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Kinetics of Oxidation of Indole in High Indole Concentration Range by Bromamine-B in Alkaline Medium Catalysed by Os(VIII)

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The kinetics of oxidation of indole (In) in high indole concentration range by sodium N-bromobenzene sulphonamide (BAB) in alkaline medium in presence of OsO_4 catalyst have been investigated at 30°C. The reaction rate shows a first order dependence of rate on $[BAB]_0$ and [Indole], and inverse first order dependence of rate on $[OH^-]$ and first order on $[OsO_4]$. Addition of halide ions and variation of ionic strength and dielectric constant of the medium do not have any signficant effect on the reaction rate. Thermodynamic parameters have been evaluated.

INTRODUCTION

A metabolic oxidation study of indole to indoxy was attempted by Laroche and Desborders[1] and indole was oxidised by sodium perborate in the presence of acetone and methyl paraoxane as promoter[2]. However, a very few kinetic investigations of indole oxidation have been attempted. The present studies were undertaken to investigate the kinetic aspects of the oxidation of indole by N-metallo-N-halo arylsulphonamides in alkaline medium catalysed by Os(VIII). Mechanistic studies of the oxidation of diverse organic substrates by these organic haloamines have already been reported,[3–5] but reports on oxidation of heterocyclic compounds by organic haloamines are scanty. We now report a detailed investigation of the kinetics of oxidation of indole (In), by bromamine-B ($C_6H_5SO_2NBrNa\cdot1.5H_2O$, BAB) in the presence of alkali and osmium tetroxide as catalyst at 303 K in 10% aqueous methanol.

EXPERIMENTAL

The oxidant, BAB, was prepared and purified using the methods reported elsewhere.[6] Its purity was checked iodometrically and through IR and ^{13}C NMR spectral data.[7] Aqueous solutions of BAB were prepared, standardized by the iodometric method and preserved in amber coloured bottles. All chemicals used

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were of analytical grade. Triply distilled water was used for preparing aqueous solutions. The ionic strength of the system was kept at a high value by using a concentrated $NaClO_4$ solution.

Stoichiometry and product analysis: Various ratios of indole and oxidant were equilibrated in the presence of NaOH and OsO_4 in [BAB] ≫ [indole]. Determination of unreacted BAB in reaction mixture showed that 1 mole of indole consumed 1 mole of BAB, conforming to the following stoichiometry:

$$PhSO_2NBrNa + C_8H_7N + H_2O \longrightarrow PhSO_2NH_2 + C_8H_6NO + Na^+ + Br^- \qquad (1)$$

The reaction mixture was made slightly acidic by adding dilute HCl and was diluted with water, when $PhSO_2NH_2$ was precipitated in bulk. The remaining $PhSO_2NH_2$ in the reaction mixture was salted out. Then the reaction mixture was extracted with chloroform and the $CHCl_3$ layer was evaporated to give a brown solid residue. The residue was subjected to column chromatography on silica gel (60–200 mesh) using gradient elution (dichloromethane to acetone). After initial separation, the reaction products were further purified by recrystallization and were characterized by ^1H NMR and materials were identified by comparison with commerically available samples.

Oxindole: Recrystallized from dichloromethanol petroleum-ether (m.p. = 118–120°C); known m.p. = 125–127°C; R_f value (0.13) determined from TLC (CH_2Cl_2), IR (KBr); 3217 (N—H stretch), 3070 and 3032 (aromatic C—H stretch), 2925 (aliphatic C—H stretch), 1701 (C═O stretch), 1619 (C═O stretch), 1473, 1333, 1234, 749, 674 and 552 cm^{-1}. NMR ($CDCl_3$); 7.22–6.83 (S, 4H, aromatic C—H); 3.54 (S, 3H, aliphatic C—H), and 1.71 (S, 1H, N—H); GC/MS, m/e, 133 (m^+); 104 ($m^+ = CHO$), 78 ($m^+ = CHNO$), 77 ($m^+ = C_2H_2NO$), 51 and 36.

