CHAPTER VII

KINETIC AND MECHANISTIC INVESTIGATION OF OXIDATION OF VITAMIN B₆ WITH CHLORAMINE-B CATALYZED BY RUTHENIUM (III) IN ACID MEDIUM
SECTION 7.1

INTRODUCTION AND BIOLOGICAL IMPORTANCE OF VITAMIN B\textsubscript{6}

Pyridoxine, pyridoxal and pyridoxamine are collectively known as vitamin B\textsubscript{6}. All three compounds are efficiently converted to the biologically active form of vitamin B\textsubscript{6}, pyridoxal phosphate. This conversion is catalyzed by the ATP requiring enzyme, pyridoxal kinase.

Pyridoxal phosphate functions as a cofactor in enzymes involved in transamination reactions required for the synthesis and catabolism of the amino acids as well as in glycogenolysis as a cofactor for glycogen phosphorylase. The requirement for vitamin B\textsubscript{6} in the diet is proportional to the level of protein consumption ranging from 1.4 - 2.0 mg/day for a normal adult. Deficiencies of vitamin B\textsubscript{6} are rare and usually are related to an overall deficiency of all the B-complex vitamins. Isoniazid and penicillamine (used to treat rheumatoid arthritis and cystinurias) are two drugs that complex with pyridoxal and pyridoxal phosphate resulting in a deficiency in this vitamin.

Thus vitamin B\textsubscript{6} has been paid special attention in clinical and pharmaceutical lines because of its extensive and essential applications in bio-metabolisms. Vitamin B\textsubscript{6} and its derivatives play a major role in gene modulation [1], sexual behavior [2], cancer research [3] and immune modulation in HIV-1 infection [4]. In biological systems, pyridoxine is oxidized to pyridoxal derivative to act as a co-enzyme for the amino group transformations [5, 6]. The oxidation kinetics and mechanism of vitamin B\textsubscript{6} are thus important to the process in vitro.

The review of available literature reveals the determination and kinetics of oxidation of vitamin B\textsubscript{6} with some oxidants.

Jayaram and Madegowda [7] have developed the titrimetric methods for the determination of pyridoxine (PRX) in solution using chloramine-T, bromamine-T bromamine-B. This method is based on the oxidation of PRX by the \textit{N}-halo amines. The oxidation involves two-electron change. The reaction products, pyridoxal and
sulfonamides were identified. The effects of variables, such as pH of the medium and presence of foreign ions on the rate of oxidation were studied.

The kinetics of oxidation of PRX by Mn(III) in aqueous AcOH was investigated [8], and is first-order with respect to [Mn(III)]. The effects of varying [Mn(III)], PRX, added Mn(II), pH, and added anion such as AcO⁻, F⁻, Cl⁻, ClO₄⁻ and SO₄²⁻ were studied. The orders in [PRX] and Mn(II) were unity and inverse-fractional respectively in both low and high [H⁺] ranges. The dependence of reaction rate on temperature was studied and activation parameters were computed from Arrhenius and Eyring plots. A mechanism consistent with the observed results is proposed and discussed.

The electro-catalytic oxidation of vitamin B₆ was demonstrated on a nafion/lead ruthenate pyrochloride modified electrode by cyclic voltammetry [9]. The catalytic activity of vitamin B₆ was explored in terms of the higher oxidation states of ruthenium species in the pyrochlore network. The mediated mechanism was derived by Michaelis-Menton kinetics.

In view of extensive biological importance of vitamin B₆, it was felt important and interesting to investigate the oxidative behavior of CAB towards vitamin B₆. The reaction of PRX with CAB in the presence of HCl medium without a catalyst was found to be sluggish, but the reaction was facile in the presence of RuCl₃ catalyst. Therefore the present chapter reports the kinetics of Ru(III)-catalyzed oxidation of PRX with CAB in HCl medium at 308 K. The objectives of the present investigations are to: (i) elucidate the reaction mechanism (ii) put forward appropriate rate laws (iii) ascertain the reactive species of CAB and (iv) identify the products of reaction.
SECTION 7.2

KINETIC AND MECHANISTIC INVESTIGATION OF OXIDATION OF VITAMIN B₆ WITH CHLORAMINE-B CATALYZED BY RUTHENIUM (III) IN HYDROCHLORIC ACID MEDIUM

This section deals with the kinetics of oxidation of vitamin B₆ (pyridoxin hydrochloride, PRX) with chloramine-B in presence of Ruthenium (III) catalyst in hydrochloric acid medium at 308 K.

