CHAPTER III

Kinetic and Mechanistic Investigation of Oxidative Degradation and Deamination of Atenolol by Diperiodatonickelate(IV) in Aqueous Alkaline Medium

The general importance of diperiodatonickelate(IV) (DPN) is given in chapter II (p.30). Nickel(IV) periodate oxidations of aliphatic amines, alcohols, acids and acetophenones in alkaline medium have been studied. DPN oxidation of some amino acids and other substrates has been made earlier in our laboratory.

The substrate, 4-(2-hydroxy-3-isopropylaminoproxy) phenylacetamide commercially known as atenolol (ATN) a β-adrenoreceptor blocking agent is used as antihypertensive drug. Atenolol is a well-known drug that finds extensive applications in pharmaceutical industries. It is also used for anti-angina treatment to relieve symptoms, improve tolerance and as an anti-arrhythmic to regulate heartbeat and infections. It is also used in management of alcohol withdrawal, in anxiety states, migraine prophylaxis, hyperthyroidism and tremor. The derivative of oxidation product of atenolol finds its importance in biological systems such as plant growth hormones, herbicides, etc.

In earlier reports on DPN oxidation, periodate had a retarding effect and order in the [OH⁻] was found to be less than unity in almost all the reactions and monoperiodatonickelate(IV), is considered to be the active species. However, in the present study we have observed entirely different kinetic observations and
diperiodatonicelate(IV), is found to be active form of the oxidant. Literature survey reveals that there are no reports on the oxidative mechanism of atenolol by any oxidant except in one case. The present chapter deals with the title reaction to investigate the redox chemistry of nickel(IV) in such media and to arrive at a plausible mechanism of the reaction on the basis of kinetic and spectral results.

**EXPERIMENTAL**

**Materials**
All chemicals used were of reagent grade. Double distilled water was used throughout the work. Solution of atenolol (S.D.Fine Chem.) was prepared by dissolving appropriate amount of recrystallised sample in double distilled water. The solid complex nickel(IV) periodate, was prepared by known method as described in chapter II (p.32). Aqueous solution of DPN was obtained by dissolving the solid complex in 1.0 mol dm$^{-3}$ KOH solution. The Ni(IV) in alkaline solution was estimated gravimetrically after reducing it to Ni(II) and precipitating Ni(II) as its dimethyl glyoxime complex. Periodate solution was prepared by weighing out the required amount of a sample in hot water and was used after keeping for 24 hours. Its concentration was ascertained iodometrically at neutral pH maintained by a phosphate buffer. The nickel(II) solution was made by dissolving weighed amount of nickel sulfate in water. Potassium hydroxide and potassium nitrate were used to provide the required alkalinity and ionic strength respectively in the reaction solutions.
Since periodate is present in excess in DPN complex, the possibility of atenolol oxidation by periodate in aqueous alkaline medium has been tested. The results indicated that the reaction between periodate and atenolol is negligibly slow compared to the rate of reaction between DPN and atenolol under the experimental conditions.

**Kinetic Procedure**

The oxidation of atenolol by DPN was followed under pseudo-first order conditions where [Atenolol] was in excess over [DPN] at 25 ± 0.1 °C unless otherwise stated. The reaction was initiated by mixing previously thermostatted solutions of DPN and atenolol of required concentrations, which also contained the required quantities of potassium hydroxide, potassium nitrate and potassium metaperiodate. The total concentration of hydroxide ion was calculated by considering the potassium hydroxide in DPN as well as the potassium hydroxide additionally added. Similarly, the total metaperiodate concentration was calculated by considering the metaperiodate present in the DPN solution and that additionally added. The reaction was followed by measuring the absorbance of the unreacted DPN in the reaction mixture in a 1 cm quartz cell in the thermostatted compartment of Hitachi U-2001 Spectrophotometer, at 410 nm where other constituents of the reaction do not absorb significantly.