RESULTS AND DISCUSSION

Effect of varying reactant concentrations: The oxidation of indole with BAB in presence of NaOH and OsO_4 in 10% methanol obeys pseudo first order kinetics for at least two half lives. At constat [OH] and [Os(VIII)] with substrate in excess, plot of log [BAB] *vs.* time was linear, indicating a first order dependence of rate on $[BAB]_0$. The rate is found to be independent of $[Indole]_0$ (Table-1).

Effect of NaOH: The reaction rate was studied at constant $[BAB]_0$, $[Indole]_0$ and [Os(VIII)], the reaction rate decrease with increase in [NaOH] (Table-2). A plot of log k′ versus log [NaOH] was linear (Fig. 1) with unit negative slope indicating an inverse first order dependence of rate on $[OH^-]$.

Effect of [Os(VIII)]: The rate increased with increase in [Os(VIII)] (Table-3). A plot of log k′ *vs.* log [Os(VIII)] was linear (Fig. 2) with unit slope.

Addition of halide ions such as Cl^- and Br^- in the form of NaBr has no

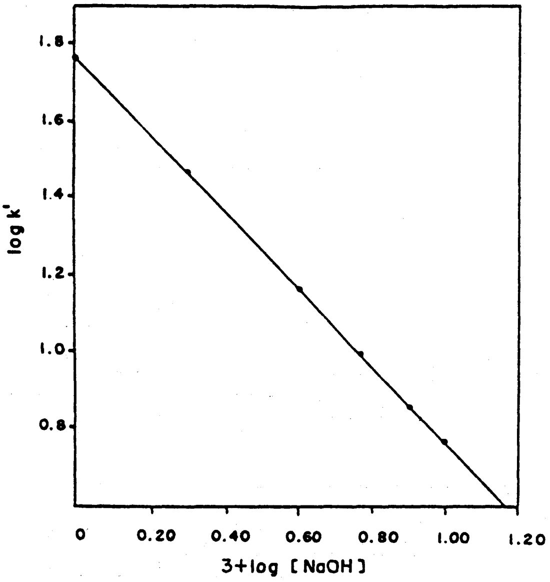

log k'
1.8
1.6
1.4
1.2
1.0
0.8
0
0.20
0.40
0.60
0.80
1.00
1.20
3+log [NaOH]

Fig. 1.

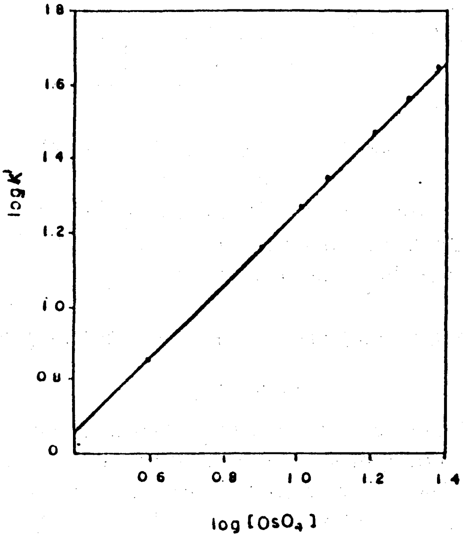

log k'
1 8
1.6
1 4
1.2
1 0
0 8
0
0 6
0 8
1 0
1.2
1 4
log [OsO4]

Fig. 2.

influence on the rate of reaction. Variation of ionic strength (0.10–0.4 mol dm^{-3}) of the medium of adding $NaClO_4$ solution has no effect on the rate of reaction.

Solvent isotope studies: Since hydroxyl ion dependence of rate was noted under high concentration of substrate, solvent isotope studies were made using D_2O with indole. The values were $(k_{obs})_{D_2O} = 1.47 \times 10^{-4}$ sec^{-1} while $(k_{obs})_{H_2O} = 2.96 \times 10^{-4}$ sec^{-1} leading to a solvent isotope effect; $k_{obs}(H_2O)/k_{obs}(D_2O) = 2.01$ with other conditions maintained as in Table-1.

