 10^3)</th>
<th>(\alpha_3) (x 10^7)</th>
<th>(\alpha_4) (x 10^{10})</th>
<th>(k_{\text{obs}}) (x 10^3\text{s}^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>0.035</td>
<td>1.086</td>
<td>3.139</td>
<td>2.305</td>
<td>0.088</td>
<td>9.631</td>
<td>4.605</td>
<td>0.865</td>
<td>0.273</td>
</tr>
<tr>
<td>0.02</td>
<td>0.044</td>
<td>1.024</td>
<td>3.765</td>
<td>2.891</td>
<td>0.085</td>
<td>11.385</td>
<td>5.138</td>
<td>1.160</td>
<td>0.385</td>
</tr>
<tr>
<td>0.05</td>
<td>0.072</td>
<td>0.787</td>
<td>5.271</td>
<td>4.710</td>
<td>0.981</td>
<td>14.250</td>
<td>4.943</td>
<td>1.585</td>
<td>1.186</td>
</tr>
<tr>
<td>0.08</td>
<td>0.101</td>
<td>0.739</td>
<td>6.614</td>
<td>5.226</td>
<td>0.979</td>
<td>14.850</td>
<td>4.837</td>
<td>1.950</td>
<td>2.564</td>
</tr>
<tr>
<td>0.10</td>
<td>0.121</td>
<td>0.698</td>
<td>7.012</td>
<td>7.830</td>
<td>0.971</td>
<td>21.030</td>
<td>6.469</td>
<td>2.300</td>
<td>4.618</td>
</tr>
</tbody>
</table>

\(\alpha_0, \alpha_1, \alpha_2, \alpha_3, \alpha_4, \text{ and } \alpha_5\) are the fractions of the total cerium(IV) species, Ce\(^{4+}\), Ce(OH)\(^{3+}\), Ce(SO\(_4\))\(^{2+}\), Ce(SO\(_4\))\(_2\), HCe(SO\(_4\))\(^3\), and H\(_5\)Ce(SO\(_4\))\(^4\) respectively.

*a All concentrations in mol dm\(^{-3}\).

*b A constant amount of H\(_2\)SO\(_4\) coming from original stock solution of cerium(IV) i.e. 1.4 \(x 10^2\) mol dm\(^{-3}\) is also present in all cases.
Figure III(iv)

Effect of acid concentration on different cerium(IV) species and also on the rate constants.

(Conditions as in Table III(iv)(p.79)).

![Graph showing the effect of acid concentration on different cerium(IV) species and rate constants.](Figure III(iv))
Figure III(v)

Spectrum of cerium(IV) with different hydrogen ion concentrations:
1) 0, 2) 0.01, 3) 0.02, 4) 0.05, 5) 0.08, 6) 0.10 : mol dm$^3$. 
indicates the possibility of various species of cerium(IV) with hydrogen ion concentration, with predominance of one species of cerium(IV) as Ce(SO₄)(HSO₄)

Effect of added products and initially added sulphate

The effect of initially added products such as cerium(III), 4-Hydroxycarboxymethoxy phenyl acetic acid and N-isopropylmethylamine did not show any significant effect on the rate of reaction. The initially added sulphate also did not affect the rate significantly.

Effect of ionic strength and solvent polarity

The effect of ionic strength was studied by varying the sodium perchlorate concentration in the reaction medium. The ionic strength of the reaction medium was varied from 0.1 to 1.0 mol dm⁻³ at constant concentrations of cerium(IV), atenolol and perchloric acid. It was found that the rate constant increased with the increase in concentration of NaClO₄ (Table III(v)(p.83)). The plot of log kₒbs versus 1/² was linear with positive slope as shown in Fig. III(vi)(p.84)(r > 0.991, S < 0.0048).

