ABSTRACT: The kinetics of oxidation of quinoline and substituted quinolines viz. 7-hydroxyquinoline, 7-chloroquinoline and 7-aminoquinoline to the corresponding quinoline–N–oxide by Bromamine-B (BAB) have been studied at 303 K in HClO₄ medium. Under comparable experimental conditions, the reaction rate shows a first-order dependence each upon [BAB]₀ and [quinoline]₀, and less than unit order dependence on [H⁺]. Addition of benzenesulfonamide showed negligible effect on the reaction rate and the dielectric effect is positive. Variation of ionic strength of the medium does not influence the rate but the rate increases with increase in dielectric constant of the medium. The solvent isotope effect was studied using D₂O. The reaction was studied at different temperatures and activation parameters have been evaluated. The stoichiometry of the reaction was found to be 1: 1 and the oxidation products of quinolines were identified as their corresponding Quinoline –N – Oxide. The rate of oxidation of quinolines increases in the order: 7-hydroxyquinoline>7-aminoquinoline>quinoline>7-chloroquinoline. An isokinetic relationship was observed with β = 328 K, which showed the reaction to be enthalpy controlled. A mechanism consistent with the experimental results is proposed and the associated rate law has been deduced.

KEYWORDS: Oxidation, Quinolines, Bromamine – B, Acid medium

I. INTRODUCTION

The diverse nature of the chemistry of N-haloamines is a consequence of their ability to act as sources of species, such as halonium ions, hypohalites and N-anions which act as bases, nucleophiles and nitrenoids[1–5]. They behave as mild oxidants and are suitable for the limited oxidation of several groups. Consequently, these reagents react with a wide variety of functional groups affecting an array of molecular transformations. Generally, monohaloamines undergo two-electron change while dihaloamines are four-electron oxidants [1]. The reduction products are the respective sulfonamide and NaCl or HCl. The dominant members of this class of chlorocompounds are chloramine-T (CAT) and chloramine-B (CAB). A review of literature reveals that although the reaction of aromatic sulfonyl chloramines has been known and extensively
investigated, [6-9] there is not much of information available on the reaction of corresponding bromamines, bromamine-T and bromamine-B. Sodium N-bromobenzenesulfonamide or bromamine-B (BAB; C₆H₅SO₂NBrNa 1.5 H₂O BAB) has gained importance as a mild oxidant and it can be readily prepared by brominating CAB. Bromamine-B is found to be a most potential oxidant among these N-haloamines. There are but a very few reports on the kinetics of oxidation of organic substrates by BAB as compared to the studies with other haloamines as oxidants from mechanistic vision.

The catalyst by platinum group metal ions in redox reactions is of recent interest and it plays an important role in understanding the mechanism of redox reactions. Subsequently, various platinum group metal catalysts have been used in the N-haloamine oxidation of various organic substrates [10,11]. In particular, ruthenium (III) chloride (Ru(III)) have been found to be highly efficient catalysts in acid and alkaline media, respectively. Further, some of these systems have proved suitable for kinetic analysis. The mechanisms of these catalysts are complicated due to the formation of different intermediate complexes, free radicals and differing oxidizing states of these catalysts [12-15]. Preliminary experimental results revealed that a micro-quantity of Ru(III) catalyzes the oxidation of quinolines with BAB in acid and alkaline media, respectively in order to realize the reaction mechanism and the rate law of the present redox systems. Such studies also provide an insight into the interaction of metal ions with the drug in biological systems. Preliminary kinetic runs reveal that the reactions between quinoline and BAB were found to be ‘too slow’ to be measured in neutral, acidic and alkaline media at ambient temperature. Alternatively, it was found that Ru(III) are excellent catalysts for the facile oxidation of quinoline by BAB in acid media. To our knowledge, this is the first report on the kinetics and mechanism of oxidation of quinolines. Objectives of the present study are to (i) accumulate the kinetic data, (ii) elucidate plausible mechanisms, (iii) design kinetic ratelaws (iv) ascertain the reactive species, (v) deduce thermodynamic parameters, (vi) characterize the products. Quinoline nucleus is a backbone of many natural products and pharmacologically significant compounds displaying a broad range of biological activity. Many functionalized quinolines are widely used as antimalarial, anti-inflammatory, anti-asthmatic, antibacterial, antihypertensive and thyrokinase PDGF–RTE inhibiting agents [16]. As they are increasingly useful and important in drugs, quinoline antibiotics has gained wide acceptance for the treatment of various infectious to the larger extent. The new heterocycles show interesting chemical properties and they are attributed as potential antitumour reactants. Sadramycin and thiocoraline z natural depsipeptides which is 3 – hydroxyquinoline – 2-carboxylic acid plays a significant role in DNA binding properties of these compounds [17].