The obedience of Beer’s law by DPN at 410 nm in the concentration range of $1.0 \times 10^{-5}$ to $1.0 \times 10^{4}$ mol dm$^{-3}$ under constant metaperiodate and alkali concentration was studied (chapter II (p.35)) with molar absorbance coefficient ‘$\varepsilon$’
as $7500 \pm 375 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ at this wavelength. The first order rate constants, $k_{obs}$, were obtained from the plots of $\log (a-x)$ versus time, where 'a' and 'x' being the initial concentration and change in concentration of diperiodatonicelate(IV) at time 't' respectively. The plots were linear upto about 85% completion of the reaction and the rate constants were reproducible within $\pm 5\%$. An example run is given in Table III (i) (p.74).

The effect of dissolved oxygen on the rate of reaction was studied by preparing the reaction mixture and following the reaction in an atmosphere of nitrogen. No significant difference between the results was observed. In view of the ubiquitous contamination of basic solutions by carbonate, the effect of carbonate on the reaction was also studied. Added carbonate had no effect on reaction rate. However, fresh solutions were used during the experiments.

In view of the modest concentration of alkali used in the reaction medium, attention was also given to the effect of the surface of the reaction vessel on the kinetics. The use of polythene or acrylic ware and quartz or polyacrylate cells gave the same results, indicating that the surface does not have any significant effect on the rate. Regression analysis of experimental data to obtain the regression coefficient, 'r' and standard deviation, 'S' of points from the regression line was performed using a Pentium-IV P.C.
Table III (i)

Example run for the Oxidation of Atenolol by Diperiodatonickelate(IV) in aqueous alkaline medium at 25 °C.

\[
\begin{align*}
[\text{DPN}] &= 1.0 \times 10^{-4}; \\
[\text{Atenolol}] &= 1.0 \times 10^{-3}; \\
[\text{OH}^{-}] &= 0.2; \\
[\text{IO}_4^{-}] &= 5.0 \times 10^{-4}; \\
I &= 1.0 / \text{mol dm}^3.
\end{align*}
\]

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Optical density (410 nm)</th>
<th>[DPN] \times 10^5 (mol dm(^{-3}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.740</td>
<td>9.86</td>
</tr>
<tr>
<td>0.4</td>
<td>0.673</td>
<td>8.97</td>
</tr>
<tr>
<td>0.8</td>
<td>0.593</td>
<td>7.91</td>
</tr>
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<td>1.2</td>
<td>0.525</td>
<td>7.00</td>
</tr>
<tr>
<td>1.6</td>
<td>0.456</td>
<td>6.08</td>
</tr>
<tr>
<td>2.0</td>
<td>0.396</td>
<td>5.28</td>
</tr>
<tr>
<td>2.4</td>
<td>0.350</td>
<td>4.66</td>
</tr>
<tr>
<td>2.8</td>
<td>0.310</td>
<td>4.13</td>
</tr>
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</tr>
<tr>
<td>3.6</td>
<td>0.230</td>
<td>3.06</td>
</tr>
<tr>
<td>4.0</td>
<td>0.199</td>
<td>2.65</td>
</tr>
<tr>
<td>4.4</td>
<td>0.174</td>
<td>2.32</td>
</tr>
<tr>
<td>4.8</td>
<td>0.150</td>
<td>2.00</td>
</tr>
<tr>
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<td>0.133</td>
<td>1.77</td>
</tr>
<tr>
<td>5.6</td>
<td>0.117</td>
<td>1.56</td>
</tr>
<tr>
<td>6.0</td>
<td>0.100</td>
<td>1.33</td>
</tr>
</tbody>
</table>
RESULTS

Stoichiometry and Product Analysis

Different reaction mixtures with different sets of concentrations of reactants where [Ni(IV)] was in excess over [Atenolol] at constant ionic strength and alkali were kept for about 6 hours at 25 ± 0.1 °C in nitrogen atmosphere and in a closed vessel. The remaining [DPN] was assayed spectrophotometrically by measuring the absorbance at 410 nm (Table III (ii) (p.76)). The results indicated that two moles of DPN consumed one mole of atenolol as in equation (1).

