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Oxidation of Methionine by Sodium N-Chlorobenzene Sulphonamide in Hydrochloric Acid Medium: A Kinetic Study

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Kinetics of oxidation of DL-methionine (Met) in the presence of HCl by sodium N-chlorobenzene sulphonamide (chloramine-B or CAB) have been performed at 30°C. The rate shows a first order dependence each on [CAB] and $[H^+]$ and zero order dependence on [Met]. The variation of the ionic strength, dielectric constant of the medium and addition of chloride ion and the reaction product of CAB (benzene sulphonamide) do not have any significant effect on the reaction rate. The activation parameters have been evaluated.

INTRODUCTION

The chemistry of aromatic sulphonyl haloamines in general and of the sodium salt of N-chlorobenzene sulphonamide (Chloramine-B or CAB or $C_6H_5SO_2NClNa \cdot 1.5H_2O$) in particular has received considerable attention[1–3]. Methionine (Met), a sulphur containing amino acid is reported to behave differently from other amino acids towards many oxidants[4, 5] due to the electron-rich sulphur centre which is easily oxidizable. In continuation of our earlier work[2–6] on oxidation of amino acids, we report here the kinetics of oxidation of methionine by chloramine-B in HCl medium.

EXPERIMENTAL

Chloramine-B was prepared and purified by the method described earlier[6]. An aqueous solution of the compound was standardized by the iodometric method and preserved in brown bottles to prevent its photochemical deterioration. Chromatographically pure DL-methionine (Merck) was further assayed by the acetous perchloric acid method[7] and its aqueous solution was prepared. All other reagents were of AnalaR grade. The ionic strength of the medium was kept at a high value by using a concentrated solution of sodium perchlorate.

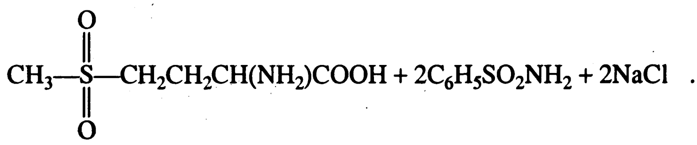
The kinetic runs were carried out in stoppered pyrex glass tubes whose outer surfaces were coated black to eliminate photochemical effects. Mixtures containing requisite amounts of methionine, $NaClO_4$, HCl and water (to maintain a constant total volume for all runs) were taken in the tube and thermally equilibrated in a water bath set at a given temperature (30 ± 0.1°C). To this solution was added a measured amount of preequilibrated CAB solution to give a known concentration. The reaction mixture was shaken well for uniform concentration. The progress of the reaction was monitored iodometrically for two half lives by withdrawing aliquots of the reaction mixture at regular intervals of time. The pseudo-first order rate constants calculated were reproducible within ±3%. Regression analyses of the experimental data were carried out on an EC-72 statistical calculator.

RESULTS AND DISCUSSION

The kinetics of oxidation of methionine by CAB was investigated at several initial concentrations of the reactants in HCl medium at 30°C.

Stoichiometry and product analysis: Varying ratios of CAB to methionine in the presence of HCl were equilibrated at 30°C for 24 h. The unreacted CAB in the reaction mixture was determined by iodometric titrations. The analysis showed that one mole of methionine reacted with two moles of CAB. The observed reaction stoichiometry is given by eqn. (1).

$CH_3SCH_2CH_2CH(NH_2)COOH + 2C_6H_5SO_2NClNa + 2H_2O \longrightarrow$



$$CH_3{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}{-}CH_2CH_2CH(NH_2)COOH + 2C_6H_5SO_2NH_2 + 2NaCl \quad \ldots (1)$$

Benzene sulphonamide ($C_6H_5SO_2NH_2$) was detected by thin layer chromatography using solvent system of petroleum ether-chloroform-1-butanol (2 : 2 : 1 v/v) in ascending irrigation and using iodine vapour as the developing reagent ($R_f = 0.88$). Identification of methionine sulphone was also made through paper chromatography[9]. The solvent system employed was *n*-butanol-glacial acetic acid-water (4 : 1 : 5 v/v) and a 0.2% solution of ninhydrin in butanol, water and acetic acid (95 : 4 : 0.5 v/v) was used as the spray reagent ($R_f = 0.17$).

