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Kinetics of Oxidation of Cysteine by Chloramine-B in $HClO_4$ Medium

T. DEMAPPA
Department of Studies and Research in Polymer Science, University of Mysore
Sir. M. Visvesvaraya, Post-Graduate Centre, Tubinakere, Mandya-571 402, India

The kinetics of oxidation of cysteine by chloramine-B in $HClO_4$ medium has been carried out at 30°C. The reaction rate shows a first order dependence each on [CAB] and [cysteine] and inverse fractional order on $[H^+]$. Addition of halide ions, ionic strength, dielectric constant of the medium and the reduction product benzenesulphonamide have no significant effect on the reaction rate. Thermodynamic parameters have been evaluated.

INTRODUCTION

There are the sources of halogen cations and hypohalite species[1–3]. The kinetic investigations of oxidation of amino acids by several oxidants has been reported[4–15] except with chloramine-B CAB. The author reports here the detailed investigation on oxidation of cysteine by CAB in $HClO_4$ medium at 30°C.

EXPERIMENTAL

Chloramine-B (CAB) was prepared by reported procedure[16]. The rate constants calculated were reproducible within ±3%. Regression analysis was carried out on an EC-72 statistical calculator.

Stoichiometry and Product Analysis

Reaction mixtures containing different compositions were equilibrated at 30°C for 24 h. The iodometric determination of unreacted CAB in the reaction mixture showed that 4 moles of CAB were consumed per mole of cysteine according to equation (1).

$$HOOC-\underset{NH_2}{\overset{H}{\underset{|}{\overset{|}{C}}}}-CH_2SH + 4PhSO_2NClNa + 5H_2O \longrightarrow$$

$$CH_3CHO + 4PhSO_2NH_2 + H_2SO_4 + NH_3 + CO_2 + 4NaCl \quad (1)$$

The presence of aldehyde which is an oxidation product of cysteine in the reaction mixture was detected by preparing 2,4-dinitrophenyl hydrazone derivatives and by using Tollens' and chromic acid tests[17]. The other product ammonia was quantitatively estimated by standard micro-Kjeldahl procedure, CO_2 was detected by the conventional lime water test. The reduction product of CAB, $PhSO_2NH_2$ was also identified by TLC using petroleum ether-chloroform-1-butanol (2 : 2 : 1 v/v/v) solvent system with ascending irrigation and using iodine as the developing reagent ($R_f = 0.88$).[18]

RESULTS AND DISCUSSION

The plot of log [CAB] versus time was found to the linear (Table-1) indicating first order dependence on [CAB]. The rate of reaction increased with increase in [Cyst] and plot of log k^1 *vs.* log [Cyst] was linear with a slope equal to unity (Fig. 1, Table-1), indicating first order dependence of rate on [Cyst]. The rate of

TABLE-1
EFFECT OF VARYING REACTANT CONCENTRATION ON THE RATE OF REACTION

$HClO_4 = 0.04$ mol dm^{-3}, $\mu = 0.2$ mol dm^{-3}, T = 303 K

10^3 [CAB] (mol dm^{-3})	10^3 [Cyst] (mol dm^{-3})	k^1 (10^4 sec^{-1})
2.0	3.0	13.63
3.0	3.0	13.64
4.0	3.0	13.63
5.0	3.0	13.63
6.0	3.0	13.62
7.0	3.0	13.64
5.0	1.0	4.54
5.0	2.0	9.08
5.0	3.0	13.63
5.0	4.0	18.17
5.0	5.0	22.65
5.0	6.0	27.23

r = 0.9999; order = 1.00

reaction decreased with increase in $[H^+]$ and plot of log k^1 *vs.* log $[H^+]$ was found to be linear (Table-2, Fig. 2) with fractional slope, indicating inverse fractional order. Addition of ClO_4, chlorine ion, reaction product benzenesulphonamide, ionic strength of the medium have no effect on the reaction. The reaction was studied at various temperatures and thermodynamic parameters were evaluated (Table-3). Pryde and Soper[19], Morries *et al.*[20], Bishop and Jennings[21] have shown the existence of similar equilibria in acid and alkaline solutions of CAB. Chloramine-B behaves as a strong electrolyte in aqueous solutions as shown in equations (2–6)