Stoichiometry and product analysis

Reaction mixtures containing different amounts of the PRX and CAB were equilibrated in the presence of 0.1 mol dm⁻³ HCl and 1 × 10⁻⁶ mol dm⁻³ RuCl₃ catalyst at 308 K for 48 h. Estimation of unreacted CAB in the mixture showed that one mole of CAB was consumed per mole of PRX according to equation (7.1),

\[ C₈H₁₁NO₃ + RNCINa \rightarrow C₈H₉NO₃ + RNH₂ + Na⁺ + Cl⁻ \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(7.1) \]

Where R = C₆H₅SO₂.

The products in the reaction mixture were extracted several times with diethyl ether. The combined ether extract was evaporated and subjected to the column chromatography on silica gel (60 – 200 mesh) using gradient elutions (from dichloromethane to chloroform). After initial separation, the products were further purified by recrystallization. The reduction product of CAB, benzenesulfonamide was detected as described in Section 2.2 of Chapter II. Pyridoxal was identified as its semicarbazone [10]. Further more, it was confirmed by its IR absorption bands at 1720 cm⁻¹ for C=O stretching mode and at 2852 cm⁻¹ for aldehydic C-H stretching mode. The IR spectrum is shown in Fig. 7.10.

Results

The kinetics of oxidation of PRX with CAB has been investigated at different initial concentrations of the reactants in the presence of HCl and RuCl₃ catalyst at 308 K.
Effect of varying reactant concentrations on the rate

The reaction was performed in the presence of RuCl$_3$ catalyst and HCl under pseudo-first-order conditions ([PRX]$_o$ $>>$[CAB]$_o$). Plots of log [CAB] versus time were linear (Table 7.1; Fig. 7.1). The linearity of these plots, together with the constancy of slope for various [CAB]$_o$, indicates a first-order dependence of the reaction rate on [CAB]. The pseudo-first-order rate constants, $k'$ obtained at 308 K are listed in Table 7.3. Under the similar experimental conditions, an increase in [PRX]$_o$ increased the rate. Plot of log $k'$ versus log [PRX]$_o$ was linear (Fig. 7.2) with a slope of 0.79 indicating a fractional-order dependence on [PRX]$_o$. Further more, a plot of 1/$k'$ versus 1/[PRX]$_o$ was linear (Fig. 7.8) with a Y-intercept confirming the fractional order dependence on [PRX].

Effect of varying [HCl] on the rate

At constant [CAB]$_o$, [PRX]$_o$, [RuCl$_3$] and temperature, the reaction rate increased with increasing [HCl] (Table 7.4). A plot of log $k'$ versus log [HCl] was linear (Fig. 7.4) with a slope of unity indicating first order dependence on [HCl].

Effect of varying [H$^+$] and [Cl$^-$] on the rate

At constant [Cl$^-$] = 0.15 mol dm$^{-3}$ maintained with NaCl, increase in the concentration of [H$^+$] using HCl increased the rate (Table 7.5). A plot of log $k'$ versus log [H$^+$] was linear (Fig. 7.5) with a slope of 0.44 indicating a fractional order dependence on [H$^+$]. Addition of Cl$^-$ in the form of NaCl keeping [H$^+$] constant (0.1 mol dm$^{-3}$) increases the reaction rate (Table 7.6). From a plot of log $k'$ versus log [Cl$^-$] (Fig. 7.5), the order with respect to [Cl$^-$] is found to be 0.58.

Effect of varying of [Ru(III)] on the reaction rate

The rate of the reaction increased with increasing [Ru(III)] (Table 7.7). Plot of log $k'$ versus log[Ru(III)] (Fig. 7.6) was linear with a slope equal to 0.36, confirming a fractional order dependence on [Ru(III)].

Effect of benzenesulfonamide on the rate

The addition of reduced product, benzenesulfonamide (2 x 10$^{-4}$ to 8 x10$^{-4}$ mol dm$^{-3}$) had no effect on the rate, indicating that it is not involved in the pre-equilibrium step prior to the rate-determining step (Table 7.8).
**Effect of ionic strength on the rate**

The effect of ionic strength of the medium on the rate was studied from (0.2 to 0.5 mol dm\(^{-3}\)) using NaClO\(_4\) solution with other constant experimental conditions. The ionic strength showed negligible effect on the reaction rate indicating the involvement of a non-ionic species in the rate-determining step (Table 7.9).

**Effect of varying dielectric permittivity of the medium on the rate**

The dielectric permittivity of the medium was varied by adding different proportions (0 - 20%, v/v) of acetonitril to the reaction mixture. The rate increased with decrease in dielectric permittivity of the reaction mixture (Table 7.10). Plot of log \(k'\) vs. \(1/D\), where \(D\) is the dielectric permittivity of the medium gave a straight line (Fig. 7.7) with a positive slope. Blank experiments performed showed that CAB did not oxidize CH\(_3\)CN under the experimental conditions employed.

