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Oxidation of 2-Hydroxypropanoic Acid with N-Chlorosuccinimide in Alkaline Medium: A Kinetic and Mechanistic Study

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ABSTRACT: Kinetics of oxidation of 2-hydroxypropanoic acid (Lactic acid LA) with *N*-Chlorosuccinimide(NCS) in a sodium hydroxide solution has been studied at 308 K. The reaction rate shows first-order dependence on [NCS] and zero order with respect to [hydroxy acid]. The rate of the reaction remained constant with increase in [NaOH]. Additions of chloride ions, perchlorate ions and the reduction product of NCS, have no effect on the reaction rate. Variations of ionic strength and dielectric permittivity of the medium have no effect on the rate. Activation parameters have been evaluated. A mechanism consistent with kinetic data is proposed.

KEYWORDS: Kinetics; Mechanism; Oxidation; Lactic acid(LA); N-chlorosuccinimide

I. INTRODUCTION

Lactic acid is a carboxylic acid with the chemical formula $C_2H_4OHCOOH$ which has a hydroxyl group adjacent to the carboxyl group, making it an alpha hydroxy acid. L-lactate is constantly produced from pyruvate via the enzyme lactate dehydrogenase (LDH) in a process of fermentation during normal metabolism and exercise in animals. It does not increase in concentration until the rate of lactate production exceeds the rate of lactate removal, which is governed by a number of factors, including monocarboxylate transporters, concentration and iso form of LDH, and oxidative capacity of tissues. The concentration of blood lactate is usually 1–2 mmol/L at rest, but can rise to over 20 mmol/L during intense exertion. In industry, lactic acid fermentation is performed by lactic acid bacteria, which convert simple carbohydrates such as glucose, sucrose, or galactose to lactic acid. These bacteria can also grow in the mouth; the acid they produce is responsible for the tooth decay known as caries [1-4]. Hydroxy acids are naturally occurring organic acids which can act both as an antioxidants and antiflammating agents. This will also be used as a preservative in some of the food industries. As a food additive it is approved for use in the EU, USA and Australia and New Zealand. Lactic acid is used as a food preservative, curing agent, and flavoring agent. It is an ingredient in processed foods and is used as a decontaminant during meat processing. Lactic acid is produced commercially by fermentation of carbohydrates such as glucose, sucrose, or lactose, or by chemical synthesis. Carbohydrate sources include corn, beets, and cane sugar. The oxidation products depend on the nature of oxidant and on the medium. Kinetic studies on the oxidation of hydroxy acid with several oxidants such as *N*-bromophthalimide [5-11], *N*-bromoacetamide [12], silver(II) [13], *N*-bromosuccinimide [14], Cr(VI) in aqueous perchloric acid medium [15], alkaline hexacyanoferate(III) [16], alkaline iodate [17] and chloramines-T [18-20] have been reported.

Literature study revealed that the oxidation of hydroxy acids by various oxidants produced keto acids/ carbonyl compounds and CO_2 . The oxidation of lactic acid is Pyruvic acid ($CH_3COCOOH$). It is the simplest of the alpha-keto acids, with a carboxylic acid and a ketone functional group. Pyruvate, the conjugate base, CH_3COCOO^- , is a key intersection in several metabolic pathways. Pyruvic acid can be made from glucose through glycolysis, converted back to carbohydrates or to fatty acids through acetyl-CoA. It can also be used to construct the amino acid alanine and be converted into ethanol. Pyruvic acid supplies energy to living cells through the citric acid cycle. Literature survey reveals that the oxidation of lactic acid by NCS was not reported. In this article, the kinetics and mechanisms of

