Mechanistic investigations of oxidation of isatins by sodium N-chlorobenzenesulfonamide in alkaline medium: A kinetic study

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Abstract: Oxidation of isatins (isatin, 5-methylisatin, 5-bromoisatin and 5-nitroisatin) to their anthranilic acids was performed efficiently with sodium N-chlorobenzenesulfonamide or chloramine-B (CAB) in alkaline medium at 35 ± 0.1 °C. The reactions follow identical kinetics for all the isatins, being first-order dependence each in [CAB]_o and [Isatin]_o and inverse fractional-order on [NaOH]. Addition of halide ions and benzenesulfonamide, reduction product of CAB, do not significantly affect the rate. Variation of ionic strength of the medium had no effect on the rate, while the dielectric effect is negative. The solvent isotope effect was studied using D_2O. Activation parameters for the overall reaction have been computed. The rates satisfactorily correlate with the Hammett σ relationship and the reaction constant ρ is -0.31 signifies that electron releasing groups accelerate the reaction while the electron withdrawing groups retard the rate. Values of ΔH# and ΔS# are linearly related and an isokinetic relationship is observed with β = 376 K, indicating the reaction is controlled by enthalpy. The stoichiometry of the title reaction is found to be 1:1. Oxidation products of isatins were identified as their corresponding anthranilic acids and the yields were found to be around 90%. The observed results have been explained by a plausible mechanism and the related rate law deduced. This method offers several advantages including high yield of the products, short reaction times, easier isolation of products, and stable, cost effective and relatively non-toxic reagents, which make the reaction process simple and smooth.

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1 Introduction

Isatins (1H-indole-2,3-diones) which occur in mammalian tissue and function as a modulator of biochemical processes have been the subject of interest [1]. Isatins, associated with amino heterocycles, have been used as pigments and dyes, since they are well known color reagents for amino acids. In the dyeing industry, isatin is used largely in the manufacture of vat dyes and also as an analytical reagent for the estimation of a number of industrially important compounds. The synthetic versatility of isatin has been evolved from the interest in the biological and pharmaceutical properties of its derivatives. Mild oxidation of isatins to anthranilic acids is an important synthetic step in organic synthesis. There are several reports in the literature about the synthesis of anthranilic acids from isatins [1]. However, there is still a need for introducing readily available, safe, stable and cost effective reagents for the oxidation of isatins to their anthranilic acids. The economic importance of anthranilic acids rests in their well-established anti-inflammatory activity.

The chemistry of N-haloamines has evinced considerable interest because they act as sources of both haloamine cations and N-anions, which act as both bases and nucleophiles. These compounds resemble hypohalites in their oxidative behavior and, although less familiar, are more stable than hypohalites [2-4]. The prominent member of this class is chloramine-T (CAT) and the mechanistic aspects of many of its reactions have been documented [5-7]. Chloramine-B (sodium N-chlorobenzenesulfonamide or CAB) is analogues to chloramine-T in aqueous solution and similar equilibria exist in acidic and alkaline solutions [8]. The oxidation potential of chloramine-B/benzenesulfonamide couple varies with the pH of the medium [9]. Although sufficient reports are available about the mechanism of oxidation of various substrates by CAT, similar information with CAB is scanty [10-11]. In continuation of our ongoing work on chloramine-B, we now report an efficient and a simple procedure for the oxidation of isatins to their corresponding anthranilic acids using chloramine-B in alkaline medium. It was therefore of interest to investigate this possibility in order to understand the relative rates, mechanisms and structure reactivity correlations by introducing different groups. Activation parameters have been calculated and isokinetic relationship being deduced. The present method offers several advantages including high yield of the products, short reaction times, ease of isolation of the products, and stable, cost effective and relatively non-toxic reagents which make the reaction process simple and smooth.

