N-Oxidation of Pyrazines by Bromamine-B in Perchloric Acid Medium: Kinetic and Mechanistic Approach

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Kinetic investigations on the oxidation of pyrazine and four 2-substituted pyrazines viz., 2-methylpyrazine, 2-ethylpyrazine, 2-methoxypyrazine and 2-aminopyrazine by bromamine-B (BAB) to the respective N-oxides have been studied in HClO₄ medium at 303 K. The reactions show identical kinetics being first-order each in [BAB]₀ and [pyrazine]₀, and a fractional- order dependence on [H⁺]. Effect of ionic strength of the medium and addition of benzenesulfonamide or halide ions showed no significant effect on the reaction rate. The dielectric effect is positive. The solvent isotope effect was studied using D₂O. The reaction has been studied at different temperatures and activation parameters for the composite reaction have been evaluated from the Arrhenius plots. The reaction showed 1:1 stoichiometry and the oxidation products of pyrazines were characterized as their respective N-oxides. Under comparable experimental conditions, the oxidation rate of pyrazines increased in the order: 2-aminopyrazine > 2-methoxypyrazine > 2-ethylpyrazine > 2-methylpyrazine > pyrazine. The rates correlate with the Hammett σ relationship and the reaction constant ρ was found to be -0.8, indicating that electron donating centres enhance the rate of reaction. An isoenergetic temperature of β = 333 K, indicated that the reaction was enthalpy controlled. A mechanism consistent with the experimental results has been proposed in which the rate determining step is the formation of an intermediate complex between the substrate and the diprotonated species of the oxidant. The related rate law in consistent with observed results has been deduced.

Key Words: Pyrazines, Oxidation kinetics, Bromamine-B, Acid medium

Introduction

The chemistry of a class of N-metallo-N-haloarylsulfonamides, known as N-haloamines, attracted the attention of many investigators due to their diverse behaviour. Their versatile nature is attributed to their ability to act both as bases and nucleophiles.² As a result of this, these compounds interact with a wide range of functional groups in aqueous, partially aqueous and non-aqueous media in presence of acids or alkalies, bringing about an array of molecular transformations. Mono- and dihaloamines in general undergo two electron change while dihaloamines act as four electron oxidants. The reduction products obtained are the respective sulfonamide and sodium chloride.³ 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 have been known and extensively investigated,¹⁻³ there is not much of information⁴⁻¹¹ 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 potent oxidant among these N-haloamines. There are but a few reports¹²⁻¹⁴ on the kinetics of oxidation of organic substrates by BAB as compared to the studies with other haloamines as oxidants from mechanistic view point. For these reasons, it was felt interesting to investigate the mechanism of oxidations of the selected pyrazines with this reagent.

Pyrazines are important class of N-heterocycles. They have as tertiary amines and their properties resembles those of the pyridines.⁶ Pyrazines possess unique and extremely potent flavor and aroma characteristics.¹⁵,¹⁶ Some of the derivatives of pyrazines find use as pharmaceutical intermediates,¹⁷ marking volatiles,³ antifungal and antiviral agents⁴ and hence they find extensive applications in flavor and pharmaceutical industries. Mild oxidation of pyrazines to N-oxides find importance in synthetic organic chemistry and a considerable work has been carried out in this direction.²⁰⁻²⁴ These N-oxides are widely used in the synthesis of various organic compounds and as bioreductive drugs.²⁵,²⁶ From the literature survey it was found there was no information available on the oxidation of pyrazines brought about by oxidants with regards to the kinetic and mechanistic points of view. Therefore, the mechanism and rate law for this redox system were obscure. Hence, the oxidation of pyrazines with these view points adds much to the knowledge of redox chemistry. These facts prompted us to undertake the title investigation.

Our preliminary kinetic studies revealed that the reactions between pyrazines and chloroamines were too slow to be measured in neutral, acidic and alkaline media at ambient temperature. Further kinetic runs also indicated that BAB is an excellent oxidant in effecting controlled conversion of pyrazines to N-oxides in presence of perchloric acid. Optimum conditions for the formation of N-oxides have been established. In view of these observations, a systematic kinetic and mechanistic study of the oxidation of pyrazine and 2-substituted pyrazines namely 2-methylpyrazine, 2-ethylpyrazine, 2-methoxypyrazine and 2-aminopyrazine brought about by BAB in perchloric acid medium at 303 K have been carried out. Objectives of the present
investigations are to (i) compile kinetic data, (ii) establish optimum conditions affecting mild oxidation of pyrazines to N-oxides, (iii) elucidate plausible mechanism, (iv) propose an appropriate kinetic model, (v) ascertain the reactive species, (vi) know the stoichiometry and to characterize the oxidation products, (vii) assess the relative rates of oxidation of pyrazines towards BAB, (viii) establish the isokinetic relationship from thermodynamic parameters and (ix) ascertain structure reactivity relationship.