Effect of reactants: At constant [H^+], with the substrate in excess, plots of log [CAB] *vs.* time were linear indicating a first order dependence of rate on [CAB]. Values of the pseudo-first order rate constants (k^1) are given in Table-1. The values of k^1 were unaffected with increase in $[Met]_0$, indicating that the rate was independent of $[amino\ acid]_0$ and the values are given in Table-1.

Effect of [H^+]: The rate increased with increase in [H^+] at constant [Cl^-]. A plot of log k^1 *vs.* log [H^+] was linear with slope equal to unity ($r = 0.9993$), indicating first order dependence on [H^+] (Table-2, Fig. 1).

Effect of benzene sulphonamide on rate: The addition of the reaction product, benzene sulphonamide ($C_6H_5SO_2NH_2$) (1×10^{-3} to 3×10^{-3} mol dm^{-3}) had no effect on the rate of reaction.

Effect of ionic strength and dielectric constant of the medium: Variation of the ionic strength of the medium (0.1 to 0.3 mol dm^{-3}) or variation of dielectric constant of the medium by adding methanol to the reaction mixture (0 to 20%) had no significant effect on the rate.

Effect of temperature: The reaction was studied at different temperatures (298 to 313 K) and from the plots of log k^1 *vs.* 1/T activation parameters were computed (Table-3).

TABLE-1
EFFECT OF VARYING REACTANT CONCENTRATION ON THE RATE

10^3 [CAB] (mol dm^{-3})	10^3 [Met] (mol dm^{-3})	k × 10^4 (s^{-1})
1.0	10.0	3.38
3.0	10.0	3.33
4.0	10.0	3.38
5.0	10.0	3.59
6.0	10.0	3.46
7.0	10.0	3.34
5.0	6.0	3.50
5.0	7.0	3.58
5.0	9.0	3.49
5.0	10.0	3.59
5.0	12.0	3.30
5.0	15.0	3.52

$[H^+] = 0.03$ mol dm^{-3}, $\mu = 0.30$ mol dm^{-3}, T = 303 K

TABLE-2
EFFECT OF VARYING $[H^+]$ ON THE RATE OF REACTION

10^2 $[H^+]$ (mol dm^{-3})	k × 10^4 (s^{-1})
2.0	2.50
2.5	3.03
3.0	3.60
5.0	5.84
7.0	8.60
9.0	11.09
10.0	12.47

[CAB] = 5.0×10^3 mol dm^{-3}, [Met] = 10.0×10^3 mol dm^{-3}, $\mu = 0.30$ mol dm^{-3}. T = 303 K.

TABLE-3
TEMPERATURE DEPENDENCE AND ACTIVATION PARAMETERS FOR THE OXIDATION OF METHIONINE BY CAB IN HCl MEDIUM

k × 10^4 (s^{-1})				E_a	$\Delta H^{\neq}$	$\Delta S^{\neq}$	$\Delta G^{\neq}$
298 K	303 K	308 K	313 K	(kJ mol^{-1})	(kJ mol^{-1})	(JK mol^{-1})	(kJ mol^{-1})
2.85	3.58	4.90	5.84	38.76	36.24	−191.37	94.22

Test for free radicals: Addition of the reaction mixture to aqueous acrylamide solution did not initiate polymerization, showing the absence of free radical species.

Pryde and Soper[10], Morris *et al.*[11] and Bishop and Jennings[12] have shown the existence of similar equilibria in acid and alkaline solutions of N-metalo-N-haloarylsulphonamides. Chloramine-B, being analogous to chloramine-T behaves as a strong electrolyte in aqueous solutions forming different species as shown in eqns. (2)–(6).

