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Kinetics of Oxidation of Some Amino Acids by N-Chlorosaccharin in Aqueous Acetic Acid Medium

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The kinetics of oxidation of some amino acids *e.g.*, glycine, alanine, aspartic acid, arginine, and histidine, (AA) by N-chlorosaccharin (NCSA) in aqueous acetic acid medium in the presence of perchloric acid have been investigated. The observed rate of oxidation is first order in [AA], [NCSA] and of inverse fractional order in [H^+]. The main product of the oxidation is the corresponding aldehyde. The ionic strength on the reaction rate has no significant effect. The effect of changing the dielectric constant of the medium on the rate indicates the reaction to be of dipole-dipole type. Hypochlorous acid has been postulated as the reactive oxidizing species. The reaction constants involved in the mechanism are derived. The activation parameters are computed with respect to slow step of the mechanism.

Key Words: Oxidation, Kinetics, N-Chlorosaccharin, Amino acids.

INTRODUCTION

The chemistry of reactions of N-halo compounds form a separate branch, which is of great synthetic importance[1]. N-Halo compounds have been extensively employed as oxidizing agents for organic substrates[2,3]. In the recent development, N-halo compounds are the source of positive halogen and have been exploited as oxidant for a variety of substrates in both acidic and alkaline media. The nature of active oxidizing species and mechanism depends on the nature of the halogen atom, the groups attached to the nitrogen and the reaction conditions. Although a quantum of works have been reported on the oxidation of organic compounds by N-halo compounds[4-7], it is to be noted that no systematic kinetic investigation on the oxidation of amino acids by N-chlorosaccharin has yet been reported in the literature. Here the results of the kinetics of the oxidation of glycine, alanine, aspartic acid, arginine and histidine, (AA) with N-chlorosaccharin (NCSA) in aqueous acetic acid medium in the presence of perchloric acid are reported.

EXPERIMENTAL

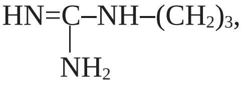
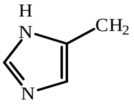
All the chemicals used were of A.R. grade. Double-distilled water was used throughout. N-Chlorosaccharin[8] were prepared using reported procedures. Standard solution of NCSA was prepared afresh. Perchloric acid (AnalaR) was used as source of hydrogen ions. Sodium perchlorate (Merck) was used to keep the ionic strength constant.

The reaction was carried out under pseudo-first order condition ([AA] > > [NCSA]). The reaction was followed by potentiometrically by setting up a cell made up of the reaction mixture into which the platinum electrode and reference electrode (SCE) were dipped. The emf of the cell was measured periodically using an Equip-Tronic potentiometer, while the reaction mixture was continuously stirred. The pseudo-first order rate constants computed from the plots of log (E_t-E_∞) against time were reproducible within ± 3 %.

RESULTS AND DISCUSSION

Stoichiometry and reaction products: Different sets of reaction mixtures containing different quantities of NCSA and amino acid at constant concentration of perchloric acid and sodium perchlorate were allowed to react for 24 h at 30ºC and then analyzed. The remaining NCSA was estimated. The oxidation products were identified as aldehyde and saccharin by their spot tests. It was confirmed by noting the mixed melting point, chemical methods and TLC techniques. The results are in good agreement with 1:1 stoichiometry.

$$\begin{aligned}&RCH(NH_2)CO_2H + C_6H_4SO_2\,CONCl + H_2O \rightarrow \\ &\qquad RCHO + C_6H_4SO_2\,CONH + CO_2 + NH_3 + HCl \qquad (1)\end{aligned}$$

where R = H, CH_3, $HOOC{-}CH_2$, 
$HN{=}\underset{\substack{| \\ NH_2}}{C}{-}NH{-}(CH_2)_3$, 

Reaction order: The kinetics of oxidation of amino acids by NCSA was investigated at several initial concentrations of the reactants in 50-80 % acetic acid-water mixture in the presence of perchloric acid. At constant [H^+] with [substrate] in excess, the plot of log (E_t-E_∞) *vs.* time is linear, indicating a first order dependence of rate on [NCSA]. Plots of log k_{obs} *vs.* log [AA] are linear with a slope of nearly unity for all the substrates (Fig. 1) and a plot of k_{obs} *vs.* [AA] is also linear passing through the origin indicating a first order dependence on [AA] (Fig. 2). The pseudo-first order rate constants decrease with increase in [H^+] in the range 0.5-1.6 mol dm^{-3} (Table-1). The linearity of the plots of log [NCSA] *vs.* time indicates the order in [NCSA] as unity.