**Experimental**

**Materials.** Bromamine-B was prepared\(^{27}\) 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 \(\text{H}_2\text{O}\), 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\(^{-3}\) \(\text{NaOH}\). 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 the 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.\(^{28}\) Pyrazines (Aldrich) of acceptable grades of purity were used without further purification. Fresh aqueous solutions of pyrazines were prepared whenever required. Heavy water (\(\text{D}_2\text{O}, 99.4\%)\) for solvent isotope studies was obtained from Bhabha Atomic Research Center, India. All other chemicals used were of analytical grade and double distilled water was used throughout the work.

**Kinetic Procedure.** Detailed kinetic runs were performed under pseudo-first order conditions of [pyrazine], \(\gg\) [oxidant], at a standard temperature of 30 ± 0.1 °C in glass stoppered pyrex boiling tubes whose outer surface was coated black to eliminate photochemical effects if any. The BAB and requisite amounts of solutions of the pyrazine, \(\text{HClO}_4\) and water (to keep the total volume constant (50 mL) for all runs) were taken in separate boiling tubes and thermostatted at 30 ± 0.1 °C till thermal equilibrium. The reaction was initiated by the rapid addition of a measured amount of BAB solution to the mixture and was shaken intermittently for uniform concentration. The progress of the reaction was monitored iodometrically by titration of unreacted BAB in known aliquots (5 mL each) of the reaction mixture withdrawn at regular time intervals. The re-}

**Stoichiometry.** Reaction mixtures having different proportions of BAB and pyrazines were equilibrated at 303 K in presence of \(5.0 \times 10^{-2}\) mol dm\(^{-3}\) \(\text{HClO}_4\) for 24 h and then analyzed. The unreacted BAB in the reaction mixture was determined iodometrically which indicated that one mole of pyrazine consumed one mole of BAB to give the corresponding N-oxide, which is stoichiometrically represented as:

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

Here R = H for pyrazine, -\(\text{CH}_3\) for 2-methylpyrazine, -\(\text{C}_2\text{H}_5\) for 2-ethylpyrazine, -\(\text{OCH}_3\) for 2-methoxypyrazine and -\(\text{NH}_2\) for 2-aminopyrazine.

**Product Analysis.** The reaction mixture in the stoichiometric ratio in presence of \(\text{HClO}_4\) under stirred condition was allowed to progress for 24 h at 303 K. After completion of the reaction (monitored by TLC), the reaction mixture was neutralized and the products were extracted with ether. The organic products were subjected to spot tests and chromatographic analysis (TLC technique). The products corresponded to N-oxides as the oxidation products of pyrazines. Pyrazine-1-oxide, 2-methylpyrazine-1-oxide, 2-methoxypyrazine-1-oxide, 2-aminopyrazine-1-oxide and 2-ethylpyrazine-1-oxide are the oxidation products of pyrazine, 2-methylpyrazine, 2-methoxypyrazine, 2-aminopyrazine and 2-ethylpyrazine, respectively. Pyrazine-1-oxide and 2-methylpyrazine-1-oxide were confirmed by GC-MS analysis. GC-MS data was obtained on a 17A Shimadzu gas chromatograph with QP-5050A Shimadzu mass spectrometer. The mass spectra showed a molecular ion peak at 96 and 110 amu clearly confirms pyrazine-1-oxide and 2-methylpyrazine-1-oxide, respectively (Figures 1 and 2). All other peaks observed in GC-MS are interpreted in accordance with the observed structure. Pyrazine-N-oxide obtained from pyrazine was extracted with ether and was quantitatively estimated. The recovery of pyrazine-N-oxide was found to be 72.9%. No further oxidation of these products was observed under the chosen kinetic conditions.

Benzenesulfonamidem, a reduction product of BAB, was also extracted with ethyl acetate and identified\(^{29}\) by TLC using pet-ether-\(\text{CHCl}_3\)-1-butanol (2:2:1, v/v) as a solvent system and iodine as a spray reagent (\(R_f = 0.88\)). It was further confirmed by GC-MS which showed a molecular ion peak of 157 amu (Figure 3).

