The study of the highest oxidation state of transition metals has intrigued many researchers. Transition metals in a higher oxidation state generally can be stabilised by chelation with suitable polydentate ligands. Metal chelates such as diperiodatoargentate(III), ditelluratoargentate(III), diperiodatonickelate(IV) and diperiodatocuprate(III) are good oxidants in a medium with appropriate pH value. In the recent past, interest in the chemistry of silver(III) species has increased significantly because of its two electron oxidant and electronically analogous to copper(III) system. The catalytic effect of Ag+ in redox reactions of S\textsubscript{2}O\textsubscript{3}\textsuperscript{2-} has been interpreted in several reports by the formation of silver(III) intermediate. There are only a few known stable complexes of silver(III). Some of these complexes such as diperidatoargentate(III) and [ethylenebis(biguanide)]silver(III) cation have been examined as oxidants. The use of diperidatoargentate(III) (DPA) as an oxidant in alkaline medium is new and restricted to a few cases due to the fact of its limited solubility in aqueous medium. Reduction of silver(III) complexes have been received a considerable attention in order to understand the nature of intermediate oxidation states of silver such as silver(II). Moreover, when silver(III) periodate is oxidant, it needs to be known which of the species is the active form of oxidant.
The study of neuroleptic drugs becomes important because of their biological significance and selectivity towards the oxidant to yield different products. Gabapentin (GP) is prescribed - usually in combination with other medications for the prevention of seizure in people suffering from seizure disorders. It is sometimes prescribed for the management of neuralgia (nerve pain).

In view of multiple equilibria embracing the different silver(III) species are involved and the complexity of the reaction, a detailed study of the title reaction is undertaken in this chapter.

**EXPERIMENTAL**

**Materials**

All chemicals used were of reagent grade. Solution of Gabapentin (M/s. S.S. Antibiotics Pvt. Ltd, Aurangabad, India) was prepared by dissolving appropriate amount of recrystallised sample in double distilled water. The solid silver(III) complex was prepared as follows: to a solution of 28g of KOH and 23 g KIO₃ in 100 cc of water, was added 8.5g of AgNO₃. This mixture was heated just to boiling, 20g of K₂S₂O₈ added slowly, and the mixture allowed to cool. After cooling, a dark solution was observed. This solution was recovered by filtering through a medium porosity fritted glass filter. To this solution was added 40 g of NaOH, whereupon a voluminous orange precipitate appeared. The precipitate was recovered by filtration through G₃ sintered crucible, washed three times with cold water. The mixture is dissolved in 50 cc of water and heated with stirring to 80°C. On cooling the orange crystals were separated out. The stock solution of DPA
was prepared in double distilled water and standardized for silver by acidifying the solution with HNO\textsubscript{3} and precipitated as AgCl by adding HCl. Ag(III) concentration was determined quantitatively by gravimetric method as AgCl.

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\textsuperscript{10} at neutral pH maintained by a phosphate buffer. Potassium hydroxide and potassium nitrate, (BDH, AR) were employed to maintain required alkalinity and ionic strength respectively.

**Kinetic procedure**

Kinetic runs were followed under pseudo-first order conditions with the Gabapentin concentration was in excess over that of the oxidant at 25 ± 0.1° C, unless otherwise stated. The reaction was initiated by mixing thermally equilibrated solutions of DPA and Gabapentin, which also contained a definite quantity of KOH, KNO\textsubscript{3} and IO\textsubscript{4}\. Here the total concentration of hydroxide ion was calculated considering the KOH in DPA as well as the KOH additionally added. Similarly, the total metaperiodate concentration was calculated by considering the amount present in the DPA solution and that additionally added. The course of reaction was followed by measuring the absorbance of unreacted DPA in the reaction mixture in a 1cm quartz cell located in the thermostatted compartment of a Peltier Accessory (temperature control) attached to Varian CARY 50 UV spectrophotometer connected to a rapid kinetic accessory (HITECH SFA-12) at its maximum absorption wavelength of 360 nm as a function of
time. Earlier it was verified that there is negligible interference from other species present in the reaction mixture at this wavelength. The obedience of Beer’s law by DPA at 360 nm was verified earlier and the molar absorbance coefficient, \( \varepsilon \) was found to be \( 13890 \pm 500 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1} \) at this wavelength (Fig. V(i)(p.132)).