II. EXPERIMENTAL

Bromamine-B was prepared [18] by the partial debromination of dibromamine-B (DBB) as follows. Pure chlorine was bubbled through an aqueous solution of chloramine-B (30 g in 560 mL water) and liquid bromine (6 mL) was added dropwise with constant stirring. A yellow precipitate of DBB formed was washed well with H2O, filtered under suction, and dried in a vacuum desiccator. Dibromamine-B (31.5 g) was digested in batches with constant stirring in 50 mL of 4 mol dm⁻³ NaOH. The resulting mass was cooled in ice, filtered under suction, and the product (BAB) was dried over anhydrous calcium chloride. The purity of BAB was tested iodometrically through its active bromine content and its FT-IR spectrum. Aqueous solutions of BAB were prepared, standardized whenever required by the iodometric method and preserved in brown bottles to prevent its photochemical deterioration. Chloramine-B (E. Merck) was used as received. Aqueous solutions of BAB were kept in brownbottles to avoid any photochemical deterioration. Quinolines were of adequate grades of purity; quinoline, 2-hydroxyquinoline, 2-chloroquinoline and 2-aminoquinoline (Sigma) were used as received. Solvent isotope studies were made with D₂O (99.4 %) supplied by BARC, Mumbai, India. Analytical grade chemicals and double distilled water was used throughout.

2. KINETIC PROCEDURE

Reactions were carried out under pseudo first-order conditions ([quinoline] >> [oxidant],) at 30±0.1°C in glass-stoppered Pyrex boiling tubes whose outersurface was coated black to eliminate any photochemical effects. The oxidant and requisite amounts of solutions of the substrate, HClO₄ and water (to keep the total volume constant (50 ml) for all runs) were taken in separate boiling tubes and thermostatted for 30 minutes at 30±0.1°C. The reaction was initiated by therapid addition of a measured amount of BAB solution to the mixture which was shaken intermittently to maintain uniform concentration. The
progress of reaction was monitored by iodometric titration of unconsumed BAB in known aliquots (5 ml each) of the reaction mixture withdrawn at regular time intervals. Their reactions were followed for more than two half-lives. The pseudo first-order rate constants (k, s⁻¹), calculated from the linear plots of log [BAB] versus time, were reproducible within ±4%. The regression coefficient r of the experimental data was calculated using an fx-350TL scientific calculator.

3. STOICHIOMETRY

Different sets of reaction mixtures containing different amounts of oxidant and substrate, in the presence of 0.1 mol dm⁻³ HClO₄ were kept for 24 h at 300 K. Iodometric determination of the unconsumed BAB indicated that one mole of oxidant was needed per mole of quinoline to give the corresponding Quinoline – N – Oxide, thus the stoichiometry is 1:1. The observed stoichiometry is

\[
\text{R}N + \text{O}^\cdot + \text{PhSO}_2\text{NBrNa} + \text{H}_2\text{O} \rightarrow \text{R}N - \text{N}_2 + \text{PhSO}_2\text{NH}_2 + \text{Na}^+ + \text{Br}^- \quad (1)
\]

Where R=H for quinoline, -OH for 7-hydroxyquinoline, -Cl for 7-chloroquinoline and -NH₂ for 7-aminoquinoline.