**Results and Discussion**

**Kinetic Orders.** The kinetics of oxidation of pyrazine and substituted pyrazines by BAB was investigated at several different initial concentrations of the reactants in \(\text{HClO}_4\) medium. Under comparable experimental conditions, the similar oxidation kinetic behaviour was observed for all the pyrazines studied. The kinetic data obtained are presented in Table 1. Under pseudo-first-order conditions of [pyrazine], \(\gg\) [BAB], at constant [pyrazine], [\(\text{HClO}_4\)] and temperature, plots of log [BAB] vs. time were linear (\(r > 0.9904\)), showing a first-order dependence of the rate on [BAB]. The values of pseudo-first-order rate constants, \(k\) (s\(^{-1}\)), are given in Table 1. The values of \(k\) remain unaffected with a change in [BAB], confirming the first-order
dependence on \([\text{BAB}]_o\). The rate increased with increase in \([\text{pyrazine}]_o\) (Table 1). Plots of \(\log k\) vs. \(\log [\text{pyrazine}]_o\) were linear \((r > 0.9945)\) with unit slopes, indicating the first-order dependence of rate on \([\text{pyrazine}]_o\). Further, plots of \(k/\) vs. \([\text{pyrazine}]_o\) gave straight lines \((r > 0.9802)\) passing through the origin, substantiating a first-order dependence of rate on \([\text{pyrazine}]_o\). Furthermore, the second order rate constants \(k' = k/\) [pyrazine]o were nearly the same for all the pyrazines except 2-methylpyrazine, establishing the first-order dependence of rate on \([\text{pyrazine}]_o\), and also the reaction intermediates formed were of transient existence \((k'/\) values are not reported).

Effect of HClO4 and Halide Ion Concentrations on the Rate. The reaction rate increased with an increase in \([\text{HClO}_4]_o\) (Table 1) and plots of \(\log k\) vs. \(\log [\text{HClO}_4]_o\) were linear \((r > 0.9804)\) with fractional slopes \((0.51 \sim 0.71)\), showing a fractional-order dependence of the rate on \([\text{HClO}_4]_o\). Addition of \(\text{Br}^-\) or \(\text{Cl}^-\) ions in the form of NaBr or NaCl \((5.0 \times 10^{-3} \text{ mol dm}^{-3})\) did not alter the rate of the reaction, suggesting that neither interhalogen nor free bromine was formed during the reaction sequence.

Effect of Benzenesulfonamide and Ionic Strength on the Rate. Addition of benzenesulfonamide \((\text{PhSO}_2\text{NH}_2)\) to the reaction mixture \((5.0 \times 10^{-3} \text{ mol dm}^{-3})\) had no effect on the rate. This is indicative of non-involvement of \(\text{PhSO}_2\text{NH}_2\) in any step prior to the rate determining in the scheme proposed (Scheme 1). The effect of ionic strength on the reaction rate was carried out in presence of 0.1 mol dm\(^{-3}\) sodium perchlorate, keeping all other experimental conditions constant. It was noticed that the ionic strength had negligible effect on the

Table 1. Effect of Varying BAB, Pyrazine and HClO4 Concentrations on the Reaction Rate at 303 K