The first order rate constants, \( k_{\text{obs}} \), were obtained from the plots of log (absorbance) versus time. The plots were linear up to about 85% completion of the reaction and the rate constants were reproducible within \( \pm 5 \% \). An example run is shown in the Table V(i) (p.133).

In view of the modest concentration of alkali used in the reaction medium, attention was also directed to the effect of the reaction vessel surface on the kinetics. Use of polythene /acrylic wares and quartz or polyacrylate cells gave the same results, indicating that the surface does not have any significant effect on the reaction rates. Kinetic runs were also carried out in an nitrogen atmosphere in order to understand the effect of dissolved oxygen on the rate of reaction. No significant difference in the results was obtained under a nitrogen atmosphere and in the presence of air. In view of the ubiquitous contamination of carbonate in the basic medium, the effect of carbonate was also studied. Added carbonate had no effect on the reaction rate, however, fresh solutions were nevertheless used while carrying out the kinetic study.
Verification of Beer's law for [DPA] at 360 nm in 0.001 mol dm$^{-3}$ alkali.
Example run for the oxidation of gabapentin by diperiodatoargentate(III) in aqueous alkaline medium at 25 °C.

\[ [\text{GBP}] = 1.0 \times 10^{-4}; \quad [\text{DPA}] = 5.0 \times 10^{-5}; \]
\[ [\text{OH}^-] = 0.001; \quad [\text{IO}_4^-] = 0.002, \]
\[ I = 0.1/\text{mol dm}^{-3}. \]

<table>
<thead>
<tr>
<th>Time (Sec)</th>
<th>Optical density (360 nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.68</td>
</tr>
<tr>
<td>20</td>
<td>0.42</td>
</tr>
<tr>
<td>40</td>
<td>0.33</td>
</tr>
<tr>
<td>60</td>
<td>0.28</td>
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<tr>
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<td>0.23</td>
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<tr>
<td>100</td>
<td>0.19</td>
</tr>
<tr>
<td>120</td>
<td>0.18</td>
</tr>
<tr>
<td>140</td>
<td>0.15</td>
</tr>
<tr>
<td>160</td>
<td>0.13</td>
</tr>
</tbody>
</table>
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-III personnel computer.

**RESULTS**

**Stoichiometry and product analysis**

Different sets of reaction mixtures containing different concentrations of gabapentin and DPA with a constant ionic strength and alkali were kept for 2 hours at 25 °C in a nitrogen atmosphere. When [DPA] was higher than [GBP], the unreacted DPA was found by measuring the absorbance at 360 nm. The results indicated that one mole of DPA consumed one mole of gabapentin as shown in equation (1).

\[
\begin{align*}
\text{H}_2\text{NH}_2\text{C} & \quad \text{CH}_2\text{COOH} \\
\text{+ Ag(III) + 2OH} & \quad \rightarrow \\
\text{HOH}_2\text{C} & \quad \text{CH}_2\text{COOH}
\end{align*}
\]

The main reaction products were extracted with solvent ether and organic product was subjected to spot tests. The main reaction product was identified as the 1-(Hydroxymethyl)cyclohexaneacetic acid by spot test\(^{11}\) for free carboxyl group and –OH. The product was also confirmed by IR spectra. In gabapentin, the IR spectra\(^{12}\) shows that it exists as Zwitter ion indicating the absence of –NH\(_2\) and –COOH groups; there is no absorption in the usual -NH stretching i.e., 3500-3300 cm\(^{-1}\) but instead the bands are observed in the region of 2800-3100 cm\(^{-1}\).
the band due to NH$_3^+$ stretching and also there is one characteristic band at 1541 cm$^{-1}$ as assignable to NH$_3^+$ deformation vibration. In addition to this there is one more band at 1607 cm$^{-1}$ which is assignable to ionic carboxyl absorption. At 1485 cm$^{-1}$ a band is appeared which is assignable to NH$_3^+$ deformation vibration (second band). Where as in the product, l-(Hydroxymethyl)cyclohexaneacetic acid, the presence of absorption band at 1681 cm$^{-1}$ indicates the free –COO$^-$ group which was absent in gabapentin (due to Zwitter ion) and there is a broad valley in the region 3098-3500 cm$^{-1}$ indicating the presence of –OH group as well as carboxylic –OH group. There is C-O stretching frequency of alcoholic –OH group (Hydroxymethyl group) at 1066 cm$^{-1}$ indicating the formation of –CH$_2$-OH group which was absent in gabapentin and –OH deformation bands occur at 1329-1320 cm$^{-1}$.