\[
\text{O-CH}_2-\text{CH-CH}_2-\text{NH-CH}_3 + 2\text{Ni(IV)} + 4 \text{OH}^- \rightarrow \text{CH}_2\text{C-CH}_3 + 2\text{Ni(II)} + \text{NH}_3 + \text{H}_2\text{O} \]

The reaction product, 4-carboxy methoxy phenyl acetic acid was extracted with ether and recrystallised from aqueous alcohol and the purity was checked by HPLC. It was identified as 4-carboxy methoxy phenyl acetic acid by its IR spectrum, which showed a band at (υ) 1690 cm\(^{-1}\) due to >C=O stretching and a broad band at 2845 cm\(^{-1}\) due to O-H stretching. 4-carboxy methoxy phenyl acetic acid was further characterised by \(^1\)H NMR spectrum (DMSO), showed chemical shifts (δ) at 10 ppm (s, due to carboxylic OH, 2H), 7.7 ppm (s, at due to aromatic,
Table III (ii)

Stoichiometry of Oxidation of Atenolol by DPN in aqueous alkaline medium at 25 °C.

\[ \text{[OH}^-\text{]} = 0.2; \quad \text{[IO}_4^-\text{]} = 5.0 \times 10^{-4}; \]

\[ I = 1.0 / \text{mol dm}^{-3}. \]

<table>
<thead>
<tr>
<th>[DPN] x 10^4 (mol dm^-3)</th>
<th>[Atenolol] x 10^4 (mol dm^-3)</th>
<th>[DPN] x 10^4 (mol dm^-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taken</td>
<td>Taken</td>
<td>Found</td>
</tr>
<tr>
<td>1.0</td>
<td>0.5</td>
<td>0.01</td>
</tr>
<tr>
<td>4.0</td>
<td>1.0</td>
<td>2.09</td>
</tr>
<tr>
<td>6.0</td>
<td>2.0</td>
<td>2.05</td>
</tr>
<tr>
<td>6.0</td>
<td>1.0</td>
<td>4.12</td>
</tr>
<tr>
<td>8.0</td>
<td>2.0</td>
<td>4.10</td>
</tr>
<tr>
<td>4.0</td>
<td>1.0</td>
<td>2.14</td>
</tr>
</tbody>
</table>
N-isopropylmethylamine, which is soluble in water, was identified by spot test.\textsuperscript{12} It was observed that the 4-carboxy methoxy phenyl acetic acid and N-isopropylmethylamine do not undergo further oxidation under the present kinetic conditions.

**Spectrofluorimetric Studies**

The fluorescence study was carried out (Hitachi F 2000 Spectrofluorimeter) in methanol as solvent. There was no interference of the solvent methanol seen in the fluorescent study. We have taken the fluorescence study of our pure compound atenolol and also for the product of the reaction of atenolol with diperiodatonickelate(IV) in aqueous alkaline medium. 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.

**Reaction Order**

The orders with respect to [Atenolol], [Alkali] and [Periodate] were found by log \( k_{obs} \) versus log concentration plots and obtained orders were also confirmed by
differential method by the plot log (±dc/dt) versus log (concentration) using the equation \( \log (±dc/dt) = \log k + n \log c \); these orders were obtained by varying the concentration of atenolol, periodate and alkali in turn while keeping others constant.

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

The concentration of diperiodatonickelate(IV) was varied in the range, 1.0 x 10^{-5} to 1.0 x 10^{-4} mol dm^{-3} at fixed [Atenolol], [OH⁻] and ionic strength. The non-variation in the pseudo-first order rate constants at various concentrations of DPN indicates the order in [DPN] as unity (Table III (iii) (p.79)). This was also confirmed from the linearity of plots of log (absorbance) versus time upto 85% completion of the reaction (Fig. III (i) (p.80) (r > 0.9994, S < 0.0145).

