CHAPTER-II

KINETICS AND MECHANISM OF OXIDATION OF SALBUTAMOL BY CHLORAMINE-T IN HClO₄ AND NAOH MEDIA
Section 2.1

OXIDATION OF SALBUTAMOL: A REVIEW

Salbutamol, [1-(4-hydroxy-3-hydroxymethyl phenyl)-2-(t-butylamino) ethanol], also known as albuterol, is \( \beta_2 \)-adrenergic receptor agonist used for the relief of bronchospasm in conditions such as asthma and chronic obstructive pulmonary disease (COPD). Salbutamol is a relevant medication for the treatment of asthma. It is also used in obstetrics as a tocolytic to delay premature labor and as a nasal decongestant. The pharmacokinetics following a therapeutic dose and the analysis of salbutamol are important in pharmaceutical research and in clinical chemistry, since the drug is widely prescribed.

The kinetic study of oxidation of this bioactive compound is of much use in understanding the mechanistic profile in redox reactions. Several analytical procedures are reported in the literature for the determination of SBL in pharmaceuticals using CAT.

Basavaiah K et al have reported the titrimetric and spectrophotometric determination of salbutamol sulphate in pharmaceuticals using chloramine - T. In both direct titrimetry and back titrimetry the unreacted oxidant is determined iodometrically after the oxidation of SBL is completed. In both methods, the reaction follows a 1:2 (SBL: CAT), reaction stoichiometry.

Yilmaz Niyazi et al has reported the voltammetric determination of salbutamol based on electrochemical oxidation at platinum and glassy carbon electrodes. The oxidative behavior of salbutamol sulfate was studied as a function of pH at platinum and activated glassy carbon electrodes.

M. Narayana Reddy et al has reported the simple and sensitive spectrophotometric method for the determination of salbutamol(SBL) based on their oxidation with Fe(III) and subsequent chelation of Fe(II) with 1,10-phenanthroline to form red colored complex (\( \lambda_{\text{max}} \), 510 nm).

Geeta, N. and Baggi, T. R have reported an improved extractive spectrophotometric method for the determination of salbutamol sulfate based on its oxidative coupling with 3-
methylbenzthiazolinone-2-hydrazone in the presence of ceric ammonium sulfate as an oxidizing agent.

Maelkki-Laine et al\textsuperscript{10} have reported the decomposition of salbutamol in aqueous solutions. The effect of buffer species, pH, buffer concentration and antioxidants has studied. Reversed-phase HPLC with diode array detection was used to follow the decomposition which obeyed apparent first-order kinetics under all conditions studied.

A review of the literature shows that kinetics of oxidation of SBL with CAT has not been reported.

The present investigations therefore were taken up to study the oxidation kinetics of this drug by CAT in acid medium to ascertain the mechanisms of metabolic conversion of SBL in biological systems and also to identify the reactive species of the oxidants in acidic and alkaline media.

Section 2.2

KINETICS OF OXIDATION OF SALBUTAMOL BY CHLORAMINE-T IN $\text{HClO}_4$ AND NaOH MEDIA

This section reports the kinetics and mechanism of oxidation of Salbutamol (SBL) by CAT in the presence of $\text{HClO}_4$ and NaOH media at 303K.

The details regarding the preparation of reagents and the experimental procedures are similar to those given in Section 1.8 of Chapter 1.

Stoichiometry

Reaction mixture containing varying ratios of CAT to SBL in the presence of 0.01 mol dm\textsuperscript{-3} $\text{HClO}_4$ or 0.001 mol dm\textsuperscript{-3} NaOH were equilibrated at 303K for 48 hrs. Estimation of unreacted CAT in the reaction mixture showed that one mole of SBL consumed two moles of oxidant in acidic medium and one mole of oxidant in alkaline medium confirming the following stoichiometry:
\[ C_{13}H_{21}O_3N + 2RNClNa + 2H_2O \rightarrow C_8H_8O_4 + HCHO + HNC (CH_3)_3 + 2RNH_2 + 2Na^+ + 2Cl^- \]  
\[ C_{13}H_{21}O_3N + RNClNa + H_2O \rightarrow C_8H_8O_3 + HCHO + HNC (CH_3)_3 + RNH_2 + Na^+ + Cl^- \]

where \( R = CH_3C_6H_4SO_2 \).