<table>
<thead>
<tr>
<th>(10^4[\text{BAB}]_o) mol dm(^{-3})</th>
<th>(10^3[\text{pyrazine}]_o) mol dm(^{-3})</th>
<th>(10^3[\text{HClO}_4]_o) mol dm(^{-3})</th>
<th>(10^4k) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>1.8</td>
<td>5.0</td>
<td>3.90 ± 0.13</td>
</tr>
<tr>
<td>1.0</td>
<td>1.8</td>
<td>5.0</td>
<td>3.75 ± 0.09</td>
</tr>
<tr>
<td>1.6</td>
<td>1.8</td>
<td>5.0</td>
<td>3.84 ± 0.11</td>
</tr>
<tr>
<td>3.0</td>
<td>1.8</td>
<td>5.0</td>
<td>3.81 ± 0.13</td>
</tr>
<tr>
<td>5.0</td>
<td>1.8</td>
<td>5.0</td>
<td>3.92 ± 0.03</td>
</tr>
<tr>
<td>1.6</td>
<td>0.5</td>
<td>5.0</td>
<td>1.15 ± 0.05</td>
</tr>
<tr>
<td>1.6</td>
<td>1.0</td>
<td>5.0</td>
<td>2.01 ± 0.13</td>
</tr>
<tr>
<td>1.6</td>
<td>1.8</td>
<td>5.0</td>
<td>3.84 ± 0.16</td>
</tr>
<tr>
<td>1.6</td>
<td>3.6</td>
<td>5.0</td>
<td>7.43 ± 0.39</td>
</tr>
<tr>
<td>1.6</td>
<td>5.2</td>
<td>5.0</td>
<td>11.2 ± 0.03</td>
</tr>
<tr>
<td>1.6</td>
<td>1.8</td>
<td>1.0</td>
<td>1.20 ± 0.06</td>
</tr>
<tr>
<td>1.6</td>
<td>1.8</td>
<td>2.0</td>
<td>1.97 ± 0.14</td>
</tr>
<tr>
<td>1.6</td>
<td>1.8</td>
<td>5.0</td>
<td>3.84 ± 0.15</td>
</tr>
<tr>
<td>1.6</td>
<td>1.8</td>
<td>10.0</td>
<td>6.60 ± 0.15</td>
</tr>
<tr>
<td>1.6</td>
<td>1.8</td>
<td>15.0</td>
<td>9.36 ± 0.21</td>
</tr>
</tbody>
</table>
reaction rate, suggesting the involvement of non-ionic species in the rate determining step. Subsequently, no attempt was made to keep ionic strength constant during kinetic runs.

**Effect of Dielectric Constant of the Medium on the Rate.** In order to find out the nature of reactive species, the dielectric constant (D) of the medium was varied by adding MeOH (0 - 30% v/v) to the reaction mixture keeping all other experimental conditions constant. The rate increased with increase in MeOH content (Table 2). Plots of log \( k \) vs. \( 1/D \) were linear (Figure 4: \( r > 0.9905 \)) with positive slopes. There was no reaction of the dielectric with the oxidant under the prevailing experimental conditions. Values of dielectric constant of MeOH-H\(_2\)O mixture reported in the literature\(^{20} \) were used.

**Effect of Solvent Isotope on the Rate.** As the rate was dependent on [H\(^+\)], solvent isotope studies were made in D\(_2\)O medium with pyrazine as a probe. Values of k (H\(_2\)O) and k (D\(_2\)O) were 3.84 \( \times \) 10\(^{-4} \) and 4.70 \( \times \) 10\(^{-4} \) s\(^{-1} \), respectively, giving a solvent isotope effect, \( k (\text{H}_2\text{O}) / k (\text{D}_2\text{O}) = 0.82 \).

**Effect of Temperature on the Rate.** The effect of temperature on the rate was studied by conducting the kinetic experiments at 293, 298, 303, 308 and 313 K, keeping other experimental conditions constant. From the linear Arrhenius plots of log \( k \) vs. 1/T (\( r > 0.9907 \)), activation parameters (\( E_a, \Delta H^\neq, \Delta S^\neq, \Delta G^\neq \) and log A) for the overall reaction were computed and the results are summarized in Table 3.

**Polymerization Study.** Addition of the reaction mixture to the acrylamide monomer did not initiate polymerization indicating the absence of any free radicals produced during the course of reaction.

**Reactive Species of BAB.** Organic haloamines have homogeneous chemical properties and hence it is expected that similar equilibria exist in solutions of these compounds.\(^{28,31,33} \) Bromamine-B, which is analogous to chloramine-T and chloramine-B, behaves like a strong electrolyte both in acidic and alkaline media.\(^{31} \) 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:

\[
\text{PhSO}_2\text{NBrNa} \rightleftharpoons \text{PhSO}_2\text{NBr}^- + \text{Na}^+ \quad (2)
\]

\[
\text{PhSO}_2\text{NBr}^- + \text{H}^+ \rightleftharpoons \text{PhSO}_2\text{NHBr} \quad (3)
\]