The product was also confirmed by $^1$H NMR spectra. From the spectra of gabapentin, it is observed that the two –CH$_2$ peaks appeared at 2.244 and 2.819 δ ppm respectively. The cyclohexyl proton appeared in the region of 1.185-1.310 δ ppm and as earlier suggested –NH$_2$ and –COOH peaks are not observed because of Zwitter ion form. In l-(Hydroxymethyl)cyclohexaneacetic acid, the cyclohexyl protons appeared in the region of 1.27-1.65 δ ppm, and two –CH$_2$ bands appeared at down field to cyclohexyl protons i.e. 2.19-3.16 δ ppm respectively. Another peak appeared at 4.6 δ ppm due to hydroxymethyl group. Another product, hydroxylamine was identified by spot test$^{12}$. It was further observed that the 1-(Hydroxymethyl) cyclohexane acetic acid and hydroxylamine do not undergo further oxidation under prevailing kinetic conditions.
Reaction order

The order with respect to [GBP] and [alkali] were found by log $k_{obs}$ versus log(concentration) plots and the obtained orders were also confirmed by differential method by the plot log(-dc/dt) versus log (concentration) using the equation log(±dc/dt) = logk + n logc; these orders were obtained by varying the concentration of gabapentin and alkali while keeping others constant.

Effect of [diperiodatoargentate(III)]

The concentration of diperiodatoargentate(III) was varied in the range, 1.0x $10^{-6}$ to 1.0x$10^{-5}$ mol dm$^{-3}$ at fixed [GBP], [OH'] and ionic strength. The non-variation in the pseudo-first order rate constants at various concentrations of DPN indicates the order in [DPA] as unity (Table V(ii)(p.139)). This was also confirmed from the linearity of plots of log (absorbance) versus time ($r \geq 0.9994$, $S \leq 0.026$) up to 85% completion of the reaction (Fig. V(ii)(p.138)).

Effect of [gabapentin]

The substrate, gabapentin was varied in the range of 5.0 x $10^{-5}$ to 5.0 x $10^{-4}$ mol dm$^{-3}$ at 25° C keeping all other reactant’s concentration and conditions constant. The $k_{obs}$ values increased with increase in concentration of gabapentin. The order was found to be less than unity in [GBP] (Table V (ii)(p.139)(Fig. V (iii) (p.141)).

Effect of [alkali]

The effect of [alkali] on the rate of reaction was studied at constant concentrations of Gabapentin, diperiodatoargentate(III) and a constant ionic strength at 0.1 mol dm$^{-3}$. 

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The rate constants increased with increase in [alkali] (Table V (ii) (p.139)). The reaction order in [OH\(^-\)] was found to be less than unity as shown in Fig. V (iii) (p.141).

**Effect of [periodate]**

The effect of [IO\(_4^+\)] was observed by varying the concentration from 5.0 x 10\(^{-4}\) to 5.0 x 10\(^{-3}\) mol dm\(^{-3}\) at constant concentrations of diperiodatoargentate (III), gabapentin, alkali and ionic strength. It was found that the rate of reaction decreases as the concentration of periodate increases (Table V (iii) (p.140)). The reaction order in [IO\(_4^+\)] was found to be inverse less than unity as shown in Fig. V (iv) (p.143).

**Effect of ionic strength**

The effect of ionic strength was studied by varying the [KNO\(_3\)] in the reaction mixture. The ionic strength of the reaction medium was varied from 0.1 to 1.0 mol dm\(^{-3}\) at constant [DPA], [GBP], [IO\(_4^+\)] and [alkali]. It was found that the rate of reaction increases as the ionic strength increases (Table V(iv)(p.144)). The plot of log \(k_{obs}\) vs \(1/2\) was linear as shown in Fig. V (v) (p.145) (r \(\geq 0.9993\), S \(\leq 0.0150\)).