**Effect of temperature on the rate**

The reaction was studied at different temperatures (303 – 319 K) (Table 7.11), keeping other experimental conditions constant. From the Arrhenius plot of log \(k'\) versus \(1/T\) (fig. 7.8), the activation parameters, namely energy of activation, enthalpy of activation, entropy of activation and Gibb’s free energy of activation were calculated. The activation parameters obtained are presented in Table 7.12.

**Test for free radicals**

The addition of the reaction mixture to aqueous acrylamide monomer solution did not initiate polymerization indicating the absence of \textit{in situ} formation of free radical species in the reaction sequence.
Table 7.1

Effect of [CAB] on the rate of oxidation of PRX
(Representative Run)

[CAB] = 5 x 10^{-4} \text{ mol dm}^{-3}, [PRX] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}, [HCl] = 10 \times 10^{-2} \text{ mol dm}^{-3}, [\text{Ru(III)}] = 1 \times 10^{-6} \text{ mol dm}^{-3}, T = 308 \text{ K}, \mu = 0.2 \text{ mol dm}^{-3}

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>V_t (ml)</th>
<th>log V_t</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>11.0</td>
<td>1.041</td>
</tr>
<tr>
<td>5</td>
<td>8.2</td>
<td>0.914</td>
</tr>
<tr>
<td>10</td>
<td>6.7</td>
<td>0.826</td>
</tr>
<tr>
<td>15</td>
<td>5.4</td>
<td>0.732</td>
</tr>
<tr>
<td>20</td>
<td>4.5</td>
<td>0.653</td>
</tr>
<tr>
<td>30</td>
<td>3.4</td>
<td>0.531</td>
</tr>
<tr>
<td>40</td>
<td>2.5</td>
<td>0.398</td>
</tr>
</tbody>
</table>

r = 0.997

k' = 5.68 \times 10^{-4} \text{ (s}^{-1})

V_t = \text{Titre volume of Na}_2S_2O_3

**Fig. 7.1:** Plot of log V_t versus time(min)
Table 7.2
Effect of varying the [CAB]₀ on the rate of oxidation of PRX

\[ [PRX] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}, \ [HCl] = 10 \times 10^{-2} \text{ mol dm}^{-3}, \ [Ru(III)] = 1 \times 10^{-6} \text{ mol dm}^{-3}, \ T = 308 \text{ K}, \ \mu = 0.2 \text{ mol dm}^{-3} \]

<table>
<thead>
<tr>
<th>[CAB] x 10^4 (mol dm⁻³)</th>
<th>k x 10⁴ (s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0</td>
<td>5.62</td>
</tr>
<tr>
<td>5.0</td>
<td>5.68</td>
</tr>
<tr>
<td>7.0</td>
<td>5.79</td>
</tr>
<tr>
<td>9.0</td>
<td>5.72</td>
</tr>
<tr>
<td>11.0</td>
<td>5.70</td>
</tr>
</tbody>
</table>

Table 7.3
Effect of varying the [PRX]₀ on the rate

\[ [CAB] = 5 \times 10^{-4} \text{ mol dm}^{-3}, \ [HCl] = 10 \times 10^{-2} \text{ mol dm}^{-3}, \ [Ru(III)] = 1 \times 10^{-6} \text{ mol dm}^{-3}, \ T = 308 \text{ K}, \ \mu = 0.2 \text{ mol dm}^{-3} \]

<table>
<thead>
<tr>
<th>[PRX] x 10² (mol dm⁻³)</th>
<th>k x 10⁴ (s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>3.84</td>
</tr>
<tr>
<td>0.8</td>
<td>4.73</td>
</tr>
<tr>
<td>1.0</td>
<td>5.68</td>
</tr>
<tr>
<td>1.2</td>
<td>6.56</td>
</tr>
<tr>
<td>1.4</td>
<td>7.49</td>
</tr>
</tbody>
</table>

\[ r = 0.999 \]

Fig. 7.2: Plot of 4+log k versus 3+log [PRX]
Fig. 7.2

![Graph showing 3+log(PRX) vs 4+log(k')](image)

Fig. 7.3: Plot of 1/k' versus 1/[PRX]
Table 7.4

Effect of varying [HCl] on the reaction rate

[CAB] = 5 x 10^{-4} \text{ mol dm}^{-3}, \quad [PRX] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}

[\text{Ru(III)}] = 1 \times 10^{-6} \text{ mol dm}^{-3} \quad T = 308 \text{ K}, \mu = 0.2 \text{ mol dm}^{-3}