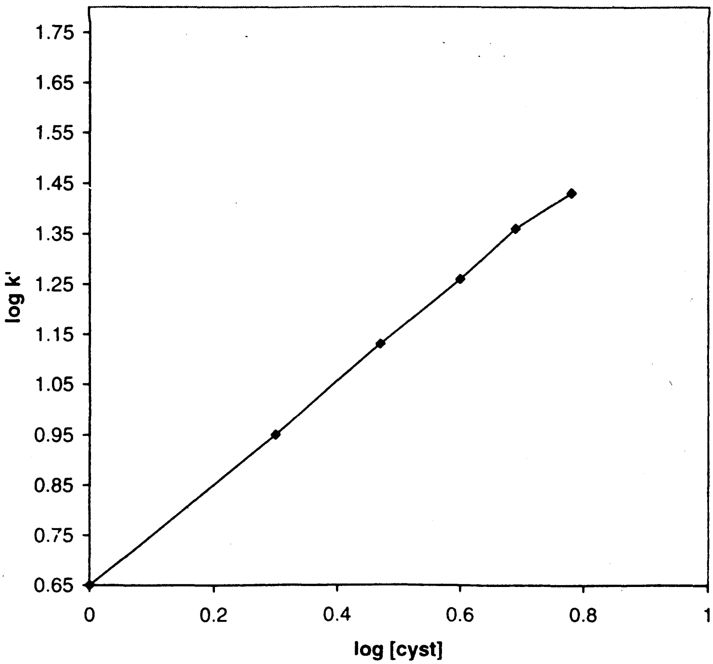


Fig. 1

TABLE-2

EFFECT OF [H^+] ON THE RATE OF REACTION AT [$NaClO_4$]

[Cyst] = 3.0×10^3 mol dm^{-3}, μ = 0.2 mol dm^{-3}, T = 303 K

[H^+] (mol dm^{-3})	k^1 (10^4 sec^{-1})
0.01	22.56
0.02	17.50
0.03	15.12
0.04	13.63
0.06	11.77
0.10	9.75
0.14	8.63
0.18	7.87

r = 0.9999; order = –0.36

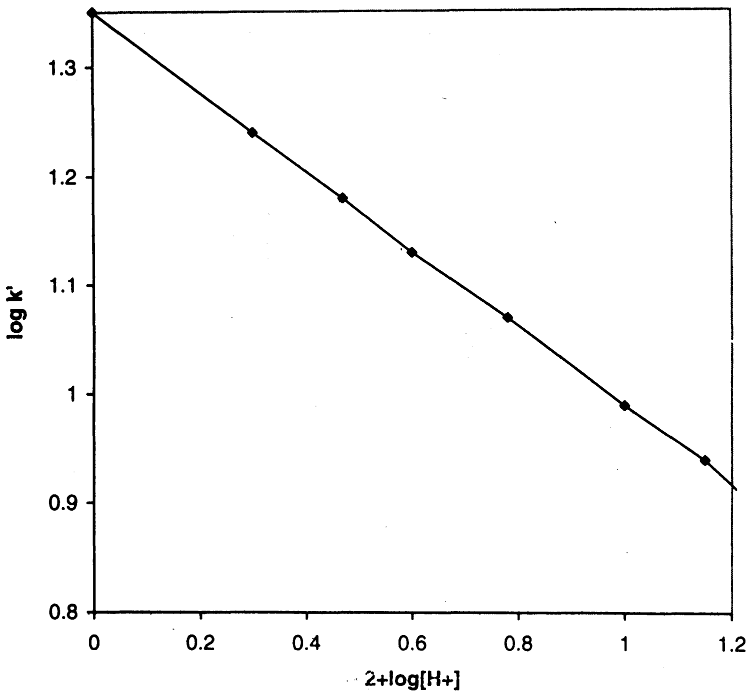


Fig. 2

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

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

$$PhSO_2NHCl + H_2O \rightleftharpoons PhSO_2NH_2 + HOCl \quad (4)$$

$$2PhSO_2NHCl \rightleftharpoons PhSO_2NH_2 + PhSO_2NCl_2 \quad (5)$$

$$HOCl + H^+ \rightleftharpoons H_2OCl^+ \quad (6)$$

In acid medium, the probable oxidizing species are the free acid ($PhSO_2NHCl$), dichloramine-B ($PhSO_2NCl_2$), HOCl and H_2OCl^+. The involve-