4. PRODUCT ANALYSIS

After completion of the reaction, the reaction products were neutralized with alkali and extracted with ether. The organic products were subjected to spot tests and chromatographic analysis (TLC technique), which revealed the formation of oxidation products of quinolines as the corresponding quinoline – N – Oxide. Their presence is confirmed by GC–MS analysis. GC–MS data was obtained on a 17A Shimadzu gas chromatograph with a QP-5050A Shimadzu mass spectrometer operating in electron-impact mode. The mass spectrum showed a molecular ion peak of 145 amu (figure 1) confirming quinoline – N – Oxide. It was also observed that there was no further oxidation of these products under the prescribed kinetic conditions. Benzenesulfonamide (BSA), the reduction product of BAB, was extracted with ethyl acetate and identified [19,20] by TLC using petroleum-ether-CHCl₃-1-butanol (2:2:1 v:v) as the solvent system and iodine as spray reagent (Rf=0.88). Further, the molecular ion peak of 157 amu (figure 2) confirmed benzenesulfonamide.

![Figure 1. GC-Mass spectrum of quinoline-N-oxide with its molecular ion peak at 145 amu](image)
RESULTS AND DISCUSSION

The kinetics of oxidation of quinoline and the three substituted quinolines by BAB was investigated at several initial concentrations of reactants in HClO$_4$ medium.

1. EFFECT OF REACTANTS CONCENTRATION ON THE RATE

Under pseudo first-order conditions of [quinolines]>>[BAB], at constant [quinoline], [HCl] and temperature, plots of log[BAB] versus time were found to be linear (r>0.9804), indicating a first order dependence of the reaction rate on [BAB]. The pseudo first-order rate constants, k', are listed in Table 1. The plots of log k'/ versus log [quinolines] are linear with slopes less than unity showing the fractional dependence with respect to [quinolines] in the range of substrate concentration [21].

2. EFFECT OF HClO$_4$, HALIDE ION AND BENZENESULFONAMIDE CONCENTRATIONS ON THE RATE

The rate increased with increase in [HClO$_4$] (Table 1) and plots of log k' versus log [HClO$_4$] were linear (r>0.9951) with fractional slopes (0.70 – 0.85), showing a fractional order dependence of the rate on [HClO$_4$]. The rate increased with increase in [H$^+$] (Table 1). However, addition of Br$^-$ ions in the form of NaBr (5.06 x 10$^{-3}$ mol dm$^{-3}$) did not influence the rate. Addition of benzenesulfonamide (BSA or PhSO$_2$NH$_2$) to the reaction mixture did not alter the rate of the reaction indicating that PhSO$_2$NH$_2$ is not involved in a fast pre-equilibrium prior to the rate-determining step.
Table 1: Effect of concentrations of oxidant, substrate and HClO₄ on the rate at 303K