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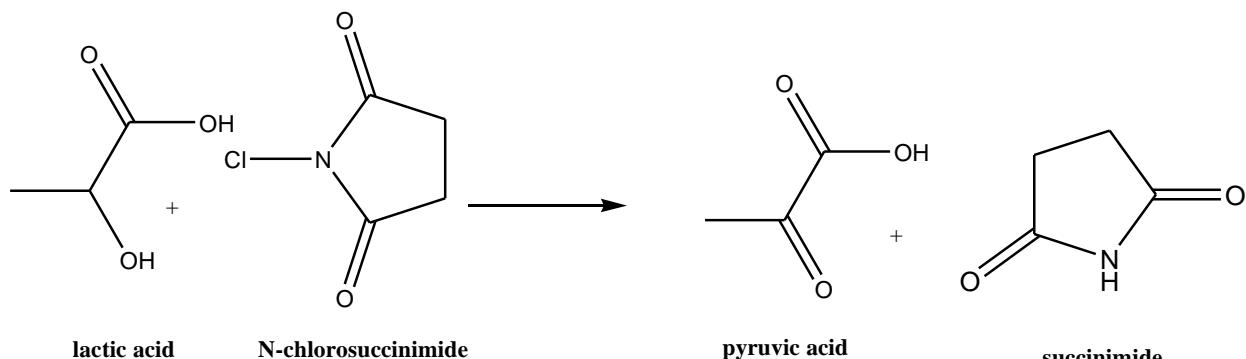
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oxidation of lactic acid by NCS is reported, in order to understand the mechanism of this biologically important hydroxyl acid because it may reveal the mechanism of lactic acid metabolism.

II. EXPERIMENTAL METHODS

A fresh solution of NCS was prepared every time before starting the experiment. Other chemicals used in this study were of analar grade and used as such without any further purification. Double distilled water was used throughout this study. The kinetics and oxidization of lactic acid by NCS in alkaline medium was investigated under pseudo first order conditions, i.e., [hydroxy acids] > [NCS]. The rate of the reaction was determined from the concentration of the unreacted[NCS] at different time intervals by iodometry.

2.1 Stoichiometry: The stoichiometry of the reaction was determined by allowing the reaction mixtures containing three times excess of [NCS] over [LA]. Simultaneously, a blank solution of the reaction mixture was also prepared by adding all the solutions without hydroxy acid. Both the reaction mixtures were allowed to stand for 48 hours and the excess of [NCS] in both the solution was estimated by iodometry. Correction for the self-decomposition of [NCS] was made. The observed stoichiometry of the reaction was calculated as [LA] : NCS = 1:1. The stoichiometric equation is given as follows.



2.2 Product analysis: The reaction mixture containing a large excess of [NCS], i.e., 3 times over [LA] in a blackened vessel was allowed to stand for 48 hours at room temperature for completion of the reaction and sodium bisulphite was added to destroy the remaining [NCS]. The reaction mixture was then extracted with dichloromethane and the sample was analyzed by TLC (thin layer chromatography) and it showed one prominent spots. The reaction mixture was purified by column chromatography. The separated products were analyzed by IR spectroscopy. The product was identical to an authentic sample of pyruvic acid.

2.3 Spectral Analysis: The reaction mixture was scanned in the Ultra-Violet and visible regions on a Perkin-Elmer LS 25 spectrometer to unravel the intermediate formed during the course of the reaction. The reaction mixture was prepared by adding NCS (2.5×10^{-5} mol dm⁻³) to [LA] (5×10^{-2} mol dm⁻³) in the alkaline medium. The spectra were taken immediately after preparing the reaction mixture in 1 cm cell at room temperature(298K). A peak was observed at λ_{max} 290 nm which disappeared during the course of the reaction. This might be due to the formation of hypochlorite and it was consumed to give the products. The reaction between hypochlorite and the hydroxy acid was very fast and hence the rate was independent of [hydroxy acid] in LA. Another peak at 230 nm was also observed in lactic acid (Figure 1).

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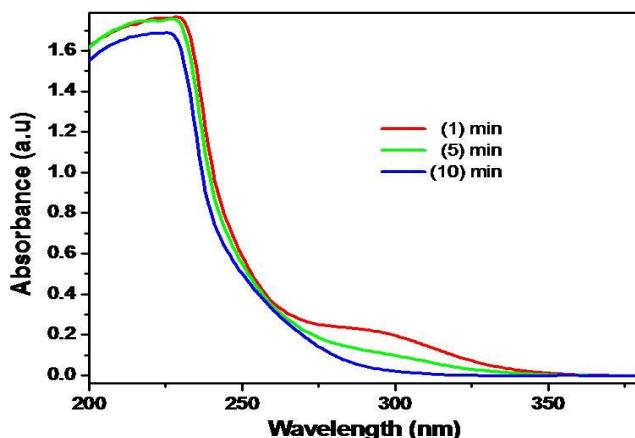


Figure 1. UV absorption spectra of the reaction mixture at various time intervals [lactic acid] = 0.005 mol dm⁻³; [sodium hydroxide] = 0.01 mol dm⁻³; [N-Chloro succinimide] = 0.008 mol dm⁻³.