2 Experimental

2.1 Materials

The purity of chloramine-B (Fluka, Switzerland) was checked [12] by determining the amount of active chlorine present in the compound. The active chlorine content was found to be about $16.1 \pm 0.2 \%$ (Merck value $16.6 \%$). An aqueous solution of CAB was prepared, standardized periodically by the iodometric titration and stored in brown
bottles to prevent its photochemical deterioration [3]. Isatins (Lancaster, England) were of acceptable grades of purity and used without further purification. Aqueous solutions of isatins were employed. All other chemicals used were of analytical grades. Heavy water (D$_2$O, 99.2 %) was obtained by the Bhabha Atomic Research Centre (Mumbai, India). Double distilled water was employed in preparing the aqueous solutions.

2.2 Kinetic measurements

Reactions were carried out under pseudo-first-order conditions ([Isatin]$_o$ $\gg$ [CAB]$_o$) in glass stoppered Pyrex boiling tubes whose outer surface was coated black to prevent photochemical effects. Solutions containing appropriate amounts of isatin, NaOH and water (to keep the total volume constant for all runs), were placed in the tube and held at 35 ± 0.1 °C. A measured amount of CAB solution, also held at the same temperature, was rapidly added to the mixture. The progress of the reaction was monitored by withdrawing known aliquots (5 ml each) from the reaction mixtures at regular time intervals and estimating the unreacted CAB iodometrically. The course of the reaction was followed up to two half-lives. Pseudo-first-order rate constants, k', calculated from log [CAB] versus time plots were reproducible within ± 3–5 %. Regression analysis of the experimental data to obtain the regression coefficient, r, was performed with an $f_x$-100W scientific calculator.

3 Results and discussion

3.1 Stoichiometry and product analysis

Different sets of reactions containing excess CAB over isatins at a constant concentration of NaOH (1.0 × 10$^{-3}$ mol dm$^{-3}$) were kept for 24 h at 35 °C and then analyzed. The unreacted oxidant in the reaction mixture was determined iodometrically and the results showed 1:1 stoichiometry according to the equation:

\[
\text{R} = \text{H for isatin, CH}_3 \text{ for 5-methylisatin, Br for 5-bromoisatin and NO}_2 \text{ for 5-nitroisatin.}
\]

where R = H for isatin, CH$_3$ for 5-methylisatin, Br for 5-bromoisatin and NO$_2$ for 5-nitroisatin.

The reaction mixtures were stirred for 24 h at 35 °C. After completion of the reaction, the reaction products were neutralized by HCl and extracted with ethyl acetate. The reaction products were separated by column chromatography on silica gel (60 -200 mesh) using dichloromethane as eluting agent. Further, the products were identified as follows:
Benzenesulfonamide (BSA): The reduction product of CAB, benzenesulfonamide (PhSO$_2$NH$_2$), was recrystallized from dichloromethane and light petroleum ether and detected [13] by thin-layer chromatography using light petroleum – chloroform – butan-1-ol (2:2:1, v/v/v) as the solvent and iodine for detection ($R_f = 0.88$). The reported $R_f$ value is consistent with those reported in literature [13]. It was further confirmed by its melting point 151 °C (theoretical m.p. 150–152 °C). Furthermore, benzenesulfonamide was confirmed by GC-Mass spectrum. GC-MS data was obtained on a 17A Shimadzu gas chromatograph with a QP-5050A Shimadzu mass spectrometer. The mass spectrum was obtained using the electron impact ionization technique. The mass spectrum showed a molecular ion peak at 157 amu clearly confirming benzenesulfonamide (Fig. 1).

Anthranilic acids: The oxidation products of isatins were found to be their corresponding anthranilic acids. The presence of anthranilic acid was detected [14] by paper chromatography ($R_f = 0.278$), with butanol : ammonia (4:1 v/v) solvent and ethanolic ferric chloride as spry reagent. Further, it was subjected to GC-MS analysis which showed a molecular ion peak of 137 amu confirming anthranilic acid (Fig. 2). Other peaks observed in GC-MS can be interpreted in accordance with the observed structure. Furthermore, the procedure for the estimation of anthranilic acid was as follows: anthranilate was precipitated as its zinc salt [15]. To the reaction mixture calculated volume of 1 mol dm$^{-3}$ NaOH was added followed by 10 ml of buffer (pH 5) and 10 ml of 1 % zinc sulfate. The precipitate formed was filtered, dried at 105-110 °C and weighed, recovery of (C$_7$H$_6$O$_2$N)$_2$Zn was 88 – 95 %. Estimation of antranilic acid as zinc anthranilate in some typical experiments, the weights of anthranilates and their percentage yield are given in Table 1. It was also observed that the anthranilic acid does not undergo further oxidation under prevailing kinetic condition. The liberated CO$_2$ was identified by lime water test.