TABLE-1

EFFECT OF VARYING REACTANT CONCENTRATION ON THE RATE OF REACTION

$[BAB]_0 = 8.0 \times 10^{-4}$ mol dm^{-3}, $[NaOH] = 2.0 \times 10^{-3}$ mol dm^{-3}

$[OsO_4] = 16.0 \times 10^{-6}$ mol dm^{-3}, MeOH = 10% (v/v)

$\mu = 0.4$ mol dm^{-3}, Temp. = 303 K

10^3 [Indole] mol dm^{-3}	10^4 K′ sec^{-1}
8.0	2.98
10.0	2.99
15.0	2.96
20.0	2.97
40.0	2.93
60.0	2.91

TABLE-2

EFFECT OF CONCENTRATION OF NaOH ON THE RATE OF REACTION

$[BAB]_0 = 8.0 \times 10^{-4}$ mol dm^{-3} $[In]_0 = 1.5 \times 10^{-2}$ mol dm^{-3}

$[OsO_4] = 16.0 \times 10^{-6}$ mol dm^{-3} MeOH = 10% (v/v)

$\mu = 0.4$ mol dm^{-3}, Temp = 303 K

10^{-4} [NaOH] mol dm^{-3}	10^4 k′ sec^{-1}
10	5.91
20	2.96
40	1.47
60	0.98
80	0.74
100	0.59
Order = 1.000	r = 0.9999

Effect of temperature: The reaction was studied at different temperature (298 K–313 K; Table-4) and from the Arrhenius plot (Fig. 3) of log k′ versus 1/T values of the activation parameters were calculated (Table-4).

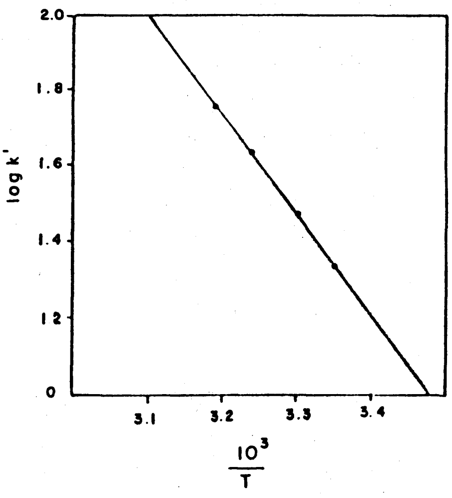


Fig. 3.

Effect of benzenesulphonamide: Benzenesulphonamide ($PhSO_2NH_2$) was detected by TLC, using petroleum ether-chloroform-1-butanol (2 : 2 : 1 v/v) as the solvent and iodine as the detecting agent ($R_f = 0.88$).

Effect of varying dielectric constant of solvent: The study of the effect of dielectric constant [D] of the solvent made in water-methanol mixtures of varying compositions. The rate decreased with increase in methanol content of the reaction mixture.

TABLE-3

EFFECT OF CONCENTRATION OF CATALYST OsO_4 ON THE RATE OF REACTION

$[BAB]_0 = 8.0 \times 10^{-4}$ mol dm^{-3}
[NaOH] = 2.0×10^{-3} mol dm^{-3}
$\mu = 0.4$ mol dm^{-3},

$[In]_0 = 1.5 \times 10^{-2}$ mol dm^{-3}
MeOH = 10% (v/v)
Temp = 303 K

10^6 [Os(VIII)] mol dm^{-3}	10^4 k' sec^{-1}
4.0	0.74
8.0	1.47
12.0	2.21
16.0	2.96
20.0	3.69
24.0	4.42
Order = 1.000	r = 0.9999

TABLE-4
KINETIC AND THERMODYNAMIC PARAMETERS FOR THE OXIDATION OF INDOLE BY BAB IN ALKALINE MEDIUM IN PRESENCE OF OsO_4

$[BAB]_0 = 8.0 \times 10^{-4}$ mol dm^{-3} $[In]_0 = 1.5 \times 10^{-2}$ mol dm^{-3}
$[OsO_4] = 16.0 \times 10^{-6}$ mol dm^{-3} MeOH = 10% (v/v)
$[NaOH] = 2.0 \times 10^{-3}$ mol dm^{-3} $\mu = 0.4$ mol dm^{-3}