**Product analysis**

The reaction was allowed to progress for 48 hrs at 303K in presence of acid and alkali separately. After completion of the reaction, the reaction products were neutralized with acid/alkali and extracted with ether. The oxidation products were purified and recrystallized. The oxidation product 4-hydroxy-3-hydroxymethylbenzoic acid in acidic medium was identified by conventional spot tests. The aldehyde, 4-hydroxy-3-(hydroxymethyl) benzaldehyde in alkaline medium was detected by conventional spot tests and also by 2, 4-DNP derivative. These were further confirmed by GC-MS analysis. The mass data were obtained using electron impact ionization technique. The mass spectrum showed a molecular ion peaks at 168 amu and 152 clearly confirming the identity of the product. The other oxidation product formaldehyde was identified by Schiff's reagent test\(^{11}\) and 2-methylpropan-2-amine was identified by spot test\(^{12}\). It was also observed that there was no further oxidation of these products under the present kinetic conditions.

The reduction product of CAT, \( p \)-toluenesulfonamide (\( CH_3C_6H_4NH_2 \)) was also extracted with ethyl acetate and identified by TLC\(^{13}\) using petroleum ether-chloroform-1-butanol (2:2:1 v/v) as the solvent system and iodine as spray reagent (\( R_f = 0.84 \)). Further, the molecular ion peak at 171 amu clearly confirms \( p \)-toluenesulfonamide (PTS). All other peaks observed in GC-MS spectra are to be interpreted in accordance with the observed structure.

**RESULTS**

The kinetics of oxidation of SBL with CAT has been kinetically investigated at different initial concentrations of reactants in the presence of \( \text{HClO}_4 \) or \( \text{NaOH} \) at 303 K. In
the present investigations we could not establish the identical experimental conditions for acid and alkaline media. For the sake of convenience the salient features obtained in these two media are discussed separately.

KINETICS OF OXIDATION IN ACIDIC MEDIUM

Effect of reactants

With the substrate in excess at constant [HClO₄], [NaClO₄] and temperature the [CAT]₀ was varied. Plots of log [CAT] versus time were linear (r > 0.995) indicating a first-order dependence of the rate on [CAT]. The pseudo-first-order rate constants (k') calculated from the slopes are given in Table 2.1. The values of k' unaltered with variation of [CAT]₀ confirming the first-order dependence of the rate on [CAT]₀. Under the similar experimental conditions an increase in [SBL]₀, increased the k' values (Table 2.1). Plots of log k' versus log [SBL] was linear (Fig.2.1; r=0.998) with a slope of 0.52 indicating a fractional-order dependence on [SBL]₀.

Effect of varying [HClO₄]

The reaction was studied with varying [HClO₄] at fixed [CAT], [SBL]. The rate decreased with increase in [HClO₄] (Table 2.1) and a plot of log k' versus log [HClO₄] was linear (Fig.2.2 r = 0.998) with a slope of -0.72 indicating an inverse-fractional-order dependence on [H⁺].

Effect of p-toluene sulfonamide (PTS) and halide ions

Addition of PTS, the reduction product of oxidant, to the reaction mixture retards the rate (Table 2.2) Plot of log k' versus log [PTS] was linear (Fig.2.3, r=0.998) with a negative fractional slope -0.42, indicating the involvement of PTS in a pre-equilibrium step prior to the rate determining step. At constant [H⁺], addition of chloride/bromide ions in the form of NaCl and NaBr does not change the rate of reaction (Table 2.2).

Effect of varying ionic strength and dielectric constant

The reaction rate remained unchanged by varying ionic strength of the medium through addition of NaClO₄ (0.1–0.8 mol dm⁻³). The dielectric permittivity of the medium
was varied by adding different proportions (0–40 % v/v) of CH₃OH to the reaction mixture. The rate decreased with increasing CH₃OH content (Table 2.3). A plot of log k' versus 1/D, where D is the dielectric permittivity of the medium, gave a straight line (Fig. 2.4, r=0.999) with a negative slope. The D values are obtained from the literature. Blank experiments performed showed that CAT did not oxidize CH₃OH under the experimental conditions employed.

**Effect of Temperature and test for free radicals**

The reaction was studied at different temperatures (293–313K) (Table 2.4), keeping other experimental conditions constant. From the linear Arrhenius plot of log k' versus 1/T (Fig. 2.5, r=0.999), activation energy and other thermodynamic parameters for the composite reaction were computed. The results are compiled in Table 2.4. The addition of aqueous acrylonitrile monomer solution to the reaction mixture in an inert atmosphere did not initiate polymerization indicating the absence of free radical species in the reaction sequence.

