Oxidation of substituted phenyl methyl sulphides by N-chloroacetamide in acidic medium: A kinetic and mechanistic study

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The kinetics of oxidation of several substituted phenyl methyl sulphides by N-chloroacetamide (NCA) yielding sulphoxides have been studied in acidic aqueous acetonitrile medium. The reaction displays first-order dependence each in [sulphide], [NCA] and [H⁺]. The reaction rate is not influenced by the addition of acetamide, mercuric acetate and acrylamide. Presence of electron releasing substituents in the phenyl ring enhances the rate while that of opposite ones retards it. A good Hammett correlation between the rate data and σ constants is obtained with a p-value of -3.29 at 313K (r=0.999). The results point to a polar mechanism involving the rate-limiting formation of a chlorosulphonium cation by the electrophilic attack of a protonated NCA on the sulphide sulphur. The chlorosulphonium cation presumably hydrolys to sulphonide in a fast step.

The kinetics of oxidation of organic sulphides by N-halo oxidants such as bromamine-T¹, chloramine-T², N-bromoacetamide³ and N-bromosuccinimide⁴ have been investigated. The nature of active oxidising species and the mechanism depend on the nature of the halogen atom, the groups attached to the nitrogen and the reaction conditions. In our recent study³ on the N-bromoacetamide oxidation of substituted phenyl methyl sulphides in the presence of Hg(II) we have found that Hg(II) introduced into the reaction mixture to trap the bromide ion catalyses the reaction and the reaction proceeds entirely through the Hg(II)-catalysed pathway. With a view to obtaining further insight into the mechanism of oxidation of sulphides by N-halo oxidants we have now studied N-chloroacetamide (NCA) oxidation of sulphides. The reaction failed to occur in neutral medium even in presence of Hg(II) demonstrating that complex between NCA and Hg(II) is not involved in the reaction in contrast to NBA oxidation involving NBA...Hg(II) complex³. However, as the reaction of sulphides with NCA has been found to proceed smoothly in presence of HClO₄ the reaction has been studied in acidic medium and the results are presented in the paper. It is to be noted that no systematic kinetic investigation on the oxidation of organic substrates by NCA has yet been reported in the literature in contrast to several oxidations by N-bromosuccinimide⁴,⁵ and N-bromoaceta-
mide³,⁶.

Materials and Methods

All the reagents employed were of the highest purity available. N-Chloroacetamide, prepared⁷ in the laboratory, was kept always in a blackened container. Solutions of NCA were prepared afresh before each kinetic run and assayed iodometrically. Acetonitrile was purified by a standard procedure⁸. All the sulphides were prepared by known methods⁹,¹⁰ and their purity checked by TLC. Doubly distilled water was employed in all kinetic runs.

Kinetic procedure

The kinetic measurements were performed in 50% (v/v) acetonitrile-water mixture under pseudo-first order conditions, viz. [sulphide] ≫ [NCA] at constant ionic strength (maintained by NaClO₄) and constant [H⁺] (maintained by HClO₄). The initial [sulphide] was in the range of 0.01-0.08 mol dm⁻³ and the [NCA] in the range of 0.0005-0.004 mol dm⁻³. The runs were conducted in blackened vessels and the kinetics followed upto 70-80% completion of the reaction by estimating un-
continued NCA iodometrically using starch as an in-
dicator. The pseudo-first order rate constants (kobs) obtained from the slopes of the linear log
[NCA] versus time plots \((r \geq 0.997)\) when divided by [sulphide] afforded the second order rate constants.

**Stoichiometry and product analysis**

Reaction mixture containing an excess of [NCA] over [MPS] was allowed to react at 313 K for 24 hr in the presence of 0.025 mol dm\(^{-3}\) HClO\(_4\). The excess of NCA remaining was estimated. The results show that one mole of MPS consumes one mole of NCA.

The product from the reaction mixture of an actual kinetic run with MPS as a substrate was isolated and analysed by co-TLC with authentic samples of MPS, methyl phenyl sulphoxide and methyl phenyl sulphone. The reaction product gave only two spots corresponding to the unchanged MPS and methyl phenyl sulphoxide, indicating that sulphoxide is the only product and further oxidation to sulphone does not occur. Hence the overall reaction can be expressed by Eq. (1).

\[
\begin{align*}
\text{C}_6\text{H}_6\text{SCH}_3 + \text{CH}_3\text{CONHCl} + \text{H}_2\text{O} & \xrightarrow{H^+} \\
\text{C}_6\text{H}_6\text{SOCH}_3 + \text{CH}_3\text{CONH}_2 + \text{H}^+\text{Cl}^- & \quad \ldots (1)
\end{align*}
\]

**Results and Discussion**

Kinetic data were collected for all the substituted phenyl methyl sulphides. As the results were similar only those of methyl phenyl sulphide (MPS) are presented in detail. The rates of oxidation at various initial [MPS] and [NCA] are listed in Table 1. The reaction exhibits a clean first order dependence in NCA as evidenced by the good linear plots of log [NCA] versus time \((r \geq 0.997)\) and by the constancy of \(k_{\text{obs}}\) at varying [NCA] (Table 1). Further, the plot of \(k_{\text{obs}}\) versus [MPS] is linear passing through the origin revealing first order dependence in MPS and ruling out the possibility of any substrate-independent path for oxidation.

