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OXIDATION OF INDOLE BY *N*-SODIO-*N*-CHLOROBENZENESULPHONAMIDE (CHLORAMINE-B) IN ALKALINE MEDIUM CATALYSED BY Os(VIII): A KINETIC AND MECHANISTIC STUDY

B. M. VENKATESHA, S. ANANDA AND D. S. MAHADEVAPPA*

Department of Studies in Chemistry, University of Mysore, Manasagangothri, Mysore-570006, India

The kinetics of oxidation of indole (In) and 5-substituted indoles (OCH_3, Br and Cl) by chloramine-B (CAB) were studied in alkaline medium with Os(VIII) as catalyst at 303 K. At low $[In]_0$ the rate law rate $= k[CAB][Os(VIII)][In]_0$ is obeyed, which changes to rate $= k[CAB][Os(VIII)][OH^-]^{-1}$ at higher substrate concentrations. Variation of ionic strength has no effect on the rate and the dielectric effect is negative. The reaction was studied at different temperatures and activation parameters were evaluated. Hammett correlation of substituent effects indicated a linear free energy relationship with $\rho^+ = -1 \cdot 0$, showing the formation of an electron-deficient transition state. From enthalpy–entropy relationships and Exner correlations, the isokinetic temperature β was found to be 330 K, indicating enthalpy as a controlling factor. The mechanism assumes the formation of a complex between oxidant and Os(VIII) at high and low $[In]_0$. Proton inventory studies in H_2O–D_2O mixtures showed the involvement of a single exchangeable proton of OH^- ion in the transition state.

INTRODUCTION

A metabolic oxidation study of indole to indoxyl was attempted by Laroche and Desbordes[1] and indole was oxidized by sodium perborate in the presence of acetone and methyl paraoxane as promoter.[2] However, very few kinetic investigations of indole oxidations have been attempted. The present studies were undertaken to investigate the kinetic aspects of the oxidation of indole and 5-substituted indoles by *N*-metallo-*N*-haloarylsulphonamides. Mechanistic studies of the oxidation of diverse organic substrates by these organic haloamines have been reported previously,[3–5] but reports on the oxidation of heterocyclic compounds by organic haloamines are scanty. We now report a detailed investigation of the kinetics of oxidation of indole (In), 5-methoxyindole (5-MI), 5-bromoindole (5-BI) and 5-chloroindole (5-CI) by chloramine-B ($C_6H_5SO_2NClNa \cdot 1 \cdot 5H_2O$; CAB) in the presence of alkali and osmium tetroxide as catalyst at 303 K in 10% aqueous methanol. Hammett linear free energy and isokinetic relationships were observed during the course of these investigations. Substituent effects at the indole 5-position were studied as this is the recognized reactive site in the ring system.

EXPERIMENTAL

Chloramine-B was prepared by passing chlorine through a solution of benzenesulphonamide in 4.0 mol dm^{-3} NaOH for 1 h at 343 K. The product was collected, dried and recrystallized from water; it had m.p. 170 °C with decomposition. The purity was checked by iodimetric titration and ^1H and ^{13}C NMR spectroscopy. An aqueous solution of CAB was standardized iodimetrically and stored in brown bottles to prevent its photochemical deterioration.

Indole (Loba Chemie), 5-methoxyindole, 5-bromoindole and 5-chloroindole (Aldrich) were of accepted grades of purity and were used as received. Solutions of the compounds were prepared in 10% (v/v) methanol. Osmium tetroxide (Johnson Matthey, London) was prepared in $0 \cdot 02$ mol dm^{-3} NaOH. All other reagents used were of analytical grade. Doubly distilled water was employed in the preparation of aqueous solutions. The ionic strength of the system was maintained at a constant high value ($\mu = 0 \cdot 5$ mol dm^{-3}) using a concentrated solution of sodium perchlorate. Solvent isotope studies were made with D_2O (99·4%) supplied by the Bhabha Atomic Research Centre (Bombay).

Regression analysis of experimental data was carried out on an EC-72 statistical calculator to obtain the

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* Author for correspondence.

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regression coefficient r and standard deviation s of the points from the regression line.

Kinetic measurements. The reaction was carried out in glass-stoppered Pyrex boiling tubes whose outer surface was coated black to eliminate photochemical effects. For each run, appropriate amounts of solutions of NaOH, $NaClO_4$, OsO_4, water and methanol (to maintain the total volume constant and 10% methanol medium throughout) were added to the tube. Indole and CAB solutions pre-equilibrated separately at 303 K were added successively to the reaction mixture to initiate the reaction. The course of the reaction was followed by iodimetric determination of unreacted CAB presented in measured aliquots of the reaction mixture withdrawn at different intervals of time. The reaction was studied for two half-lives. The pseudo-first-order rate constants (k') calculated were reproducible to within 3%.