**KINETICS OF OXIDATION IN ALKALINE MEDIUM**

**Effect of reactants**

Under the pseudo-first-order conditions, at constant [OH⁻], [NaClO₄] and temperature, the [CAT]₀ was varied. Plots of log [CAT] versus time were found linear (r > 0.997) indicating a first-order dependence of the rate on [CAT]₀. The values of k' unaltered with variation of [CAT]₀ confirming the first-order dependence of the rate on [CAT]₀ (Table 2.5). Under the similar conditions an increase in [SBL]₀ increases the k' values (Table 2.5). Plots of log k' versus log [SBL] was linear (Fig 2.1; r = 0.998) with a slope 0.78 showing a fractional-order dependence of rate on [SBL]₀.

**Effect of varying [OH⁻]**

The rate decreased with increase in [OH⁻] (Table 2.5), and a plot of log k' versus log [OH⁻] was linear (Fig. 2.2, r=0.999) with a negative slope (-0.43) indicating an inverse-fractional-order with respect to [OH⁻].
**Effect of p-toluene sulfonamide (PTS) and halide ions**

The addition of reduced product, PTS retards the rate. Plot of log k' versus log [PTS] was linear (Fig.2.3, r=0.997) with a negative fractional slope – 0.36 (Table 2.2), indicating the involvement of PTS in a pre-equilibrium step prior to the rate determining step. At constant [OH'], addition of chloride/bromide ions in the form of NaCl and NaBr does not change the rate of reaction (Table 2.2).

**Effect of ionic strength and dielectric constant**

The reaction rate remained unchanged by varying ionic strength of the medium through addition of NaClO₄ (0.1–0.8 mol dm⁻³). The dielectric permittivity of the medium was varied by adding different proportions of (0–40 % v/v) of CH₃OH to the reaction mixture. The rate decreased with increase in CH₃OH content (Table 2.3) and a plot of log k' versus 1/D was linear (Fig. 2.4, r = 0.998) with a negative slope.

**Effect of Temperature and test for free radicals**

The reaction was studied at different temperatures (293K-313K) (Table 2.4), keeping other experimental conditions constant. From the linear Arrhenius plot of log k' versus 1/T (Fig.2.5, r=0.999), activation energy and other thermodynamic parameters for the composite reaction were computed. These are given in Table 2.4. Addition of aqueous acrylonitrile monomer solution to the reaction mixture in an inert atmosphere did not initiate polymerization, which indicates the absence of free radical in the reaction mixture.
Table 2.1
Effect of varying concentrations of oxidant, substrate, acid on the reaction rate constant at 303K

<table>
<thead>
<tr>
<th>$10^4$ [CAT] (mol dm$^{-3}$)</th>
<th>$10^3$ [SBL] (mol dm$^{-3}$)</th>
<th>$10^3$ [HClO4] (mol dm$^{-3}$)</th>
<th>$k \times 10^4$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.0</td>
<td>6.0</td>
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</tr>
<tr>
<td>10.0</td>
<td>6.0</td>
<td>10</td>
<td>2.06</td>
</tr>
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<td>12.0</td>
<td>6.0</td>
<td>10</td>
<td>2.02</td>
</tr>
<tr>
<td>8.0</td>
<td>1.0</td>
<td>10</td>
<td>0.84</td>
</tr>
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<td>2.0</td>
<td>10</td>
<td>1.20</td>
</tr>
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<td>10</td>
<td>2.80</td>
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<td>10</td>
<td>3.92</td>
</tr>
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<td>50.0</td>
<td>10</td>
<td>5.90</td>
</tr>
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<td>1.0</td>
<td>13.5</td>
</tr>
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<td>4.80</td>
</tr>
<tr>
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<td>6.0</td>
<td>5.0</td>
<td>3.50</td>
</tr>
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<td>6.0</td>
<td>10</td>
<td>2.00</td>
</tr>
<tr>
<td>8.0</td>
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<td>1.23</td>
</tr>
<tr>
<td>8.0</td>
<td>6.0</td>
<td>40</td>
<td>0.75</td>
</tr>
</tbody>
</table>

$\mu = 0.5$ mol dm$^{-3}$

Table 2.2
Effect of varying concentrations of $p$-toluenesulfonamide, NaCl and NaBr on the rate

