Kinetics and mechanism of oxidation of ketoacids by N-bromophthalimide in aqueous acetic acid medium

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ABSTRACT

The kinetics and mechanism of oxidation of keto acids viz., Pyruvic acid (PA) and Levulinic acid (LA) by N-Bromophthalimide (NBP) in the presence of mercuric acetate have been investigated in aqueous acetic acid medium at $35^o C$. The reaction follows first order kinetics each in [NBP] and [keto acid]. The activation parameters have been evaluated. Based on the observed kinetic results, a probable mechanism has been proposed.

Keywords: Kinetics, oxidation, keto acid, N-Bromophthalimide.

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INTRODUCTION

The keto acids are especially important in biology as they are involved in the Krebs citric acid cycle and in Glycolysis. Keto acids are readily decarboxylated by several metallic and non-metallic oxidizing agents such as ceric sulphate, potassium permanganate, lead tetra acetate and hydrogen peroxide [1]. Pyruvic acid (PA) is one of the smallest biomolecule with a keto acid function. Previous studies of pyruvic acid oxidation by higher valent metal oxidants are rather limited in the literature [2-9]. In recent years, studies of the oxidation of various organic compounds by N-halo compounds in acidic medium have attracted considerable attention. They are the sources of a positive halogen and the mechanism of these reactions depends on the nature of the active oxidizing species, which may differ depending on the nature of halogen atom, the groups attached to the nitrogen atom and the reaction conditions [10-17]. However, no study involving pyruvic acid (PA) and levulinic acid (LA) with N-Bromophthalimide has been reported so far. Keeping these points in mind, we thought it appropriate to study the kinetics and mechanism of oxidation of keto acids, viz. pyruvic acid (PA) and levulinic acid (LA) in aqueous acetic acid medium with N-Bromophthalimide (NBP) in the temperature range of 308-328K.

EXPERIMENTAL SECTION

The reagents employed were Pyruvic acid and levulinic acid (Merck) and N-Bromophthalimide (Sigma Aldrich). All the chemicals used were of analytical grade. Acetic acid was refluxed with chromic oxide and acetic anhydride for 6 h and then fractionally distilled according to literature procedures [18].The solution of NBP was always prepared freshly and was standardized iodometrically. All aqueous solutions were prepared in doubly distilled water.

KINETIC METHOD

All kinetic measurements were performed under pseudo-first-order conditions with [keto acid] at least 10-fold in excess over [NBP] at a constant ionic strength (μ) were thermally equilibrated for an hour at the desired temperature. The reaction was initiated by the addition of previously thermostated solutions of NBP and keto acid solution of the

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requisite concentration which also contained necessary quantities of acid and mercuric acetate. The progress of the reaction was followed by iodometric determination of the unreacted [NBP] in aliquots of the reaction mixture withdrawn into aqueous KI solutions at regular time intervals. The iodine liberated was titrated against standard sodium thiosulphate (hypo) solution using starch indicator.

STOICHIOMETRY AND PRODUCT ANALYSIS

The stoichiometry of the reaction was determined by taking known excess of [NBP] over [keto acid] in aqueous acetic acid media at desired temperature. The progress of the reaction was followed to ensure the completion of the reaction. The unreacted [NBP] in aliquots was estimated till a constancy in the titer value is obtained. Final analysis indicated that one mole of keto acid was consumed for one mole of NBP. To estimate the end products, we added a solution of 1.33×10^{-3} M keto acid to the solution of 2.66×10^{-2} M NBP in acetonitrile medium. After the reaction was completed, the unreacted NBP was estimated by an iodometric determination method, using starch indicator. Acetic acid was distilled from the solution and the content of the distillate was determined by alkalimetry.
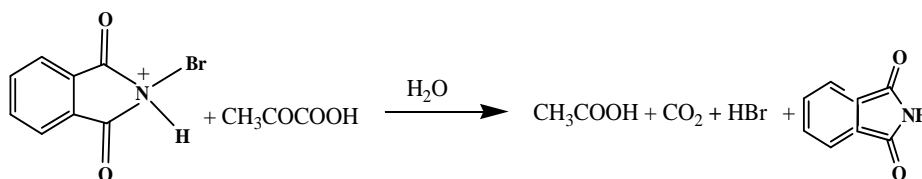
RESULTS AND DISCUSSION