Stoichiometry. Various ratios of indole and oxidant were equilibrated in the presence of NaOH and OsO_4 in 10% methanol for 24 h (303 K) under the condition [CAB] $\gg$ [indole]. Determination of unreacted CAB in reaction mixture showed that 1 mol of indole consumed 1 mol of CAB, conforming to the following stoichiometry:

$$PhSO_2NClNa + XC_8H_6N + H_2O \rightarrow PhSO_2NH_2 + XC_8H_6NO + Na^+ + Cl^- \quad (1)$$

where X = H, OCH_3, Br and Cl for indole, 5-methoxyindole, 5-bromoindole and 5-chloroindole, respectively.

Product analysis. The reaction mixture was made slightly acidic by adding dilute HCl and was diluted with water, $PhSO_2NH_2$ being precipitated in bulk. The remaining $PhSO_2NH_2$ in the reaction mixture was salted out. The reaction mixture was then extracted with chloroform and the chloroform layer was evaporated to dryness 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 ^{1}H NMR spectroscopy and identified by comparison with commercially available samples.

Oxindole. Recrystallized from dichloromethane–petroleum ether, m.p. 118–120 °C (known m.p. = 125–127 °C). R_F value 0·13, determined by thin-layer chromatography (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}. ^{1}H NMR ($CDCl_3$): 7·22–6·83 (m, 4H, aromatic CH), 3·54 (s, 3H, aliphatic CH), 1·71 (s, 1H, NH). Gas chromatography–mass spectrometry: m/z 133 (M^+), 104 ($M^+ - CHO$), 78 ($M^+ - C_2HNO$), 77 ($M^+ - C_2H_2NO$), 51, 36.

Benzenesulphonamide. Benzenesulphonamide ($PhSO_2NH_2$ or BSA) was detected by TLC, using light petroleum–chloroform–butan-1-ol (2:2:1 v/v/v) as the solvent and iodine for detection ($R_F = 0·88$).

RESULTS

The kinetics of oxidation of indole by CAB were investigated for two different ranges of indole concentration in 10% methanol medium. Blank experiments with methanol, however, showed that there is a slight decomposition of the solvent (<2%) under the experimental conditions used. This was allowed for in the calculation of the net reaction rate constant for the oxidation of indole:

(1) low concentration range of indole:
$[\text{indole}]_0 = 8·0 \times 10^{-4}–45·0 \times 10^{-4}$ mol dm^{-3}
(2) high concentration range of indole:
$[\text{indole}]_0 = 50·0 \times 10^{-4}–150·0 \times 10^{-4}$ mol dm^{-3}

Effect of reactants

The oxidation of indoles with CAB in the presence of NaOH and OsO_4 in 10% methanol obeys pseudo-first-order kinetics for at least two half-lives. At constant [OH^-] and [Os(VIII)] with substrate in excess, plots of log[CAB] versus time were linear in both ranges, indicating a first-order dependence of rate on $[\text{CAB}]_0$. Values of psuedo-first-order rate constants (k') are given in Table 1. At low indole concentrations (range 1) the rate increases with increase in $[\text{indole}]_0$, levelling off at higher $[\text{indole}]_0$ (range 2). A plot of log k' versus log$[\text{indole}]_0$ was linear [$r = 0·9994$, $s < 0·01$, Figure 1(a)] with a slope of unity (Table 1) in range 1. The rate is independent of substrate concentration at higher $[\text{indole}]_0$ (Table 1).

Effect of NaOH concentration

At constant $[\text{CAB}]_0$, $[\text{indole}]_0$ and [Os(VIII)] the rate is independent of [NaOH] (Table 2) at low concentrations of indole, but at higher concentrations of indole the rate decreases with increase in [NaOH] (Table 2). A plot of log k' versus log[NaOH] was linear ($r = 0·9975$, $s < 0·016$) with a negative slope of unity, indicating an inverse first-order dependence of rate on [alkali].

Effect of Os(VIII) concentration

The rate increases with increase in [Os(VIII)] (Table 2) in both ranges. A plot of log k' versus log[Os(VIII)]

Table 1. Effect of varying reactant concentrations on the rate[a]

	Low [indole] range		High [indole] range	
$[\mathrm{CAB}] \times 10^4$ (mol dm^{-3})	$[\mathrm{In}]_0 \times 10^4$ (mol dm^{-3})	$k' \times 10^5$ (s^{-1})	$[\mathrm{In}]_0 \times 10^4$ (mol dm^{-3})	$k' \times 10^5$ (s^{-1})
6·0	25·0	12·63	70·0	20·50
7·0	25·0	11·92	70·0	19·95
8·0	25·0	12·53	70·0	20·20
9·0	25·0	12·92	70·0	21·00
10·0	25·0	12·35	70·0	19·88
12·0	25·0	12·13	70·0	20·00
8·0	8·0	4·20 (4·00)	30·0	20·65
8·0	12·0	5·88 (6·01)	50·0	20·71
8·0	20·0	10·20(10·02)	80·0	20·11
8·0	30·0	14·80(15·03)	90·0	20·22
8·0	40·0	19·30(20·04)	100·0	20·32
8·0	45·0	21·15(22·55)	150·0	19·93
8·0	60·0	21·25(30·07)		
8·0	80·0	21·10(40·09)		