The relative permittivity(εr) effect was studied by varying the acetic acid-water content in the reaction mixture, all other conditions being maintained constant as in Table III(v)(p.83). Attempts to measure the relative permittivities were not successful. However, they were computed from the values of pure liquids¹³ as given in chapter II(p.45). There was no reaction of the solvent with the oxidant under the experimental conditions used. It was found that an increase in the percentage of acetic acid, rate constant, kₒbs decreased. The plot of logkₒbs versus 1/εr was linear with negative slope as shown in Fig. III(vi)(p.84)(r > 0.983, S < 0.0047).
Table III(v)

Effect of ionic strength (I) and dielectric constant ($\varepsilon_T$) on the oxidation of atenolol by cerium(IV) in aqueous perchloric acid medium at 25 °C.

\[
\begin{align*}
[\text{ATN}] &= 2.0 \times 10^{-3}; \\
[\text{Ce(IV)}] &= 2.0 \times 10^{-4}; \\
[H^+] &= 0.05 \text{ mol dm}^{-3} \\
I &= 0.50 \text{ /mol dm}^{-3}.
\end{align*}
\]

<table>
<thead>
<tr>
<th>$I$ (mol dm$^{-3}$)</th>
<th>$k_{\text{obs}} \times 10^3$ (s$^{-1}$)</th>
<th>% of AcOH-Water (v/v)</th>
<th>$\varepsilon_T$</th>
<th>$k_{\text{obs}} \times 10^3$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>3.28</td>
<td>5</td>
<td>74.88</td>
<td>4.01</td>
</tr>
<tr>
<td>0.2</td>
<td>3.39</td>
<td>10</td>
<td>71.27</td>
<td>3.15</td>
</tr>
<tr>
<td>0.5</td>
<td>3.80</td>
<td>15</td>
<td>67.66</td>
<td>2.40</td>
</tr>
<tr>
<td>0.8</td>
<td>4.04</td>
<td>20</td>
<td>64.05</td>
<td>1.91</td>
</tr>
<tr>
<td>1.0</td>
<td>4.21</td>
<td>25</td>
<td>60.43</td>
<td>1.45</td>
</tr>
</tbody>
</table>
Figure III(vi)

Effect of ionic strength (I) and dielectric constant (e_T) on the oxidation of atenolol in aqueous perchloric acid medium at 25 °C.

(Conditions as in Table III(v)(p.83))
Polymerization study

The reaction mixture containing acrylonitrile was kept for 24 hours in an inert atmosphere. On diluting the reaction mixture with methanol, we obtained a precipitate indicating the presence of free radical intervention in the reaction. The blank experiments of either Ce(IV) or ATN alone with acrylonitrile did not induce any polymerization under the same condition as those induced reaction mixture. Added acrylonitrile decreases the rate of reaction indicating free radical intervention, as in earlier work.14

Effect of temperature

The rate of reaction was measured at different temperatures under varying [ATN] keeping other conditions constant. The rate constants, k of the slow step of Scheme 1 were obtained from the intercept of the plots of 1/k_{obs} versus 1/[ATN] at four different temperatures. The values of k are given in Table III(vi)(p.86). From the plot of log k versus 1/T(Fig. III(vii)(p.87);(r>0.955, S<0.005)), the activation parameters have been calculated as in Chapter II(p. 47) and are tabulated in Table III(vi)(p.86).

DISCUSSION

The reaction between ATN and cerium(IV) in acidic medium has a stoichiometry of 1:2 with fractional order dependence on acid and less than unit order dependence on atenolol concentrations and a first order dependence on [Ce(IV)]. No effect of the products was observed. The variation of rate with acidity was shown (results section), to parallel the trend of variation of concentration of the
Table III(vi)

(a) Effect of temperature on the slow step of the mechanism of oxidation of atenolol by cerium(IV) in aqueous perchloric acid medium.

<table>
<thead>
<tr>
<th>Temp (K)</th>
<th>k x 10^3 (s^-1)</th>
<th>log k (Y)</th>
<th>1/T x 10^3 (X)</th>
<th>Y^* calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>298</td>
<td>5.09</td>
<td>-2.2934</td>
<td>3.35</td>
<td>-2.2856</td>
</tr>
<tr>
<td>303</td>
<td>6.05</td>
<td>-2.2183</td>
<td>3.30</td>
<td>-2.2182</td>
</tr>
<tr>
<td>308</td>
<td>7.20</td>
<td>-2.1426</td>
<td>3.24</td>
<td>-2.1499</td>
</tr>
<tr>
<td>313</td>
<td>8.56</td>
<td>-2.0676</td>
<td>3.19</td>
<td>-2.0675</td>
</tr>
</tbody>
</table>

* Calculated

(b) Thermodynamic activation parameters for the oxidation of atenolol by acidic cerium(IV) with respect to slow step of Scheme 1.