<table>
<thead>
<tr>
<th>[PTS] $\times 10^2$ mol dm$^{-3}$</th>
<th>$10^4 k'(s^{-1})$</th>
<th>$10^4$ [NaCl] mol dm$^{-3}$</th>
<th>$10^4 k'(s^{-1})$</th>
<th>$10^4$ [NaBr] mol dm$^{-3}$</th>
<th>$10^4 k'(s^{-1})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Acid]</td>
<td>[Alkali]</td>
<td>[*Acid]</td>
<td>[Alkali]</td>
<td>[*Acid]</td>
<td>[Alkali]</td>
</tr>
<tr>
<td>0.0</td>
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<td>5.70</td>
<td>0.0</td>
<td>2.00</td>
<td>5.70</td>
</tr>
<tr>
<td>1.0</td>
<td>0.70</td>
<td>4.10</td>
<td>5.0</td>
<td>2.21</td>
<td>5.68</td>
</tr>
<tr>
<td>5.0</td>
<td>0.51</td>
<td>3.70</td>
<td>10.0</td>
<td>2.08</td>
<td>5.53</td>
</tr>
<tr>
<td>10.0</td>
<td>0.42</td>
<td>3.00</td>
<td>20.0</td>
<td>2.14</td>
<td>5.75</td>
</tr>
<tr>
<td>20.0</td>
<td>0.34</td>
<td>2.10</td>
<td>30.0</td>
<td>2.15</td>
<td>5.72</td>
</tr>
</tbody>
</table>

$^[\text{CAT}] = 8 \times 10^{-4}$ mol dm$^{-3}$, $[^\text{SBL}] = 6 \times 10^{-3}$ mol dm$^{-3}$, $[^\text{HClO4}] = 1 \times 10^{-2}$ mol dm$^{-3}$, $\mu = 0.5$ mol dm$^{-3}$, $[\text{NaOH}] = 1 \times 10^{-3}$ mol dm$^{-3}$, $\mu = 0.5$ mol dm$^{-3}$, $T = 303$K.

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Table 2.3

Effect of Solvent composition on the reaction rate constant at 303 K

<table>
<thead>
<tr>
<th>CH$_3$OH, (%) (v/v)</th>
<th>10$^4$ k'(s$^{-1}$)</th>
<th>μ</th>
<th>10$^4$ k'(s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D</td>
<td>*Acid</td>
<td>#Alkaline</td>
</tr>
<tr>
<td>0</td>
<td>76.73</td>
<td>2</td>
<td>5.70</td>
</tr>
<tr>
<td>10</td>
<td>72.37</td>
<td>1.66</td>
<td>4.00</td>
</tr>
<tr>
<td>20</td>
<td>67.48</td>
<td>0.98</td>
<td>2.80</td>
</tr>
<tr>
<td>30</td>
<td>62.71</td>
<td>0.52</td>
<td>1.20</td>
</tr>
<tr>
<td>40</td>
<td>58.06</td>
<td>0.32</td>
<td>0.70</td>
</tr>
</tbody>
</table>

* [CAT] = 8 x 10$^{-4}$ mol dm$^{-3}$, [SBL] = 6 x 10$^{-3}$ mol dm$^{-3}$, [HClO$_4$] = 1 x 10$^{-2}$ mol dm$^{-3}$, μ = 0.5 mol dm$^{-3}$

# [CAT] = 1 x 10$^{-3}$ mol dm$^{-3}$, [SBL] = 1 x 10$^{-2}$ mol dm$^{-3}$, [NaOH] = 1 x 10$^{-3}$ mol dm$^{-3}$, μ = 0.5 mol dm$^{-3}$

Table 2.4

Effect of varying temperature on the reaction rate constant and thermodynamic parameters for the oxidation of SBL with CAT

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>10$^4$ k' (s$^{-1}$)</th>
<th>Thermodynamic Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>*Acid</td>
<td>#Alkaline</td>
</tr>
<tr>
<td>293</td>
<td>0.84</td>
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<tr>
<td>298</td>
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<td>4.35</td>
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<tr>
<td>303</td>
<td>2.00</td>
<td>5.70</td>
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<tr>
<td>308</td>
<td>2.98</td>
<td>8.20</td>
</tr>
<tr>
<td>313</td>
<td>4.40</td>
<td>10.55</td>
</tr>
</tbody>
</table>

* [CAT] = 8 x 10$^{-4}$ mol dm$^{-3}$, [SBL] = 6 x 10$^{-3}$ mol dm$^{-3}$, [HClO$_4$] = 1 x 10$^{-2}$ mol dm$^{-3}$, μ = 0.5 mol dm$^{-3}$

# [CAT] = 1 x 10$^{-3}$ mol dm$^{-3}$, [SBL] = 1 x 10$^{-2}$ mol dm$^{-3}$, [NaOH] = 1 x 10$^{-3}$ mol dm$^{-3}$, μ = 0.5 mol dm$^{-3}$
Table 2.5

Effect of varying concentrations of oxidant, substrate, and alkali on the rate constant