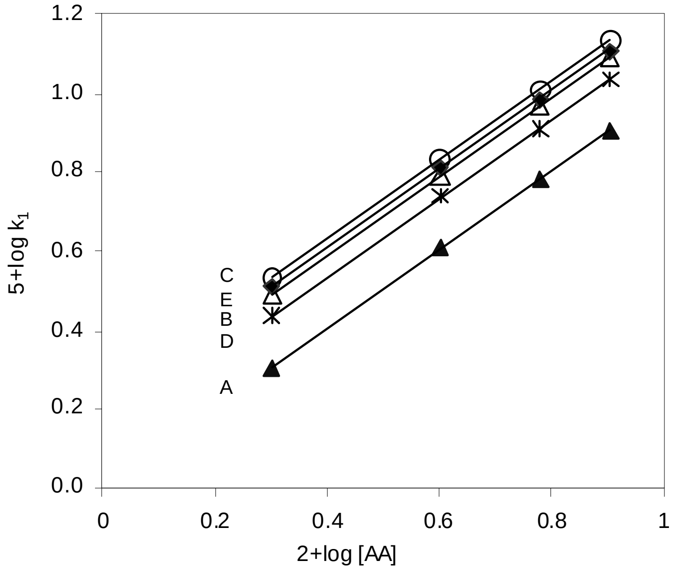


Fig. 1. Plots of log [AA] *vs.* log k_1 (A = Glycine; B = Alanine; C = Histidine; D = Arginine; E = aspartic acid)

TABLE-1
EFFECT OF VARYING [AMINO ACID], [NCSA] AND [H^+] ON THE RATE OF REACTION AT 30ºC[a]

10^2 [AA] (mol dm^{-3})	10^3 [NCSA] (mol dm^{-3})	H^+ (mol dm^{-3})	$10^5 \times k_{obs}$ s^{-1}				
			Gly	Ala	His	Arg	Asp
2.0	1.0	0.5	2.02	3.11	3.41	2.72	3.23
4.0	1.0	0.5	4.07	6.19	6.81	5.48	6.46
6.0	1.0	0.5	6.07	9.29	10.23	8.11	9.67
8.0	1.0	0.5	8.06	12.40	13.65	10.86	12.84
2.0	3.0	0.5	2.05	3.14	3.43	2.74	3.24
2.0	5.0	0.5	2.03	3.07	3.41	2.71	3.26
2.0	7.0	0.5	2.05	3.10	3.38	2.69	3.23
2.0	1.0	0.8	5.26	2.45	2.81	2.11	2.61
2.0	1.0	1.2	5.37	1.64	1.85	1.46	1.74
2.0	1.0	1.6	5.38	1.21	1.42	0.98	1.31

[a] General conditions: [$NaClO_4$] = 0.5 mol dm^{-3}, solvent composition: 50 % acetic acid : 50 % water (v/v).

The rate increases with increase in dielectric constant of the medium. A plot of log k_{obs} *vs.* [D-1/2D+1], where D is the dielectric constant of the medium, is linear with positive slope indicating a dipole- dipole type of interaction. The reaction have been studied in the temperature range 30-50ºC. By the use of Arrhenius equation, the thermodynamic parameters have been calculated (Table-2). The oxidation of amino acids by NCSA under nitrogen atmosphere fails to induce polymerization of added acrylonitrile, thus ruling out radical oxidation. The retarding effect of added saccharin suggests that the pre-equilibrium step involves hydrolysis of NCSA to give saccharin and HOCl (eqn. 2).

$$C_6H_4SO_2CONCl + H_2O \xrightleftharpoons{K_1} C_6H_4SO_2CONH + HOCl \qquad (2)$$

Of the four probable oxidizing species in the reaction, *viz.* NCSA, $NCSAH^+$, HOCl and H_2OCl^+, HOCl is considered as the active oxidizing species since the rate is an inverse function of [saccharin] and $[H^+]$.