**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 constant. Attempts to measure the relative permittivities of the mixture of t-butyl alcohol-water were not successful. However, they were computed from the values of pure liquids\(^{13}\). There was no reaction of the solvent with the oxidant under the
First order plots of oxidation of Gabapentin in aqueous alkaline diperiodatoargentate(III) at 25 °C.

\[ [DPA] \times 10^4 \text{ (mol dm}^{-3}) \text{):} \]

(1) 0.1, (2) 0.3, (3) 0.5, (4) 0.8, (5) 1.0

(Conditions as in Table V (ii)(p.139)
Table V (ii)

Effect of variation of [DPA] and [GBP] on the oxidation of gabapentin by diperiodatoargentate(III) in aqueous alkaline medium at 25 °C.

\[
\begin{align*}
[\text{IO}_4^-] &= 2.0 \times 10^{-4}; \\
[\text{OH}^-] &= 0.001; \\
I &= 0.10 / \text{mol dm}^{-3}.
\end{align*}
\]

<table>
<thead>
<tr>
<th>[DPA] (\times 10^4) (mol dm(^{-3}))</th>
<th>[GBP] (\times 10^4) (mol dm(^{-3}))</th>
<th>(k_{\text{obs}} \times 10^2) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>1.0</td>
<td>0.63</td>
</tr>
<tr>
<td>0.3</td>
<td>1.0</td>
<td>0.59</td>
</tr>
<tr>
<td>0.5</td>
<td>1.0</td>
<td>0.59</td>
</tr>
<tr>
<td>0.8</td>
<td>1.0</td>
<td>0.64</td>
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<td>1.0</td>
<td>0.61</td>
</tr>
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<td>0.35</td>
</tr>
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<td>0.5</td>
<td>1.0</td>
<td>0.62</td>
</tr>
<tr>
<td>0.5</td>
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<tr>
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<td>3.0</td>
<td>0.90</td>
</tr>
<tr>
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<td>5.0</td>
<td>1.20</td>
</tr>
<tr>
<td>0.5</td>
<td>1.0</td>
<td>0.61</td>
</tr>
<tr>
<td>0.5</td>
<td>2.0</td>
<td>0.77</td>
</tr>
<tr>
<td>0.5</td>
<td>5.0</td>
<td>1.20</td>
</tr>
</tbody>
</table>

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Table V (iii)

Effect of variation of \([\text{OH}^-]\) and \([\text{IO}_4^-]\) on the oxidation of gabapentin by dipерiodatoargentate(III) in aqueous alkaline medium at 25 °C.

\[
[DPA] = 5.0 \times 10^{-5}; \\
[GBP] = 1.0 \times 10^{-4}; \\
1 = 0.10 / \text{mol dm}^{-3}.
\]

<table>
<thead>
<tr>
<th>([\text{OH}^-]\times 10^3) (mol dm(^{-3}))</th>
<th>([\text{IO}_4^-]\times 10^3) (mol dm(^{-3}))</th>
<th>(k_{\text{obs}} \times 10^4) (s(^{-1}))</th>
<th>Found</th>
<th>Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>2.0</td>
<td>0.33</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>0.62</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>2.0</td>
<td>0.84</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>3.0</td>
<td>2.0</td>
<td>1.05</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>5.0</td>
<td>2.0</td>
<td>1.40</td>
<td>1.35</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>0.5</td>
<td>0.84</td>
<td>0.80</td>
<td></td>
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<td>0.71</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>0.62</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
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<td>0.54</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>5.0</td>
<td>0.44</td>
<td>0.43</td>
<td></td>
</tr>
</tbody>
</table>
Figure V (iii)

Order in [AA] and [OH\textsuperscript{-}] on the diperiodatoargentate(III) oxidation of gabapentin in aqueous alkaline medium at 25 °C.

(Conditions as in Table V (ii)(p.139) and Table V (iii)(p.140))
experimental conditions used. It was found that the rate of the reaction increased with decrease in the dielectric constant of the medium. The plot of log $k_{obs}$ versus $1/\varepsilon T$ was linear with positive slope as shown in Table V (iv) (p.144) and Fig. V (v) (p.145) ($r \geq 0.9993$, $S \leq 0.0150$).

**Effect of initially added products**

The initially added products, hydroxylamine and 1-(Hydroxymethyl)cyclohexane acetic acid and Ag(I) did not show any significant 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 one hour 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 DPA or Gabapentin alone with acrylonitrile did not induce polymerization under the same condition as those induce with reaction mixtures. Initially added acrylonitrile decreases the rate indicating the free radical intervention, which is the case in earlier work.¹⁴

**Effect of temperature**

The rate of the reaction was measured at four different temperatures, with varying [GBP], keeping other conditions constant. The rate was found to increase with increase in temperature. The rate constants $k$, of the slow step of Scheme 1
Order of $[\text{IO}_4^-]$ on the oxidation of gabapentin by diperiodatoargentate(III) in aqueous alkaline medium at 25 °C.