3.2 Kinetic orders

Oxidation of isatins to their anthranilic acids was performed efficiently using chloramine-B in alkaline medium. The kinetics of oxidation of isatins by CAB was investigated at several initial concentrations of the reactants. Similar oxidation behaviour was observed for all the four isatins studied.

Under pseudo-first-order conditions in which [Isatin]$_o$ $\gg$ [CAB]$_o$ and at constant [OH$^-$], plots of log [CAB] versus time were linear ($r = 0.9916$) for each [CAB]$_o$. The pseudo-first-order rate constants, $k'_{o}$, obtained by these plots were constant for different initial concentrations of CAB employed (Table 2), thus indicating a first-order dependence of rate on [CAB]$_o$. Values of $k'_{o}$ increases with increase in [Isatin]$_o$ (Table 2). Plots of log $k'$ versus log [Isatin] were linear ($r > 0.9990$) with unit slope, showing a first-order dependence of rate on [Isatin]$_o$. Also, the second-order rate constants $k^{''}_{o} = k'/[Isatin]_{o}$ were fairly constant (values are not reported) establishing a first-order dependence on [Isatin]$_o$. Furthermore, plots of $k'$ versus [Isatin] were linear ($r > 0.9960$), passing through the origin, confirming the first-order dependence on [Isatin]$_o$ and also the intermediates formed are of transient existence.
There was a decrease in rate with increase in [NaOH] (Table 3) and plots of log \( k' \) versus log [NaOH] were linear (\( r > 0.9961 \)) with negative fractional slopes (0.28 - 0.35), indicating an inverse fractional-order dependence of rate on hydroxyl ion concentration for all the four isatins. Addition of the reduction product, benzenesulfonamide (\( R\text{SO}_2\text{NH}_2 \), 5.0 \( \times \) \( 10^{-4} \) – 15.0 \( \times \) \( 10^{-4} \) mol dm\(^{-3} \)), did not affect the rate. It may thus be inferred that the sulfonamide is not involved in a pre-equilibrium step with the oxidant.

Variation of ionic strength of the medium (0.1–0.4 mol dm\(^{-3} \)) had no significant effect on the rate indicating the involvement of non-ionic species in the rate determining step. Hence no attempt was made to keep ionic strength constant for kinetic runs. Addition of \( \text{Cl}^- \) or \( \text{Br}^- \) ions in the form of NaCl or NaBr (2.0 \( \times \) \( 10^{-2} \)–8.0 \( \times \) \( 10^{-2} \) mol dm\(^{-3} \)) had no significant effect on the rate, indicating that neither interhalogen nor free chlorine was formed.

The rates were also studied in aqueous methanol of varying composition (0 – 30 % v/v). It was observed that an increase in methanol concentration decreases the rate of the reaction (Table 4) and hence plots of log \( k' \) versus \( 1 / D \), where \( D \) is the dielectric constant of the medium, gave straight lines (\( r > 0.9960 \)) with negative slopes. Values of \( D \) of MeOH-H\(_2\)O mixtures reported in literature [16] were employed. Blank experiments showed that the methanol oxidation by CAB was negligible under the present experimental conditions. Studies on the reaction rate in D\(_2\)O medium for isatin and 5-methylisatin revealed that while \( k' \) (H\(_2\)O) = 7.67 \( \times \) \( 10^{-4} \) s\(^{-1} \) and 9.30 \( \times \) \( 10^{-4} \) s\(^{-1} \), \( k' \) (D\(_2\)O) = 5.59 \( \times \) \( 10^{-4} \) s\(^{-1} \) and 7.08 \( \times \) \( 10^{-4} \) s\(^{-1} \) respectively. The solvent isotope effect \( k' \) (H\(_2\)O)/\( k' \) (D\(_2\)O) = 1.37 and 1.31 for the two isatins.