Tempearute (K)	10^4 k′ sec^{-1}	E_a kJ mol^{-1}	$\Delta H^{\#}$ kJ mol^{-1}	$\Delta S^{\#}$ kJ mol^{-1}	$\Delta G^{\#}$ kJ mol^{-1}
298	2.19	50.7	48.2	–153.5	95.0
303	2.96				
308	4.36				
313	5.75				

The first order dependence of reaction rate on [Os(VIII)] and $[BAB]_0$ and inverse first order in $[OH^-]$ and zero order in $[Indole]_0$ indicate that the formation of an intermediate species between OsO_4 and BAB is the most probable rate controlling step.

A first order retardation by OH^- has been observed in many chloraminometric reactions, which has been attributed to hydrolysis of the anion to generate the conjugate acid. During the oxidation of α-hydroxyacids, aldehydes and ketones by alkaline CAT catalyzed by OsO_4, Mushran *et al.*[8] assume the formation of a cyclic complex between $P—CH_3—C_6H_4$, NHCl and OsO_4 which interacts with the substrate. In subsequent steps, complexation decreases the electron density around the nitrogen atom of the conjugate acid, thus increasing its electrophilic character and hence the hydride ion abstracting capacity which results in a fast interaction with the substrate. Hardy and Jonhston[9] have carried out a detailed investigation on alkaline bromamine-B solutions and have shown that conjugate acid $C_6H_5SO_2NHBr$ is the active species in the oxidation of nitrophenols and reported the following equilibria in alkaline solutions of BAB:

$$PhSO_2NBr^- + H_2O \rightleftharpoons PhSO_2NHBr + OH^- \quad (2)$$

$$PhSO_2NHBr + H_2O \rightleftharpoons PhSO_2NH_2 + HOBr \quad (3)$$

Equation (3) indicates a slow hydrolysis; if HOBr were the primary oxidizing species, a first-order retardation of the rate by the added $PhSO_2NH_2$ would be expected which is contrary to the experimental observations. Therefore in the present studies a first order retardation of the rate by $[OH^-]$ observed indicates that $PhSO_2NHBr$ is the active species. It can be assumed that a complex of $PhSO_2NHBr$ and OsO_4 serves as an oxidant. Further, the oxidation of indole does not occur with either OsO_4 or BAB alone. In view of these facts the following mechanism can be proposed:

$$PhSO_2NBr^- + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} PhSO_2NHBr + OH^- \quad K_1 = k_1/k_{-1} \qquad \text{Fast} \qquad (4)$$

$$PhSO_2NHBr + OsO_4 \xrightarrow{k_2} X \qquad \text{r.d.s.} \qquad (5)$$

$$X + In \xrightarrow{k_3} \text{products} \qquad \text{Fast} \qquad (6)$$

Scheme-I

From Scheme-I we get

$$\text{rate} = k_2[PhSO_2NHBr][Os(VIII)] \qquad (7)$$

Applying steady state conditions to [$PhSO_2NHBr$], we get

$$\frac{d[PhSO_2NHBr]}{dt} = k_1[BAB][H_2O] - k_{-1}[PhSO_2NHBr][OH^-] - k_2[PhSO_2NHBr]\,[Os(VIII)] = 0 \qquad (8)$$

