

# Bio-mimic Oxidation Kinetics of Nicotinic Acid by $\mu$ - Peroxo Complex in Aqueous Medium

Mohanraja M <sup>#1</sup> and Sekar A <sup>\*2</sup>

<sup>#</sup> Department of Chemistry, Arignar Anna Govt Arts College, Attur 636 121, Tamil Nadu, India

<sup>\*</sup> Department of Chemistry, Nehru Memorial College, Puthanampatti, Tiruchirappalli 621 007, Tamil Nadu, India

<sup>1</sup>[mmabimohan@gmail.com](mailto:mmabimohan@gmail.com)

<sup>2</sup>[alagansek66@gmail.com](mailto:alagansek66@gmail.com)

**Abstract** - The complex ( $\mu$ -peroxo)( $\mu$ -hydroxo)bis[bis(bipyridyl)-cobalt(III)] was synthesized by solution route. The prepared  $\mu$ -peroxo complex was confirmed by FT-IR and Electronic Spectroscopy. The biomimic oxidation kinetics of nicotinic acid by  $\mu$ -peroxo complex in aqueous medium was studied potentiometrically. The reaction exhibit first order dependence of rate with respect to each in the dioxygen  $\mu$ -peroxo complex concentration and hydrogen ion concentration. The substrate concentration was maintained at pseudo first order condition. The increase in ionic strength does not affect the rate of reaction. The reaction did not induce the formation of free radicals by the addition of acrylonitrile. The activation and thermodynamic parameters have been calculated from the effect of temperature on the reaction rate. The main product was identified by the spot test. A plausible reaction mechanism consistent with the experimental observation has been proposed.

**Keywords:** Kinetics,  $\mu$ -Peroxo Complex, Nicotinic Acid, Oxidation, Mechanism.

## 1. INTRODUCTION

The chemistry of oxygen requiring enzymes is of major importance in a large number of metabolically, medicinally and industrially relevant systems [1]. The attention has been focused on the mechanism of enzymatic reaction. A large number of model systems have been established. There are still many unsolved problems for most enzymes utilizing oxygen. The studies on the non-enzymatic oxygenation reactions as biomimic have contributed to understanding of oxidation reactions. It is well known that complexation of dioxygen plays a important role in many biological systems. They interact with a wide range of functional groups, affecting a variety of molecular transformation. Therefore an extensive research has focused on the coordination chemistry of naturally occurring dioxygen complexes.

Nicotinic acid also called Niacin and vitamin B<sub>3</sub>. It occurs naturally in plants and animals and is added to many foods as a vitamin supplement. Niacin is used to treat and prevent a lack of natural niacin in the body and to lower cholesterol and triglycerides in the blood. As the precursor for NAD and NADP, niacin is also involved in DNA repair [2], [3]. It is used to lower the risk of heart attack in people with high cholesterol who have already had a heart attack. It is also known as pellagra-preventive factor (p-p factor). It plays a vital role in cell respiration, release of carbohydrates, fats and proteins.

It has been oxidized by some oxidizing agents. The importance of oxidation of vitamins from chemical point of view is on its mechanism of metabolism. Consequently, it is imperative to explore more redox reactions of this compound with a wide range of oxidants. Hence oxidation of nicotinic acid may help in understanding some aspects of enzyme kinetics.

The reports on kinetic study of oxidation reactions of nicotinic acid are scanty. The kinetics of oxidation of nicotinic acid have been studied by reagents such as Ruthenium (III) catalyzed oxidation of niacin by

Bromamine-B [4], Ruthenium (III) catalyzed oxidation of niacin by Chloramine-B [5], by peroxomonosulfate [6], nicotinic acid hydrazide by thallium (III) [7],  $\text{KMnO}_4$  [8] and some other well-known oxidizing agents. But there seems to be no work reported in the literature on the oxidation kinetics of Nicotinic acid by  $(\mu\text{-peroxo})(\mu\text{-hydroxo})$  bis[bis(bipyridyl)-cobalt(III)] complex. Hence we have considered it to study the kinetics and mechanism of oxidation of Nicotinic acid by this  $\mu\text{-peroxo}$  complex.