<table>
<thead>
<tr>
<th>$10^2$ [CAT] (mol dm$^{-3}$)</th>
<th>$10^2$ [SBL] (mol dm$^{-3}$)</th>
<th>$10^2$ [NaOH] (mol dm$^{-3}$)</th>
<th>$10^4$ k' (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>10.0</td>
<td>1.0</td>
<td>5.70</td>
</tr>
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<td>2.0</td>
<td>10.0</td>
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<td>5.0</td>
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<td>1.0</td>
<td>5.65</td>
</tr>
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<td>1.00</td>
<td>1.0</td>
<td>0.54</td>
</tr>
<tr>
<td>1.0</td>
<td>2.00</td>
<td>1.0</td>
<td>1.10</td>
</tr>
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<td>1.0</td>
<td>5.70</td>
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<td>7.10</td>
</tr>
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<td>1.0</td>
<td>5.70</td>
</tr>
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<td>10.0</td>
<td>5.0</td>
<td>3.50</td>
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<tr>
<td>1.0</td>
<td>10.0</td>
<td>10.0</td>
<td>2.80</td>
</tr>
<tr>
<td>1.0</td>
<td>10.0</td>
<td>20.0</td>
<td>2.20</td>
</tr>
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</table>

$\mu = 0.5$ mol dm$^{-3}$, $T = 303$ K.

Table 2.6

Effect of varying [SBL] at different temperatures in acidic and alkaline media

<table>
<thead>
<tr>
<th>[SBL]$\times 10^3$ (mol dm$^{-3}$)</th>
<th>*acid $10^4$ k'(s$^{-1}$) 293K</th>
<th>303K</th>
<th>308K</th>
<th>313K</th>
<th>*alkaline $10^4$ k'(s$^{-1}$) 298K</th>
<th>303K</th>
<th>308K</th>
<th>313K</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>0.48</td>
<td>1.12</td>
<td>1.66</td>
<td>2.31</td>
<td>2.0</td>
<td>1.15</td>
<td>1.40</td>
<td>2.10</td>
</tr>
<tr>
<td>4.0</td>
<td>0.69</td>
<td>1.61</td>
<td>2.55</td>
<td>3.32</td>
<td>5.0</td>
<td>2.40</td>
<td>2.98</td>
<td>4.63</td>
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<td>6.0</td>
<td>0.84</td>
<td>2.00</td>
<td>2.98</td>
<td>4.42</td>
<td>10.0</td>
<td>4.35</td>
<td>5.70</td>
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<td>8.0</td>
<td>0.99</td>
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<td>3.72</td>
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<td>7.60</td>
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<td>14.5</td>
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<td>4.11</td>
<td>5.54</td>
<td>40.0</td>
<td>14.14</td>
<td>17.4</td>
<td>25.5</td>
</tr>
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<td>5.76</td>
<td>8.00</td>
<td>45.0</td>
<td>17.20</td>
<td>19.7</td>
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* [CAT] = $8\times 10^{-4}$ mol dm$^{-3}$, [HClO$_4$] = $1\times 10^{-2}$ mol dm$^{-3}$, $\mu = 0.5$ mol dm$^{-3}$.

# [CAT] = $1\times 10^{-3}$ mol dm$^{-3}$, [NaOH] = $1\times 10^{-3}$ mol dm$^{-3}$, $\mu = 0.5$ mol dm$^{-3}$.
Table 2.7

Activation parameters for the rate limiting step

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>$10^4xk_4$</th>
<th>Activation Parameters *acidic</th>
<th>$10^3xk_9$</th>
<th>Activation Parameters *alkaline</th>
</tr>
</thead>
<tbody>
<tr>
<td>293</td>
<td>2.63</td>
<td>$E_a$(kJ mol$^{-1}$) 55.5</td>
<td>298</td>
<td>1.67</td>
</tr>
<tr>
<td>303</td>
<td>6.25</td>
<td>$\Delta H^\circ$(kJ mol$^{-1}$) 52.0</td>
<td>303</td>
<td>2.50</td>
</tr>
<tr>
<td>308</td>
<td>8.34</td>
<td>$\Delta S^\circ$(J K$^{-1}$ mol$^{-1}$) -129.9</td>
<td>308</td>
<td>3.34</td>
</tr>
<tr>
<td>313</td>
<td>12.5</td>
<td>$\Delta G^\circ$(kJ mol$^{-1}$) 91.0</td>
<td>313</td>
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</table>

* $[\text{CAT}] = 8 \times 10^{-4}$ mol dm$^{-3}$, $[\text{HClO}_4] = 1 \times 10^{-2}$ mol dm$^{-3}$, $\mu = 0.5$ mol dm$^{-3}$.