[a] [NaOH] = 0·002 mol dm^{-3}; [Os(VIII)] = $15{\cdot}7 \times 10^{-6}$ mol dm^{-3}; $\mu = 0{\cdot}50$ mol dm^{-3}; $T = 303$ K. Values in parentheses are the predicted rate constants calculated from equation (11).

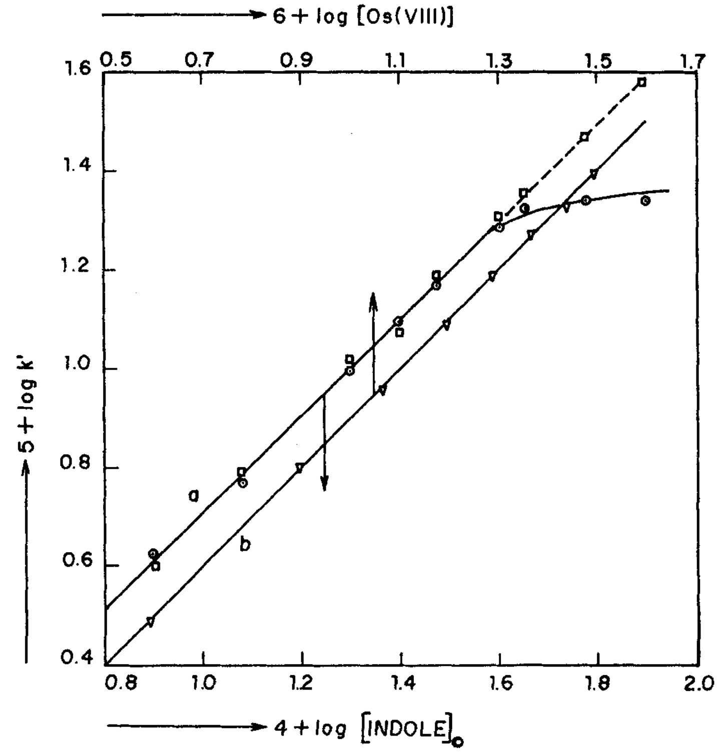


Figure 1. (a) Plot of log k' versus $\log[\mathrm{In}]_0$. [CAB] = 0·0008 mol dm^{-3}; [NaOH] = 0·002 mol dm^{-3}; [Os(VIII)] = $15{\cdot}7 \times 10^{-6}$ mol dm^{-3}; temperature = 303 K; $\mu = 0{\cdot}5$ mol dm^{-3}. (□) Points on the theoretical curve. (b) Plot of log k' versus log [Os(VIII)]. $[\mathrm{In}]_0 = 0{\cdot}0025$ mol dm^{-3}; other conditions as in (a)

Table 2. Effect of varying [NaOH] and [Os(VIII)] on the rate[a]

[Os(VIII) × 10^6 (mol dm^{-3})	[NaOH] × 10^4 (mol dm^{-3})	k' × 10^5 (s^{-1}) Low [In]$_0$ range	High [In]$_0$ range
3·93	20·00	3·09	5·10
7·86	20·00	6·37	10·60
11·78	20·00	9·12	—
15·70	20·00	12·50	20·20
19·62	20·00	15·32	—
23·60	20·00	18·82	28·80
27·50	20·00	21·55	35·50
31·40	20·00	24·53	—
15·70	8·00	12·22	—
15·70	10·00	12·50	38·05
15·70	15·00	12·53	26·80
15·70	25·00	12·27	15·13
15·70	30·00	12·10	13·18
15·70	40·00	12·15	—

[a] [CAB] = 0·0008 mol dm^{-3}; [In]$_0$ = 0·0025 and 0·007 mol dm^{-3} for low and high [indole]$_0$ range, respectively; T = 303 K; μ = 0·5 mol dm^{-3}.

was linear [$r = 0·9998$, $s < 0·01$, Figure 1(b)] with a slope of unity in both ranges.

Effect of halide ions

Addition of halide ions such as Cl^- in the form of NaCl and Br^- in the form of NaBr had no influence on the rate in both ranges.

Effect of benzenesulphonamide

Addition of the reaction product, benzenesulphonamide ($1·0 \times 10^{-4}$–$6·0 \times 10^{-4}$ mol dm^{-3}) had no effect on the rate in both ranges.

Effect of ionic strength

Variation of the ionic strength of the medium by adding $NaClO_4$ (0·005–1·0 mol dm^{-3}) had no effect on the rate in both ranges.