## II. EXPERIMENTAL METHODS

### A. Complex Preparation

Reagents and solvents used were of commercially available reagent quality without further purification. All solutions were prepared with distilled water. The  $(\mu\text{-O}_2)(\mu\text{-OH})[(\text{Co}(\text{bpy})_2)_2]^{3+}$  (bpy=bipyridyl) complex was prepared [9] by bubbling oxygen in the dark through a solution containing 2,2'-dipyridyl and cobalt nitrate with pH adjusted to 9 and subsequently  $\text{NaClO}_4 \cdot \text{H}_2\text{O}$  dissolved in ethanol was added. The resulting solution was maintained at  $10^\circ\text{C}$ . Brown crystals were filtered, washed with cold ethanol and were characterized using UV-Visible and Fourier Transformed Infrared (FTIR) spectrophotometers.

### B. Kinetic Procedure

The kinetic runs were carried out under pseudo first order condition with [Nicotinic acid]  $\gg$  [ $\mu\text{-peroxo}$  complex]. Requisite amounts of nicotinic acid, sulphuric acid, sodium sulphate and water were pipetted out into a double walled beaker provided with an inlet and outlet for water circulation from the thermostat set at desired temperature. The kinetic reaction was started by the addition of appropriate quantity of  $\mu\text{-peroxo}$  complex solution, which had also been thermo stated for nearly half an hour. The total volume of the reaction mixture was 40 ml for all the experiment.

The kinetic reaction was followed by setting up a cell [SCE<sup>-</sup>/substrate-complex/Pt<sup>+</sup>] made up of the reaction mixture into which the platinum electrode and reference electrode (SCE) were dipped. The reaction mixture was stirred continuously using a magnetic stirrer throughout the experiment. The emf of the cell was measured periodically using Equiptronics Potentiometer.

In order to study the effect of atmospheric oxygen, some experiments were carried out in an inert atmosphere by bubbling nitrogen gas in the reaction mixture and it was ascertained that the velocity constants were reproducible within  $\pm 3\%$ . The rate of reaction was not in much variation between the air and inert atmosphere; hence the entire experiment was done in air atmosphere. Sodium sulphate solution ( $2.5 \times 10^{-2} \text{mol dm}^{-3}$ ) was used to keep ionic strength constant in the reaction mixture.

The rate constants were calculated from linear ( $r > 0.99$ ) plots of  $\log(E_t - E_\infty)$  versus time by least square method by using Microsoft Office Excel program. Duplicate kinetic runs showed that the rate constants were reproducible to within  $\pm 3\%$ . The pseudo first order rate constant ( $K_{\text{obs}}$ ) was expressed in terms of seconds.

## III. RESULTS AND DISCUSSION

### A. Characterization of $\mu\text{-Peroxo}$ Complex

The electronic absorption spectrum of the  $\mu\text{-peroxo}$  complex was recorded in aqueous medium. The bridged  $\mu\text{-peroxo}$  complex has an absorption maximum at 305 nm. The spectrum shows that there is no characteristic transition in visible region, but an intense charge transfer band near 200nm due to the transfer of electron from the peroxide to metal. This clearly shows the presence of a single bridge peroxo-ligand in the  $\mu\text{-peroxo}$  complex.

The FT-IR spectrum of  $\mu$ -peroxo complex was recorded on a Perkin Elmer Spectrum RSI spectrometer using KBr pellet technique in the wavelength range  $400\text{-}4000\text{cm}^{-1}$ . The broad band centered at  $3443\text{cm}^{-1}$  shows the presence of O-H stretching in  $\mu$ -peroxo complex. The band at  $2346\text{cm}^{-1}$  confirms the presence of coordinated nitrogen in  $\mu$ -peroxo complex. The strong peaks of  $1589$  and  $1385\text{cm}^{-1}$  confirm the presence of C-H and  $\text{-OH}$  bending vibrations respectively. The peak at  $1091\text{cm}^{-1}$  and  $624\text{cm}^{-1}$  shows the presence of C-N stretching and  $\text{ClO}_4$  stretching vibrations in the  $\mu$ -peroxo complex. The peak at  $855\text{cm}^{-1}$  shows the presence of O-O stretching vibration in the  $\mu$ -peroxo complex.