The reaction was studied at five different temperatures (298, 303, 308, 313 and 318 K), keeping other experimental conditions constant. From the Arrhenius plots of log \( k' \) versus \( 1 / T \) (\( r > 0.9987 \)), values of activation parameters, energy of activation \( E_a \), enthalpy of activation \( \Delta H^\ddagger \), entropy of activation \( \Delta S^\ddagger \), Gibb’s free energy of activation \( \Delta G^\ddagger \) and log \( A \) for each temperature were computed and the average values of each parameters are reported along with errors. These results are summarized in Table 5. Addition of reaction mixture to aqueous acrylamide solution did not initiate any polymerization and hence confirms the absence of free radical species in the reaction mixture.

### 3.3 Reaction mechanism and rate law

Chloramine-B is analogous to chloarmine-T and behaves like a strong electrolyte in aqueous solutions, and the several equilibria present are predominantly pH dependant [5]. Bishop and Jennings [2], Morris et al [3] and Hardy and Johnston [8] have explained the several types of equilibria present in acidic solutions of N-haloamines.

The oxidizing species in acidic solutions of CAB are \( \text{R SO}_2\text{NHCl} \), \( \text{R SO}_2\text{NCl}_2 \), HOCI and possibly \( \text{HOCl}^+ \). In alkaline solutions of CAB dichloramine (\( \text{R SO}_2\text{NCl}_2 \)) does not exist, and the possible species are the \( \text{R SO}_2\text{NCl}^- \) and \( \text{OCI}^- \) anions which would be transformed into more reactive oxidizing species \( \text{R SO}_2\text{NHCl} \) and HOCI in the course of the reaction in alkaline medium. A retarding influence of \( \text{OH}^- \) ion on the reaction
rate noticed [10, 17-22] in several chloraminometric reactions has been attributed to the formation of the conjugate acid PhSO₂NHCl from PhSO₂NCl⁻ in a base retarding step. An inverse fractional-order dependence of rate on [OH⁻] observed in the oxidation of isatins by CAB indicates that a fraction of the overall reaction proceeds via an alternative path involving the anion PhSO₂NCl⁻. In view of these facts, Schemes 1 and 2 have been proposed to account for the observed kinetics of the oxidation of isatins by CAB in alkaline solutions:

| Scheme 1 | General mechanistic scheme for the oxidation of isatins by CAB in alkaline medium. |
|----------|---------------------------------------------------------------------------------|
| PhSO₂NCl⁻ + H₂O ⇌[k₁] PhSO₂NHCl + OH⁻ (i) slow |
| PhSO₂NCl⁻ + S ⇌[k₂] X (ii) slowest and rate determining step |
| X ⇌[k₃] Products (iii) fast |

| Scheme 2 | General mechanistic scheme for the oxidation of isatins by CAB in alkaline medium. |
|----------|---------------------------------------------------------------------------------|
| PhSO₂NCl⁻ + S ⇌[k₄] X' + PhSO₂NH⁻ (i) slow and rate determining step |
| X' ⇌[k₅] Products (ii) fast |
| PhSO₂NH⁻ + H₂O ⇌[k₆] PhSO₂NH₂ + OH⁻ (iii) fast |

Here S = substrate, X and X' = complex intermediate species.

Scheme 1 and rate law 2 show a first-order dependence on both [CAB]₀ and [Isatin]₀, and an inverse first-order dependence in [OH⁻], while Scheme 2 and rate law 3, indicate the rate to be independent of [OH⁻].

\[-\frac{d[CAB]}{dt} = k₁k₂[CAB] \frac{[Isatin]}{k_{-1}[OH^{-}]} \]

\[-\frac{d[CAB]}{dt} = k₄[CAB] \frac{[Isatin]}{} \]

The net outcome of the two paths, results in the combined rate law 4 from which the inverse-fractional dependence of rate on [OH⁻] can be inferred.

\[-\frac{d[CAB]}{dt} = k₁k₂[CAB] \frac{[Isatin]}{k_{-1}[OH^{-}]} + k₄[CAB] \frac{[Isatin]}{} \]