Effect of temperature on the rate

The reaction was studied at different temperatures (298–313 K) and from the Arrhenius plots ($r > 0·9998$) of log k' versus $1/T$, values of the activation parameters were calculated in both ranges (Tables 3 and 4).

Solvent isotope studies

As a dependence of the rate on hydroxyl ion concentration was noted at high concentrations of substrate, solvent isotope studies were made using D_2O with indole as the probe in range 2. The values were $(k_{obs})_{D_2O} = 9·95 \times 10^{-5}\ s^{-1}$ and $(k_{obs})_{H_2O} = 20·20 \times 10^{-5}\ s^{-1}$, leading to a solvent isotope effect, $k_{obs}(H_2O)/k_{obs}(D_2O) = 2·03$, with other conditions maintained as in Table 1. Proton inventory studies were made in H_2O–D_2O mixtures with the same probe and the results are shown in Table 5. The corresponding proton inventory plot for the rate constant k^n_{obs} in a

Table 3. Temperature dependence of the oxidation of 5-substituted Indoles by CAB[a]

Indole	k' × 10^5 (s^{-1}) 298 K	303 K	306 K	309 K	313 K	$k_2 = k'/[In]$ ($dm^3\ mol^{-1}\ s^{-1}$)
Indole	7·24 (13·80)	10·50 (20·20)	13·05 (24·90)	16·23 (31·05)	21·00 (40·02)	$4·2 \times 10^{-2}$
5-MI	9·33	13·08	15·95	19·00	24·37	$5·23 \times 10^{-2}$
5-BI	3·34	5·48	7·35	9·83	14·00	$2·19 \times 10^{-2}$
5-Cl	2·82	4·92	6·70	9·29	13·34	1.96×10^{-2}

[a] [CAB] = 0·0008 mol dm^{-3}; [substrate]$_0$ = 0·0025 mol dm^{-3}; [NaOH] = 0·002 mol dm^{-3}; [Os(VIII)] = $15·7 \times 10^{-6}$ mol dm^{-3}; μ = 0·5 mol dm^{-3}. Values in parentheses are rate constants for the high [In]$_0$ range.

Table 4. Kinetic and thermodynamic parameters for oxidation of 5-substituted indoles by CAB[a]

Indole	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J K^{-1} mol^{-1})	$\Delta G^{\neq}$ (kJ mol^{-1})	E_a (kJ mol^{-1})
In	52·7	−147·3	97·8	55·3
	(52·6)	(−142·2)	(96·2)	(55·21)
5-MI	46·9	−164·6	97·3	49·5
5-BI	71·8	−89·7	99·2	74·3
5-CI	78·2	−69·6	99·5	80·7

[a] Values in parentheses are the parameters for the high [In]$_0$ range.

Table 5. Proton inventory studies for indole in H_2O–D_2O mixtures at 303 K[a]

Atom fraction of deuterium (n)	$k^n_{obs} \times 10^4$ (s^{-1})
0·000	20·20
0·248	17·40
0·497	14·60
0·745	11·95
0·947	9·95

[a] [CAB]$_0$ = 0·0008 mol dm^{-3}; [In]$_0$ = 0·007 mol dm^{-3}; μ = 0·5 mol dm^{-3}; [NaOH] = 0·002 mol dm^{-3}; [Os(VIII)] = 15·7 × 10^{-6} mol dm^{-3}.

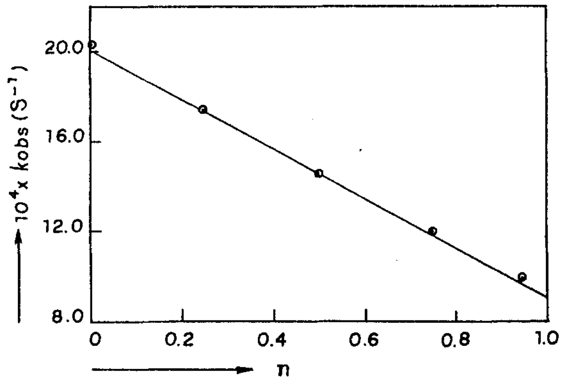


Figure 2. Proton inventory plot of k_{obs} versus the deuterium atom fraction n in H_2O–D_2O mixtures

solvent mixture of deuterium atom fraction n is given in Figure 2.

Effect of varying dielectric constant of medium

Rate studies were made in water–methanol mixtures of various compositions. In both ranges the rate decreased with increase in methanol content in the reaction mixture and a plot of log k' versus $1/D$, where D is the dielectric constant of the medium, gave a straight line with negative slope, supporting a rate-limiting step with charge dispersal.

Test for free radicals

Addition of the reaction mixture to acrylamide did not initiate polymerization, showing the absence of free radical species during the reaction sequence in both ranges.