* $[\text{CAT}] = 1 \times 10^{-3}$ mol dm$^{-3}$, $[\text{NaOH}] = 1 \times 10^{-3}$ mol dm$^{-3}$, $\mu = 0.5$ mol dm$^{-3}$.
Fig 2.1 Plot of $\log k'$ versus $\log[SBL] + 4\log[SBL]$

Fig 2.2. Plot of $\log k'$ versus (a) $\log[\text{HClO}_4]$ and (b) $\log[\text{OH}^-]$
Fig. 2.3 Plot of log $k'$ versus log[$PTS$] vs log[$PTS$]

Fig. 2.4. Plot of log $k'$ versus $1/D$ vs $10^2/D$
Fig. 2.5 Plot of log$k'$ versus $1/T$

Fig. 2.6 Plot of $1/k'$ versus $1/[SBL]$
Fig. 2.7 Plot of $\log k_4$ and $\log k_5$ versus $1/T$ 10$^9/T$

Fig. 2.8 Plot of $[\text{SBL}]^{-1}$ versus $(k')^{-1}$
DISCUSSION

Bishop and Jennings\textsuperscript{17}, Hardy and Johnston\textsuperscript{18}, Morris et al\textsuperscript{19} and Pryde and Soper\textsuperscript{20} have formulated the following equilibria in acid and alkaline solutions of CAT:

\[
\text{RNClNa} \rightleftharpoons \text{RNCI}^+ + \text{Na}^+ \tag{2.3}
\]
\[
\text{RNCI}^+ + \text{H}^+ \rightleftharpoons \text{RNHCl} \tag{2.4}
\]
\[
\text{RNHCl} + \text{H}_2\text{O} \rightleftharpoons \text{RNH}_2 + \text{HOCl} \tag{2.5}
\]
\[
2\text{RNHCl} \rightleftharpoons \text{RNH}_2 + \text{RNCI}_2 \tag{2.6}
\]
\[
\text{RNCI}_2 + \text{H}_2\text{O} \rightleftharpoons \text{RNHCl} + \text{HOCl} \tag{2.7}
\]
\[
\text{HOCl} \rightleftharpoons \text{H}^+ + \text{OCl}^- \tag{2.8}
\]
\[
\text{HOCl} + \text{H}^+ \rightleftharpoons \text{H}_2\text{OCl}^+ \tag{2.9}
\]

Where R = \text{CH}_3\text{C}_6\text{H}_4\text{SO}_2.

Mechanism and rate law in acid medium

The possible oxidizing species in acidified CAT solutions are RNHCl, RNCI\textsubscript{2}, HOCl and possibly H\textsubscript{2}OCl\textsuperscript{+}. If RNCI\textsubscript{2} were to be the reactive species then the rate law predicts the second-order dependence on [CAT], which is not in agreement with the experimental results, since a first-order with respect to [CAT] was noticed. There was a negative fractional order observed with respect to PTS and [H\textsuperscript{+}] respectively. Many studies have been reported that RNHCl further undergo protonation. Thus it is reasonable to assume HOCl is the reactive species. Based on the preceding discussion, Scheme 2.1 for SBL-CAT reaction in acid medium has been proposed to substantiate the observed kinetics.

\[
\text{RNH}_2\text{Cl} \rightleftharpoons \text{RNHCl} + \text{H}^+ \tag{i}
\]
\[
\text{RNHCl} + \text{H}_2\text{O} \rightleftharpoons \text{RNH}_2 + \text{HOCl} \tag{ii}
\]
\[
\text{HOCl} + \text{SBL} \rightleftharpoons X \tag{iii}
\]
\[
X \rightleftharpoons X' \tag{iv}
\]
\[
X' + \text{HOCl} \rightleftharpoons \text{products} \tag{v}
\]

Scheme 2.1
Here SBL represents the substrate, whereas X and X' are the complex intermediate species whose structures are shown in Scheme 2.3.