TABLE-3
THERMODYNAMIC PARAMETERS FOR OXIDATION OF CYSTEINE BY CHLORAMINE-B

Temperature K	k^1 (10^4 sec^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (kJ mol^{-1})	$\Delta G^{\neq}$ (kJ mol^{-1})	E_a (kJ mol^{-1})
298	8.49	45.33	–150.57	91.35	47.89
303	13.63				
308	18.90				
313	26.50				

ment of $PhSO_2NCl_2$ in the mechanism leads to a second order rate law according to equation (5) which is contrary to experimental observations. If HOCl were the primary oxidizing species, a first order retardation of the rate by the added $PhSO_2NH_2$ would be expected contrary to experimental result. Hardy and Johnston[19] have studied the pH dependent relative concentration of the species present in acidified haloamines. $PhSO_2NCl$ is the likely oxidizing species in acid medium. Narayanan *et al.*[22] and Subramanian[23] have reported that monohaloamine can be further protonated at pH < 2 as shown in the following equations (7) and (8) for CAT and CAB respectively.

$$CH_3C_6H_4SO_2NHCl + H^+ \rightleftharpoons CH_3C_6H_4SO_2N^+H_2Cl \qquad (7)$$

$$C_6H_5SO_2NHCl + H^+ \rightleftharpoons C_6H_5SO_2N^+H_2Cl \qquad (8)$$

In the present case the inverse fractional order in (H^+) suggests that the deprotonation of $PhSO_2NH_2Cl^+$ results in the regeneration of $PhSO_2NHCl$ which is likely to be the active oxidizing species involved in the mechanism of the cysteine oxidation. Based on the preceding discussion a mechanism (Scheme–I) is proposed for the reaction.

SCHEME-I

$$PhSO_2NH_2Cl \overset{K_1}{\rightleftharpoons} PhSO_2NHCl + H^+ \qquad \text{(i) Fast}$$

$$PhSO_2NHCl + S \xrightarrow{k_2} X \qquad \text{(ii) Slow}$$

$$X \xrightarrow{k_3} \text{Products}$$

In Scheme-I, S represents the cysteine substrate, while X represents the complex intermediate species. A detailed mechanistic interpretation of cysteine-CAB reaction in acid medium is represented in Scheme-II.

