May, 1984] © 1984 The Chemical Society of Japan NOTES Bull. Chem. Soc. Jpn., 57, 1439—1440 (1984) 1439

Kinetics and Mechanism of Oxidation of Pyridoxine by Sodium *N*-Chlorobenzenesulfonamidate

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(Received May 16, 1983)

Synopsis. Oxidation of pyridoxine (PRX) by chloramine-B (CAB) in HCl medium at 313 K shows first order dependence each on oxidant, substrate and Cl^- ion concentrations, but is independent of $[H^+]$. A first-order retardation of rate is observed by the addition of reaction product, benzenesulfonamide. Suitable mechanism is proposed.

Aromatic *N*-halosulfonamides are compounds containing positive halogen and they act as both chlorinating and oxidising agents. The important members of this class of compounds are chloramine-T (CAT) and chloramine-B (sodium *N*-chlorobenzenesulfonamidate, CAB). Although sufficient reports are available about the mechanism of oxidation of substrates by CAT[1], information about CAB is scanty. Pyridoxine (PRX) find extensive application in pharmaceutical industries but mechanistic studies of its oxidation are meagre. It has been oxidised to pyridoxal by MnO_2[2] and $KMnO_4$[3] in acidic and alkaline media respectively. We report here the kinetics and mechanism of pyridoxine by CAB in HCl medium at 313 K.

Experimental

Chloramine-B was prepared and purified by standard procedures.[4] Pyridoxine (Fluka) was used without further purification. Aqueous solutions of the compounds were prepared in double distilled water. Heavy water (99.8%) was obtained from BARC, Bombay, India. All other reagents used were of AR grade. The reactions were followed under pseudo-first order conditions by estimating the unreacted CAB iodometrically. Experimental details are described elsewhere.[1]

Stoichiometry. Varying proportions of CAB and pyridoxine solutions in presence of HCl (0.04—0.14 M, 1M $=1$ mol dm^{-3}) were mixed and the unreacted CAB was estimated. Values of $\Delta[CAB]/\Delta[PRX]$ and $\Delta[pyridoxal]/\Delta[CAB]$ in Table 1 suggest the overall reaction:

$$C_8H_{11}NO_3 + RNClNa \longrightarrow C_8H_9NO_3 + RNH_2 + NaCl.$$
$$(R = C_6H_5SO_2)$$

Benzenesulfonamide among the reaction product was detected by TLC technique.[5] Pyridoxal was identified and estimated as semicarbazone[6] (mp 509 K).

Table 1. Stoichiometry of oxidation of pyridoxine by CAB at 313 K

[HCl]/M	Δ[CAB]/Δ[PRX]	Δ[Pyridoxal]/Δ[CAB]
0.02	0.89	0.86
0.04	0.92	0.90
0.06	0.94	0.93
0.08	0.99	1.01
0.10	1.01	1.01
0.12	1.02	0.99
0.14	0.99	1.00

Results and Discussion

Oxidation of PRX by CAB was carried out at 313 K in the presence of various concentrations of HCl, H_2SO_4, and $HClO_4$ (0.04—0.14 M) but the reaction was found to be facile only in the presence of chloride ion in the solution. Hence, a detailed study was made on the kinetics of oxidation of PRX by CAB in HCl medium.

At constant [HCl] and [PRX], plots of log $(a-x)$ *vs.* time were linear indicating a first-order dependence of rate on [CAB]. The value of first-order rate constant k was independent of [CAB] (Table 2). Values of k increase with increase in [PRX] (Table 2) and a plot of log k *vs.* log [PRX], gives a straight line of slope unity, indicating first order dependence of rate on [PRX].

The rate also increases with increase in [HCl]. A plot of log k *vs.* log [HCl], shows a first-order dependent of rate on [HCl]. At constant $[H^+]$, addition of NaCl increased the rate. Plot of log k *vs.* log $[Cl^-]$ was linear with unit slope, showing first-order dependence of rate on $[Cl^-]$. The effect of $[H^+]$ at constant $[Cl^-]$ was studied. It was observed that the rate is independent of $[H^+]$ (Table 3).

Tble 2. Effect of concentration of reactants on the rate

10^4[CAB]/M	10^3[PRX]/M	$10^4k/s^{-1}$
3.0	5.0	4.69±0.10
4.0	5.0	4.71±0.09
5.0	5.0	4.64±0.09
6.0	5.0	4.59±0.08
7.0	5.0	4.62±0.11
5.0	2.0	1.99±0.04
5.0	4.0	3.71±0.10
5.0	6.0	5.84±0.11
5.0	8.0	7.31±0.18
5.0	10.0	9.59±0.21
5.0	5.0	4.35±0.08[a]
5.0	5.0	4.21±0.11[b]

[HCl]=0.1 M; temp: 313 K; a) : with 0.5 M $NaClO_4$; b) : In D_2O medium.

Table 3. Dependence of reaction rate on $[H^+]$ and $[Cl^-]$ at 313 K

[HCl]/M	[NaCl]/M	$10^4k/s^{-1}$
0.06	0.08	7.53±0.15
0.08	0.06	7.59±0.15
0.10	0.04	7.55±0.18
0.12	0.02	7.60±0.16
0.14	—	7.57±0.19
0.08	—	3.98±0.11
0.08	0.02	5.10±0.14
0.08	0.04	5.96±0.10
0.08	0.06	7.20±0.16
0.08	0.08	7.71±0.16

$[CAB]=5\times10^{-4}$ M; $[PRX]=5\times10^{-3}$ M.