III. RESULTS AND DISCUSSION

The oxidation of lactic acid was studied in perchloric acid medium and also in acetic acid/sodium acetate buffered medium. However the reaction was very sluggish in the above medium and did not proceed at all even after 4hours. Hence the reaction was studied in alkaline medium. The results obtained for the oxidation of LA by NCS in an alkaline medium are given below. The rate constant obtained for the variation of reactants, temperature and ionic strength for lactic acid is tabulated in Table 1.

Table 1: Effect of the variations of NCS, Sodium hydroxide, and temperature on the reaction rate of LA at 308K.

$10^3[\text{NCS}] \text{ mol dm}^{-3}$	$10^2[\text{LA}] \text{ mol dm}^{-3}$	$10^2 [\text{NaOH}] \text{ mol dm}^{-3}$	T (k)	$10^5 k_{\text{obs}} \text{s}^{-1}$
2.00	5.00	15.00	308	2.80
4.00	5.00	15.00	308	3.30
6.00	5.00	15.00	308	2.95
8.00	5.00	15.00	308	2.98
4.00	5.00	15.00	308	2.80
4.00	7.50	15.00	308	3.00
4.00	10.00	15.00	308	2.90
4.00	12.50	15.00	308	3.07
4.00	5.00	07.50	308	2.69
4.00	5.00	10.00	308	3.84
4.00	5.00	11.50	308	2.84
4.00	5.00	13.00	308	2.95
4.00	5.00	15.00	308	2.56
4.00	5.00	15.00	301	8.00
4.00	5.00	15.00	308	22.02
4.00	5.00	15.00	312	52.70
4.00	5.00	15.00	321	143.90

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3.1 Effect of [NCS] on k_{obs} : The oxidation of LA by NCS in alkaline medium was investigated under pseudo-first order conditions. The oxidation followed first order with respect to NCS as evidenced by the linear of $\log [NCS]_t$ vs time upto 80% conversion of [NCS] (Figure 2). Further, the values of k_{obs} calculated from the different plots were independent of $[NCS]_0$, indicating that the rate of reaction was first order in [NCS].

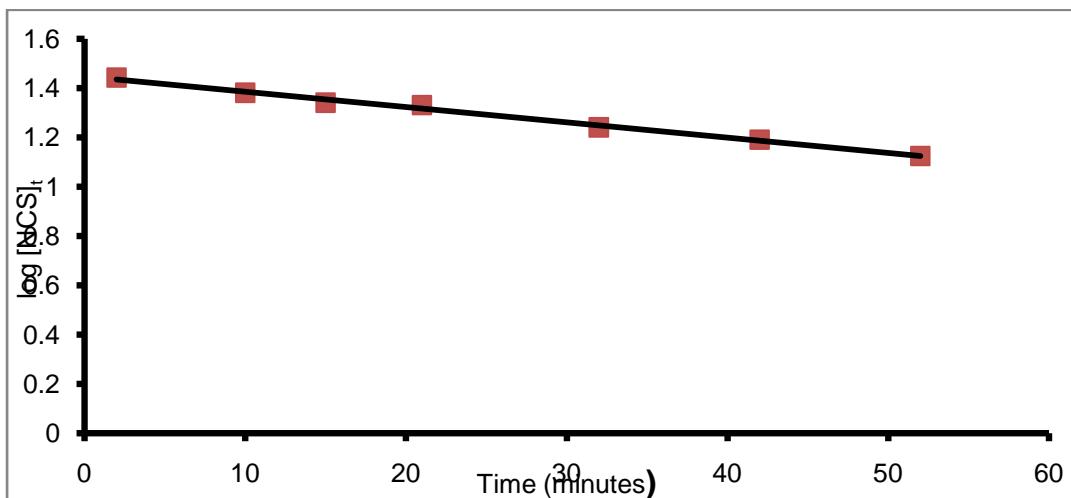


Figure 2. Plot of $\log [NCS]_t$ versus time at 308 K. Lactic acid = 0.05 M ; [sodium hydroxide] = 0.1 M ; [N-Chloro succinimide] = 0.004 mol dm⁻³.