**Table 2.** Effect of Varying Dielectric Constant (D) of Medium on the Reaction Rate at 303 K

<table>
<thead>
<tr>
<th>% CH(_3)OH v/v</th>
<th>D</th>
<th>( 10^4 ) k (s(^{-1} ))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>pyrazine 2-methyl pyrazine 2-ethyl pyrazine 2-methoxy pyrazine 2-amino pyrazine</td>
</tr>
<tr>
<td>0</td>
<td>76.7</td>
<td>3.84 ± 0.08</td>
</tr>
<tr>
<td>5</td>
<td>74.5</td>
<td>4.22 ± 0.06</td>
</tr>
<tr>
<td>10</td>
<td>72.4</td>
<td>4.89 ± 0.12</td>
</tr>
<tr>
<td>20</td>
<td>69.7</td>
<td>6.10 ± 0.05</td>
</tr>
<tr>
<td>30</td>
<td>67.5</td>
<td>7.85 ± 0.31</td>
</tr>
</tbody>
</table>

\([\text{BAB}]_o = 1.6 \times 10^{-4} \text{ mol dm}^{-3}; [\text{pyrazine}]_o = 1.8 \times 10^{-3} \text{ mol dm}^{-3}; [\text{HClO}_4] = 5.0 \times 10^{-3} \text{ mol dm}^{-3} \).
N-Oxidation of Pyrazines

2 PhSO2NHBBr $\rightleftharpoons$ PhSO2NH2 + PhSO2NBr2 (4)

PhSO2NBr2 + H2O $\rightleftharpoons$ PhSO2NHBBr + HOBr (5)

PhSO2NHBBr + H2O $\rightleftharpoons$ PhSO2NH2 + HOBr (6)

HOBr $\rightleftharpoons$ H+ + OBr$^-$ (7)

HOBr + H+ $\rightleftharpoons$ H2O+Br (8)

The possible oxidizing species in acidified BAB solutions are therefore the free acid (PhSO2NHB), 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 reaction by the added benzesulfonylamide would be expected, which is contradictory to the observed experimental results. Since pKa of PhSO2NHB is 4.95 at 298 K, it is likely that under the present acidic conditions BAB may exist primarily as PhSO2NHB and any dependence of rate on [H+] could be attributed to the addition of a second proton to PhSO2NHB. Furthermore, Narayanan and Rao$^{34}$ and Subhashini et al$^{35}$ have reported that monochloramines can be further protonated at pH 2 as shown in eq. (9) and eq. (10) for chloramine-T and chloramine-B, respectively.

p-CH3C6H4SO2NHCl + H+ $\rightleftharpoons$ (p-CH3C6H4SO2NH2Cl)$^+$ (9)

PhSO2NHCl + H+ $\rightleftharpoons$ (PhSO2NH2Cl)$^+$ (10)

The second protonation constants for CAT and CAB are 102 M$^{-1}$ and 61 ± 5 M$^{-1}$ respectively at 298 K. Because organic haloamines have similar chemical properties, it is reasonable to expect the formation of an identical species of the type PhSO2NH2Br$^+$ for BAB also. In the present investigations, the acceleration of rate by H$^+$ ion indicates that PhSO2NH2Br$^+$ is the active oxidizing species. Further, variations of ionic strength of the medium or addition of the reaction product, benzene-sulfonylamine have virtually no effect on the rate. Based on the preceding discussion and experimental facts, Scheme 1 is proposed to explain the reaction mechanism for the oxidation of pyrazines by BAB in HClO4 medium.

A detailed mode of oxidation of pyrazines by BAB in acid medium and the structure of intermediate are depicted in Scheme 2. In Scheme 2, an initial equilibrium involves protonation of PhSO2NHBBr forming the active oxidizing species of BAB, PhSO2NH2Br$^+$ (step (i)). In the next slow/rate determining step (step (ii)), nucleophilic attack on the positive bromine of PhSO2NH2Br$^+$ by a lone pair of electrons on nitrogen atom of pyrazine, results in the formation of a complex cation X with the elimination of PhSO2NH2. In the next step (step (iii)), followed by several fast steps, the complex cation X undergoes hydrolysis leading to the formation of N-oxide with the elimination of HBr.

If [BAB]$\text{eq}$ is the total effective concentration of BAB, then

\[
[BAB]\text{eq} = [\text{PhSO2NHB}]+ [\text{PhSO2NH2Br}^+] \tag{11}
\]

\[
\text{PhSO2NHB} + H^+ \rightleftharpoons \text{PhSO2NHBr}^+ \quad \text{(i) fast}
\]

\[
\text{PhSO2NHBr}^+ + \text{Pyrazine} \rightarrow X + \text{PhSO2NH}_2 \quad \text{(ii) slow and rds}
\]

\[
X + \text{H}_2\text{O} \rightarrow \text{Products} + \text{HBr} \quad \text{(iii) fast}
\]

Scheme 1. A general reaction scheme for the oxidation of pyrazines by BAB in HClO4 medium

From steps (i) and (ii) of Scheme 1, the following rate law (12) is obtained,

\[
\text{rate} = \frac{K_1 k_2 \text{[BAB]} \text{[pyrazine]} [H^+]}{1 + K_1 [H^+]} \tag{12}
\]

Rate law (12) is in good agreement with the experimental results, wherein a first-order dependence each on [BAB], and [pyrazine], and fractional-order on [H$^+$] was observed.