(Conditions as in Table V (iii)(p.140))
Table V (iv)

Effect of variation of ionic strength (I) and solvent polarity (ε_T) on the oxidation of gabapentin aqueous alkaline diperiodatoargentate(III) at 25° C.

\[
\begin{align*}
[DPA] &= 5.0 \times 10^{-5}; \\
[GBP] &= 1.0 \times 10^{-4}; \\
[OH^-] &= 0.001; \\
[IO_4^-] &= 2.0 \times 10^{-3}/\text{mol dm}^{-3}. \\
I &= 0.10 /\text{mol dm}^{-3}.
\end{align*}
\]

<table>
<thead>
<tr>
<th>I (mol dm^-3)</th>
<th>k_{obs} \times 10^2 (s^{-1})</th>
<th>%of *t-butanol-water</th>
<th>ε_T</th>
<th>k_{obs} \times 10^2 (s^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>0.62</td>
<td>5.0</td>
<td>75.12</td>
<td>0.70</td>
</tr>
<tr>
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<td>0.74</td>
<td>10</td>
<td>71.74</td>
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<td>0.99</td>
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<td>0.8</td>
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<td>1.0</td>
<td>1.50</td>
<td>25</td>
<td>59.12</td>
<td>1.14</td>
</tr>
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</table>

\*t-butanol-water (v/v)
Effect of variation of ionic strength (I) and solvent polarity ($\varepsilon_T$) on the oxidation of gabapentin aqueous alkaline diperiodatoargentate(III) at 25° C.

(Conditions as in Table V (iv)(p.144))
were obtained from the slopes and intercepts of the plots of $1/k_c$ versus $1/[\text{OH}^-]$ ($r \geq 0.9986$, $S \leq 0.041$), $1/k_{\text{obs}}$ versus $1/[	ext{GBP}]$ and $1/k_{\text{obs}}$ versus $[\text{H}_2\text{IO}_6^2^-]$ ($r \geq 0.9994$, $S \leq 0.050$). The values of $k$ are given in the Table V (v a)(p.147). The activation parameters were evaluated from the Arrhenius plot of $\log k$ versus $1/T$ ($r \geq 0.9976$, $S \leq 0.035$)(Fig. V(vi)(p.148)). The values of $E_a$, $\Delta H^\#, \Delta S^\#$ and $\Delta G^#$ were obtained and are given in Table V (v b)(p.147).

DISCUSSION

The diperidatoargentate(III)$^5$ complex is diamagnetic and exhibits square planer configuration with dsp$^2$ hybrid bonds. Periodate acts as bidentate ligand and contributes to the stabilization of Ag(III). The structure and cell dimensions of DPA compound resembles those of Ag(III)$^9$,$^{15}$. The Ag(III) periodate complex ion can be represented as $[\text{Ag}^{\text{II}}\text{O}_6\text{O}_6(H_2\text{O})_2]^2^-$ and in solution it can be considered as hydroxyaquodiperiodatoargentate(III).

Crouthamel et al.$^6$ from an extensive study of the equilibria between various periodate anionic species by UV spectrophotometry concluded that the following equilibria exists in aqueous solution of periodate at different pH values.

$$
\text{H}_3\text{IO}_6 \rightleftharpoons K_1 \rightarrow \text{H}_4\text{IO}_6^- + \text{H}^+,
K_1 = 2.30 \times 10^{-2}
$$

$$
\text{H}_4\text{IO}_6^- \rightleftharpoons K_2 \rightarrow \text{H}_3\text{IO}_6^{2-} + \text{H}^+,
K_2 = 4.35 \times 10^{-9}
$$

$$
\text{H}_3\text{IO}_6^{2-} \rightleftharpoons K_3 \rightarrow \text{H}_2\text{IO}_6^{3-} + \text{H}^+,
K_3 = 4.60 \times 10^{-11}
$$

The formation of dimerised species of periodate is possible only at high concentration of periodates in alkaline medium as per following equilibrium.
Table V (v)

(a) Effect of temperature on the slow step of the mechanism of oxidation of gabapentin by alkaline diperiodatoagentate(III).