3.2 Effect of [LA] on k_{obs} : By keeping all parameters at constant values, the values of k_{obs} for different concentration of [LA] were found to be constant with increase in [LA]. The reaction between active form of NCS and the hydroxy acid was very fast and hence the rate was independent of [hydroxy acid]. This showed that the order of the reaction was zero.

3.3 Effect of [NaOH] on k_{obs} : The effect of [NaOH] on k_{obs} was studied by varying [NaOH] and keeping the other parameters at constant values. The rate constant k_{obs} did not alter with increase in [NaOH] in both the cases. The concentration of NaOH was varied from 0.15M to 0.20 M i.e., $[NaOH]_f=0.1M$.

3.4 Effect of [succinimide] on k_{obs} : By keeping all parameters at constant values, the values of k_{obs} for different concentrations of succinimide, the reduction product of the oxidant were determined. The rate of the reaction remained constant ruling out the dimerisation of NCS.

3.5 Effect of ionic strength (μ) on k_{obs} : The effect of ionic strength on the reaction rate was studied by the addition of sodium perchlorate ($5 \times 10^{-2}M$ to $20 \times 10^{-2}M$) with NaOH concentration of 0.15M in the case of LA by maintaining other parameter at constant values. It was observed that the k_{obs} value had a negligible effect on the reaction rate, which may be attributed to the involvement of neutral species in the rate determining step. Since [NaOH] was kept at predetermined values so pH remained constant throughout the study.

3.6 Effect of temperature: The oxidation was carried out at four different temperatures, namely 301, 308, 312 and 321 K. The k_{obs} values increased with increase in the temperature. Further the plot of $\log k_{obs}$ Vs $1/T$ were straight lines. The thermodynamic parameter ΔH^* , ΔS^* and ΔG^* were calculated from the Eyring plot of $\log k_{obs}/T$ Vs $1/T$ and tabulated (Table3). Negative values of entropy of activation suggested the formation of a rigid transition state with a reduction of the degree of freedom of the molecules involved than the reactants.

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Table 3: Kinetic and Activation Parameters for the oxidation of [LA] by [NCS].

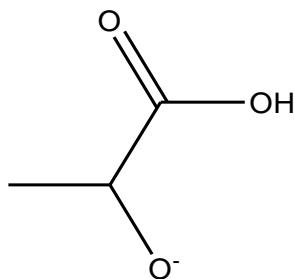
Activation parameters	Lactic acid
$10^4 E_a$ (J/mol)	5.30
$10^4 \Delta H^*$ (J/mol)	5.15
ΔS^* (J/mol)	-73.75
$10^4 \Delta G^*$ (J/mol)	7.75

3.7 Test for free radicals: To test the intervention of the free radical during the course of the reaction, acrylonitrile monomer was added to the reaction mixture and kept for 2 hours under a nitrogen atmosphere. No precipitate was obtained, which revealed that the oxidation of LA by NCS did not involve a free radical. Further ESR study confirmed that the reaction did not proceed through free radical as intermediate since no signal was obtained in the study. Thus, one electron oxidation giving rise to free radicals is unlikely.

3.8 Effect of polarity on the rate constant: By keeping all parameters at constant values, the values of k_{obs} were calculated by changing the polarity of the solvent. The rate of the reaction was studied by varying the composition of acetonitrile-water mixture. The result revealed that k_{obs} did not change with respect to the change in the solvent composition (0-20%) ruling out the formation of more polar intermediate than the reactants.

IV. CONCLUSION

Lactic acid can lose a proton from the carboxyl group in solution, producing the lactate ion $\text{CH}_3\text{CH}(\text{OH})\text{COO}^-$. This higher acidity is the consequence of the intramolecular hydrogen bridge between the α -hydroxyl and the carboxylate group, making the latter less capable of strongly attracting its proton. Due to the occupation of electrons of the carboxylic oxygens in the hydrogen bonding, the acidic proton is held less strongly, as the same electrons are used in bonding that hydrogen too. So the pK_a of lactic acid is 3.86. At the given experimental condition lactic acid exist as



In alkaline medium NCS will react with OH^- to give OCl^-



UV-Visible spectral studies revealed that there were two absorptions maximum for the reaction mixtures, one at 290nm and the other at 230nm in lactic acid. Time history of the spectrum revealed that absorbance at 290nm decreased within 15 minutes. However the absorbance at 230nm also decreased with increases with time. The peak at 290nm was due to the formation of hypochlorite. The effect of hydroxy acid on the rate of the reaction revealed that the rate of the reaction was zero order with respect to [hydroxy acid]. Moreover the reaction between hypochlorite and hydroxy acid was fast and hence the rate did not depend on the concentration of hydroxy acid.