**Effect of [Atenolol]**

The substrate, atenolol was varied in the range of 1.0 x 10^{-4} to 1.0 x 10^{-3} mol dm^{-3} at 25 °C keeping all other reactants concentrations and conditions constant. The \( k_{obs} \) values were not changed with increase in concentration of atenolol which indicates a zero order dependence in atenolol concentration (Table III (iii) (p.79)).

**Effect of [Alkali]**

The effect of [Alkali] on the rate of reaction in the range 0.1 to 1.0 mol dm^{-3} was studied at constant concentrations of atenolol, DPN and ionic strength at 1.0 mol dm^{-3}. The rate constants increased with increase in [Alkali]. The order in [alkali] was found to be less than unity as shown in Table III (iv) (p.82) and Figure III (ii) (p.83) (r ≥ 0.9997, S ≤ 0.0135).
Table III (iii)

Effect of variation of [DPN] and [Atenolol] on Oxidation of Atenolol by DPN in aqueous alkaline medium at 25 °C.

\[ [\text{IO}_4^-] = 5.0 \times 10^{-4}, \quad [\text{OH}^+] = 0.2; \quad I = 1.0 / \text{mol dm}^{-3}. \]

<table>
<thead>
<tr>
<th>[DPN] x 10^5 (mol dm(^{-3}))</th>
<th>[Atenolol] x 10^3 (mol dm(^{-3}))</th>
<th>(k_{\text{obs}} \times 10^3 \text{ (s}^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>1.0</td>
<td>5.61</td>
</tr>
<tr>
<td>3.0</td>
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<td>5.64</td>
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<td>6.0</td>
<td>1.0</td>
<td>5.63</td>
</tr>
<tr>
<td>8.0</td>
<td>1.0</td>
<td>5.62</td>
</tr>
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<td>1.0</td>
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<td>5.59</td>
</tr>
<tr>
<td>10</td>
<td>0.8</td>
<td>5.60</td>
</tr>
<tr>
<td>10</td>
<td>1.0</td>
<td>5.64</td>
</tr>
</tbody>
</table>
First order plots of Oxidation of Atenolol by Diperiodatonickelate(IV) in aqueous alkaline medium at 25 °C.

\[ [\text{Ni(IV)}] \times 10^3 \text{ mol dm}^{-3}; \]

(1) 1.0; (2) 3.0; (3) 6.0; (4) 8.0; (5) 10

(Conditions as given in Table III (iii) (p.79))
Effect of [Periodate]

The effect of \([\text{IO}_4^-]\) was studied by varying the concentration from \(1.0 \times 10^{-4}\) to \(1.0 \times 10^{-3}\ \text{mol dm}^{-3}\) keeping all other reactants concentrations constant. It was found that the added periodate has no significant effect on the rate of reaction (Table III (iv) (p.82)).

Effect of Initially Added Products

Effects of initially added reaction products such as Ni(II) in the form of NiSO₄ and 4-carboxy methoxy phenyl acetic acid were studied in the concentration ranges from \(1.0 \times 10^{-5}\) to \(1.0 \times 10^{-4}\ \text{mol dm}^{-3}\), keeping all other reactant concentrations constant (Table III (v) (p.84)). It was found that the added product had negligible effect on rate of reaction.

Effect of Ionic Strength

The effect of ionic strength was studied by varying the potassium nitrate concentration in the reaction medium. The ionic strength of the reaction medium was varied from 0.2 to 2.0 \(\text{mol dm}^{-3}\) at constant concentration of DPN, atenolol and alkali as shown in Table III (vi) (p.85). It was found that the rate constant enhanced with increase in KNO₃ concentration and the plot of \(\log k_{\text{obs}}\) versus \(I^{1/2}\) was linear with positive slope. (Fig. III (iii) (p.86)) (\(r > 0.9989\), \(S < 0.0224\)).
Table III (iv)

Effect of variation of [OH\(^-\)] and [IO\(_4^-\)] on Oxidation of Atenolol by Diperiodatonickelate(IV) in aqueous alkaline medium at 25 °C.