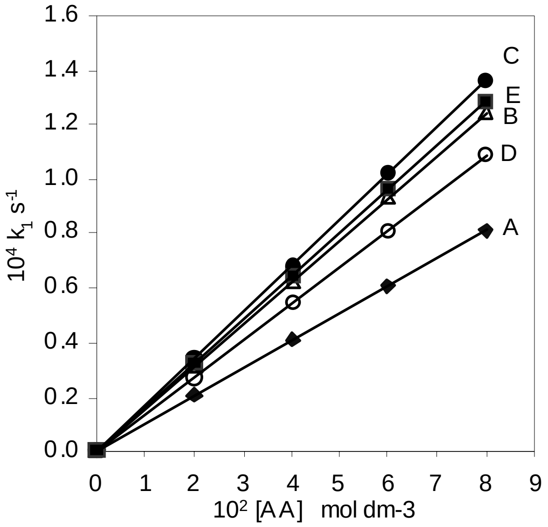


Fig. 2. Plots of [AA] *vs.* k_1 (A = glycine; B = alanine; C = histidine; D = arginine; E = aspartic acid)

TABLE-2
ACTIVATION PARAMETERS FOR THE OXIDATION OF AMINO ACIDS BY NCSA[a]

Parameters	Glycine	Alanine	Histidine	Arginine	Aspartic acid
10^5 k_{obs} (s^{-1})	2.02	3.11	3.41	2.72	3.23
E_a (k J mol^{-1})	42.80	48.70	51.70	45.70	49.80
ΔH^* (k J mol^{-1})	40.30	46.20	49.20	43.20	47.30
ΔS^* (JK^{-1} mol^{-1})	38.50	41.20	43.20	40.20	42.40
ΔG^* (k J mol^{-1})	54.60	62.40	67.20	61.10	65.20

[a]General conditions: $[NaClO_4]$ = 0.5 mol dm^{-3}, Solvent composition: 50 % acetic acid – 50% water (v/v) [AA] = 0.02 mol dm^{-3}, [NCSA] = 0.001 mol dm^{-3}.

The retarding effect of $[H^+]$ on the rate of reaction can be explained by considering the equilibrium (3) between the substrate (AA) and H^+.

$$S + H^{+} \underset{}{\overset{k_2}{\rightleftharpoons}} SH^{+} \qquad (3)$$

This effect coupled with the solvent effect does point out that the reaction with unprotonated amino acid should be more predominant.

Mechanism

The first order dependence each on [AA] and [NCSA] reveals that overall rate may involve the interaction of HOCl and amino acid in the rate determining step to give a mono ester similar to that reported by Reddy & Sundaram[9] and Gopalkrishnan and Hogg[10] for N-bromoacetamide oxidations. The mono ester involving O-Cl linkage may then undergo a series of fast steps as shown in **Scheme-I** to give aldehyde and ammonia.

$$RCH(NH_3^{+})COO^{-} + HOCl \xrightarrow[slow]{k_2} [RCH(NH_2)COOCl] + H_2O \qquad (4)$$

$$[RCH(NH_2)COOCl] \xrightarrow[fast]{} R\overset{+}{C}H(NH_2) + CO_2 + Cl^{-} \qquad (5)$$

$$R\overset{+}{C}H(NH_2) \xrightarrow[fast]{} RCH = NH + H^{+} \qquad (6)$$

$$RCH = NH + H_2O \xrightarrow[fast]{} RCHO + NH_3 \qquad (7)$$

Scheme-I

The rate law based on **Scheme-I** is represented by eq. (8)

$$\frac{-d[NCSA]}{dt} = \frac{k_1k_3\ [NCSA]\ [SH^{+}]}{k_2[H^{+}]\ [C_6H_4SO_2CONH]} \qquad (8)$$

Equation (8) clearly points out the observed results, *i.e.* first order in [NCSA], [AA] and inverse first order in $[H^{+}]$ negligible influence of changes in ionic strength and the effect of dielectric constant of the medium on the rate of oxidation.

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