Based on the above results the following mechanism was proposed.

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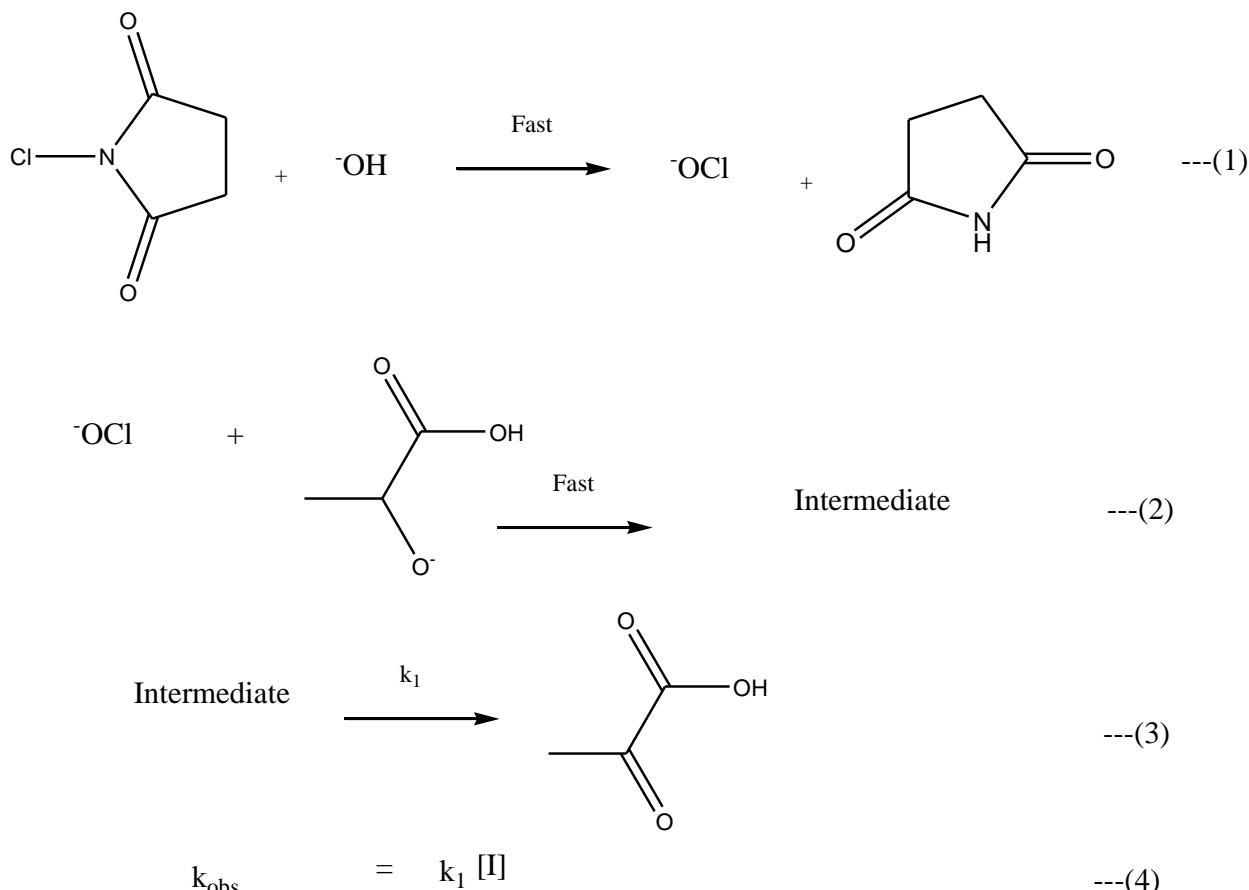
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Lactic acid - Scheme I



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