\[
[\text{DPN}] = 1.0 \times 10^{-4}; \quad [\text{Atenolol}] = 1.0 \times 10^{-3};
\]

\[I = 1.0 / \text{mol dm}^{-3}.\]

<table>
<thead>
<tr>
<th>[OH(^-)] (mol dm(^{-3}))</th>
<th>[IO(_4^-)] \times 10^4 (mol dm(^{-3}))</th>
<th>(k_{\text{obs}} \times 10^4) (s(^{-1}))</th>
<th>Found</th>
<th>Calculated</th>
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<td>5.64</td>
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<td>-</td>
</tr>
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<td>0.2</td>
<td>8.0</td>
<td>5.62</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>0.2</td>
<td>10</td>
<td>5.63</td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

82
Figure III (ii)

Order in [OH'] on the Oxidation of Atenolol by DPN in aqueous alkaline medium at 25 °C.

(Conditions as in Table III (iv) (p.82))
Table III (v)

Effect of Initial Added Products, Ni(II) and 4-carboxy methoxy phenyl acetic acid on the Oxidation of Atenolol by DPN in aqueous alkaline medium at 25 °C.

\[
[\text{DPN}] = 1.0 \times 10^{-4}; \\
[\text{Atenolol}] = 1.0 \times 10^{-3}; \\
[\text{OH}^{-}] = 0.2; \\
[I_{O_4}^{-}] = 5.0 \times 10^{-4}, \\
I = 1.0 \text{ / mol dm}^{-3}.
\]

<table>
<thead>
<tr>
<th>[Ni(II)] (\times 10^5) (mol dm(^{-3}))</th>
<th>[4-carboxy methoxy phenyl acetic acid] (\times 10^5) (mol dm(^{-3}))</th>
<th>(k_{obs} \times 10^3) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>-</td>
<td>5.65</td>
</tr>
<tr>
<td>2.0</td>
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<td>5.64</td>
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<td>5.67</td>
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<td>8.0</td>
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<td>5.63</td>
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<td>4.0</td>
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<td>10</td>
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</tbody>
</table>

84
Table III (vi)

Effect of Ionic Strength (I) and Relative Permittivity ($\varepsilon_r$) on the Oxidation of Atenolol by DPN in aqueous alkaline medium at 25 °C.

\[
[\text{DPN}] = 1.0 \times 10^{-4}; \quad [\text{DPN}] = 1.0 \times 10^{-4};
\]

\[
[\text{Atenolol}] = 1.0 \times 10^{-3}; \quad [\text{Atenolol}] = 1.0 \times 10^{-3};
\]

\[
[\text{OH}^-] = 0.2; \quad [\text{OH}^-] = 0.2;
\]

\[
[\text{IO}_4^-] = 5.0 \times 10^{-4}/\text{mol dm}^3. \quad [\text{IO}_4^-] = 5.0 \times 10^{-4};
\]

\[
I = 1.0/\text{mol dm}^3.
\]

<table>
<thead>
<tr>
<th>I (mol dm$^3$)</th>
<th>$k_{obs} \times 10^3$ (s$^{-1}$)</th>
<th>% of $\varepsilon_r$</th>
<th>$k_{obs} \times 10^3$ (s$^{-1}$)</th>
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</thead>
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<td>76.47</td>
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<td>3.68</td>
<td>5</td>
<td>75.12</td>
</tr>
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<td>0.8</td>
<td>4.77</td>
<td>10</td>
<td>71.74</td>
</tr>
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<td>1.0</td>
<td>5.64</td>
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<td>68.36</td>
</tr>
<tr>
<td>2.0</td>
<td>8.20</td>
<td>20</td>
<td>64.98</td>
</tr>
</tbody>
</table>

*t-butanol-water (V/V)
Figure III (iii)

Effect of Ionic Strength (I) on the Oxidation of Atenolol by Diperiodatonicelate(IV) in aqueous alkaline medium at 25 °C.