<table>
<thead>
<tr>
<th>Activation parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ea (kJ mol^-1)</td>
<td>27 ± 2</td>
</tr>
<tr>
<td>ΔH^&quot; (kJ mol^-1)</td>
<td>25 ± 2</td>
</tr>
<tr>
<td>ΔS^&quot; (J K^-1mol^-1)</td>
<td>-208 ± 10</td>
</tr>
<tr>
<td>ΔG^&quot; (kJ mol^-1)</td>
<td>88 ± 3</td>
</tr>
</tbody>
</table>
Figure III(vii)

Effect of temperature on the slow step of the mechanism of oxidation of atenolol by cerium(IV) in aqueous perchloric acid medium.

(Conditions as in Table III(vi)(p.86))
Ce(SO₄)₂(HSO₄)⁺ species with the acidity (Table III(iv)(p.79)). Although the variation of Ce(SO₄)²⁺, also parallels the acidity and rate, since no effect of sulphate on the rate of reaction is observed in this case and in view of apparent less than unit order in [H⁺], sulphate complexes of cerium(IV) do not play role in the reaction. Hence Ce(SO₄)₂(HSO₄)⁺ is considered to be the active species (Fig. III(iv)(p.80)) of cerium(IV). This type of species is also observed in earlier work¹⁵. Atenolol is an amide and it is existed as in the following hydrolyzed form in aqueous medium.

\[
\begin{align*}
\text{OH} & \\
\text{O-CH₂-CH₂-NH-CH-(CH₃)₂} & + 2\text{H₂O} \quad \rightleftharpoons \quad \text{O-CH₂-CH₂-NH-CH-(CH₃)₂} \\
\text{CH₂-C} & \quad \text{NH₂} \\
\end{align*}
\]

The added acrylonitrile monomer polymerizes under an inert atmosphere indicating the presence of free radical intervention in the reaction. The apparent less than unit order in substrate(ATN), presumably results from a complex formation between the oxidant and substrate prior to the formation of products. Indeed, it is to be noted that, the plot of 1/\(k_{obs}\) versus 1/[ATN] (Fig. III(viii)(p.94);(r>0.990, S ≤ 0.0046)), shows an intercept, is in agreement with such complex formation.

The results indicate that the active Ce(IV) species, i.e., Ce(SO₄)₂(HSO₄)⁺ is formed in a prior equilibrium. This active species, Ce(SO₄)₂(HSO₄)⁺ reacts with hydrolyzed form of atenolol, to give a complex, which then decomposes in a slow step to give a free radical derived from ATN and the cerium(III) product. Thus
formed free radical reacts with another molecule of the active species of cerium(IV) in a subsequent fast step to yield the products. Attempts to obtain spectral evidence for the complex formation between oxidant and substrate were not successful, since there is no change in UV-Vis spectra of Ce(IV) and mixture of Ce(IV) and ATN at room temperature. However, at lower temperature (nearly 5 °C), a bathochromic shift of about 4 nm from 236 to 240 nm of Ce(IV) and hyperchromicity at 240nm was observed for the spectra of Ce(IV) and ATN. The formation of complex is proved kinetically also by the non-zero intercept (Fig. III(viii)(p.94); r ≥ 0.990, S ≥ 0.0046) of the plot of 1/k_{obs} versus 1/[ATN] (Michaelis-Menten plot). Such complex formation between substrate and oxidant has been observed earlier. These results indicate a mechanism of the type as in Scheme 1.

\[
\begin{align*}
H^+ + SO_4^- & \rightleftharpoons K \quad HSO_4^- \\
Ce(SO_4)_2 + HSO_4^- & \rightleftharpoons HCe(SO_4)_3^- \\

\text{Complex (C)} + Ce(SO}_4\text{)}^2(aq) & \rightleftharpoons K_4 \quad \text{Complex(C)} \\