<table>
<thead>
<tr>
<th>[HCl] x 10^2 (mol dm^{-3})</th>
<th>k x 10^4 (s^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.0</td>
<td>3.61</td>
</tr>
<tr>
<td>8.0</td>
<td>4.61</td>
</tr>
<tr>
<td>10.0</td>
<td>5.68</td>
</tr>
<tr>
<td>14.0</td>
<td>7.51</td>
</tr>
<tr>
<td>16.0</td>
<td>9.12</td>
</tr>
</tbody>
</table>

r = 0.996

Fig. 7.4: Plot of 4+log k’ versus 2+log [HCl]
Table 7.5
Effect of varying [H\(^+\)] on the rate of reaction

\([\text{CAB}] = 5 \times 10^{-4} \text{ mol dm}^{-3}, \quad [\text{PRX}] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}, \quad [\text{Cl}^{-}] = 0.15 \text{ mol dm}^{-3}, \quad \text{[Ru(III)]} = 1 \times 10^{-6} \text{ mol dm}^{-3}. \quad T = 308 \text{ K}, \quad \mu = 0.2 \text{ mol dm}^{-3}\)

<table>
<thead>
<tr>
<th>[H(^+)] x 10(^2) (mol dm(^{-3}))</th>
<th>k x 10(^4) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0</td>
<td>5.30</td>
</tr>
<tr>
<td>6.0</td>
<td>6.25</td>
</tr>
<tr>
<td>8.0</td>
<td>6.99</td>
</tr>
<tr>
<td>10.0</td>
<td>7.68</td>
</tr>
<tr>
<td>12.0</td>
<td>8.37</td>
</tr>
</tbody>
</table>

\(r = 0.999\)

Fig. 7.5: Plot of 4+\log{k}' versus 2+\log{[H\(^+\)]}

Table 7.6
Effect of varying [Cl\(^-\)] on the reaction rate

\([\text{CAB}] = 5 \times 10^{-4} \text{ mol dm}^{-3}, \quad [\text{PRX}] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}, \quad [\text{H}^+] = 0.1 \text{ mol dm}^{-3}, \quad \text{[Ru(III)]} = 1 \times 10^{-6} \text{ mol dm}^{-3}, \quad T = 308 \text{ K}, \quad \mu = 0.2 \text{ mol dm}^{-3}\)

<table>
<thead>
<tr>
<th>[Cl(^-)] x 10(^2) (mol dm(^{-3}))</th>
<th>k x 10(^4) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>6.91</td>
</tr>
<tr>
<td>12</td>
<td>7.35</td>
</tr>
<tr>
<td>14</td>
<td>8.02</td>
</tr>
<tr>
<td>15</td>
<td>8.23</td>
</tr>
<tr>
<td>17</td>
<td>8.94</td>
</tr>
<tr>
<td>20</td>
<td>9.75</td>
</tr>
</tbody>
</table>

\(r = 0.999\)

Fig. 7.5: Plot of 4+\log{k}' versus 2+\log{[Cl\(^-\)]}
Fig. 7.5
Table 7.7

Effect of varying [Ru(III)] on the reaction rate

$[\text{CAB}] = 5 \times 10^{-4} \text{ mol dm}^{-3}$, $[\text{PRX}] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}$

$[\text{HCl}] = 10 \times 10^{-2} \text{ mol dm}^{-3}$, $T = 308 \text{ K}$, $\mu = 0.2 \text{ mol dm}^{-3}$

<table>
<thead>
<tr>
<th>[Ru(III)] $\times 10^6$ (mol dm$^{-3}$)</th>
<th>$k \times 10^4$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.8</td>
<td>5.199</td>
</tr>
<tr>
<td>1.0</td>
<td>5.681</td>
</tr>
<tr>
<td>2.0</td>
<td>7.295</td>
</tr>
<tr>
<td>3.0</td>
<td>8.609</td>
</tr>
<tr>
<td>4.0</td>
<td>9.572</td>
</tr>
</tbody>
</table>

$r = 0.999$

Fig. 7.6: Plot of $4\log k$ versus $7\log [\text{Ru(III)}]$
Table 7.8
Effect of varying benzenesulfonamide on the rate

\[ [\text{CAB}] = 5 \times 10^{-4} \text{ mol dm}^{-3}, \ [\text{PRX}] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}, \ [\text{HCl}] = 10 \times 10^{-2} \text{ mol dm}^{-3} \]
\[ [\text{Ru(III)}] = 1 \times 10^{-6} \text{ mol dm}^{-3}, \ T = 308 \text{ K}, \ \mu = 0.2 \text{ mol dm}^{-3} \]

<table>
<thead>
<tr>
<th>[BSA] x 10^4 (mol dm^{-3})</th>
<th>k x 10^4 (s^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>5.69</td>
</tr>
<tr>
<td>4.0</td>
<td>5.68</td>
</tr>
<tr>
<td>6.0</td>
<td>5.76</td>
</tr>
<tr>
<td>8.0</td>
<td>5.69</td>
</tr>
</tbody>
</table>