(Conditions as in Table III (vi) (p.85))
Effect of Solvent Polarity

The relative permittivity ($\varepsilon_r$) effect was studied by varying the t-butyl alcohol-water content in the reaction mixture with all other conditions being maintained constant as in Table III (vi) (p.85). Attempts to measure the relative permittivities were not successful. However, they were computed from the values of pure liquids as in chapter II (p.45). There was no reaction of the solvent with the oxidant under the experimental conditions used. It was found that change in relative permittivity has negligible effect on the rate of the reaction.

Test for Free Radicals

To test the intervention of free radicals, the reaction mixture was mixed with acrylonitrile monomer and kept for 24 hours under nitrogen atmosphere. On dilution with methanol, white precipitate of polymer was formed, indicating the presence of intervention of free radicals in the reaction. The blank experiment of either DPN or atenolol in with acrylonitrile alone did not induce polymerization under the same condition as those induce with reaction mixture. Initially added acrylonitrile decreases the rate indicating the free radical intervention, which is the case in earlier work.

Effect of Temperature

The rate of reaction was measured at different temperatures under varying [Atenolol], keeping other conditions constant. The rate constants, $k$, of the slow step of mechanism were obtained from the intercepts of the plots of $1/k_{obs}$ versus $1/[OH^-]$ at four different temperatures. The data are subjected to least square
analysis as in chapter II (p.50) and were tabulated in Table III (vii a) (p.89)). The energy of activation corresponding to these constants was evaluated from the plot (Y*ca) log k versus 1/T (Fig. III (iv) (p.90)) (r ≤ 0.9999, S ≤ 0.0224) and other activation parameters are obtained as in chapter II (p.50) and are tabulated in Table III (vii b) (p.89).

DISCUSSION

The water soluble Ni(IV) periodate complex is reported \(^3,4\) to be [Ni(HIO\(_6\))\(_2\)(OH)\(_2\)]\(^{6-}\). Although periodate is involved in multiple equilibria which prevail to varying extents depending on the pH employed, under the conditions of high pH as maintained in this study, periodate is likely to exist \(^1\) as [H\(_3\)IO\(_6\)]\(^2-\). Hence, the species of Ni(IV) in alkali can be expected to be [Ni(H\(_3\)IO\(_6\))(H\(_2\)IO\(_6\))(OH)\(_2\)]\(^{3+}\) (DPN), a conclusion is also supported by earlier work.\(^2,15,16\)

The reaction between DPN and atenolol in alkaline medium has 2:1 stoichiometry of oxidant to reductant with first order dependence each in [DPN], the apparent order of less than unity in [OH\(^-\)] and zero order in [Atenolol]. It is interesting to note the zero order in [Atenolol] which is rarely observed. In most of the reports\(^1,6\) on DPN oxidation, periodate had a retarding effect and order in the [OH\(^-\)] was found to be less than unity and monoperiodonickelate(IV) (MPN), is considered to be the active species. However, in the present kinetic study, different kinetic observations have been obtained i.e., periodate has totally no effect on the rate of reaction. Accordingly, the deprotonated DPN is considered to be as the
Table III (vii)

(a) Effect of temperature on the slow step of the mechanism of Oxidation of Atenolol by Diperiodatonickelate(IV) in aqueous alkaline medium.

\[
\begin{align*}
[\text{DPN}] &= 1.0 \times 10^{-4}; \\
[\text{OH}^-] &= 0.2; \\
I &= 1.0 / \text{mol dm}^3.
\end{align*}
\]

\[
\begin{array}{cccc}
\text{Temperature (K)} & \text{k} \times 10^2 (s^{-1}) & \log k (Y) & 1/T \times 10^3 (X) \\
298 & 2.2 & -1.6576 & 3.35 \\
303 & 2.8 & -1.5528 & 3.30 \\
308 & 3.8 & -1.4202 & 3.24 \\
313 & 5.1 & -1.2924 & 3.19 \\
\end{array}
\]

*Calculated

(b) Activation Parameters with respect to slow step of Scheme 1.