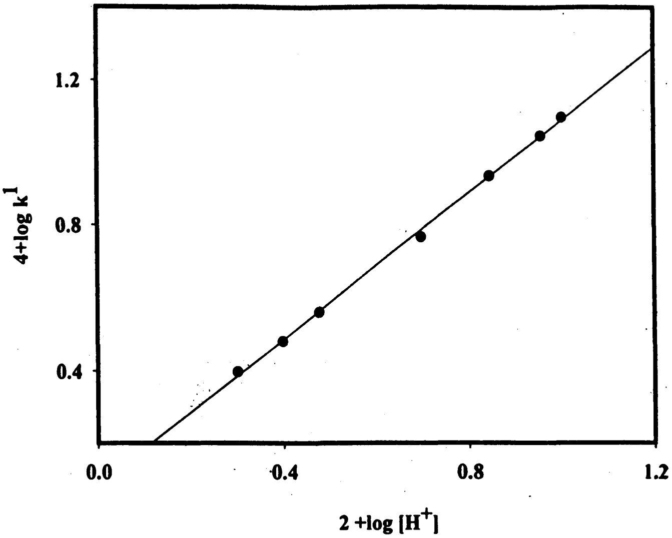


Fig. 1. Plot of log k^1 *vs.* log [H$^+$]
[CAB] = 5.0 × 10^3 mol dm^{-3}, [Met] = 10.0 × 10^3 mol dm^{-3}, μ = 0.30 mol dm^{-3}, T = 303 K.

$$C_6H_5SO_2NClNa \rightleftharpoons C_6H_5SO_2NCl^- + Na^+ \tag{2}$$

$$C_6H_5SO_2NCl^- + H^+ \rightleftharpoons C_6H_5SO_2NHCl \tag{3}$$

$$C_6H_5SO_2NHCl + H_2O \rightleftharpoons C_6H_5SO_2NH_2 + HOCl \tag{4}$$

$$2C_6H_5SO_2NHCl \rightleftharpoons C_6H_5SO_2NH_2 + C_6H_5SO_2NCl_2 \tag{5}$$

$$HOCl + H^+ \rightleftharpoons H_2OCl^+ \tag{6}$$

The possible oxidizing species in acidified CAB solution are $C_6H_5SO_2$ NHCl, $C_6H_5SO_2NCl_2$, HOCl and H_2OCl^+. If $C_6H_5SO_2NCl_2$ were to be the reactive species, then the rate law predicts a second order dependence of rate on $[CAB]_0$ according to eqn. (5) which is contrary to the experimental observations. If HOCl were the primary oxidizing species first order retardation of rate by the added benzene sulphonamide would be expected. However, no such effect was noticed in this study. Hardy and Johnston[13] have studied the pH dependence of relative concentrations of the species present in acidified chloramine-T solution of comparable molarities and have shown that monohaloamine is the likely oxidizing species in acid solution. Narayanan and Rao[14] and Subhashini *et al.*[15] have reported that monohaloamines can be further protonated at pH < 2 as shown in the following eqns. (7) and (8) for chloramine-T and chloramine-B respectively.

$$CH_3C_6H_4SO_2NHCl + H^+ \rightleftharpoons CH_3C_6H_4SO_2\overset{+}{N}H_2Cl \tag{7}$$

$$C_6H_5SO_2NHCl + H^+ \rightleftharpoons C_6H_5SO_2\overset{+}{N}H_2Cl \tag{8}$$

In the present investigations, the first order in [H$^+$] indicates that the protonation of $C_6H_5SO_2NHCl$ results in the formation of $C_6H_5SO_2NH_2Cl$. The protonated monochloramine-B produced can undergo hydrolysis to form $C_6H_5SO_2NH_2$ and H_2OCl^+.

Based on the above discussion, Scheme-1 is proposed for the oxidation of methionine by CAB.

Scheme-1

$$C_6H_5SO_2NHCl + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_6H_5SO_2\overset{+}{N}H_2Cl \qquad \text{fast} \quad (9)$$

$$C_6H_5SO_2\overset{+}{N}H_2Cl + H_2O \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C_6H_5SO_2NH_2 + H_2OCl^+ \qquad (10)$$

Forward step is rate determining

$$H_2OCl^+ + Met \xrightarrow{k_3} Products \qquad \text{fast} \quad (11)$$

Scheme-1 leads to rate law

$$Rate = k_2K_1[CAB][H^+] \qquad (12)$$

indicating that the substrate is oxidized in a fast step. Swain and Crist[16] have pointed out in their studies on the chlorination of anisole by HOCl that hypochlorous acidium ion H_2OCl^+ formed in a prior equilibrium before the rate limiting step is a better electrophile than HOCl.