<table>
<thead>
<tr>
<th>10⁻⁴ [BAB] (mol/dm³)</th>
<th>10⁻³ [substrate] (mol/dm³)</th>
<th>10⁻³ [HClO₄] (mol/dm³)</th>
<th>2-chloro quinoline</th>
<th>2-amino quinoline</th>
<th>2-hydroxy quinoline</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>1.7</td>
<td>4.8</td>
<td>2.15</td>
<td>2.93</td>
<td>5.35</td>
</tr>
<tr>
<td>1.0</td>
<td>1.7</td>
<td>4.8</td>
<td>2.22</td>
<td>2.82</td>
<td>5.30</td>
</tr>
<tr>
<td>1.5</td>
<td>1.7</td>
<td>4.8</td>
<td>2.16</td>
<td>2.88</td>
<td>5.32</td>
</tr>
<tr>
<td>3.2</td>
<td>1.7</td>
<td>4.8</td>
<td>2.18</td>
<td>2.80</td>
<td>5.28</td>
</tr>
<tr>
<td>5.0</td>
<td>1.7</td>
<td>4.8</td>
<td>2.17</td>
<td>2.86</td>
<td>5.35</td>
</tr>
<tr>
<td>1.5</td>
<td>0.6</td>
<td>4.8</td>
<td>0.64</td>
<td>0.86</td>
<td>1.59</td>
</tr>
<tr>
<td>1.5</td>
<td>1.0</td>
<td>4.8</td>
<td>1.13</td>
<td>1.50</td>
<td>2.77</td>
</tr>
<tr>
<td>1.5</td>
<td>1.7</td>
<td>4.8</td>
<td>2.16</td>
<td>2.88</td>
<td>5.32</td>
</tr>
<tr>
<td>1.5</td>
<td>3.5</td>
<td>4.8</td>
<td>4.17</td>
<td>5.57</td>
<td>10.3</td>
</tr>
<tr>
<td>1.5</td>
<td>5.2</td>
<td>4.8</td>
<td>6.30</td>
<td>8.41</td>
<td>15.5</td>
</tr>
<tr>
<td>1.5</td>
<td>1.7</td>
<td>0.8</td>
<td>0.67</td>
<td>0.90</td>
<td>1.66</td>
</tr>
<tr>
<td>1.5</td>
<td>1.7</td>
<td>2.5</td>
<td>1.10</td>
<td>1.47</td>
<td>2.71</td>
</tr>
<tr>
<td>1.5</td>
<td>1.7</td>
<td>4.8</td>
<td>2.16</td>
<td>2.88</td>
<td>7.85</td>
</tr>
<tr>
<td>1.5</td>
<td>1.7</td>
<td>8.0</td>
<td>3.71</td>
<td>4.95</td>
<td>10.1</td>
</tr>
<tr>
<td>1.5</td>
<td>1.7</td>
<td>12.0</td>
<td>5.26</td>
<td>7.02</td>
<td>11.2</td>
</tr>
</tbody>
</table>

3. Effect of dielectric constant of the medium on the rate

In order to elucidate the nature of the reactive species, the dielectric constant (D) of the medium was varied by adding MeOH (0 – 30% v/v) to the reaction mixture with all other experimental conditions being held constant (Table 2). The plots of log \( k \) versus 1/D were linear (r > 0.9905) with positive slopes. Blank experiments showed that the oxidation of MeOH by BAB under the experimental conditions employed is negligible (51%). Values of the dielectric constant of MeOH-H₂O mixtures reported in the literature [22] were employed.
Table 2 Effect of dielectric constant on rate at 303K

<table>
<thead>
<tr>
<th>%CH₂OH v/v</th>
<th>D</th>
<th>2-chloro quinoline</th>
<th>quinoline</th>
<th>2-amno quinoline</th>
<th>2-hydroxy quinoline</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>76.7</td>
<td>2.16</td>
<td>2.88</td>
<td>5.32</td>
<td>7.85</td>
</tr>
<tr>
<td>5</td>
<td>74.5</td>
<td>2.37</td>
<td>3.16</td>
<td>5.75</td>
<td>9.67</td>
</tr>
<tr>
<td>10</td>
<td>72.4</td>
<td>2.74</td>
<td>3.66</td>
<td>6.77</td>
<td>11.5</td>
</tr>
<tr>
<td>20</td>
<td>69.7</td>
<td>3.42</td>
<td>4.57</td>
<td>8.45</td>
<td>13.8</td>
</tr>
<tr>
<td>30</td>
<td>62.7</td>
<td>4.41</td>
<td>5.88</td>
<td>10.8</td>
<td>27.5</td>
</tr>
</tbody>
</table>

4. Effect of Ionic Strength of the Medium on the Rate
The effect of the ionic strength of the medium was studied by varying the sodium perchlorate concentration in a range of 0.10 – 0.30 mol dm⁻³ by keeping the other experimental conditions constant. It was found that ionic strength has a negligible effect on the reaction rate. Hence, the ionic strength of the system was not kept constant for kinetic runs.