DISCUSSION

N-Metallo-*N*-haloarylsulphonamides are mild oxidants and the prominent member of this class of compounds is chloramine-T, whose properties have been well established.[6] *N*-Chloro-*N*-sodiobenzenesulphonamide (CAB) is similar to chloramine-T and acts as an oxidizing agent in both acidic and alkaline media. In general, CAB undergoes a two-electron change in its reactions, the products being benzenesulphonamide (BSA) and sodium chloride. The oxidation potential of the CAB–BSA system is dependent on the pH of the medium (1·14 V at pH 0·65 and 0·5 V at pH 12 for chloramine-T). Depending on the pH of the medium, CAB furnishes different types of reactive species in solution, such as the conjugate acid $PhSO_2NHCl$, the dichloramine $PhSO_2NCl_2$, HOCl and possibly H_2OCl^+ in acidic solution. In alkaline medium the expected reactive species are $PhSO_2NHCl$, ClO^- ion and the anion $PhSO_2NCl^-$ itself.

This potent oxidant is of special interest for reaction mechanisms as it behaves as both a chlorinating and an oxidizing agent. *N*-Metallo-*N*-haloarylsulphonamides behave like strong electrolytes in aqueous solution and dissociate as shown in equation (2). It has been suggested that the reactivity of CAB in weakly alkaline solutions is due to the formation of a more potent oxidant, namely the conjugate acid $PhSO_2NHCl$ from $PhSO_2NCl^-$ in a base retarding step [equation (3)], while ClO^- ion is formed as in equation (4). Therefore, the possible oxidant species of CAB in alkaline solution are $PhSO_2NHCl$ and OCl^- in addition to the parent ion $PhSO_2NCl^-$.

$$PhSO_2NClNa \rightleftharpoons PhSO_2NCl^- + Na^+ \quad (2)$$

$$PhSO_2NCl^- + H_2O \rightleftharpoons PhSO_2NHCl + OH^- \quad (3)$$

$$PhSO_2NCl^- + H_2O \rightleftharpoons PhSO_2NH_2 + ClO^- \quad (4)$$

Low concentration range of indole

Under these conditions, the rate shows a first-order dependence each on $[CAB]_0$, [Os(VIII)] and $[indole]_0$ and is independent of [NaOH]. Further, the rate becomes zero order in substrate at higher $[indole]_0$. An absence of rate retardation by OH^- or the reaction product benzenesulphonamide indicates that $PhSO_2NHCl$ or OCl^- ion are not the reactive species. Hence the anion $PhSO_2NCl^-$ is the most likely oxidizing species. It has been shown that OsO_4 is stable as Os(VIII)[7-9] and exists in the following equilibria in alkaline medium:

$$OsO_4 + OH^- + H_2O \rightleftharpoons [OsO_4(OH)H_2O]^- \quad (5)$$

$$[OsO_4(OH)H_2O]^- + OH^- \rightleftharpoons [OsO_4(OH)_2]^{2-} + H_2O \quad (6)$$

Both $[OsO_4(OH)H_2O]^-$ and $[OsO_4(OH)_2]^{2-}$ possess octahedral geometry and they may not be able to form effective complexes with the oxidant. It is more realistic to postulate OsO_4, which possesses tetrahedral geometry, as the active species that can effectively form the complex with the oxidant species. The results of oxidation of indole at low concentration can be explained by Scheme 1

$$\text{(i)} \quad PhSO_2NCl^- + OsO_4 \underset{k_{-1}}{\overset{k_1\,(\text{fast})}{\rightleftharpoons}} X'$$

$$\text{(ii)} \quad X' + In \xrightarrow[\text{rate-limiting step}]{k_2} \text{products}$$

Scheme 1

According to Scheme 1,

$$\text{rate} = k_2[X'][In] \quad (7)$$

Assuming a steady state for $[X']$, we obtain

$$\frac{d[X']}{dt} = k_1[CAB][Os(VIII)] - k_{-1}[X'] - k_2[X'][In] = 0$$

or

$$[X'] = \frac{k_1[CAB][Os(VIII)]}{k_{-1} + k_2[In]} \quad (8)$$

Substituting for $[X']$ in equation (7), we obtain

$$\text{rate} = \frac{-d[CAB]}{dt} = \frac{k_2k_1[CAB][Os(VIII)][In]}{k_{-1} + k_2[In]} \quad (9)$$

