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KINETICS OF OXIDATION OF KETOGLUTARIC ACIDS BY ALKALINE CHLORAMINE-T SOLUTION

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Abstract - Kinetics of the oxidation of α-ketoglutaric and β-ketoglutaric acids by chloramine-T (CAT) have been investigated in highly alkaline media. The reactions show first order dependence in chloramine-T and fractional order in substrates. The order in hydroxide ions has been found to be second but shows a slight decrease at high concentration of alkali. No effect of p-toluene-sulphonamide was evident. Observed stoichiometry, positive effects of ionic strength and dielectric constant point to a mechanism involving formation of an intermediate in a termolecular rate determining slowest step among hypochlorite ion, hydroxide ion and enolic anion of keto acids followed by a fast step leading to products. Activation parameters have been computed and formaldehyde and formic acid were identified as end-products.

INTRODUCTION

The present communication reports the complex kinetics in oxidation of ketoglutaric acids by alkaline solution of chloramine-T in contrast to very simple kinetic observations, so far, obtained in chloramine-T oxidation of aldehydes,[1,2] ketones,[3,4] and aldoses[5] in alkaline media. In order to shed some further light on chloramine-T oxidations, the kinetic observations of the present invesigation have been discussed and a suitable mechanism has been presented.

MATERIALS AND METHODS

All the reagents used were of highest purity available. Chloramine-T (E. Merck proanalysis) was used and stored in black coated bottles. Koch-Light (England) sample of p-toluene-sulphonamide was used. All other reagents were of analar grade. The solutions of α-ketoglutaric acid (E. Merck) and β-ketoglutaric acid (Loba Chemie) were prepared by direct weighing and dissolving in double distilled water. The reaction stills were blackened from outside to avoid any photochemical influence.

All reactants except keto acid were allowed to mix and the reaction was initiated by adding subsequently appropriate amount of ketoglutaric acid. The progress of the reaction was monitored by estimating unconsumed CAT iodometrically using starch as indicator. All the rate studies were carried out at constant temperature (± 0.1).

Stoichiometry and product analysis Reaction mixture containing excess of CAT over ketoglutaric acid was allowed to equilibrate at 35°C for 48 hours in presence of 2.00×10^{-1} M NaOH. Excess of CAT left was estimated. The results showed that two moles of CAT were consumed per mole oxidation of ketoglutaric acid (Table 1) and accordingly the following stoichiometric equation could be formulated, where R represents $-CH_2.CO.COOH$ and $-CO.CH_2COOH$ groups in the substrate molecule. The end products formic acid (tested by chromatographic technique) and formaldehyde were tested by conventional methods.[6]

$$R.CH_2COOH + 2\ CH_3C_6H_4SO_2N.NaCl + 4\ OH^- =$$

$$2\ CH_3C_6H_4.SO_2NH_2 + 2\ NaCl + 4\ HCOO^- + HCHO \ldots\ldots\ldots\ldots\ldots (1)$$

RESULTS AND DISCUSSION

Kinetics of the oxidation of α-ketoglutaric and β-ketoglutaric acids were investigated at several initial concentrations of the reactants at constant ionic strength. Owing to the high concentration of alkali (pH > 12) it was not possible to use a buffer. The results show first order dependence in chloramine-T and fractional order in ketoglutaric acid concentration (Table 2). The order of the reaction in ketoglutaric acids was found as 0.54 (Fig. 1) from the slope of the plot of log k_1 against log [ketoglutaric acid].

The most interesting feature of the oxidation of ketoglutaric acids by chloramine-T is the dependence on alkali of the rate of oxidation. The results show that the reactions are highly susceptible to a change in alkalinity (Table 3). The order of the reaction in hydroxide ions was calculated from the slope of the plots of log k_1 vs log $[OH^-]$. It was observed that the reactions follow second-order kinetics in hydroxide ions at lower alkali concentrations while at higher concentrations the order decreases (Fig. 2).