5. Effect of Temperature on the Rate
The effect of temperature on the rate was studied by performing kinetic runs at different temperatures, in the range of 293 to 313K keeping other experimental conditions constant. From the linear Arrhenius plots of log k' versus 1/T (r > 0.9963), values of activation parameters (Eₐ, ΔH°, ΔS°, ΔG°) for the overall reaction were computed. These data are summarized in Table 3.
Table 3 Effect of temperature on rate and activation parameters for oxidation of quinolines by BAB in acid medium

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>2-chloro quinoline</th>
<th>2-amino quinoline</th>
<th>2-hydroxy quinoline</th>
</tr>
</thead>
<tbody>
<tr>
<td>293</td>
<td>1.08</td>
<td>1.44</td>
<td>2.66</td>
</tr>
<tr>
<td>298</td>
<td>1.46</td>
<td>1.95</td>
<td>3.60</td>
</tr>
<tr>
<td>303</td>
<td>2.16</td>
<td>2.88</td>
<td>5.32</td>
</tr>
<tr>
<td>308</td>
<td>2.94</td>
<td>3.92</td>
<td>7.25</td>
</tr>
<tr>
<td>313</td>
<td>4.65</td>
<td>6.21</td>
<td>11.4</td>
</tr>
</tbody>
</table>

$E_a$(kJ mol$^{-1}$) | 55.5 | 53.6 | 45.9 | 38.3 |
$\Delta H^\ne$ (kJ mol$^{-1}$) | 51.1 | 54.9 | 53.0 | 35.8 |
$\Delta S^\ne$ (JK$^{-1}$ mol$^{-1}$) | -162 | -175 | -180 | -202 |
$\Delta G^\ne$ (kJ mol$^{-1}$) | 65.9 | 71.6 | 63.4 | 91.8 |
Log A | 8.64 | 9.43 | 9.7 | 9.2 |

6. TEST FOR FREE RADICALS
Addition of an aqueous solution of acrylamide to the reaction mixture did not cause polymerization. This suggests the absence of free radical involvement during the oxidation reaction.

IV. DISCUSSION

1. Reactive species of BAB
Organic haloamines have homogeneous chemical properties and hence it is expected that similar equilibria exist in solutions of these compounds. [23-25] Bromamine-B, which is analogous to Chloramine-T and Chloramine-B, behaves like a strong electrolyte both in acidic and alkaline media. The oxidation potential of BAB/ PhSO$_2$NH$_2$ is pH dependent and decreases with increase in the pH of the medium (1.4 V at pH 0.65 and 0.50 V at pH 12.0). In acid solutions, BAB exists in the following equilibria:
The possible oxidizing species in acidified BAB solutions are therefore the free acid (PhSO₂NHBr), dibromamine-B (PhSO₂NBr₂), hypobromous acid (HOBr) and possibly H₂O⁻Br. The involvement of PhSO₂NBr₂ in the mechanism should correspond to a second-order rate law, which is contrary to the experimental observations. If HOBr were the primary oxidizing species, a first-order retardation of the rate by the added benzenesulfonamide would be expected, which is conflicting the investigations. Since pKa of PhSO₂NHBr is 4.95 at 298 K, it is likely that under the present acidic conditions BAB may exist primarily as PhSO₂NHBr and any dependence of rate on [H⁺] could be attributed to the addition of a second proton to PhSO₂NHBr. Furthermore, Narayanan and Rao [26] and Subhashini et al [27] have reported that monochloramines can be further protonated at pH 2 as shown in eq. (9) and for chloramine-T and chloramine-B, respectively

\[
\text{PhSO}_2\text{NHCl} + \text{H}^+ \rightarrow (\text{PhSO}_2\text{N}{\text{H}_2}\text{Cl})^+ \quad (9)
\]

The second protonation constants for CAT and CAB are 102 M⁻¹ and 61 ± 5 M⁻¹ respectively at 300 K. Because organic haloamines have similar chemical properties, it is reasonable to expect the formation of an identical species of the type PhSO₂NBr⁺ for BAB also. In the present investigations, the acceleration of rate by H⁺ ion indicates that PhSO₂NBr⁺ is the active oxidizing species. Further, variations of ionic strength of the medium or addition of the reaction product, benzenesulfonamide have virtually no effect on the rate.