Table 7.9
Effect of ionic strength on the rate

\[ [\text{CAB}] = 5 \times 10^{-4} \text{ mol dm}^{-3}, \ [\text{PRX}] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}, \ [\text{HCl}] = 10 \times 10^{-2} \text{ mol dm}^{-3} \]
\[ [\text{Ru(III)}] = 1 \times 10^{-6} \text{ mol dm}^{-3}, \ T = 308 \text{ K} \]

<table>
<thead>
<tr>
<th>[NaClO_4] x 10^2 (mol dm^{-3})</th>
<th>k x 10^4 (s^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>5.70</td>
</tr>
<tr>
<td>20</td>
<td>5.68</td>
</tr>
<tr>
<td>30</td>
<td>5.68</td>
</tr>
<tr>
<td>40</td>
<td>5.69</td>
</tr>
</tbody>
</table>
Table 7.10

Effect of dielectric permittivity of the medium on the rate

\[ [\text{CAB}] = 5 \times 10^{-4} \text{ mol dm}^{-3}, \ [\text{PRX}] = 1.0 \times 10^{-2} \text{ mol dm}^{-3}, \ [\text{HCl}] = 10 \times 10^{-2} \text{ mol dm}^{-3}, \ [\text{Ru(III)}] = 1 \times 10^{-6} \text{ mol dm}^{-3}, \ T = 308 \text{ K}, \ \mu = 0.2 \text{ mol dm}^{-3} \]

<table>
<thead>
<tr>
<th>(%CH₃CN (v/v))</th>
<th>D</th>
<th>( k' \times 10^{-4} ) (s⁻¹)</th>
<th>( 10^2/D )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>73.6</td>
<td>5.68</td>
<td>1.359</td>
</tr>
<tr>
<td>5</td>
<td>71.8</td>
<td>6.34</td>
<td>1.393</td>
</tr>
<tr>
<td>10</td>
<td>70.0</td>
<td>7.03</td>
<td>1.429</td>
</tr>
<tr>
<td>15</td>
<td>68.2</td>
<td>7.95</td>
<td>1.466</td>
</tr>
<tr>
<td>20</td>
<td>66.5</td>
<td>8.92</td>
<td>1.504</td>
</tr>
</tbody>
</table>

\( r = 0.999 \)

Fig. 7.7: Plot of \(4 + \log k'\) versus \(10^2/D\)

---

Fig. 7.7
Table 7.11

**Effect of temperature on the reaction rate**

\[
[CAB] = 5 \times 10^{-4} \text{ mol dm}^{-3}, \ [PRX] = 1.0 \times 10^{-2} \text{ mol dm}^{-3} \\
[HCl] = 10 \times 10^{-2} \text{ mol dm}^{-3}, \ [Ru(III)] = 1 \times 10^{-6} \text{ mol dm}^{-3}, \ \mu = 0.2 \text{ mol dm}^{-3}
\]

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>( k' \times 10^4 ) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>303</td>
<td>4.03</td>
</tr>
<tr>
<td>308</td>
<td>5.68</td>
</tr>
<tr>
<td>313</td>
<td>9.21</td>
</tr>
<tr>
<td>316</td>
<td>11.75</td>
</tr>
<tr>
<td>319</td>
<td>14.47</td>
</tr>
</tbody>
</table>

\( r = 0.998 \)

**Fig. 7.8**: Plot of 4 + log \( k' \) versus \( 10^3/T \)
Table 7.12
Kinetic and thermodynamic parameters for the oxidation of PRX with CAB in the presence of HCl and Ru(III) – catalyst.

<table>
<thead>
<tr>
<th>Activation parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_a = 64.95 \text{ kJ mol}^{-1}$</td>
</tr>
<tr>
<td>$\Delta H^\circ = 62.36 \text{ kJ mol}^{-1}$</td>
</tr>
<tr>
<td>$\Delta S^\circ = -104.38 \text{ JK}^{-1} \text{ mol}^{-1}$</td>
</tr>
<tr>
<td>$\Delta G^\circ = 94.91 \text{ kJ mol}^{-1}$</td>
</tr>
</tbody>
</table>

Table 7.13
Double reciprocal plot of $1/k'$ versus $1/[\text{Ru(III)}]$ at constant [PRX] and [HCl]

<table>
<thead>
<tr>
<th>$1/[\text{Ru(III)}]$</th>
<th>$10^3/k$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1923</td>
<td>1250</td>
</tr>
<tr>
<td>1760</td>
<td>1000</td>
</tr>
<tr>
<td>1371</td>
<td>500</td>
</tr>
<tr>
<td>1162</td>
<td>333</td>
</tr>
<tr>
<td>1045</td>
<td>1045</td>
</tr>
</tbody>
</table>