The influence of several other factors on the rate of oxidation of ketoglutaric acids by chloramine-T was also studied. Table 4 records positive effect of ionic strength variation (affected by addition of suitable amounts of sodium perchlorate solution), negative effect of addition of ethanol (5-30%) and negligible effect of addition of p-toluenesulphonamide (the reduction product of chloramine-T) and effect of variation of temperature. The effect of temperature was quite marked. Average values of energy of activation ($\Delta E^{\ddagger}$) and entropy of activation ($\Delta S^{\ddagger}$) were calculated from the values of rate constants at four temperatures (30-45°) and were found to be 7.54 Kcal mol^{-1} and -40.60 e.u., respectively (α-ketoglutaric acid) and 9.15 Kcal mol^{-1} and -35.89 e.u., respectively (β-ketoglutaric acid).

The results of the oxidation of α-ketoglutaric and β-ketoglutaric acids, recorded here, have revealed that the reactions have identical kinetics and thus appear to have a common mechanism. Base catalysed oxidation of ketoglutaric acids clearly indicates that the enolic anion of ketoglutaric acids is involved in the oxidation process and not their keto form by chloramine-T.

.... (2)

(S) (S^-)

where R' = -COOH and R" = $-CH_2CH_2COOH$ in α-ketoglutaric acid and R' = R" = CH_2COOH in β-ketoglutaric acid and R"' ⟶ $=CHCH_2COOH$ (α-ketoglutaric acid) and R"' ⟶ =CHCOOH (β-ketoglutaric acid).

In aqueous alkaline solutions, chloramine-T (CAT)[7] hydrolyses to p-toluenesulphochloramide (CAT*) and p-toluenesulphonamide (TSA) as follows:

$$\underset{CAT}{CH_3C_6H_4SO_2N.NaCl+H_2O} \qquad \underset{CAT*}{CH_3C_6H_4SO_2N.HCl + NaOH} \quad \ldots\ldots\ldots\ldots\ldots\ldots (3)$$

$$\underset{CAT*}{CH_3C_6H_4SO_2N.HCl+NaOH} \qquad \underset{TSA}{CH_3C_6H_4SO_2NH_2+NaClO} \quad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Chloramine-T in aqueous solution thus provides four oxidizing species viz. CAT itself, CAT*, hypochlorite ion and dichloramine-T. The possibility of dichloramine-T acting as main oxidising species is ruled out, as in alkaline media it does not exist even in traces. When either CAT or CAT* is assumed as oxidising species of chloramine-T, the rate law obtained does not conform to second order dependence of the reactions on hydroxide ion concentration and positive effect of ionic strength. Hence these species cannot be expected to be involved in the rate-determining step. The only choice left is hypochlorite ion. Considering all experimental data, the mechanism of oxidation of ketoglutaric acids may be summarised by the following steps. Step (ii) is slow.

$$CAT + H_2O \underset{k_{-1}\ \text{fast}}{\overset{k_1}{\rightleftharpoons}} TSA + ClO^- + Na^+ \qquad \text{..........................} \quad (i)$$

$$S + OH^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} S^- + H_2O \qquad \text{..............................} \quad (ii)$$

$$S^- + OH^- + OCl^- \xrightarrow{k_3} \text{Intermediate (X)} \qquad \text{.......................} \quad (iii)$$

Slowest and rate-determining

$$X + OCl^- \xrightarrow[\text{fast}]{k_4} \text{Products} \qquad \text{..............................} \quad (iv)$$

but not as slow as the rate-determining step (iii). Applying steady-state conditions to S, the rate of disappearance of hypochlorite is given by eqn (5).

$$\genfrac{}{}{0pt}{}{-d\,[ClO^-]}{dt} \qquad \genfrac{}{}{0pt}{}{2\,k_2k_3[S][ClO^-][OH^-]^2}{k_{-2}\,[H_2O] + k_3\,[ClO^-][OH^-]} \qquad \text{..................} (5)$$