Since, rate $= k'$ [BAB]$\text{eq}$, eq. (12) can be transformed as:

\[
k' = \frac{K_1 k_2 \text{[pyrazine]} [H^+]}{1 + K_1 [H^+]} \tag{13}
\]

\[
\frac{1}{k'} = \frac{1}{K_1 k_2 \text{[pyrazine]} [H^+]} + \frac{1}{k_2 \text{[pyrazine]}} \tag{14}
\]

Based on eq. (14), plots of 1/k$'$ vs. 1/[H$^+$] (values are taken from Table 1) at constant [BAB]$\text{eq}$, [pyrazine]$\text{eq}$, and temperature
has been found to be fairly linear (Figure 5: $r > 0.9576$) for each pyrazine. The protonation constants ($K_i$) of PhSO2NHBr and the decomposition constant ($k_d$) were calculated from slope and intercept of these plots for the standard run with $[\text{BAB}]_o = 1.6 \times 10^{-4} \text{ mol dm}^{-3}$; $[\text{pyrazine}]_o = 1.8 \times 10^{-3} \text{ mol dm}^{-3}$ at 303 K. Further the values of deprotonation constant, $K_i' = 1/K_i$ were also determined. All these values are presented in Table 4. The proposed mechanism and the rate law derived are supported by the experimental findings given below.

**Solvent Isotope Effect.** Reactions in aqueous medium that are susceptible to acid-base catalysis have been studied in heavy water (D2O) after equilibrium. Since most oxidation reactions of organic compounds involve the cleavage of C-H bond, deuterium isotope effect on such reactions gives information regarding the nature of the rate determining step. In the present investigations, solvent isotope studies have shown that the rate of reaction is higher in D2O medium. For a reaction involving a fast equilibrium H$^+$ or OH$^-$ ion transfer, the rate increases in D2O medium since D$_2$O or OD$^-$ are a stronger acid and a stronger base, respectively, than H$_2$O and OH$^-$ ions. The observed solvent isotope effect of $k$ (H$_2$O) / $k$ (D$_2$O) < 1 is due to the greater acidity of D$_2$O compared to H$_2$O. However, the magnitude of increase in rate in D$_2$O is small (expected value is 2 ± 3 times greater). This may be due to the fractional order dependence of rate on [H$^+$]. Hence, this observation supports the proposed mechanism.

**Dielectric Constant Effect.** A change in solvent composition by varying methanol content affects the reaction rate. The effect of solvent on the reaction kinetics has been described in detail in the well-known monographs of Moelwyn-Hughes, Benson, Frost and Pearson, Laidler and Amis. For the limiting case of zero angle of approach between two dipoles or an ion-dipole system, Amis has shown that a plot of log $k$ vs. 1/D gives a straight line with a negative slope for a reaction involving a negative ion and a dipole or between the dipoles, while a positive slope results for a positive ion-dipole interaction. The latter argument agrees with the observed results, where, a positive ion and a dipole are involved in the rate determining step of Scheme 2.

<table>
<thead>
<tr>
<th>Pyrazine</th>
<th>$10^{-2} K_i$ (dm$^3$ mol$^{-1}$)</th>
<th>$k_d$ (s$^{-1}$)</th>
<th>$10^{-2} K_i'$ (mol dm$^{-3}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyrazine</td>
<td>0.93</td>
<td>0.79</td>
<td>1.07</td>
</tr>
<tr>
<td>2-methylpyrazine</td>
<td>0.77</td>
<td>0.85</td>
<td>1.29</td>
</tr>
<tr>
<td>2-ethylpyrazine</td>
<td>1.30</td>
<td>0.79</td>
<td>0.76</td>
</tr>
<tr>
<td>2-methoxypyrazine</td>
<td>1.75</td>
<td>0.85</td>
<td>0.57</td>
</tr>
<tr>
<td>2-aminopyrazine</td>
<td>0.94</td>
<td>1.98</td>
<td>1.06</td>
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</tbody>
</table>