$r = 0.992$

Fig. 7.9 Plot of $1/k'$ versus $1/[\text{Ru(III)}]$
Fig. 7.9
Discussion and mechanism

Bishop and Jennings [11], Morris et al [12] and Higuchi and co-workers [13] have shown the existence of similar equilibria in acid and alkaline solutions of metal salts of N-haloarenesulfonamides. Chloramine-B an analogue to chloramine-T behaves as a strong electrolyte in aqueous solutions which furnishes different types of reactive species in acidic solutions. To confirm this hypothesis, conductometric and pH-titrations between aqueous solutions of CAB and HCl were performed. The conductometric behavior of CAB is identical with that of CAT [14, 15], while the pH titration curves observed are similar to those noted by Morris et al [12]. The possible equilibria in acidified CAB solutions are,

\[
\text{RNClNa} \rightleftharpoons \text{RNCI}^- + \text{Na}^+ \quad \ldots \ldots (7.2)
\]
\[
\text{RNCI}^- + \text{H}^+ \rightleftharpoons \text{RNHCl} \quad \ldots \ldots (7.3)
\]
\[
\text{RNHCl} + \text{H}_2\text{O} \rightleftharpoons \text{RNH}_2 + \text{HOCl} \quad \ldots \ldots (7.4)
\]
\[
2\text{RNHCl} \rightleftharpoons \text{RNH}_2 + \text{RNCI}_2 \quad \ldots \ldots (7.5)
\]
\[
\text{HOCl} + \text{H}^+ \rightleftharpoons \text{H}_2\text{OCl}^+ \quad \ldots \ldots (7.6)
\]

where R = C₆H₅SO₂.

Therefore the possible oxidizing species in acid solution of CAB are free acid (RNHCl), RNCI₂, HOCl and H₂OCl⁺. The involvement of RNCI₂ in the mechanism leads to a second-order rate law and negative effect of RNH₂ according to equation (7.5), which is contrary to the experimental observations. If HOCl were the primary oxidizing species, a first-order retardation of the rate by the added RNH₂ would be expected. However no such effect is noticed. Hardy and Johnston [16], who studied the pH dependent relative concentrations of the species present in acidified bromamine-B solutions of comparable molar concentrations, have shown that C₆H₄SO₂NHBr is the probable oxidizing species in acid medium. Narayanan and Rao [17] and Subhashini et al [18] have reported that monohaloamines can be further protonated at pH < 2 as shown in equations (7.7) and (7.8) and the values of the second protonation constants are 102 and 61 ± 2 at 25 °C for chloramine-T and chloramine-B, respectively.
\[ \text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NHCl} + \text{H}^+ \rightleftharpoons \text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NH}_2\text{Cl} \] 

\[ \text{C}_6\text{H}_5\text{SO}_2\text{NHCl} + \text{H}^+ \rightleftharpoons \text{C}_6\text{H}_5\text{SO}_2\text{NH}_2\text{Cl} \] 

\( (7.7) \)

\( (7.8) \)

Cady and Connick\textsuperscript{[19]} and Connick and Fine\textsuperscript{[20]} based on ion exchange properties and UV-spectral studies have shown that the octahedral complexes such as [RuCl\(_5\)(H\(_2\)O)]\(^2-\), [RuCl\(_4\)(H\(_2\)O)\(_2\)]\(^+\), [RuCl\(_3\)(H\(_2\)O)\(_3\)] \(^+\), [RuCl\(_2\)(H\(_2\)O)\(_4\)] \(^+\) and [RuCl(H\(_2\)O)\(_5\)] \(^2+\) may not exist in aqueous solutions of RuCl\(_3\), however other studies\textsuperscript{[21, 23]} have shown that the following ligand substitution equilibrium exists in acidic solutions,

\[ \text{RuCl}_3\text{xH}_2\text{O} + 3\text{HCl} \rightarrow \text{[RuCl}_6\text{]}\text{H}_2\text{O} + 3\text{H}^+ \]

\[ \text{[RuCl}_6\text{]}\text{H}_2\text{O} + \text{H}_2\text{O} \rightarrow \text{[RuCl}_6\text{]}\text{(H}_2\text{O)}\text{]2-} + \text{Cl}^- \] 

\( (7.9) \)

Singh et al\textsuperscript{[24, 25]} have employed the above equilibrium in the ruthenium (III) chloride catalyzed oxidation of primary alcohols with bromamine-T and ethylene glycols with N-bromocetamide in HClO\(_4\) medium. In the present studies, increasing effect of added chloride ion on the rate suggests that [RuCl\(_6\)]\(^3-\) is the more likely catalyzing species\textsuperscript{[20, 23]}.