2. REACTION SCHEME AND KINETIC RATE LAW

Based on the experimental results Scheme 1 is proposed to explain the reaction mechanism for the oxidation of quinolines and 2–substituted quinolines by BAB in HClO₄ medium.

PhSO₂NHBr + H⁺ \[\overset{K_1}{\longrightarrow}\] PhSO₂NH₂Br⁺ (i) fast

PhSO₂NH₂Br⁺ + S \[\overset{k_2}{\longrightarrow}\] X + PhSO₂NH₂ (ii) slow & rds

X + H₂O \[\overset{k_3}{\longrightarrow}\] Products + HBr (iii) fast

The structure of the complex intermediate species (X) is shown in Scheme 2 where a detailed mechanistic interpretation of the quinolines –BAB reaction in HClO₄ medium is presented.
From steps (i) and (ii) of Scheme 1, the following rate law (10) is obtained,

\[
\text{rate} = \frac{K_1 k_2 [\text{BAB}][\text{quinoline}][H^+]}{1 + K_3[H^+]} \tag{10}
\]

Rate law (10) is in good agreement with the experimental results, wherein a first-order dependence each on [BAB] and [quinoline], and fractional-order on [H^+] was observed.

3. EFFECT OF SOLVENT ISOTOPE ON THE RATE:
A dependence of the rate on the H^+ ion concentration having been noted, solvent isotope studies of the rate in D_2O for quinoline and 2-hydroxy quinoline revealed that \( k/(H_2O) = 2.88 \times 10^{-4} \text{s}^{-1} \) and \( 1.78 \times 10^{-4} \text{s}^{-1} \), and \( k/(D_2O) = 3.25 \times 10^{-4} \text{s}^{-1} \) and \( 16.2 \times 10^{-4} \text{s}^{-1} \), respectively. The solvent isotope effect \( k/(H_2O)/k/(D_2O) = 0.81 \) and 0.83 for two quinolines. [28,29]

4. ISOKINETIC RELATIONSHIP
The relative magnitudes of the activation energies for the oxidation of quinolines in Table 3, which concur with the preceding trend, indicate that the reactions are enthalpy controlled. This is verified by calculating the isokinetic temperature \( \beta \) from the slope of the linear plot of \( \Delta H^\ne \) versus \( \Delta S^\ne \) (Figure 3: \( r = 0.9887 \)). The \( \beta \) value of 331 K, which is higher than the experimental range used in the present study, implies that the quinoline oxidation is enthalpy controlled. A further confirmation of the existence of the isokinetic relationship was inferred from the Exner criterion [31], by plotting log
\( k'_{(293)} \) versus \( \log k'_{(303)} \), which yielded a linear plot. The Exert slope gave a value of \( \beta \) 328 K. The large negative values of \( \Delta S^\neq \) indicate the formation of a more ordered, rigid associative transition state in each case. The change in the ionic strength of the medium did not alter the rate indicating that non-ionic species were involved in the rate-determining step. All these observations are also in conformity with the proposed mechanism and the derived rate law.

**Figure 3.** Isokinetic plots of (a) \( \Delta H^\neq \) vs. \( \Delta S^\neq \), (b) \( \log k'_{(293 \text{ K})} \) vs. \( \log k'_{(303 \text{ K})} \). Experimental conditions are as in Table 3.

**V. CONCLUSION**

The kinetics of oxidation of quinoline and three substituted quinolines viz.: 7-hydroxyquinoline,7-aminoquinoline, quinoline, 7-cloroquinoiline to the corresponding quinoline-N-oxide by BAB have been studied at 303 K. The reaction follows identical kinetics for all the quinolines studied and obeys the rate law where \( x, y \) and \( z \) is less than unity. Activation parameters and isokinetic temperature were deduced. On the basis of the experimental results a suitable mechanism and appropriate rate law have been derived.

**REFERENCES**