The iodometric titre value for the reaction mixture corresponds to both chloramine-T and hypochlorite and chloramine-T is consumed only in the formation of hypochlorite. Thus eqn (5) may be written as eqn (6).

$$\frac{-d[CAT]}{dt} = \frac{2\,k_2k_3\,[S][CAT][OH^-]^2}{k_{-2}\,[H_2O] + k_3\,[CAT][OH^-]} \qquad \text{.....................} \quad (6)$$

The rate law (6) is well in agreement with observed first order dependence on chloramine-T and a second order dependence on OH when $k_{-2}\,[H_2O] >> k_3\,[CAT][OH]$. k_{-2} is fairly large and k_3 is small, being the constant for the rate determining step and thus the above approximation will be valid for low concentrations of hydroxide ion and the order in alkali will be two. At higher alkali concentrations the approximation will not strictly hold and the order in alkali will decrease. The experimental observations (Fig. 2) show a decrease in order with respect to alkali at higher concentration of alkali and are, therefore, consistent with the rate law (6). The fractional order (i.e. 0.54) with respect to substrates (Fig. 1) does not conform to the first order dependence of the reactions on substrates according to the rate law (6). The decrease in order with respect to substrates may be ascribed due to decrease in dielectric constant of the medium on increasing the concentration of ketoglutaric acids.

The rate determining step (iii) involves an interaction between similarly charged ions which would require a positive effect of ionic strength. In fact, positive effect of ionic strength has been observed and is thus consistent with the rate determining step (iii). The values of energy of activation, entropy of activation and positive effect of dielectric constant also confirm the rate controlling step (iii) in the proposed mechanism.

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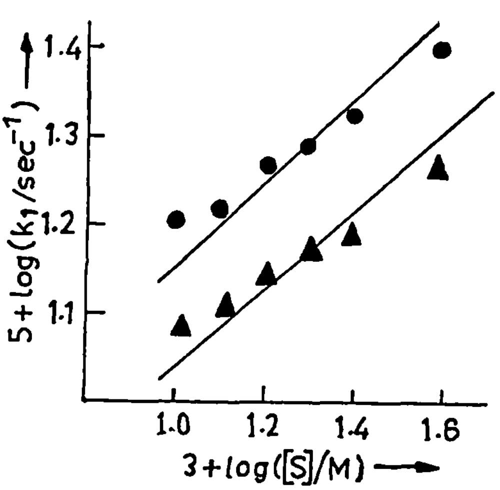

Fig. 1: Plot of log k_1 against log [KGA]
[Chloramine-T] = 2.00 x 10^{-3};
μ = 0.20 M
[NaOH] = 8.00 x 10^{-2}M, Temp. 35°
●—● (α - Ketoglutaric acid)
▲—▲ (β - Ketoglutaric acid)

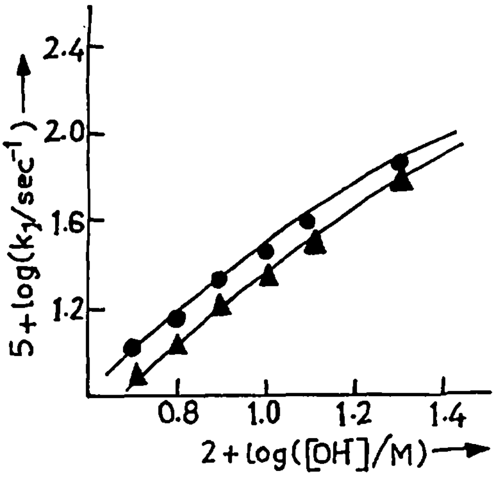

Fig. 2: Plot of log k_1 against
log [OH$^-$] at 35°
[chloramine-T] = 2.00 x 10^{-3}M,
μ = 0.20 M
●—● (α - Ketoglutaric
acid] = 2.00 x 10^{-2} M
▲—▲ (β - Ketoglutaric
acid] = 2.00 x 10^{-2} M