Based on the preceding discussion, a detailed mechanistic interpretation (Scheme 7.1) for the Ru(III)-catalyzed PRX-CAB reaction in acid medium has been proposed to substantiate the observed kinetics.

\[ \text{RNHCl} + \text{H}^+ \xrightarrow{K_1} \text{RNH}_2\text{Cl} \quad \text{fast} \] 

\[ \text{RNH}_2\text{Cl} + \text{S} \xrightarrow{K_2} \text{X} \quad \text{fast} \] 

\[ \text{X} + \text{Ru(III)} \xrightarrow{K_3} \text{X}' \quad \text{fast} \] 

\[ \text{X}' \xrightarrow{k_4} \text{Products} \quad \text{slow and r.d.s} \]

Scheme 7.1
In Scheme 7.1, S, X and X' represents the substrate and complex intermediate species whose structures are shown in Scheme 7.2, where a detailed mechanistic interpretation of the ruthenium (III) chloride catalyzed PRX-CAB reaction in acid medium is illustrated.

From Scheme 7.1, rate = $k_4[X']$  ……(7.10)

If [CAB]$_t$ represents the total effective concentration of CAB,

$$[\text{CAB}]_t = [\text{RNHCl}] + [\text{RN}^+\text{H}_2\text{Cl}] + [\text{X}] + [\text{X}']$$  ……(7.11)

By substituting [RNHCl], [RN$^+$H$^+_2$Cl] and [X] from equilibrium steps (i), (ii) and (iii) in equation (7.11) one obtains,

$$[\text{CAB}]_t = \frac{[X']}{K_1K_2K_3[H^+][S][\text{Ru(III)}]} + \frac{[X']}{K_2K_3[S][\text{Ru(III)}]} + \frac{[X']}{K_3[\text{Ru(III)}]} + [X']$$

or

$$[\text{CAB}]_t = \frac{[X']}{K_1K_2K_3[S][\text{Ru(III)}]} \frac{[H^+][S]}{[1 + K_1[H^+][1 + K_2[S] + K_2K_3[S][\text{Ru(III)}]]}$$  ……(7.12)

or

$$[X'] = \frac{K_1K_2K_3[S][\text{CAB}]_t[H^+][S][\text{Ru(III)}]}{1 + K_1[H^+][1 + K_2[S] + K_2K_3[S][\text{Ru(III)}]]}$$  ……(7.13)

Substituting for [X'] from equation (7.13) into equation (7.10), the following rate law (equation 7.14) is obtained.

$$\text{rate} = \frac{K_1K_2K_3k_4[\text{CAB}]_t[H^+][S][\text{Ru(III)}]}{1 + K_1[H^+][1 + K_2[S] + K_2K_3[S][\text{Ru(III)}]]}$$  ……(7.14)

Since rate = $k'[\text{CAB}]_t$, equation (7.14) can be transformed into equations (7.15) - (7.17),

$$k' = \frac{K_1K_2K_3k_4[H^+][S][\text{Ru(III)}]}{1 + K_1[H^+][1 + K_2[S] + K_2K_3[S][\text{Ru(III)}]]}$$  ……(7.15)

$$\frac{1}{k'} = \frac{1}{K_1K_2K_3k_4[H^+][S][\text{Ru(III)}]} + \frac{1}{K_2K_3k_4[S][\text{Ru(III)}]} + \frac{1}{K_3k_4[\text{Ru(III)}]} + \frac{1}{k_4}$$  ……(7.16)
Based on equation (7.17), the plot of $1/k'$ versus $1/[\text{Ru(III)}]$ at constant $[S]$, $[H^+]$ and temperature was found to be linear (Fig. 7.9). From the intercept of the above plot, the decomposition constant ($k_4$) for the standard run was found to be $1.234 \times 10^{-3}$ s$^{-1}$. The rate law (7.14) is in agreement with the observed kinetic data. The proposed scheme and the derived rate law are also supported by the experimental observations.

Addition of chloride ion increased the rate and a fractional order dependence on $[\text{Cl}^-]$ was observed in the oxidation of PRX. The following Scheme 7.3 is proposed for the effect of added chloride ion,

\[
\begin{align*}
\text{RNHCl} + H^+ & \underset{\text{fast}}{\overset{K_1}{\rightleftharpoons}} \text{R}^+ \text{Cl} \\
\text{R}^+ \text{Cl} + \text{Cl}^- & \underset{\text{fast}}{\overset{K_5}{\rightleftharpoons}} \text{R}^+ \text{Cl}^- \\
\text{R}^+ \text{Cl}^- + \text{S} & \underset{\text{fast}}{\overset{K_6}{\rightleftharpoons}} \text{X} \\
\text{X} + \text{Ru(III)} & \underset{\text{fast}}{\overset{K_7}{\rightleftharpoons}} \text{X}^' \\
\text{X}^' & \underset{k_8}{\rightleftharpoons} \text{Products}
\end{align*}
\]