In limiting cases, at low $[In]_0$, $k_2[In] \ll k_{-1}$ and hence

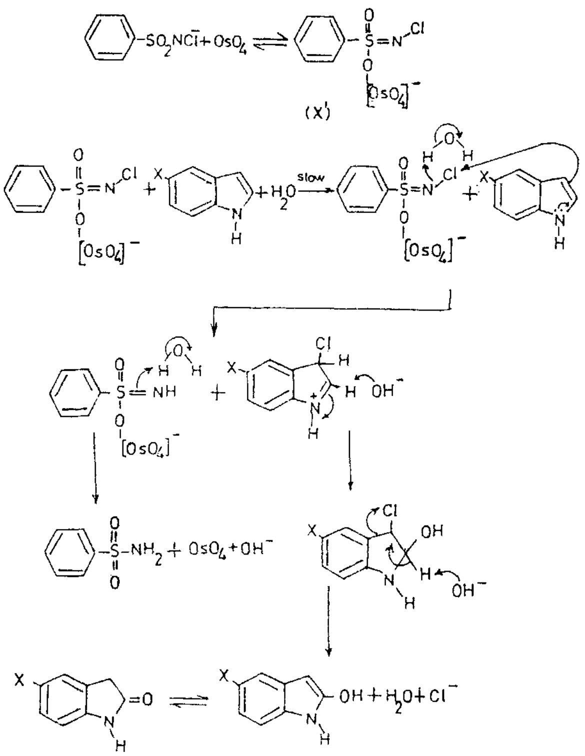
$$\text{rate} = k_2K_1[CAB][Os(VIII)][In] \quad (10)$$

Equation (10) accounts for the observed first order each in [CAB], [Os(VIII)] and $[indole]_0$. Equation (10) can be transformed into

$$k_{obs} = K_1k_2[Os(VIII)][In] \quad (11)$$

The product k_2K_1 was calculated from the value of k_{obs} for the standard run ($[CAB] = 0{\cdot}0008\ mol\,dm^{-3}$; $[In]_0 = 0{\cdot}0025\ mol\,dm^{-3}$; $T = 303$ K). Using this value of k_2K_1 the predicted rate constants for different indole concentrations were obtained from equation (11). These are given in Table 1 and the corresponding plot is shown in Figure 1.

The most probable structure of X′ is shown in Scheme 2, where CAB first coordinates with OsO_4. This activates chloramine-B via stabilization of the nitrogen—chlorine bond, which is followed by the rate-limiting reaction with the substrate to give products.



Scheme 2

Effect of varying dielectric constant of the medium

The effect of varying solvent composition on the rate of reaction has been described in several publications. For the limiting case of zero angle of approach between two dipoles or an anion–dipole system, Amis[10] has shown that a plot of log k_{obs} versus $1/D$ gives a straight line with a negative slope for reaction between a negative ion and a dipole or between two dipoles, while a positive slope indicates a reaction between a positive ion and a dipole. Since the dielectric effect is negative in the present studies, it supports the interaction of two dipoles as in the rate limiting step (ii) of Scheme 1.

Structure–reactivity correlations

It was interesting to test for a linear free energy relationship in the oxidation of indoles by CAB. A plot of log k'_2 (second-order constant k'_2) versus σ_p parameters for the ring substituents was made (Figure 3). The Hammett correlations[11,12] were fitted with the $\sigma_p = \sigma_I + \sigma_R^-$ scale (values of σ_R^- are available in the literature with the ionizations of anilinium ion in water at 25 °C as the basis[12]) The value of ρ^+ was found to be $-1{\cdot}00$, indicating the formation of an electron-deficient transition state. The low sensitivity of k'_2 to ring substituents indicates significant bond formation between the substrate and the oxidant in the rate-limiting step. It can also be seen from Table 3 that the rate decreases as the ring substituent becomes more electron withdrawing, demonstrating the operation of a $+I$ effect.

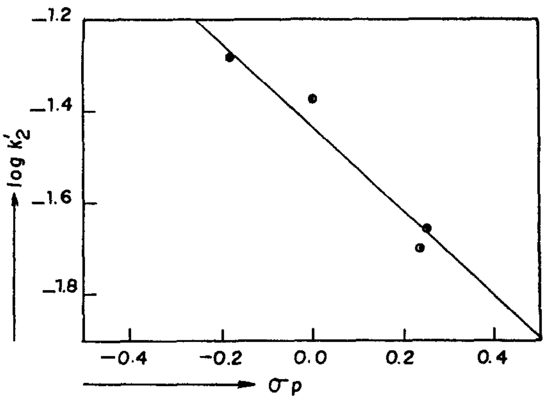


Figure 3. Hammett plot of log k'_2 versus σ_p

Isokinetic relationship

The mechanism is supported by the low enthalpy of activation. The value of $\Delta S^{\neq}$ reflects the formation of a more ordered transition state. The activation enthalpies and entropies of oxidation of indole, 5-methylindole, 5-bromoindole and 5-chloroindole are linearly related in a plot of $\Delta H^{\neq}$ versus $\Delta S^{\neq}$ ($r = 0{\cdot}9998$). From the slope, the calculated value of the isokinetic temperature β is 330 K. The relationship was proved to be genuine through the Exner criterion[13] by plotting log k'_{303} versus log k'_{313} ($r = 0{\cdot}9995$, $s = 0{\cdot}016$). The value of β was calculated from the equation

$$\beta = \frac{T_1(1 - q)}{(T_1/T_2) - q} \tag{12}$$

where q is the slope of the Exner plot and $T_2 > T_1$; β was found to be 330 K. The values of β from both the calculated plots are higher than the experimental temperature (303 K), indicating enthalpy as a controlling factor in the reaction sequence.