Detailed mechanisms involved in the electron transfer during the oxidation of isatins to corresponding anthranilic acids by PhSO₂NHC and PhSO₂NCl⁻ are shown in Scheme 3 and Scheme 4 respectively. In Scheme 3 the oxidant species PhSO₂NCl⁻ anion hydrolyses to give the corresponding conjugate acid PhSO₂NHCl. In the next slow and rate determining step isatins reacts with a mole of PhSO₂NHC giving an intermediate complex, oxychloro compound (X). This intermediate complex in the fast step, in presence of base, loses the chloride ion followed by decarboxylation to yield the corresponding anthranilic
acids. In Scheme 4, the anion PhSO$_2$NCl$^-$ reacts with isatin in the rate determining step, ultimately giving the corresponding anthranilic acids. The intermediate steps involved in Scheme 4 are similar to those of Scheme 3. The proposed mechanism and the derived rate law are supported by the following experimental facts:

3.4 Effect of solvent isotope

The proposed mechanism is supported by the decrease of rate in D$_2$O medium. For a reaction involving a fast pre-equilibrium H$^+$ or OH$^-$ ion transfer, the rate increases in D$_2$O since D$_3$O$^+$ and OD$^-$ are 2 to 3 times stronger acids and stronger bases respectively, than H$_3$O$^+$ and OH$^-$ ions [23-24]. The reverse also holds good for reactions involving retardation by H$^+$ or OH$^-$ ions. The decrease of reaction rate with D$_2$O in the present studies indicate retardation by OH$^-$ ion and the observed solvent isotope effect $k'_{(H_2O)}/k'_{(D_2O)} > 1$ confirm the above theory. However, the magnitude of retardation in D$_2$O is small due to the hydrolysis step which to make the normal kinetic isotope effect $k_{H_10}/k_{D_10} > 1$ for the slow step (i) in Scheme 1 and also attributed to the inverse fractional-order dependence of rate on [OH$^-$].

3.5 Effect of dielectric constant

The negative dielectric effect of methanol provides support for the proposed mechanism. The effect of changing the solvent composition on the rate of reaction has been discussed in detail in the well-known publications by Benson [25], Frost and Pearson [26], Laidler [27], Amis [28] and Entelis and Tiger [29]. For the limiting case of zero angle of approach between two dipoles or an ion-dipole system, Amis [28] has shown that a plot of log $k'$ versus 1/D gives a straight line, with a negative slope for a reaction between a negative ion and a dipole or between two dipoles, while a positive slope results for a positive ion-dipole interaction. The former concept agrees with our observation, where a negative ion and a dipole and two dipoles are involved in the rate determining steps of schemes 1 and 2.

3.6 Effect of substituents

Substituent effect was used to probe the reaction mechanism. Structure reactivity relationships [30-31] are ascertained by employing three para-substituted isatins and the kinetic observations reveal that electron releasing group enhances the reactivity while electron withdrawing groups inhibit the rate. The rate data are correlated with the Hammett plot of log $k'$ versus $\sigma$ which is fairly linear ($r = 0.9552$). From the above plot, the value of the reaction constant $\rho$ is found to be -0.31 signifies that the electron releasing group (CH$_3$) in the benzene ring accelerates the reaction while the electron withdrawing groups (Br and NO$_2$) retard the rate. From an inspection of the rate data, the rate of oxidation of isatins follows the order: 5-methylisatin > isatin > 5-bromoisatin > 5-nitroisatin. The
trend may be attributed to the inductive effect of both the electron donating and electron withdrawing groups in the present study.