\[ [\text{GBP}] = 1.0 \times 10^{-4}; \]
\[ [\text{DPA}] = 5.0 \times 10^{-5}; \]
\[ [\text{OH}^-] = 0.001; \]
\[ [\text{IO}_4^-] = 2.0 \times 10^{-3}; \]
\[ I = 1.0 /\text{mol dm}^{-3}. \]

<table>
<thead>
<tr>
<th>T (K)</th>
<th>k x10^2 (s^-1)</th>
<th>log k (Y)</th>
<th>1/T x10^3 (X)</th>
<th>Y_{calc}^*</th>
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<td>-1.6144</td>
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</table>

*Calculated

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

<table>
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<th>Parameters</th>
<th>Values</th>
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<tbody>
<tr>
<td>( E_a ) (kJ mol(^{-1}))</td>
<td>19.5 ± 0.5</td>
</tr>
<tr>
<td>log A</td>
<td>6.1± 0.1</td>
</tr>
<tr>
<td>( \Delta H^# ) (kJ mol(^{-1}))</td>
<td>17.0 ± 0.5</td>
</tr>
<tr>
<td>( \Delta S^# ) (J K(^{-1}) mol(^{-1}))</td>
<td>-48 ± 2</td>
</tr>
<tr>
<td>( \Delta G^# ) (kJ mol(^{-1}))</td>
<td>31 ± 1</td>
</tr>
</tbody>
</table>
Effect of temperature on the slow step of the mechanism of oxidation of gabapentin by diperiodatoargentate (III) alkaline medium. 

(Condition as in Table V (ii) (p.139)
However, formation of the species is not possible under conditions employed for the kinetic study. The study of various equilibria of periodates in alkaline solutions, reported\textsuperscript{17} that $\text{H}_3\text{IO}_6^{2-}$ and $\text{H}_2\text{IO}_6^{3-}$ predominates rather than the dehydrated species $\text{HIO}_5^{2-}$ and $\text{IO}_5^{3-}$.

The fully deprotonated periodate complex does not seem likely for the Ag(III) systems since solid salts of the complex precipitated from basic solutions generally have formulate involving at least two and more often four portions. It was therefore concluded that though periodate is known to get hydrated in solution, the exact nature of species in basic media is difficult to predict. Therefore, Ag(III)-periodate complex in basic media is represented as $[\text{Ag} (\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-}$, a conclusion also supported by earlier work\textsuperscript{5}. The precipitation of periodate in the oxidation reaction is ruled out in view of the high potential of the the Ag(III) – Ag(II) system.

Increase of reaction rate with increase in [OH\textsuperscript{-}] has been explained in terms of equilibrium between a deprotonated reactive species and a protonated unreactive species.

\[
[\text{Ag(OH)}_2(\text{H}_2\text{IO}_6)]^{5-} + \text{OH}^- \rightleftharpoons [\text{Ag(OH)}_2(\text{HIO}_6)]^{3-} + \text{H}_2\text{IO}_6^{3-} + \text{H}_2\text{O}
\]

The reaction between diperiodatoargentate(III) complex and gabapentin in alkaline medium has a 1:1 stoichiometry of reductant to oxidant with first order dependence on [DPA], apparent less than unit order in [GBP], fractional order in
[OH'] and inverse fractional order in [IO₄⁻]. In view of the negative less than unit order in periodate on rate of reaction, monoperiodate silver(III) complex is considered to be the active species of silver(III) complex. The less than unit order in [GBP] presumably results a complex (C) formation between the oxidant and substrate prior to the formation of the products. Then this complex (C) decomposes in a slow step to form an intermediate free radical species of gabapentin and Ag(II) intermediate species. This intermediate species of Ag(II) further reacts with free radical species in a fast step to yield the products. All the results lead to a mechanism as given in Scheme 1.

\[
[\text{Ag(OH)}_2(\text{H}_2\text{IO}_6)]^{6-} + \text{OH}^- \rightleftharpoons K_4 \quad [\text{Ag(OH)}_2(\text{H}_2\text{IO}_6)]^{3-} + \text{H}_2\text{IO}_6^{3-} + \text{H}_2\text{O}
\]