The oxidation reactions of keto acids were conducted under the conditions [NBP] $<<<$ [S] (where S denotes the substrate i.e., Levulinic acid / Pyruvic acid) and in presence of excess of $Hg(OAc)_2$. The progress of the reaction was monitored by estimating the unreacted [NBP] at different intervals of time. The plots of log (a/a-x) Vs time (where 'a' and (a-x) corresponds to the concentration of NBP at zero time and at time 't') were found to be linear passing through the origin indicating first order dependence of rate on [NBP] (Figure 1). From the slopes of such plots pseudo first order rate constants (k') were evaluated.
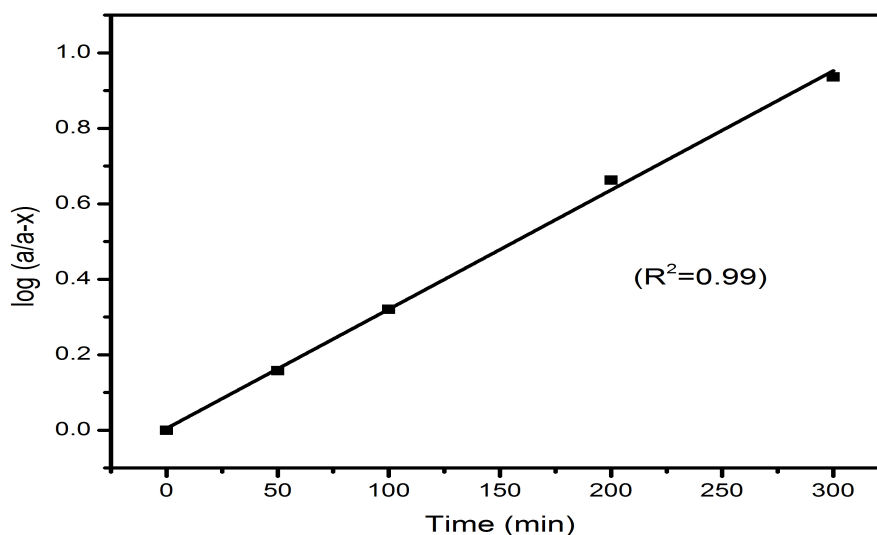

Figure1: Order in [NBP] in the oxidation of Levulinic acid.
[NBP] = 1.33x10^{-3} mol dm^{-3} ; [LA] = 2.66x10^{-2} mol dm^{-3} ; [HOAc] = 30 % (v/v); [Hg(OAc)_2] = 2x10^{-3} mol dm^{-3}; Temp = 308 K

An increase of [Substrate] increased the rate of oxidation. The plot of log k' versus log [Substrate] was linear (with slopes for PA, n=1.16 and for LA, n=1.06 and r = 0.99), indicating first order dependence of rate on [Substrate] (Figure 2).
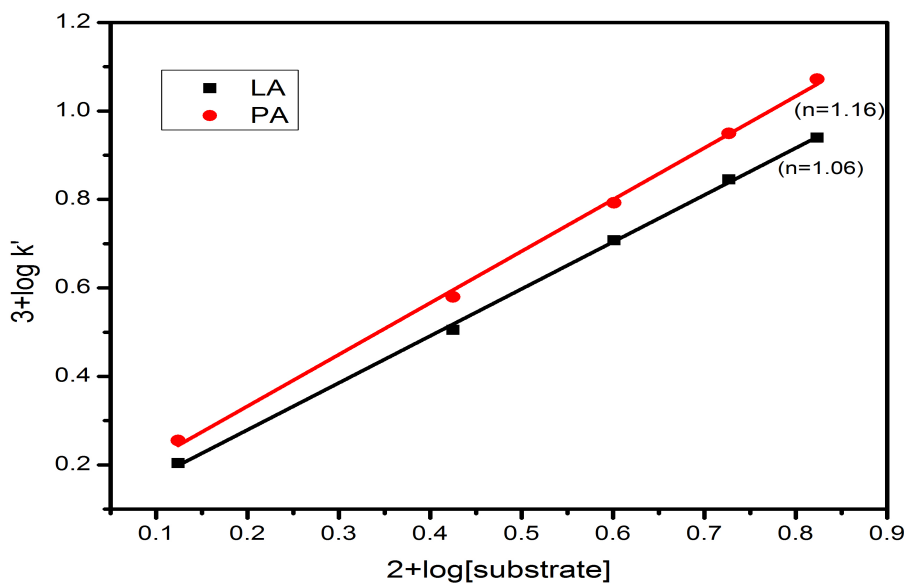
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Figure 2: Effect of [Substrate] on k' in NBP-keto acid reactions
[NBP] = 1.33x10⁻³mol dm⁻³; [Hg(OAc)₂]= 2x10⁻³mol dm⁻³; [HOAc] = 30% v/v;Temp = 308 K

Table 1 Effect of temperature on k' in the oxidation of Pyruvic acid by NBP
[NBP] = 1.33x10⁻³ mol dm⁻³; [Hg(OAc)₂] = 2x10⁻³mol dm⁻³; [HOAc] = 30% v/v