The reaction rate increases with increase in \([H^+]\) at constant ionic strength (Table 2). A plot of \(k_{\text{obs}}\) versus \([H^+]\) is linear passing through the origin showing that the reaction proceeds completely through the acid-catalysed pathway and the order in \([H^+]\) is unity. The reaction rate increases with increase in ionic strength of the medium and in the proportion of water in the solvent mixture (Table 2).

In an atmosphere of nitrogen, the addition of acrylamide into the reaction mixture failed to affect the rate and no visible polymerisation of the monomer was noted. This rules out the intermediacy of free radicals in the reaction.

In an acidified solution of NCA, the probable active oxidising species are the NCA itself, the disproportionation product, viz. N,N-dichloroacetamide (CH\(_3\)CONCl\(_2\)), the hydrolytic product (HOCl) and their protonated forms (see Eqs 2 and 3). The strict first order dependence in NCA and the absence of rate retardation by added acetaldehyde (0.05 mol dm\(^{-3}\)) preclude the involvement of CH\(_3\)CONCl\(_2\) (2) and HOCl (3) and their protonated forms in the rate-limiting step.

\[
\begin{align*}
2\text{CH}_3\text{CONHCl} & \rightleftharpoons \text{CH}_3\text{CONCl}_2 + \text{CH}_3\text{CONH}_2 \\
\text{CH}_3\text{CONHCl} + \text{H}_2\text{O} & \rightleftharpoons \text{CH}_3\text{CONH}_2 + \text{HOCl} \quad \ldots (2)
\end{align*}
\]

This leaves CH\(_3\)CONHCl or its protonated species as the most likely oxidising species. The linear increase in the reaction rate with increase in \([H^+]\) is clearly in favour of the protonated NCA, i.e. CH\(_3\)CONH\(_2\)Cl as the active oxidant (Eq. 4). The fact that the plot of \(k_{\text{obs}}\) vs \([H^+]\) is linear \((r = 0.999)\) with no levelling off at higher

\[
\text{CH}_3\text{CONHCl} + H^+ \xrightarrow{K} \text{CH}_3\text{CONH}_2\text{Cl} \quad \ldots (4)
\]
[H+] suggests that the protonation equilibrium constant, K, is of small magnitude. This is not surprising as even in acetamide the K-value is 0.234 and N-chloroacetamide is anticipated to have a still lesser K-value.

All the above results are in accord with a rate-limiting electrophilic attack of CH3CONH2Cl on the sulphide sulphur (Eq. 5). The absence of rate retardation by added acetamide excludes the possibility of step (5) being an equilibrium.

The resulting chlorosulphonium cation in step (5) presumably undergoes a fast hydrolysis to the sulphoxide (Eq. 6).

\[ \text{CH}_3\text{CONH}_2\text{Cl} + \text{S}_2\text{Cl}_2 \rightarrow \text{CH}_3\text{CONH}_2 + 2\text{H}^+ + \text{Cl}^- \]

The overall rate law is given by Eq. (7)

\[ -\frac{d[\text{NCA}]}{dt} = k_1[\text{MPS}]\text{[NCA]}[\text{H}^+] \]

\[ = Kk_1[\text{MPS}]\text{[NCA]}[\text{H}^+] \]

\[ = k_{\text{obs}}[\text{MPS}]\text{[NCA]} \text{ at constant [H]}^+ \] \( \cdots \) (7)

The above rate law is clearly in accord with the experimental observations.

**Substituent effects**

With a view to obtaining more information into the nature of the transition state, the rates of oxidation of several substituted phenyl methyl sulphides by NCA have been measured. The rate data at 303, 313 and 323 K and the activation parameters computed from the slopes and intercepts of the Eyring’s plots are listed in Table 3. Both entropies of activation and enthalpies of activation vary with the nature of the substituent. However, the plot of ΔH‡ versus ΔS‡ is found to be scattered. From the plot of log \( k_2 \) (50°C) versus log \( K_2 \) (30°C) the isokinetic temperature has been calculated to be \(-351.4\) K. The entropies of activation presented in Table 3 are largely negative in consonance with a bimolecular-rate-limiting reaction involving an ordered transition state relative to the reactants. The data in Table 3 further show that the reaction rate increases with increase in the electron donating character of the substituent. The rate data give an excellent correlation with Hammett \( \sigma \) constants, the \( \rho \)-value at 313K being \(-3.3\) (r = 0.999). The large negative \( \rho \)-value indicates that the sulphide molecule acquires high electron deficiency in the rate-limiting step. Almost equal \( \rho \)-value (\(-3.2\)) has been encountered in the bromine oxidation of alkyl phenyl sulphides involving the formation of bromosulphonium cation. Similar nucleophilic role by sulphides and consequent negative \( \rho \)-values have been recorded in several oxidations. The effect of solvent composition also is in accordance with the mechanism. With increase in water content of the medium both the polarity and nucleophilicity of the solvent medium increases. This facilitates the formation of the chlorosulphonium cation with a polar transition state in the rate-limiting step. The high \( \rho \)-value and the absence of influence by the radical trap on the rate are all consistent with the polar mechanism advanced for this reaction.

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**References**