Step (iv) of Scheme 2.1 determines the overall rate,

\[ \text{rate} = -\frac{d[\text{CAT}]}{dt} = k_4[X] \quad (2.10) \]

If \([\text{CAT}]_t\) represents the total effective concentration of CAT in solution then,

\[ [\text{CAT}]_t = [\text{RNH}_2^+\text{Cl}^-] + [\text{RNHCl}] + [\text{HOCl}] + [X] \quad (2.11) \]

From which, solving for \([X]\), one obtains

\[ [X] = \frac{K_1K_2K_4[\text{CAT}][\text{SBL}][\text{H}_2\text{O}]}{[\text{RNH}_2^-][\text{H}^+] + K_1[\text{RNH}_2^-] + K_1K_2[\text{H}_2\text{O}]\{1 + K_3[\text{SBL}]\}} \quad (2.12) \]

Substituting equation (2.12) in equation (2.10), the following rate law can be obtained:

\[ \text{rate} = -\frac{d[\text{CAT}]}{dt} = \frac{K_1K_2K_4[\text{CAT}][\text{SBL}][\text{H}_2\text{O}]}{[\text{RNH}_2^-][\text{H}^+] + K_1[\text{RNH}_2^-] + K_1K_2[\text{H}_2\text{O}]\{1 + K_3[\text{SBL}]\}} \quad (2.13) \]

Since \(\text{rate} = k' [\text{CAT}]_t\),

Equation (2.13) can be transformed into equations (2.14)–(2.16).

\[ k' = \frac{K_1K_2K_4[\text{CAT}][\text{SBL}][\text{H}_2\text{O}]}{[\text{RNH}_2^-][\text{H}^+] + K_1[\text{RNH}_2^-] + K_1K_2[\text{H}_2\text{O}]\{1 + K_3[\text{SBL}]\}} \quad (2.14) \]

\[ \frac{1}{k'} = \frac{[\text{RNH}_2^-][\text{H}^+]}{K_3K_4[\text{SBL}][\text{H}_2\text{O}]} + \frac{[\text{RNH}_2^-]}{K_2K_4[\text{SBL}][\text{H}_2\text{O}]} + \frac{1}{k_4} \quad (2.15) \]

\[ \frac{1}{k'} = \frac{1}{K_3K_4[\text{SBL}]} \left( \frac{[\text{RNH}_2^-][\text{H}^+]}{K_1K_2[\text{H}_2\text{O}]} + \frac{[\text{RNH}_2^-]}{K_2[\text{H}_2\text{O}]} + 1 \right) + \frac{1}{k_4} \quad (2.16) \]

The rate law (2.13) is in agreement with the experimental results with first order dependence on \([\text{CAT}]_0\), a fractional order in \([\text{SBL}]\) and an inverse fractional order in \([\text{H}^+]\) and PTS.
(RNH₂) respectively. Based on equation (2.16), plot of 1/k' versus 1/[SBL] (Fig.2.6, r = 0.997) at constant [H⁺] and temperature was found to be linear. The decomposition constant (k₄) was calculated from the intercept of the above plot and it was found to be k₄ = 6.25 × 10⁻⁴ s⁻¹ for the standard run.

Since the rate was fractional order in [SBL], Michaelis-Menten type of kinetics was adopted. The effect of [SBL] on the rate at different temperatures (293-313K) was studied (Table 2.6) and by plotting 1/k' vs 1/ [SBL] (Fig 2.6) values of decomposition constants k₄ were calculated. Activation parameters for the rate limiting step were computed from the Arrhenius plot of log k₄ vs 1/T (Fig. 2.7, r=0.988) yielded the activation parameters for the rate limiting step. These results are presented in Table 2.7.

**Mechanism and rate law in alkaline medium**

In alkaline solutions of CAT, RNCI₂ does not exist and hence the expected reactive species are RNHCl, HOCl and RNCI⁻. Further, Hardy and Johnston reported the following equilibria in alkaline solutions of bromamine-B:

\[
\text{RNBr}^- + \text{H}_2\text{O} \rightleftharpoons \text{RNHBr} + \text{OH}^- \quad (2.17)
\]

\[
\text{RNHBr} + \text{H}_2\text{O} \rightleftharpoons \text{RNH}_2 + \text{HOBr} \quad (2.18)
\]

A retarding influence of OH⁻ ions on the several reaction rates noticed in several haloamino metric reactions. Since the halo amines have similar properties, the above argument can be extended to CAT also. This supports the formation of RNHCl from RNCI⁻ in base retarding step (Eqn. 2.17). Since the negative fractional order is observed with respect to PTS (Eqn.2.18), HOCl is considered as the significant oxidizing species.