\text{Complex (C)} & \xrightarrow{k_{\text{slow}}} \\

\text{Ce(III)} + H_2SO_4
\end{align*}
\]
Scheme 1

The probable structure of the complex (C) is

The thermodynamic quantities for the first equilibrium step in Scheme 1 can be evaluated as follows: The H⁺ concentration was varied at several temperatures, and values of β₃ were determined at each temperature. The values of β₃ (dm³ mol⁻¹) were obtained as 98.05, 140.30, 264.61, and 343.88 at 25, 30, 35 and 40 °C respectively. A van't Hoff plot was made for the variation of β₃ with temperature (i.e., log β₃ versus 1/T)(r ≥ 0.9860, S ≤ 0.0110) and the values of the enthalpy of the reaction, ΔH, entropy of the reaction, ΔS, and free energy of reaction, ΔG, were calculated as 68.5 ± 2.0 kJ mol⁻¹, 268 ± 10 J K⁻¹ mol⁻¹ and -13.3 ± 0.5 k J mol⁻¹, respectively. A
comparison of the latter values with those obtained for the slow step of the reaction shows that these values mainly refer to the rate limiting step, supporting the fact that the reaction before the rate determining step are fairly slow and involves higher activation energy\(^{17}\).

Since Scheme 1 is in accordance with the generally well accepted principle of non-complementary oxidations taking place in sequence of one electron steps, the reaction between the substrate and oxidant would afford radical intermediate. A free radical scavenging experiment revealed such a possibility. This type of radical intermediate has also been observed in earlier work\(^{18}\) on the cerium(IV) oxidations of various organic substrates in acid medium.

Scheme 1 leads to the following rate law.

\[
\text{Rate} = - \frac{d[\text{Ce(IV)}]}{dt} = k [C] = k K_3 K_4 [\text{ATN}]_r [\text{Ce(SO}_4)_2]_r [\text{H}^+]_r [\text{SO}_4^{2-}]_r
\]

The total \([\text{Ce(IV)}]_t\), \([\text{Ce(IV)}]_f\) is given as (where the subscripts t and f stand for total and free respectively)

\[
[\text{Ce(IV)}]_t = [\text{Ce(SO}_4)_2]_r + [\text{Ce(SO}_4)_2(\text{HSO}_4)] + [C]
\]

\[
= [\text{Ce(IV)}]_r + \beta_3 [\text{Ce(IV)}][\text{H}^+][\text{SO}_4^{2-}] + K_5 [\text{ATN}][\text{Ce(SO}_4)_2(\text{HSO}_4)]
\]

\[
= [\text{Ce(IV)}]_r + \beta_3 [\text{Ce(IV)}][\text{H}^+][\text{SO}_4^{2-}] + K_4 K_5 [\text{ATN}][\text{Ce(IV)}][\text{H}^+][\text{SO}_4^{2-}]
\]

\[
= [\text{Ce(IV)}]_r (1 + K \beta_3 [\text{H}^+][\text{SO}_4^{2-}] + K \beta_3 K_5 [\text{ATN}][\text{H}^+][\text{SO}_4^{2-}])
\]

Therefore,

\[
[\text{Ce(IV)}]_f = \frac{[\text{Ce(IV)}]_r}{1 + K \beta_3 [\text{H}^+][\text{SO}_4^{2-}] + K \beta_3 K_5 [\text{ATN}][\text{H}^+][\text{SO}_4^{2-}]}
\]

Similarly,

\[
[\text{ATN}]_f = [\text{ATN}]_r + [C]
\]

\[
= [\text{ATN}]_r + \beta_3 K_5 [\text{ATN}][\text{H}^+][\text{SO}_4^{2-}][\text{Ce(IV)}]
\]
\[ [\text{ATN}]_t = \frac{[\text{ATN}]}{1 + K \beta_3 K_s [H^+] [SO_4^{2-}] [\text{Ce(IV)}]} \]  
\[ [H^+]_f = \frac{[H^+]_t}{1 + K \beta_3 [\text{Ce(IV)}] [SO_4^{2-}] + K \beta_3 K_s [\text{ATN}] [SO_4^{2-}] [\text{Ce(IV)}]} \]