or

$$[PhSO_2NHBr] = \frac{k_1[BAB][H_2O]}{k_1[OH^-] + k_2[Os(VIII)]}$$

At higher [OH^-], the inequality $k_1[OH^-] \gg k_2[Os(VIII)]$ holds and

$$[PhSO_2NHBr] = \frac{K_1[BAB][H_2O]}{[OH]} \qquad (9)$$

Substituting for [$PhSO_2NHBr$] in equation (7),

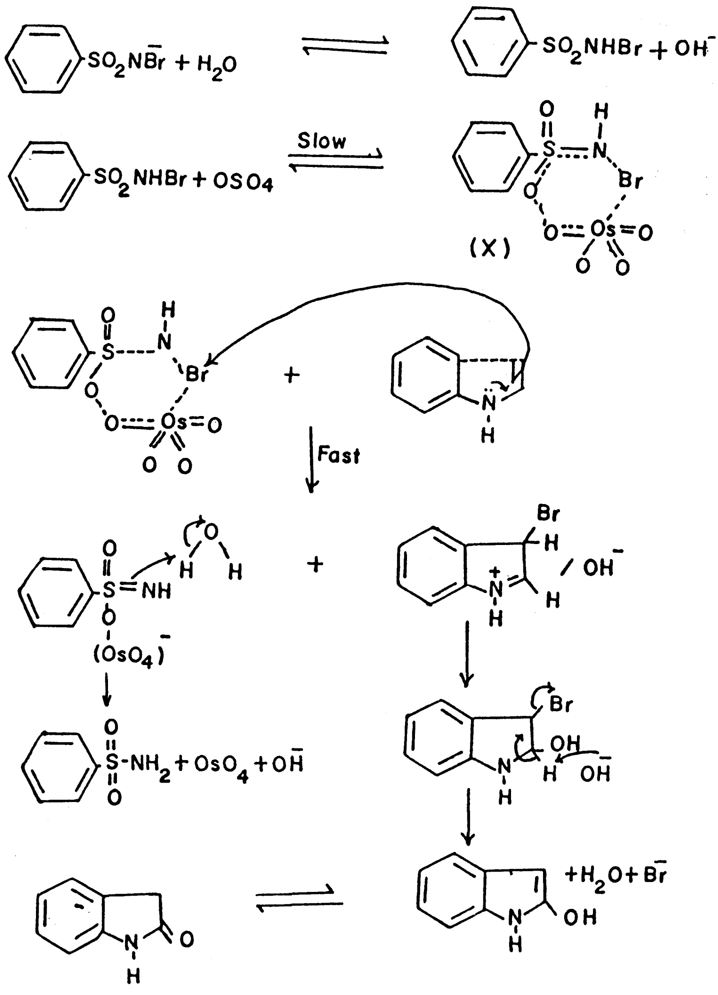
$$\text{Rate} = \frac{k_2k_1[BAB][H_2O][Os(VIII)]}{[OH^-]} \qquad (10)$$

Equation (10) accounts for the observed first order each in [oxidant] and [catalyst], and inverse first order in [OH^-].

The proposed mechanism is also supported by the magnitude of solvent isotope effect. For a reaction involving a fast pre-eqilibrium H^+ or OH^- ion transfer, the rate increases in D_2O medium since D_3O^+ and OD^- are stronger acid and stronger base respectively than H_3O^+ and OH^- ions. The reverse holds for rections involving retardation by H^+ or OH^- ions. Hence the proposed mechanism is also supported by the decrease of rate in D_2O medium indicating retardation by OH^- (Scheme-I).

In Scheme-2, the electron density around the nitrogen atom is lowered resulting in a weakening of the N—Br bond. Subsequent oxidizing capacity of N-bromobenzene *p*-sulphonamide is increased after complexation, which then interacts with the appropriate form of the substrate. The alkaline catalyzed indole bromination *via* activated bromamine-B (X) affords 3-bromo-indolenine and a nitrogen-protonated bromamine-B-osmium tetroxide complex, which then results in the formation of benzenesulphonamide, a hydroxide ion and osmium tetroxide.

Hydration of 3-bromo-indolenine to 3-bromo-2-hydroxy-indolenine followed by alkaline catalyzed removal of hydrogen bromide produces 2-hydroxyindole, which is in equilibrium with its more stable keto form, oxindole.



Scheme-2

Further, this mechanism is supported by the low enthalphy of activation. The value ΔS$^{\#}$, though negativen, is small indicates very little rearrangement in the transition state pointing towards the loose nature of the activated complex.

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