Considering the above facts and all the experimental data, the following Scheme 2.2 may be suggested for the oxidation of SBL with CAT in alkaline medium:
\[
\begin{align*}
\text{RNCl}^+ + \text{H}_2\text{O} & \quad \xrightleftharpoons{\kappa_6} \quad \text{RNHCl} + \text{OH}^- \quad \text{fast (i)} \\
\text{RNHCl} + \text{H}_2\text{O} & \quad \xrightleftharpoons{\kappa_7} \quad \text{RNH}_2 + \text{HOCl} \quad \text{fast (ii)} \\
\text{SBL} + \text{HOCl} & \quad \xrightleftharpoons{\kappa_8} \quad \text{X} \quad \text{fast (iii)} \\
\text{X} & \quad \xrightarrow{\kappa_9} \quad \text{products} \quad \text{slow and r.d.s (iv)}
\end{align*}
\]

**Scheme 2.2**

From the slow step (iii) of Scheme 2.2,

\[
\text{rate} = k_9[X]
\]

(2.19)

Assuming total effective concentration of CAT,

\[
[\text{CAT}] = [\text{RNCl}^+] + [\text{RNHCl}] + [\text{HOCl}] + [X]
\]

(2.20)

From which and solving for \([X]\), one obtains

\[
[X] = \frac{K_6K_7K_8[SBL][\text{CAT}][\text{H}_2\text{O}]^2}{[\text{RNH}_2][\text{OH}^-] + K_6[\text{H}_2\text{O}]} + K_6K_7[\text{H}_2\text{O}]^2 + K_8K_7[SBL][\text{H}_2\text{O}]^2
\]

(2.21)

By substituting equation (2.21) in equation (2.19), the following rate law can be obtained

\[
\text{rate} = \frac{K_6K_7K_8K_9[SBL][\text{CAT}][\text{H}_2\text{O}]^2}{[\text{RNH}_2][\text{OH}^-] + K_6[\text{H}_2\text{O}]} + K_6K_7[\text{H}_2\text{O}]^2 + K_8K_7[SBL][\text{H}_2\text{O}]^2
\]

(2.22)

Since \(\text{rate} = k'[\text{CAT}]\), equation (2.22) can be written as,

\[
k' = \frac{K_6K_7K_8K_9[SBL][\text{H}_2\text{O}]^2}{[\text{RNH}_2][\text{OH}^-] + K_6[\text{H}_2\text{O}]} + K_6K_7[\text{H}_2\text{O}]^2 + K_8K_7[SBL][\text{H}_2\text{O}]^2
\]

(2.23)

\[
\frac{1}{k'} = \frac{[\text{RNH}_2]}{K_6K_7K_8K_9[SBL][\text{H}_2\text{O}]^2} + \frac{[\text{RNH}_2]}{K_7K_8K_9[SBL][\text{H}_2\text{O}]} + \frac{1}{K_8K_9[SBL]} + \frac{1}{k_9}
\]

(2.24)
The rate equation (2.22) is in good agreement with the experimental results with first order dependence on $[\text{CAT}]_0$, fractional order in $[\text{SBL}]$ and an inverse fractional order in $[\text{OH}^-]$ and PTS ($\text{RNH}_2$) respectively. From equation (2.25), plot of $1/k'$ versus $1/[\text{SBL}]$ (Fig.2.8, $r=0.988$) at constant $[\text{SBL}]$ and temperature was found to be linear. The decomposition constant, $k_9$ was calculated from the intercept of the above plot ($k_9 = 2.5 \times 10^{-3}$ s$^{-1}$) for the standard run.

The effect of $[\text{SBL}]$ on the rate at different temperatures (298-313K) was studied (Table 2.6) and by plotting $1/k'$ vs $1/[\text{SBL}]$ (Fig 2.8, $r\geq 0.988$) values of decomposition constants $k_9$ were calculated. Activation parameters for the rate limiting step were computed from the Arrhenius plot of log $k_4$ vs $1/T$ (Fig. 2.7, $r=0.978$) yielded the activation parameters for the rate limiting step. These results are presented in Table 2.7. A comparison with the activation parameters obtained for the composite reaction in acidic and alkaline media shows that the values largely refer to the rate limiting step supporting the fact that reaction before the rate limiting step is fast, involving low activation energy.

The plausible mechanism for alkaline medium given in scheme 2.4. The effect of solvent on the reaction kinetics has been described by Laidler$^{25}$ and Amis$^{26}$. In the present investigation, a plot of log $k'$ versus $1/D$ was linear with a negative slope. This observation indicates the ion-dipole nature of the rate determining step in the reaction sequence and also points to extending of charge to the transition state.

The retardation of the rate by the added PTS and negligible influence of variation of ionic strength of the medium are in agreement with the proposed mechanism. The proposed mechanism is also supported by the moderate values of energy of activation and other thermodynamic parameters (Table 2.4). The moderate value of $\Delta H^\ddagger$ and the large negative value of $\Delta S^\ddagger$ indicate that, the transition state is more ordered than the reactants.
REFERENCES