Scheme 1
The probable structure of complex (C) is given by

Attempt to obtain UV-Vis spectral for complex between substrate and oxidant were not successful at room temperature due to weak interaction, since there is no change UV-Vis spectra of DPA and mixture of DPA and gabapentin. However, at lower temperature (nearly 5°C), bathochromic shift $\lambda_{\text{max}}$ of about 9nm from 360 to 369 nm of DPA and hyperchromicity at 360 nm was observed. Such complex formation between substrate and oxidant has been observed earlier. 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 a radical intermediate. A free radical scavenging experiment revealed such a possibility. This type of radical intermediate has also been observed in earlier work. Scheme 1 leads to the following rate law as follows.

$$\text{Rate} = - \frac{d[DPA]}{dt} = k K_4 K_5 [GBP] [DPA] [OH'] [H_2IO_6^{-}]$$

(5)

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The total concentration of DPA is given by

\[ [\text{DPA}]_t = [\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5+} + [\text{Ag} (\text{HIO}_6) (\text{OH})_2]^{3-} + C \]

\[ = [\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-} + \frac{K_4[\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-}[\text{OH}^-]}{[\text{H}_2\text{IO}_6]^{3-}} + K_4K_5[\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-}[\text{GBP}] [\text{OH}^-] \]

\[ = [\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-} (\text{H}_2\text{IO}_6^{3-} + K_4[\text{OH}^-] + K_4K_5[\text{GBP}] [\text{OH}^-]) \]

\[ =\frac{[\text{DPA}]_t [\text{H}_2\text{IO}_6^{3-}]}{[\text{H}_2\text{IO}_6^{3-}] + K_4[\text{OH}^-] + K_4K_5[\text{GBP}] [\text{OH}^-]} \quad \text{(6)} \]

\[ [\text{OH}^-]_t = [\text{OH}^-]_f + [\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{3+} + C \]

\[ = [\text{OH}^-]_f + K_4K_5[\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{3-} [\text{GBP}] [\text{OH}^-] + K_4[\text{OH}^-] [\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-} \]

\[ = \frac{[\text{GBP}]_t [\text{H}_2\text{IO}_6^{3-}]}{[\text{H}_2\text{IO}_6^{3-}] + [\text{GBP}]_f + K_4K_5[\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-} + [\text{OH}^-] [\text{GBP}]_f} \]

The subscriptions \( t \) and \( f \) stand for total and free concentrations. In view of low concentration of DPA used, the terms may be neglected.

\[ [\text{OH}^-]_t = [\text{OH}^-]_f \quad \text{(7)} \]

Similarly,

\[ [\text{GBP}]_t = [\text{GBP}]_f + C \]

\[ [\text{GBP}]_t = [\text{GBP}]_f + K_4K_5[\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-} + [\text{OH}^-][\text{GBP}]_f \]

\[ [\text{GBP}]_t = \frac{[\text{GBP}]_f [\text{H}_2\text{IO}_6^{3-}] + K_4K_5[\text{Ag}(\text{H}_2\text{IO}_6)_2(\text{OH})_2]^{5-} + [\text{OH}^-]}{[\text{H}_2\text{IO}_6^{3-}]} \]
\[
\text{GBP}_f = \frac{[\text{GBP}]_f [\text{H}_2\text{I}_6^{2-}]}{[\text{H}_2\text{I}_6^{2-}] + K_4 K_5 [\text{Ag} (\text{H}_2\text{I}_6) \text{OH}][\text{GBP}]}\tag{8}
\]

In view of low concentration of DPA is used, the terms in denominators of eqn (8) approximately to unity. Therefore

\[
[\text{GBP}]_f = [\text{GBP}]_f \tag{9}
\]

Substituting the equations (6), (7), and (9) in eqn (5) (omitting the subscripts \(t\) and \(f\)), we get eqn (10)

\[
k_{\text{obs}} = \frac{\text{Rate}}{[\text{DPA}]} = \frac{k K_4 K_5 [\text{OH}][\text{GBP}]}{[\text{H}_2\text{I}_6^{2-}] + K_4 [\text{OH}^+] + K_4 K_5 [\text{DPA}][\text{OH}^+]} \tag{10}
\]

Equation (10) can be rearranged to equation (11) which is suitable for verification.

\[
\frac{1}{k_{\text{obs}}} = \frac{[\text{H}_2\text{I}_6^{2-}]}{k K_4 K_5 [\text{GBP}][\text{OH}]} + \frac{1}{k K_5 [\text{GBP}]} + \frac{1}{k} \tag{11}
\]