Similarly, 

Substituting the values of (b), (c) and (d) in equation (a) (omitting subscripts t and f), we get

\[
\text{Rate} = \frac{k K \beta_3 K_s [\text{Ce(IV)}] [\text{ATN}] [H^+] [SO_4^{2-}]}{1 + K \beta_3 [H^+] [SO_4^{2-}] + K \beta_3 K_s [\text{ATN}] [H^+] [SO_4^{2-}]} \times \frac{1}{(1 + K \beta_3 [\text{Ce(IV)}] [SO_4^{2-}] + K \beta_3 K_s [\text{ATN}] [SO_4^{2-}])} 
\]

The terms \((1 + K \beta_3 [\text{Ce(IV)}] [SO_4^{2-}] + K \beta_3 K_s [\text{ATN}] [\text{Ce(IV)}] [SO_4^{2-}]\) and \((1 + K \beta_3 K_s [\text{ATN}] [SO_4^{2-}] [\text{Ce(IV)}] [H^+] [SO_4^{2-}]\) in the denominator of equation (8) approximate to unity in view of the low concentration of [Ce(IV)]. Therefore, equation (8) can be written as,

\[
\frac{\text{Rate}}{[\text{Ce(IV)}]} = k_{\text{obs}} = \frac{k K \beta_3 K_s [\text{ATN}] [H^+] [SO_4^{2-}]}{1 + K \beta_3 [H^+] [SO_4^{2-}] + K \beta_3 K_s [\text{ATN}] [H^+] [SO_4^{2-}]} 
\]

The equation (9) can be rearranged to equation (10) which is suitable for verification.

\[
\frac{1}{k_{\text{obs}}} = \frac{1}{k K \beta_3 K_s [\text{ATN}] [H^+] [SO_4^{2-}]} + \frac{1}{k K_s [\text{ATN}]} + \frac{1}{k} 
\]

According to equation (10), the plots of \(1/k_{\text{obs}}\) versus \(1/[\text{ATN}]\) \((r \geq 0.990, S \geq 0.0046)\) and \(1/k_{\text{obs}}\) versus \(1/[H^+]\) \((r > 0.988, S \leq 0.0045)\) should be linear. This is verified in Fig. III(viii)(p.94). From the slopes and intercepts of such plots, the calculated values of \(k\), \(\beta_3\) and \(K_s\) at 25 °C were \((5.1 \pm 0.1) \times 10^3 \text{ s}^{-1}, 98 \pm 3 \text{ dm}^3 \text{ mol}^{-1}\)
5038 ± 40 dm³ mol⁻¹ respectively. The value of K is taken as 8.3 from literature¹⁹. Using these values, the rate constants under different experimental conditions were calculated and compared with experimental values as given in Table III(iii)(p.73). Experimental and calculated values agree reasonably well supporting the assumptions of Scheme 1. The value of β₃ (=101.17) is in good agreement with the earlier reported value³.

The effect of ionic strength on the rate can be understood essentially on the basis ionic species. The effect of solvent on the reaction rate is described elsewhere²⁰. The plot of log kₒᵢₑᵣ versus 1/ₑᵣ is expected to be linear with a negative slope for a reaction between a negative ion and neutral molecule, whereas a positive slope results for a positive ion and neutral molecule. In the present study, a plot of log kₒᵢₑᵣ versus 1/ₑᵣ is linear with negative slope which supports the involvement of negative ion as given in Scheme 1.

The negative value of ΔSᵣ value suggests that the complex(C) is more ordered than the reactants. The observed modest enthalpy of activation and higher rate constant of slow step indicate that the oxidation presumably occurs by inner-sphere mechanism. This conclusion is supported by the results of earlier work²¹.
Verification of rate law (9) in the form of (10) on the oxidation of atenolol by cerium(IV) in aqueous perchloric acid medium at 25 °C.

(Conditions as in Table III(iii)p.73;iv)p.79)
Importance of Chapter III

Among the various species of Cerium(IV) in acid medium, Ce(SO₄)₂(HSO₄)⁻ is considered to be predominant species. The active species involved in the mechanism play an important role in the reaction. The description of the mechanism is consistent with all the evidences including kinetics, spectral and products.
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