Scheme 7.3

From the slow step of Scheme 7.3

\[
\text{rate} = k_8 [\text{X}']
\]

....(7.18)

If $[\text{CAB}]_t$ represents the total effective concentration of CAB,

\[
[\text{CAB}]_t = [\text{RNHCl}] + [\text{RN}^+\text{H}_2\text{Cl}] + [\text{RN}^+\text{H}_2\text{Cl}…\text{Cl}^-] + [\text{X}] + [\text{X}']
\]

....(7.19)

By substituting $[\text{RNHCl}]$, $[\text{RN}^+\text{H}_2\text{Cl}]$, $[\text{RN}^+\text{H}_2\text{Cl}…\text{Cl}^-]$ and $[\text{X}]$ from equilibrium steps (i), (ii), (iii) and (iv) in equation (7.19), one obtains


\[
[CAB]_t = \frac{[X'][1 + K_1[H^+] + K_5 K_4[H^+][Cl^-] + K_1 K_2 K_3[H^+][Cl^-][S] + K_5 K_3 K_7[H^+][Cl^-][Ru(III)][S]}}{K_1 K_5 K_5[Cl^-][S][Ru(III)]}
\]

or \[X'] = \frac{K_1 K_5 K_7[KAB][H^+][Cl^-][S][Ru(III)]}{1 + K_1[H^+] + K_5 K_3[H^+][Cl^-] + K_1 K_5 K_7[H^+][Cl^-][S] + K_5 K_3 K_7[H^+][Cl^-][Ru(III)][S]}

.....(7.20)

substituting for \[X'] \text{ from equation (7.20) into equation (7.18) the following rate law is obtained,}

\[
\text{rate} = \frac{K_1 K_5 K_5 K_7 k_8[CA][H^+][S][Cl^-][Ru(III)]}{1 + K_1[H^+]([1 + K_5[Cl^-]] + K_1 K_5 K_7[H^+][Cl^-][S][1 + K_7[Ru(III)]})
\]

..... (7.21)

Since \text{rate} = k'[CAB]_t, equation (7.21) can be transformed into equation (7.22),

\[
k' = \frac{K_1 K_5 K_5 K_7 k_8[H^+][S][Cl^-][Ru(III)]}{1 + K_1[H^+]([1 + K_5[Cl^-]] + K_1 K_5 K_7[H^+][Cl^-][S][1 + K_7[Ru(III)]})
\]

..... (7.22)

The rate expression (7.21) clearly demonstrates the fractional-order dependence of the rate on \[Cl^-\] and it is in good agreement with the experimental data.

Laidler [26] and Amis [27] have described the effect of solvent composition on the reaction kinetics. For limiting case of zero angle of approach between two dipoles or an ion-dipole system, Amis [27] has shown that a plot of log \(k'\) versus \(1/D\) gives a straight line with a positive slope for a reaction involving a positive ion and a dipole and a negative slope for a negative ion-dipole or dipole-dipole interactions. In the present investigations, increasing the content of CH₃CN in the reaction medium leads to an increased effect on the rate of reaction, which seems to be contrary to the expected reaction between neutral and anionic species in media of lower relative permittivity. However, an increase in the rate of the reaction with decreasing relative permittivity may be due to stabilization of the complex \((X')\) at low relative permittivity, which is less solvated at higher relative permittivity because of its larger size. The reduction product of the oxidant, benzenesulfonamide did not influence the rate showing that it is not involved in any pre-equilibrium. The proposed mechanism is also supported by the values of energy of activation and other activation parameters. The fairly high positive
values of Gibb’s free energy of activation and enthalpy of activation indicate that the
transition state is highly solvated, while the high negative value of entropy of activation
accounts for the formation of a compact transition state in which several degrees of
freedom are lost.
Scheme 7.2
References

**Research Publications**


**Papers presented at Conference/Symposium**

1. Ruthenium (III) catalyzed oxidation of 2-phenylethylamine with chloramine-B in hydrochloric acid medium: A kinetic and mechanistic study (PP-40). *National Symposium on Bio-organic and Medicinal Chemistry (NSBM) held at DOS in Chemistry, Manasagangotri, University of Mysore, Mysore, India during Oct, 5-7, 2005.*

2. Kinetic and mechanistic investigation of oxidation of vitamin B₆ with chloramine-B catalyzed by ruthenium (III) in hydrochloric acid medium (OP-07). *International Conference on Materials for the Millennium (Mat-Con-2007) held at Department of Applied Chemistry, Cochin University of Science and Technology, Kochin, India, during Mar, 1-3, 2007.*