According to equation (11), the plots of \(1/k_{\text{obs}}\) versus \(1/[\text{GBP}]\) (\(r \geq 0.9995, S \leq 0.0160\)) (Table V(ii)(p.139)) and \(1/k_{\text{obs}}\) versus \(1/[\text{OH}^+]\) and \(1/1/k_{\text{obs}}\) versus \([\text{H}_2\text{I}_6^{2-}]\) (\(r \geq 0.9998, S \leq 0.0210\)) (Table V (iii)(p.140)) should be linear as shown in Fig. V (vii)(p.155). From the slopes and intercepts, the values of \(K_4, K_5\) and \(k\) could be derived as \(2.2 \pm 0.1\) mol dm\(^{-3}\), \((1.4 \pm 0.1) \times 10^4\) dm\(^3\) mol\(^{-1}\) and \((1.5 \pm 0.1) \times 10^2\) s\(^{-1}\) respectively. 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 V(ii)(p.139)) and Table V(iii)(p.140)), which supplements the proposed mechanism.
The effect of increasing ionic strength on the rate qualitatively explains the reaction between two negatively charged ions as shown in Scheme 1. The effect of solvent on the reaction rate has been described elsewhere\textsuperscript{20}. Increasing the content of t-butyl alcohol content in the reaction medium leads to increase in the rate of the reaction, contrary to the expected slower reaction between like ions in the media of lower relative permitivity. Perhaps this effect is countered substantially by the formation of active reactive species to a greater extent in low relative permitivity media leading to the net increase in the reaction rate\textsuperscript{21}.

The thermodynamic quantities for the first step in Scheme 1 can be evaluated as follows. The [GBP] and hydroxide ion concentration as in Table V(ii)(p. 139) and Table V(iii)(p. 140) was varied at four different temperatures. The plots of $1/k_{obs}$ versus $1/[GBP]$ ($r \geq 0.9995$, $S \leq 0.0160$) and $1/k_{obs}$ versus $[OH^-]$ ($r \geq 0.9998$, $S \leq 0.0210$) should be linear. From the slopes and intercepts, the values of $K_4$ were calculated at different temperatures and these values are given in Table V(vi a)(p.156). A van't Hoff plot was made for the variation of $K_4$ with temperature [i.e., log $K_4$ versus $1/T$ ($r \geq 0.9994$, $S \leq 0.0101$)] and the values of the enthalpy of reaction $\Delta H$, entropy of reaction $\Delta S$, and free energy of reaction $\Delta G$, were calculated. These values are given in Table V(vi b)(p. 156). 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 fast and involves low activation energy\textsuperscript{22}.
Verification of rate law (10) in the form of (11)

(Conditions as in Table V(ii)(p.139))
Table V (vi)

(a) Effect of temperature on values of $K_4$ for the oxidation of gabapentin by DPA in alkaline medium.

<table>
<thead>
<tr>
<th>Temp. (K)</th>
<th>$K_4$ (dm$^3$mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>298</td>
<td>2.10</td>
</tr>
<tr>
<td>303</td>
<td>2.74</td>
</tr>
<tr>
<td>308</td>
<td>3.34</td>
</tr>
<tr>
<td>313</td>
<td>3.82</td>
</tr>
</tbody>
</table>

(b) Thermodynamic quantities using $K_4$ values

<table>
<thead>
<tr>
<th>Thermodynamic quantities</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta H$ (kJ mol$^{-1}$)</td>
<td>$30.5 \pm 0.5$</td>
</tr>
<tr>
<td>$\Delta S$ (J K$^{-1}$ mol$^{-1}$)</td>
<td>$24 \pm 0.5$</td>
</tr>
<tr>
<td>$\Delta G$ (kJ mol$^{-1}$)</td>
<td>$-23.4 \pm 0.5$</td>
</tr>
</tbody>
</table>
The moderate values of $\Delta H^\#$ and $\Delta S^\#$ were both favorable for electron transfer processes. The negative value of $\Delta^\#$ indicates that the complex is more ordered than reactants$^{23}$.  

**Importance of Chapter V**

Among various species of DPA in alkaline medium, monoperiodatoargentate(III)(DPA) is considered as active species for the title reaction. It becomes apparent that in carrying out this reaction, the role of pH in the reaction medium is crucial. 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. The overall mechanistic sequence described here is consistent with product, mechanistic and kinetic studies.
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