3.7 Isokinetic relationship

The data given in Table 5 indicates that the activation energy is highest for the slowest reaction and vice-versa confirming that the reaction is enthalpy controlled. Further, the values of $\Delta H^\neq$ and $\Delta S^\neq$ can be correlated linearly (Fig. 3; $r = 0.9981$), resulting in an isokinetic relation, which indicates the operation of similar mechanism for the oxidation of all the four isatins by CAB. From the slope, the value of isokinetic temperature ($\beta$) is 376 K, which is much higher than the experimental value, 308 K. The genuine nature of the isokinetic relationship was verified by the Exner criterion [32] by plotting log $k'(308\text{K})$ versus log $k'(298\text{K})$ (Fig. 3; $r = 0.9960$). The value of $\beta$ was calculated from the equation $\beta = T_1 (1-q)/(T_1/T_2) - q$ where $q$ is the slope of Exner plot and $T_1 > T_2$. The value of $\beta$ is 373 K, which is higher than the experimental temperature indicating a common enthalpy-controlled pathway for the reactions. The moderate values of energy of activation observed supports the proposed mechanism. The large negative $\Delta S^\neq$ values point towards the formation of a more ordered activated complex, while the near constant values of $\Delta G^\neq$ values indicate that all the four isatins are oxidized by a similar mechanism.

4 Conclusions

Oxidation of isatins to their corresponding anthranilic acids was performed efficiently with chloramine-B in alkaline medium at 35 ± 0.1 °C. All four reactions followed identical kinetics with a first-order dependence both on [CAB]$_o$ and [Isatin]$_o$ and a negative fractional-order dependence on [NaOH]. Activation parameters and isokinetic temperature were deduced. Relative reactivity of these isatins follows the order: 5-methylisatin > isatin > 5-bromoisatin > 5-nitroisatin and the Hammett relationship is observed for the reaction with $\rho = -0.31$, showing that the electron donating group enhances the rate and the electron withdrawing groups retard the rate. The present method developed for the oxidation of isatins to their anthranilic acids using CAB offers several advantages including high yield of products, short reaction times, ease of isolation of products, and stable, cost effective and relatively non-toxic reagents which make the reaction process simple and smooth.

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| Isatin        | Corresponding anthranilic acid | Weight and % of zinc anthranilate (mg) |
|--------------|-------------------------------|---------------------------------------|
| Isatin       | Anthanilic acid               | 264 (286) 92 %                        |
| 5-Methylisatin | 5-Methylanthranilic acid       | 304 (327) 93 %                        |
| 5-Bromoisatin | 5-Bromoanthranilic acid        | 224 (254) 88 %                        |
| 5-Nitroisatin | 5-Nitroanthranilic acid        | 295 (310) 95 %                        |

Values in parentheses refer to expected weights.

**Table 1** Estimation of zinc anthranilates
| $10^3 [\text{CAB}]_o$ (mol dm$^{-3}$) | $10^3 [\text{S}]_o$ (mol dm$^{-3}$) | 5-Methyl-isatin | 1.0 | 4.0 | 7.70 | 9.25 | 6.25 | 4.98 |
|----------------------------------|----------------------------------|----------------|-----|-----|------|------|------|-----|
| 2.0                              | 4.0                              | 6.79           | 9.10| 6.04| 4.85 |
| 4.0                              | 4.0                              | 7.67           | 9.30| 6.00| 4.90 |
| 7.0                              | 4.0                              | 7.61           | 9.40| 6.05| 4.51 |
| 10.0                             | 4.0                              | 7.71           | 9.20| 5.90| 4.91 |
| 10.0                             | 1.0                              | 1.99           | 2.25| 1.81| 1.31 |
| 4.0                              | 2.0                              | 3.84           | 4.80| 3.35| 2.55 |
| 4.0                              | 4.0                              | 7.67           | 9.30| 6.00| 4.90 |
| 4.0                              | 8.0                              | 15.2           | 17.8| 12.1| 10.1 |
| 4.0                              | 16.0                             | 31.5           | 36.3| 24.5| 20.0 |

**Table 2** Effect of varying reactant concentrations on the rate of reaction at $[\text{NaOH}] = 1.0 \times 10^{-3}$ mol dm$^{-3}$; temp = 308 K.
| $10^3$ [NaOH] (mol dm$^{-3}$) | $10^4 k'$ (s$^{-1}$) Isatin | 5-Methylisatin | 5-Bromoisatin | 5-Nitroisatin |
|-----------------------------|-----------------|----------------|---------------|---------------|
| 0.1                         | 13.2            | 17.7           | 12.6          | 11.2          |
| 0.5                         | 8.90            | 11.5           | 7.90          | 6.41          |
| 1.0                         | 7.67            | 9.30           | 6.00          | 4.90          |
| 2.0                         | 6.00            | 7.15           | 4.65          | 3.81          |
| 6.0                         | 4.40            | 5.18           | 3.35          | 2.85          |