\[
\begin{array}{cc}
\text{Activation Parameters} & \text{Values} \\
\text{Ea (kJ mol}^{-1}\text{)} & 43 \pm 2 \\
\log A & 6.0 \pm 0.3 \\
\Delta H^\circ (kJ mol}^{-1}\text{)} & 41 \pm 2 \\
\Delta S^\circ (JK}^{-1}\text{ mol}^{-1}\text{)} & -138 \pm 4 \\
\Delta G^\circ (kJ mol}^{-1}\text{)} & 83 \pm 3 \\
\end{array}
\]
Figure III (iv)

Effect of temperature on the Oxidation of Atenolol by Diperiodatonicelate(IV) in aqueous alkaline medium.

(Conditions as in Table III (vii a) (p.89))

\[
\frac{1}{T} \times 10^3 \text{ (K}^{-1})
\]

3.16 3.20 3.24 3.28 3.32 3.36 3.40

\[
\log k \text{ (Y cal.)}
\]
active species of the oxidant. In view of the zero order in atenolol, the deprotonated form of DPN decomposes in a slow step to give Ni(III) species and hydroxyl radical. This type of hydroxyl radical (OH') is evidenced from literature.\textsuperscript{17} The active hydroxyl free radical (OH') interacts with a molecule of atenolol in a fast step to form an intermediate and amino free radical (NH₂). Such a type of free radical (NH₂) formation is in accordance with earlier work.\textsuperscript{18} This intermediate reacts with nickel(III) species and free radical (NH₂) in further fast steps to give the products. A free radical scavenging experiment revealed the intervention of free radicals in the reaction (infra). Based on the observed kinetic results a mechanism involving free radical has been proposed which is shown in Scheme 1.

\[
[Ni(H_3IO_6)_2(OH)_2]^2^- + [OH^-] \rightleftharpoons [Ni(H_3IO_6)(H_2IO_6(OH)_2)]^{3^-} + H_2O
\]

\[
[Ni(H_3IO_6)(H_2IO_6(OH)_2)]^{3^-} \xrightarrow{k_{slow}} Ni(OH)^{2+} + OH + 2H_2IO_6^{3-} + H^+
\]

\[
\begin{align*}
\text{O} - \text{C}H_2 - \text{CH} - \text{CH}_2 - \text{NH} - \text{HC} - \text{CH}_3 + \text{OH} \xrightarrow{\text{fast}} \text{O} - \text{C}H_2 - \text{CH} - \text{CH}_2 - \text{NH} - \text{HC} - \text{CH}_3 + \text{NH}_2
\end{align*}
\]

\[
\text{O} - \text{C}H_2 - \text{CH} - \text{CH}_2 - \text{NH} - \text{HC} - \text{CH}_3 + \text{NH}_2
\]
Scheme 1 leads to the rate law equation (6).

\[
\text{Rate} = k [\text{Ni(IV)}] \tag{2}
\]

\[
= k K [\text{Ni(OH)}_2(\text{H}_3\text{IO}_6)_2]^2[\text{OH}^-]^r \tag{3}
\]

The total [\text{Ni(IV)}], [\text{Ni(IV)}]_t, is given as in equation (4) (where the subscripts \( t \) and \( f \) stand for total and free respectively)

\[
[\text{Ni(IV)}]_t = [\text{Ni(OH)}_2(\text{H}_3\text{IO}_6)_2]^2 + [\text{Ni(OH)}_2(\text{H}_2\text{IO}_6)(\text{H}_3\text{IO}_6)]^3
\]

\[
= [\text{Ni(OH)}_2(\text{H}_3\text{IO}_6)_2]^2 + K[\text{Ni(OH)}_2(\text{H}_2\text{IO}_6)(\text{H}_3\text{IO}_6)]^3[\text{OH}^-]
\]

\[
= [\text{Ni(OH)}_2(\text{H}_3\text{IO}_6)_2]^2 (1 + K[\text{OH}^-])
\]
\[ [\text{Ni(OH)}_2(\text{H}_3\text{IO}_6)_2]^2 ] = \frac{[\text{Ni(IV)}]_t}{(1 + K[\text{OH}^\text{-}])} \]  