Since rate = k_{obs} [CAB], eqn. (12) can be transformed into eqn. (13).

$$\frac{1}{k_{obs}} = \frac{1}{k_2K_1[H^+]} \qquad (13)$$

A plot of $\frac{1}{k_{obs}}$ *vs.* $\frac{1}{[H^+]}$ was found to be linear passing through the origin (Fig. 2). The value of $K_1k_2(12.22 \times 10^{-3})$ has been calculated.

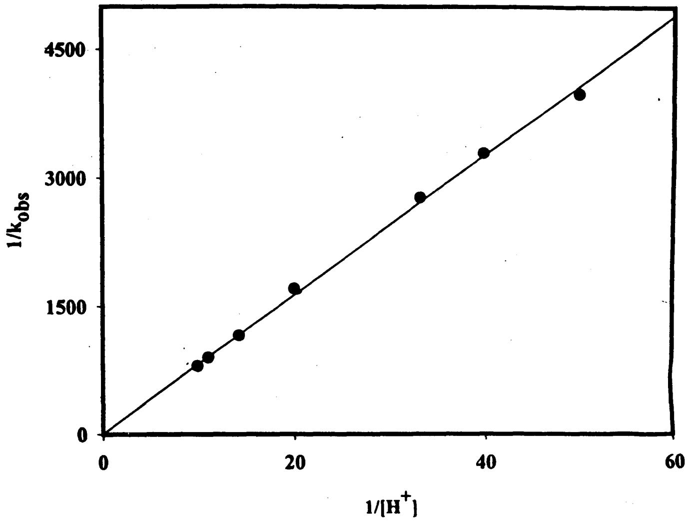


Fig. 2. Plot of $\frac{1}{k_{obs}}$ *vs.* $\frac{1}{[H^+]}$

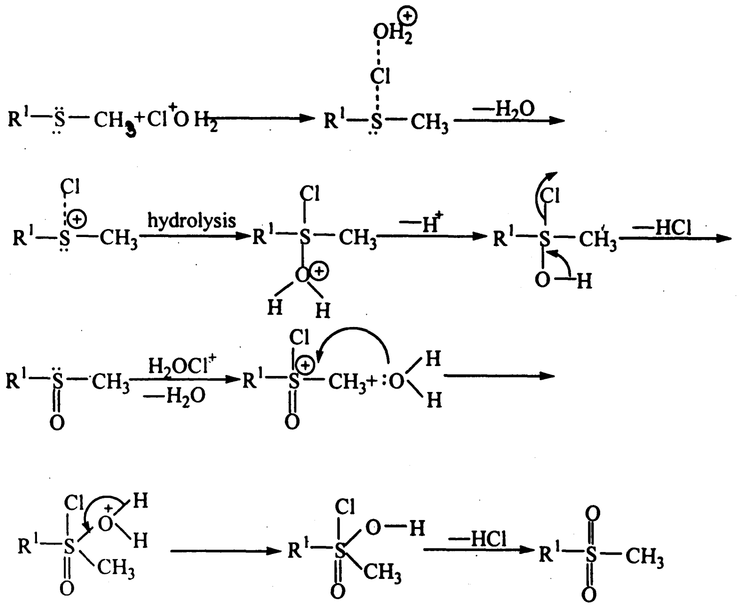
[CAB] = 5.0×10^3 mol dm^{-3}, [Met] = 10.0×10^3 mol dm^{-3}, $\mu = 0.30$ mol dm^{-3}, T = 303 K.

Variation of the dielectric constant of the medium does not affect the rate. An explanation may be offered in terms of the Born treatment applied by Laidler[17] for dipole-dipole reactions.

The moderate value of enthalpy of activation ($\Delta H^{\neq}$) is supportive of the proposed mechanism in Schemes 1 and 2.

A detailed mechanism of the oxidation of methionine by CAB in HCl solution is given in Scheme-2.

Scheme-2



Assuming H_2OCl^+ as the reactive species a reaction scheme can be formulated in which the substrate is attacked at the nucleophilic sulphur site by the oxidant to form a sulphurane-type intermediate and the latter is attacked by the dipolar solvent. Elimination of H^+ and HCl results in the formation of methionine sulphoxide, which is oxidized by the second molecule of the oxidant to methionine sulphone. The four electron stoichiometry shown for the reaction clearly rules out the formation of a sulphimide as a minor product which was observed during the oxidation of sulphides[18] by chloramine-B.

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