Table 3: Effect of varying NaOH concentration on the rate of reaction at $[CAB]_o = 4.0 \times 10^{-4}$ mol dm$^{-3}$; $[S]_o = 4.0 \times 10^{-3}$ mol dm$^{-3}$; temp = 308 K.
| % [MeOH] (v/v) | D  | 10^4k’ (s^-1) |
|---------------|----|--------------|
|               | Isatin | 5-Methyl-isatin | 5-Bromo-isatin | 5-Nitro-isatin |
| 0.0           | 76.73 | 7.67         | 9.30           | 6.00           | 4.90          |
| 10.0          | 72.37 | 6.00         | 6.45           | 4.30           | 3.51          |
| 20.0          | 67.48 | 4.20         | 4.80           | 3.00           | 2.40          |
| 30.0          | 62.71 | 2.82         | 3.20           | 1.81           | 1.35          |

Table 4: Effect of varying dielectric constant (D) of the medium on the rate of reaction at [CAB]_o = 4.0 × 10^{-4} mol dm^{-3}; [S]_o = 4.0 × 10^{-3} mol dm^{-3}; [NaOH] = 1.0 × 10^{-3} mol dm^{-3}; temp = 308 K.
| Temperature (K) | $10^4k' \text{ (s}^{-1}\text{)}$ | Isatin | 5-Methylisatin | 5-Bromoisatin | 5-Nitroisatin |
|----------------|--------------------------------|--------|----------------|---------------|---------------|
| 298            |                                | 3.75   | 5.10           | 2.80          | 2.0           |
| 303            |                                | 5.65   | 7.15           | 4.52          | 3.42          |
| 308            |                                | 7.67   | 9.30           | 6.00          | 4.90          |
| 313            |                                | 11.3   | 13.5           | 10.0          | 9.10          |
| 318            |                                | 16.5   | 17.8           | 14.5          | 13.5          |
| $E_a$/kJ mol$^{-1}$ |                      | 59.1   | 51.5           | 67.0          | 74.5          |
| $\Delta H^\#$/kJ mol$^{-1}$ |          | 56.5 ± 0.07 | 48.9 ± 0.02 | 64.4 ± 0.02 | 71.9 ± 0.10 |
| $\Delta G^\#$/kJ mol$^{-1}$ |          | 93.8 ± 0.11 | 96.2 ± 0.10 | 94.4 ± 0.20 | 94.8 ± 0.14 |
| $\Delta S^\#$/J K$^{-1}$ mol$^{-1}$ |          | -121 ± 0.22 | -144 ± 0.46 | -97.2 ± 0.21 | -74.5 ± 0.14 |
| log A          |                                | 6.91 ± 0.01 | 5.71 ± 0.01 | 6.16 ± 0.01 | 9.35 ± 0.01 |

Table 5 Temperature dependence on the rate of reaction and activation parameters for the oxidation of isatins by CAB in NaOH medium at [CAB]$_o$ = $4.0 \times 10^{-4}$ mol dm$^{-3}$; [S]$_o$ = $4.0 \times 10^{-3}$ mol dm$^{-3}$; [NaOH] = $1.0 \times 10^{-3}$ mol dm$^{-3}$. 
(i) \[
\text{PhSO}_2\text{NCl} + \text{H}_2\text{O} \rightleftharpoons \text{PhSO}_2\text{NHCl} + \text{OH}^{-}
\]

Scheme 3 Oxidation of isatins by PhSO₂NHCl species.
Scheme 4 Oxidation of isatins by PhSO$_2$NCl$^-$ species.
Fig. 1 GC-Mass spectrum of benzenesulfonamide with its molecular ion peak at 157 amu.
Fig. 2 GC-Mass spectrum of anthranilic acid with its molecular ion peak at 137 amu.
Fig. 3 Iso kinetic plots of a) $\Delta H^\neq$ versus $\Delta S^\neq$ and b) $\log k'(306K)$ versus $\log k'(298K)$. 