The linear correlation and constancy of $\Delta G^{\neq}$ values (Table 4) indicate that indole and substituted indoles undergo oxidation via the same mechanism.

High concentration range of indole

The first-order dependence of the reaction rate on [Os(VIII)] and $[\mathrm{CAB}]_0$, inverse first-order dependence on $[\mathrm{OH}^-]$ and zero-order dependence on $[\mathrm{indole}]_0$ indicate that the formation of an intermediate species from OsO_4 and CAB is the most probable rate-controlling step.

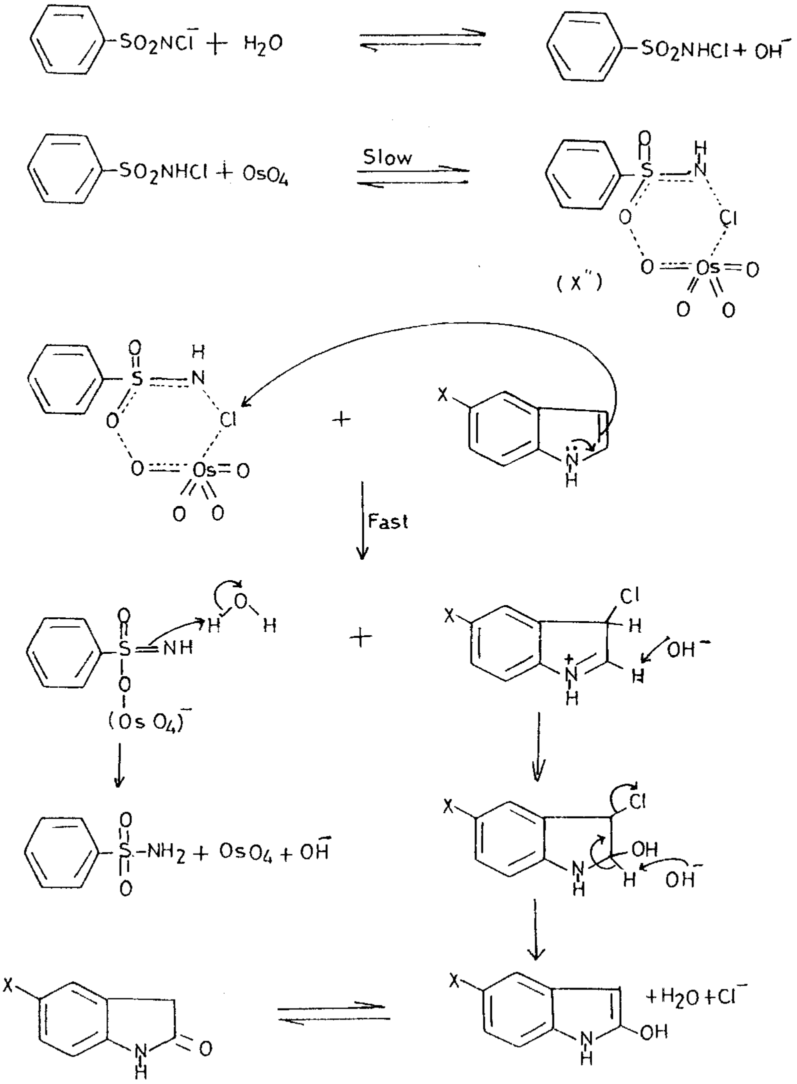
A first-order retardation by OH^- has been observed in many chloraminometric reactions, and has been attributed to the hydrolysis of the anion to generate the conjugate acid. Hardy and Johnston[14] carried out a detailed investigation on alkaline bromamine-B solutions and showed that the conjugate acid $C_6H_5SO_2NHBr$ is the active species in the oxidation of nitrophenols. During the oxidation of α-hydroxy acids, aldehydes and ketones by alkaline CAT catalysed by OsO_4, Mushran and co-workers[15] assumed the formation of a cyclic complex between p-$CH_3C_6H_5SO_2NHCl$ 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. This is illustrated in Schemes 3 and 4. Hence it is probable that the change in mechanism (from that in Scheme 1) may be attributed to the fact that the oxidation of indole does not occur with either OsO_4 or CAB alone. It can be assumed[16] that a complex of these two serves as an oxidant and the possible oxidizing species in this case would be $PhSO_2NHCl$. In view of these facts the mechanism shown in Scheme 3 can be proposed.