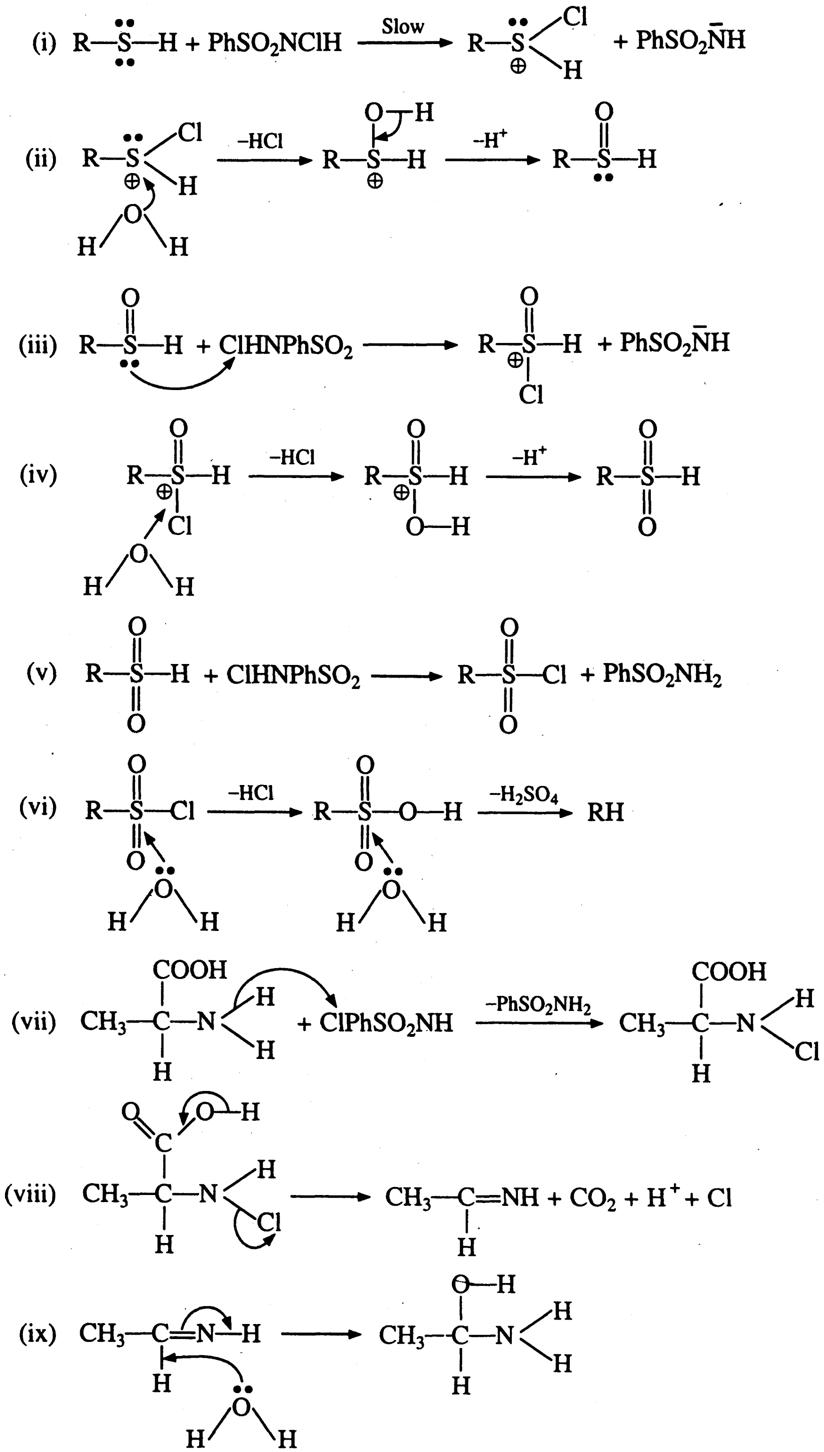
From Scheme-I,

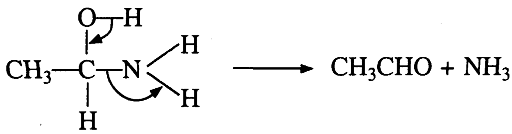
$$\text{Rate} = \frac{k_2K_1[CAB][S]}{[H^+] + K_1} \qquad (9)$$

which is in agreement with experimental data including a first order in [CAB] and [Cysteine] and inverse fractional order in $[H^+]$. Since rate = k^1 [CAB] under pseudo first order condition, the rate equation can be transformed into equation (10).

$$\frac{1}{k^1} = \frac{[H^+]}{k_2K_1[S]} + \frac{1}{k_2[S]} \qquad (10)$$

Based on equation (10) the plot of $1/k^1$ *vs.* $[H^+]$ at constant [CAB], [Substrate] and temparature was found to be linear. The value of K_1 and k_2 were calculated from the slope and intercept of the plot ($k_2 = 46.229 \times 10^{-2}$ and $K_1 = 5.041 \times 10^{-2}$). The value of deprotonation constant ($K_1 = 5.041 \times 10^{-2}$) of step (i) of Scheme-I is calculated from equation (10). Therefore the value of protonation constant (K_p) is obtained by $K_p = 1/K_1$. Further the value of K_p 19.837 is equal to that of values obtained in oxidation of primary amines by bromamine-T in HCl medium and in presence of Ru(III) catalyst.[24] Therefore the constancy of


Slow
–HCl
–H⁺
–H₂SO₄
RH
–PhSO₂NH₂

(x) 

Here R = HOOC—CH(NH_2)—CH_2

K_p or K_1 values forms a strong indirect evidence for the existence of the reacting species $PhSO_2NH_2Cl$ of oxidant. Supporting the proposed mechanism of oxidation of cysteine by CAB **(Scheme-II).**

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