TABLE 1

Stoichiometry of the Oxidation of Ketoglutaric Acids (KGA)

[KGA] 10^3M	[CAT] 10^2M	Unconsumed [CAT] 10^3M	Consumed [CAT] 10^3M	Stoichiometry $\frac{\text{consumed [CAT]}}{\text{[KGA]}}$
1.00	2.00	17.98	2.02	2.02[a]
2.00	2.00	15.80	4.20	2.10[a]
2.00	1.00	6.04	3.96	1.98[a]
1.00	1.00	7.94	2.06	2.06[b]
1.00	2.00	18.04	1.96	1.96[b]
2.00	2.00	15.76	4.24	2.12[b]

[a] -- α-ketoglutaric acid and [b] --- β-ketoglutaric acid

TABLE 2

Effect of Concentrations of Reactants on the Rate at 35°C

[NaOH] = 8.00 x 10^{-2} M; μ = 0.20 M

10^3M [CAT]	10^2M [KGA]	k_1 x 10^4 sec^{-1}	
		α-KGA	β-KGA
0.80	2.00	1.92	1.42
1.00	2.00	1.93	1.43
1.34	2.00	1.95	1.43
1.60	2.00	1.97	1.50
2.67	2.00	2.00	1.52
4.00	2.00	2.07	1.53
2.00	1.00	1.62	1.25
2.00	1.25	1.73	1.33
2.00	1.67	1.87	1.43
2.00	2.50	2.13	1.57
2.00	4.00	2.50	1.87

CAT ---- Chloramine-T and KGA ---- Ketoglutaric acid

TABLE 3

Effect of Concentration of Alkali on Rate at 35°

[CAT] = 2.00×10^{-3}M; [KGA] = 2.00×10^{-2}M; and $\mu = 0.20$ M

[NaOH] x 10^2M	$k_1 \times 10^4$ sec^{-1}	
	α-KGA	β-KGA
5.00	1.02	0.85
6.25	1.38	1.10
8.00	1.97	1.50
10.00	2.27	2.37
12.50	3.68	3.58
20.00	7.08	6.33

KGA ---- Ketoglutaric acid

TABLE 4

Effect of Ionic Strength (μ), Ethanol Concentration and Temperature Variation on Rate. [CAT] = 2.00×10^{-3}M; [KGA] = 2.00×10^{-2}M; [NaOH] = 8.00×10^{-2}M.

Temperature °C	μ	Ethanol % (v/v)	$k_1 \times 10^4$ sec^{-1}	
			α-KGA	β-KGA
35	0.80	-	1.33	1.12
35	0.20	-	1.97	1.50
35	0.30	-	2.83	2.12
35	0.40	-	3.52	2.75
35	0.50	-	3.95	3.40
35	0.20	5.00	1.62	1.25
35	0.20	10.00	1.30	1.07
35	0.20	20.00	1.00	0.85
35	0.30	30.00	0.82	0.75
30	0.20	-	1.60	1.17
40	0.20	-	2.30	1.87
45	0.20	-	2.82	2.32

KGA ---- Ketoglutaric acid

REFERENCES

1. R. Sanehi, M.C. Agrawal and S.P. Mushran, Indian J. Chem., 12, 311 (1974).
2. S.P. Mushran and M.C. Agrawal, Z. Naturforsch., 27B, 401 (1972).
3. S.P. Mushran, R. Sanehi and A.K. Bose, Acta Chim. Acad. Sci., Hungaricae, 84(2), 135 (1975).
4. Bharat Singh, A.K. Samant and B.B.L. Saxena, Tetrahedron, 38, 2591 (1982).
5. M.C. Agrawal and S.P. Mushran, J. Chem. Soc. (Perkin II), 762 (1973).
6. F. Feigl, Spot Tests in Organic Analysis, 5th edn. (Elsevier, Amsterdam), p.331 (1956).
7. R. Dietzel and K. Taufel, Apoth.-Ztg., 44, 989 (1929).