$$\text{(i)}\ \mathrm{PhSO_2NCl^- + H_2O \underset{}{\overset{K_4}{\rightleftharpoons}} PhSO_2NHCl + OH^{-}}\ ^{1}$$

$$\text{(ii)}\ \mathrm{PhSO_2NHCl + OsO_4} \xrightarrow[\text{rate-determining step}]{k_5} \mathrm{X''}$$

$$\text{(iii)}\ \mathrm{X'' + In} \xrightarrow[\text{fast}]{k_6} \text{products}$$

Scheme 3



Scheme 4

From Scheme 3, we obtain

$$\text{rate} = k_5[\mathrm{PhSO_2NHCl}]\,[\mathrm{os(VIII)}] \tag{13}$$

Applying steady-state conditions to $[\mathrm{PhSO_2NHCl}]$, we have

$$\begin{aligned}\frac{d[\mathrm{PhSO_2NHCl}]}{dt} &= k_4[\mathrm{CAB}]\,[\mathrm{H_2O}] \\ &\quad - k_{-4}[\mathrm{PhSO_2NHCl}]\,[\mathrm{OH^-}] \\ &\quad - k_5[\mathrm{PhSO_2NHCl}]\,[\mathrm{Os(VIII)}] \\ &= 0\end{aligned} \tag{14}$$

or

$$[\mathrm{PhSO_2NHCl}] = \frac{k_4[\mathrm{CAB}]\,[\mathrm{H_2O}]}{k_{-4}[\mathrm{OH^-}] + k_5[\mathrm{Os(VIII)}]}$$

At higher $[\mathrm{OH^-}]$, the inequality

$$k_{-4}[\mathrm{OH^-}] \gg k_5[\mathrm{Os(VIII)}]$$

holds and

$$\begin{aligned}[\mathrm{PhSO_2NHCl}] &= \frac{k_4[\mathrm{CAB}]\,[\mathrm{H_2O}]}{k_{-4}[\mathrm{OH^-}]} \\ &= \frac{K_4[\mathrm{CAB}]\,[\mathrm{H_2O}]}{[\mathrm{OH^-}]}\end{aligned} \tag{15}$$

Substituting for [$PhSO_2NHCl$] in equation (13),

$$\text{rate} = \frac{k_5K_4[\text{CAB}][H_2O][\text{Os(VIII)}]}{[OH^-]} \qquad (16)$$

Equation (16) accounts for the observed first order each in [oxidant] and [catalyst] and inverse first order in [OH^-].

Solvent isotope effect

For a reaction involving a fast pre-equilibrium H^+ or OH^- ion transfer, the rate increases in D_2O medium since D_3O^+ and OD^- are a stronger acid and a stronger base, respectively, than H_3O^+ and OH^- ions. The reverse holds for reactions involving retardation by H^+ or OH^- ions. Hence the proposed mechanism is also supported by the decrease in rate in D_2O medium, indicating retardation by OH^- (Scheme 3). Proton inventory studies in H_2O–D_2O mixtures could throw light on the nature of the transition state. The dependence of the rate constant (k_{obs}) on n, the atom fraction of deuterium in a solvent mixture of D_2O and H_2O, is given[17,18] by a form of Gross–Butler equation as in

$$\frac{k^0_{\text{obs}}}{k^n_{\text{obs}}} = \frac{\Pi^{\text{TS}}(1 - n + n\phi_i)}{\Pi^{\text{RS}}(1 - n + n\phi_j)} \qquad (17)$$

where ϕ_i and ϕ_j are the isotopic fractionation factors for isotopically exchangeable hydrogen sites in the transition and reactant states, respectively. Equation (17) allows the calculation of the fractionation factor of TS if reactant fractionation factors are known. However, the curvature of the proton inventory plot could reflect the number of exchangeable protons in the reaction.[19] A plot of k^n_{obs} versus the deuterium atom fraction n in the present case is more or less a straight line, which clearly shows that the process involves a single proton or H–D exchange during the reaction sequence from the hydroxyl ion. Hence the participation of OH^- ion in the formation of transition state is inferred.

In Schemes 2 and 4 the electron density around the nitrogen atom is lowered, resulting in a weakening of the N—Cl bond. The subsequent oxidizing capacity of *N*-chlorobenzene-*p*-sulphonamide is increased after complexation, and it then interacts with the appropriate form of the substrate. The alkali-catalysed indole chlorination via activated chloramine-B (X′ or X″) affords 3-chloroindolinine and a nitrogen-protonated chloramine-B–osmium tetroxide complex, which then results in the formation of benzenesulphonamide, a hydroxide ion and osmium tetroxide. Hydration of 3-chloroindolenine to 3-chloro-2-hydroxyindolenine followed by alkali-catalysed removal of hydroben chloride produces 2-hydroxyindole, which is in equilibrium with its more stable keto form oxindole.

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