**Structure Reactivity Correlation.** Structural modification of a reactant molecule may influence the rate or equilibrium constant of a reaction through inductive, polar, steric and resonance effects which can be used to probe into the reaction mechanism. Out of a number of empirical models proposed in describing the relationships between structure and reactivity, the most successful and extensively investigated are the linear free energy relationships with the Hammett equation as the most prominent example. The Hammett treatment describes the substituent effects on rate and equilibria of aromatic molecules. In the present system, structure reactivity relationship is ascertained by utilizing different groups at the second position of the pyrazine ring and tested to fit into the results to the Hammett equation. The Hammett plot (log $k$ vs. $\sigma$) is reasonably linear ($r = 0.9846$). From a plot of log $k$ vs. $\sigma$, the value of the reaction constant $\rho$ is found to be -0.8 signifying that the electron releasing groups in the pyrazine ring enhances the rate. The negative $\rho$ value implies the formation of cationic transition state X (Scheme 2). The positive inductive effect of the substituents increases the electron density at nitrogen of pyrazine and subsequently the lone pair of electrons of nitrogen of pyrazine easily attacks the positive bromine of reactive oxidizing species to form cationic transition state. Further, the positive inductive effect of the substituents in the present system increases in the order: -NH$_2$ > -OCH$_3$ > -C$_2$H$_5$ > -CH$_3$ > H, which justified by the observed reactivity trend: 2-aminopyrazine > 2-methoxypyrazine > 2-ethylpyrazine > 2-methylpyrazine > pyrazine for pyrazines oxidations.

**Isokinetic Relationship.** The activation energy is highest for the slowest reaction (Table 3) indicating that the reaction is enthalpy controlled. Within a reaction series, the variation in the rate may be caused by changes in either the enthalpy or the entropy of activation or both. Among the recognized categories, changes in rate are caused by changes in both enthalpy and entropy of activation quantities in a parallel fashion is one of the important categories. In this class, enthalpy and entropy of activation are correlated by linear relationship $\Delta H^\dagger = \Delta H^\circ + \beta \Delta S^\circ$, which is called the isokinetic relationship and $\beta$ is the isokinetic temperature. When the experimental temperature $T < \beta$, the reaction rate is controlled mainly by the enthalpy change. In the present case, the enthalpies and entropies of activation for the oxidation of the pyrazines are linearly related by plotting $\Delta H^\dagger$ vs. $\Delta S^\circ$ (Figure 6: $r = 0.9920$). From the slope, the value of isokinetic temperature ($\beta$) is computed and found to
The kinetics of oxidation of pyrazine and substituted pyrazines to the respective pyrazine-N-oxides by BAB has been studied at 303 K. The oxidation reaction follows the identical kinetic characteristics for all the pyrazines and obeys the rate law: rate = \k \beta \alpha \beta [\text{pyrazine}]_0 [\text{H}^+]_x, where x is less than unity. The rate of oxidation of pyrazines increased in the order: 2-aminoypyrazine > 2-methoxypyrazine > 2-ethylpyrazine > 2-methylpyrazine > pyrazine. The Hammett relationship is observed for the reaction with \rho = -0.8, showing that the electron donating groups enhance the rate. Activation parameters and isokinetic temperature were deduced. On the basis of experimental results, a suitable mechanism and appropriate rate law have been worked out.

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Figure 6. Isokinetic plots of (a) \Delta H^\circ vs. \Delta S^\circ, (b) log k/(293 K) vs. log k/(303 K). Experimental conditions are as in Table 3.

Summary

The kinetics of oxidation of pyrazine and substituted pyrazines to the respective pyrazine-N-oxides by BAB has been studied at 303 K. The oxidation reaction follows the identical kinetic characteristics for all the pyrazines and obeys the rate law: rate = k [BAB]_0 [pyrazine]_0 [H]^+^x, where x is less than unity. The rate of oxidation of pyrazines increased in the order: 2-aminoypyrazine > 2-methoxypyrazine > 2-ethylpyrazine > 2-methylpyrazine > pyrazine. The Hammett relationship is observed for the reaction with \rho = -0.8, showing that the electron donating groups enhance the rate. Activation parameters and isokinetic temperature were deduced. On the basis of experimental results, a suitable mechanism and appropriate rate law have been worked out.

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