(4)

Similarly,

\[ [\text{OH}^\text{-}]_t = [\text{OH}^\text{-}]_i \]  

(5)

Substituting the values of (4) and (5) in equation (3), we get (omitting the subscript t and f)

\[
\text{Rate} = \frac{d[\text{Ni(IV)}]}{dt} = \frac{kK[\text{Ni(IV)}][\text{OH}^\text{-}]}{(1 + K[\text{OH}^\text{-}]) (1 + K[\text{Ni(IV)}])}
\]  

(6)

In view of the low concentration of Ni(IV) used, the term \((1 + K[\text{Ni(IV)}])\) in the denominator is approximated to unity

Therefore

\[
k_{\text{obs}} = \frac{\text{Rate}}{[\text{Ni (IV)}]} = \frac{k K[\text{OH}^\text{-}]}{1 + K[\text{OH}^\text{-}]} \]  

(7)

Equation (7) can be arranged to (8), which is suitable for verification

\[
\frac{1}{k_{\text{obs}}} = \frac{1}{k} \frac{1}{K[\text{OH}^\text{-}]} + \frac{1}{k}
\]  

(8)

According to equation (8), other conditions being constant, the plot of \(1/k_{\text{obs}}\) versus \(1/[\text{OH}^\text{-}]\) \((r \geq 0.9991, S \leq 0.0213)\), should be linear as shown in Figure III (v) (p.94). From the slope and intercepts, the values of K and k could be derived as \(1.53 \pm 0.07 \text{ dm}^3 \text{ mol}^{-1}\) and \((2.2 \pm 0.1) \times 10^{-2} \text{ s}^{-1}\) respectively. The value of K is in agreement with earlier value. Using these constants, the rate constants were calculated over different experimental conditions and there is a reasonable agreement between the calculated and experimental values (Table III (iv) (p.82)).
Figure III (v)

Verification of rate law (7) in the form of (8)

(Conditions as in Table III (iv) (p. 82)

![Graph showing the verification of rate law (7) in the form of (8). The graph plots 1/K_{obs} \times 10^2 (s) against 1/[OH] (dm^3 mol^{-1}).]
which verifies the proposed mechanism. Since Scheme 1 is in accordance with the
generally well-accepted principle of non-complimentary oxidations taking place in
a sequence of one-electron steps, the reaction between the substrate and oxidant
would afford a radical intermediate. A free radical scavenging experimental
revealed such a possibility. The same type of radical intermediate has also been
observed earlier in the context of alkaline nickel(IV) oxidation of various
substrates.\textsuperscript{19}

The effect of ionic strength on the rate qualitatively explains the reaction
between the charged ions of similar kind as shown in Scheme 1. The effect of
solvent of the reaction rate has been described in detail in the literature.\textsuperscript{20,21} The
negligible effect of dielectric constant on the rate indicates the involvement of a
neutral molecule and an ion, which supports the proposed mechanism.\textsuperscript{22} The
moderate values of $\Delta H^\circ$ and $\Delta S^\circ$ were both favorable for electron transfer
processes. The value of $\Delta H^\circ$ was due to energy of solution changes in the
transition state. The negative values of $\Delta S^\circ$ within the range of radical reaction has
been ascribed\textsuperscript{23} to the nature of electron pairing and electron unpairing processes.
Spectrofluorimetric studies reveal that the fluorescence intensity is quenched
which may be due to the electron transfer reaction.\textsuperscript{24}
IMPORTANCE OF CHAPTER III

Among various species of Ni(IV) in alkaline medium, in earlier reports the monoperiodatonickelate(IV) was the active species, whereas, deprotonated diperiodateonickelate(IV) is considered to be the active species for the title reaction. Rate constant of slow step and other equilibrium constants involved in the mechanism are evaluated and activation parameters with respect to slow step of reaction were computed.
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