The effect of temperature on the rate of oxidation of PRX by CAB in HCl medium was studied. The values of k at various temperatures (K) —303, 308, 313, 318, 323 are 1.77 ± 0.03, 3.11 ± 0.08, 4.64 ± 0.09, 7.90 ± 0.15, and 13.51 ± 0.24, $(\times 10^4\,\mathrm{s}^{-1})$ respectively. From the Arrhenius plot of log k *vs.* $1/T$ ($r = -0.9984$) values of E_a (82.6 kJ mol^{-1}), $\Delta S^{\neq}$ (—45.5 J K^{-1}), $\Delta G^{\neq}$ (94.0 kJ mol^{-1}), $\Delta H^{\neq}$ (80.0 kJ mol^{-1}), and A ($2.8 \times 10^{10}\,\mathrm{s}^{-1}$) were computed.

The effect of the dielectric constant of the medium was studied by adding methanol to the reaction system. A plot of log k *vs.* $1/D$, where D is dielectric constant of the medium, gives a straight line with a positive slope of value 0.8642 ($r = 0.9976$).

Change in the ionic strength of the medium (0.1—0.5 M) (with $NaClO_4$) had no effect on the rate of reaction (Table 2). The effect of reaction product was studied by adding benzenesulfonamide(BSA). The rate of reaction decreased with increase in BSA, showing a first-order retardation of rate by [BSA] (Fig. 1). The reaction was also studied in D_2O medium. The solvent isotope effect was found to be 0.907.

Eqilibria present in acidified CAT solution has been clearly established.[7] No detailed information is available about the oxidative species present in acidic solution of CAB. Zilberg[8] has shown that acidification of CAB gives dichloramine-T ($RNCl_2$) and RNH_2. Mogilevski *et al.*[9] have reported the presence of HOCl in acidic CAB solution. It is likely that equilibria similar to those of CAT exist in acidified CAB solution.

Hence the probable oxidizing species are RNHCl, $RNCl_2$ and HOCl. A strict first-order dependence of rate on [CAB] (Table 2) rules out $RNCl_2$ as the oxidizing species. In acidic chloride solution, HOCl forms Cl_2 while RNHCl can be further protonated to give RN^+H_2Cl.[10] Kinetic data obtained with Cl_2 water were found to be identical with those of CAB under comparable experimental conditions. First order retardation of rate by the addition of BSA further supports the involvement of Cl_2 in the reaction sequence. Hence free chlorine can be assumed to be the reactive species, which oxidizes PRX present in the protonated form, SH^+ in acid solution.[11] Based on these facts, the following reaction scheme may be proposed:

$$RN^+H_2Cl + Cl^- \overset{K}{\rightleftharpoons} RNH_2 + Cl_2, \qquad (1)$$

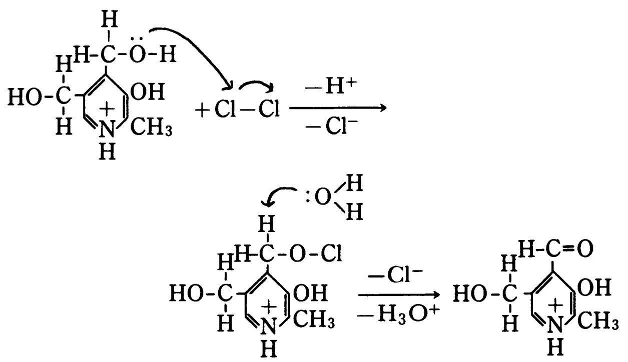
$$Cl_2 + SH^+ \xrightarrow{k} \text{products}. \qquad (2)$$

Scheme

From Eqs. 1 and 2, the rate law becomes,

$$\text{Rate} = \frac{kK[SH^+][CAB][Cl^-]}{[RNH_2]}. \qquad (3)$$

The mechanism of oxidation of primary alcohol usually involves the hydride transfer which accounts for the high solvent isotope effect[12] ($k_{D_2O}/k_{H_2O} \approx 4$ to 7). In the present system hydride transfer is unlikely in view of the observed low solvent isotope effect (0.907). Therefore a mechanism involving the formation of hypochlorite is suggested. The electron flow during oxidation is depicted as follows:



The negative entropy of activation indicates the formation of the compact hypochlorite species at the determining step. The observed neutral salt effect and slight positive dielectric constant effect on the rate support the proposed mechanism.

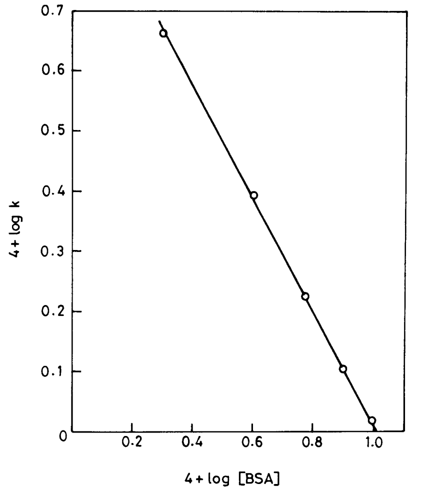


Fig. 1. Plots of log k *vs.* log [BSA]. [PRX]=5×10^{-3} M; [CAB]=5×10^{-4} M; [HCl]= 0.1 M; temp=313 K.

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