Temp (K)	$10^3/T$	10^3 k' (min^{-1})	3+log k'
308	3.24	3.8	0.579
313	3.19	5.5	0.740
318	3.14	7.2	0.857
323	3.09	9.4	0.973
328	3.04	12.7	1.103

According to the theory of absolute reaction rates (Eyring's theory), the rate constant k and free energy of activation $\Delta G^{\#}$ correlated as,

$$k = (RT/Nh) \exp(-\Delta G^{\#}/RT)$$

Where R is the gas constant, h is the Plank's constant, N, the Avogadro's number and T the temperature in absolute scale. The above equation is used to calculate the free energy of activation ($\Delta G^{\#}$) at various temperatures. Accordingly Free energy of activation $\Delta G^{\#}$ has been calculated from the rearranged form of Eyring's equation at different temperatures.

$$\Delta G^{\#} = RT \ln(RT/Nhk)$$

Free energy of activation ($\Delta G^{\#}$) values thus obtained were further used in Gibbs-Helmholtz plot of ($\Delta G^{\#}$) versus T, using the following equation for the evaluation of enthalpy of activation ($\Delta H^{\#}$) and entropy of activation ($\Delta S^{\#}$), as shown in Table-2.

$$\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#}$$

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Table 2 Activation parameters for the oxidation of PA and LA by NBP
[NBP] = 1.33x10⁻³mol dm⁻³; [Substrate] = 2.66x10⁻²mol dm⁻³; [Hg(OAc)₂]= 2x10⁻³mol dm⁻³; [HOAc] = 30% v/v

Substrate	Temp (K)	10^3 k (dm³/mol/min)	$\Delta G^{\neq}$ (kJ/mol)	Gibbs-Helmholtz $\Delta G^{\neq} = \Delta H^{\neq} - T\Delta S^{\neq}$ Equation with (R²)	$\Delta H^{\neq}$ (kJ/mol)	$-\Delta S^{\neq}$ (J/K/mol)
Pyruvic acid	308	8.75	87.64			
	313	12.67	88.15	y = 132.14x + 46885		
	318	16.58	88.88	R² = 0.9965	46.88	132.14
	323	21.65	89.61			
	328	29.25	90.22			
Levulinic acid	308	7.37	88.08			
	313	10.59	88.61	y = 125.63x + 49326		
	318	14.97	89.15	R² = 0.9944	49.32	125.63
	323	19.11	89.94			
	328	25.79	90.56			

Table 3 Effect of variation of [Phthalimide], ionic strength, solvent and [HClO₄] on the rate of oxidation of LA by NBP
[NBP] = 1.33x10⁻³mol dm⁻³; [LA] = 2.66x10⁻²mol dm⁻³; [Hg(OAc)₂] = 2x10⁻³mol dm⁻³; [HOAc] = 30 % v/v; Temp = 308 K

| [NHP] $\times 10^2$ mol dm⁻³	[NaClO₄] $\times 10^2$ mol dm⁻³	HOAc % (v/v)	[H⁺]$\times 10^2$ mol dm⁻³	k'$\times 10^3$
0.0	-	-	-	3.2
0.6	-	-	-	3.0
1.3	-	-	-	3.1
2.0	-	-	-	2.8
2.6	-	-	-	3.1
-	0.0	-	-	3.2
-	0.6	-	-	3.8
-	1.3	-	-	3.3
-	2.0	-	-	3.1
-	2.6	-	-	3.4
-	-	30	-	3.2
-	-	40	-	3.3
-	-	50	-	3.5
-	-	60	-	3.4
-	-	70	-	3.6
-	-	-	0.0	3.2
-	-	-	0.6	3.6
-	-	-	1.3	4.4
-	-	-	2.0	5.5
-	-	-	2.6	6.4

REACTIVE SPECIES AND MECHANISM:

NBP exists as free NBP, protonated NBP, Br+, HOBr, and (H₂OBr)⁺ in acidic medium according to the following equilibrium:

$$NBP + H_2O \rightleftharpoons HOBr + NHP \qquad (i)$$

$$NBP + H^+ \rightleftharpoons NHP + Br^+ \qquad (ii)$$

$$NBP + H^+ \rightleftharpoons (NBPH)^+ \qquad (iii)$$

$$HOBr + H^+ \rightleftharpoons (H_2OBr)^+ \qquad (iv)$$

Since the reactions were conducted in the presence of excess of Hg(OAc)₂, it eliminates Br⁺ via complexation, thus any possible oxidation due to Br⁺ or Br₂ is eliminated. If HOBr were to be the reactive species the rate should have indicated inverse dependence on [Phthalimide], but addition of Phthalimide had insignificant effect on rate of reaction. It was observed that an increase in the [NaClO₄] did not alter the rate significantly. Kinetic study in different compositions of binary solvent mixtures of acetic and water provided information about the variation of dielectric constant on reaction rate. An increase in acetic acid composition in binary solvent mixture of Acetic acid-Water had shown insignificant effect on rate of reaction, almost same reaction rates were observed either in acetic acid or in acetonitrile medium. While acidity variation [HClO₄] recorded rate accelerations (Table 3) suggesting the formation and participation of cationic species (NBPH)⁺ in the rate limiting step. We therefore assume the protonated NBP could be the most probable oxidizing species under the experimental conditions employed. This

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discussion together with the observed kinetics, the first-order dependence of rate on [NBP] and unit order dependence of rate on [keto acid].From the foregoing kinetic features and discussion most probable mechanism for the oxidation of Pyruvic acid by NBP could be given as shown in the following scheme.

$$(NBPH)^+ + \text{Pyruvic acid} \xrightarrow[H_2O]{k} \text{Products}$$
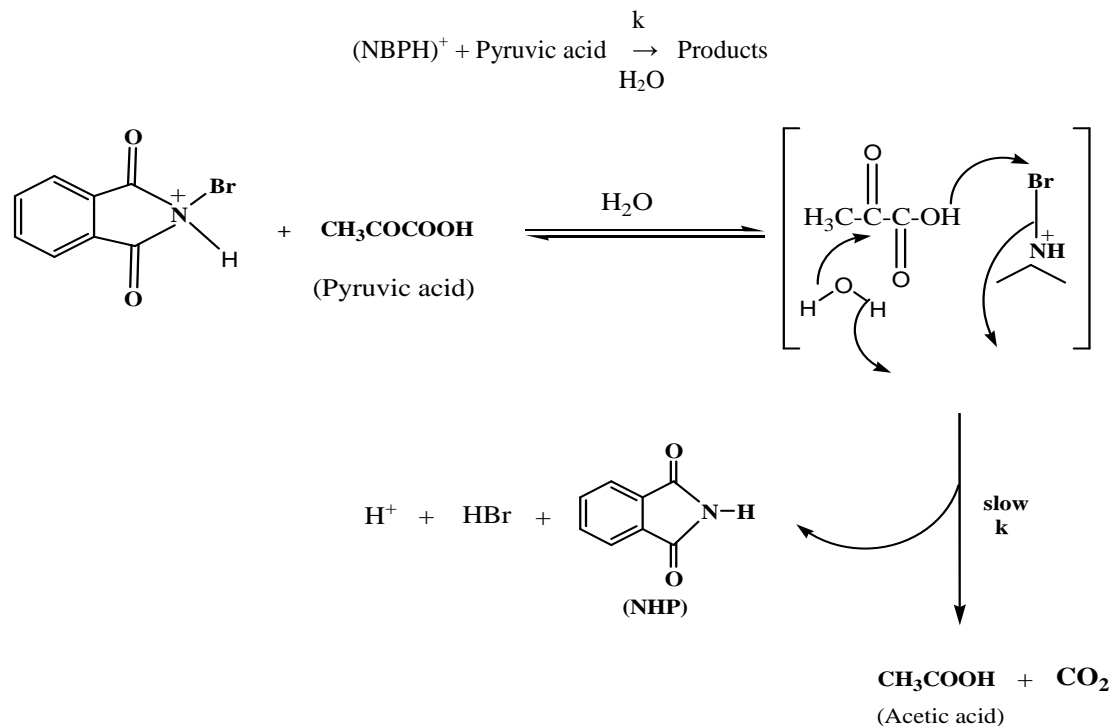
On the basis of observed kinetic results the rate law for the oxidation of ketoacids by NBP can be written as,

$$\text{Rate} = \frac{-d[NBP]}{dt} = k''[\text{Ketoacid}][\text{NBP}]$$

CONCLUSION

The oxidation reactions of ketoacids were conducted under the conditions [NBP] << [ketoacid] in presence of excess of $Hg(OAc)_2$. From the observed kinetic data, first order dependence of rate on both [NBP] and [ketoacid] was observed. The reactivity of Pyruvic acid was greater than that of Levulinic acid and this may be attributed to the greater interaction of adjacent carbonyl moiety present in Pyruvic acid, whereas in case of Levulinic acid the adjacent group may exert +I effect rather than –I effect. Activation parameters have been evaluated for both the oxidation of Pyruvic acid and Levulinic acid and the most probable mechanism has been proposed.

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