*B. Effect of Concentration of Nicotinic Acid on the Rate of Reaction*

In order to study the effect of substrate (Nicotinic acid) on the rate, the rate of oxidation was determined over a wide range of initial nicotinic acid concentration and by keeping constant [peroxo complex],  $[\text{H}_2\text{SO}_4]$  and  $[\text{Na}_2\text{SO}_4]$  at  $313\text{K}$ . The rate of the reaction is independent of initial concentration of the substrate. Hence the order with respect to nicotinic acid is zero (Table I).

TABLE I

EFFECT OF VARYING [NICOTINIC ACID] ON THE RATE OF OXIDATION BY  $\mu$ -PEROXO COMPLEX

$[\text{Peroxo Complex}] = 2.0 \times 10^{-3}\text{mol dm}^{-3}$

Solvent = Water

$[\text{Na}_2\text{SO}_4] = 2.5 \times 10^{-2}\text{mol dm}^{-3}$

Temperature =  $313\text{K}$

$[\text{H}_2\text{SO}_4] = 4.0 \times 10^{-2}\text{mol dm}^{-3}$

<b><math>10^2</math> [Nicotinic Acid] (<math>\text{mol dm}^{-3}</math>)</b>	1.0	2.0	3.0	4.0
<b><math>10^4 k_{\text{obs}} \text{S}^{-1}</math></b>	4.6	4.6	4.7	4.7

*C. Effect of Ionic Strength on the Rate of Reaction*

The effect of variation of added salt strength on the rate of oxidation of nicotinic acid was studied by varying the concentration of the initially added sodium sulphate and by keeping the concentrations of nicotinic acid,  $\text{H}_2\text{SO}_4$  and peroxo complex constant. The rate of the reaction was almost constant with increasing concentration of added salt (Table II).

TABLE II

EFFECT OF VARYING  $[\text{Na}_2\text{SO}_4]$  ON THE REACTION RATE AT  $313\text{K}$

$[\text{Peroxo Complex}] = 2.0 \times 10^{-3}\text{mol dm}^{-3}$

Temperature =  $313\text{K}$

$[\text{Nicotinic Acid}] = 2.0 \times 10^{-2}\text{mol dm}^{-3}$

Solvent = Water

$[\text{H}_2\text{SO}_4] = 4.0 \times 10^{-2}\text{mol dm}^{-3}$

<b><math>10^2</math> <math>[\text{Na}_2\text{SO}_4]</math> (<math>\text{mol dm}^{-3}</math>)</b>	1.0	1.5	2.0	2.5
<b><math>10^4 k_{\text{obs}} \text{S}^{-1}</math></b>	4.6	4.7	4.7	4.6

D. Effect of Concentration of  $\mu$ -Peroxo Complex on the Rate of Oxidation of Nicotinic Acid

The oxidation of nicotinic acid was carried with different initial concentrations of the oxidant i.e.  $\mu$ -peroxo complex and by keeping constant [Nicotinic Acid],  $[\text{Na}_2\text{SO}_4]$  and  $[\text{H}_2\text{SO}_4]$  at 313K. The rate constants were increased by increasing the initial concentration of the oxidant. The reaction is first order with respect to oxidant at every one of these concentrations (Table III).

The plot of  $5 + \log [\text{complex}]$  versus  $5 + \log k_{\text{obs}}$  for different initial concentration of  $\mu$ -peroxo complex is linear with positive unit slope presents the first order dependence of rate on  $\mu$ -peroxo complex (Fig.1).

TABLE III

EFFECT OF VARYING [ $\mu$ -PEROXO COMPLEX] ON THE RATE OF OXIDATION OF NICOTINIC ACID

[Nicotinic Acid] =  $2.0 \times 10^{-2} \text{ mol dm}^{-3}$                       Solvent = Water  
 [ $\text{Na}_2\text{SO}_4$ ] =  $2.5 \times 10^{-2} \text{ mol dm}^{-3}$                       Temperature = 313K  
 [ $\text{H}_2\text{SO}_4$ ] =  $4.0 \times 10^{-2} \text{ mol dm}^{-3}$

$10^3 [\text{Complex}]$ ( $\text{mol dm}^{-3}$ )	1.0	2.0	3.0	4.0
$10^4 k_{\text{obs}} \text{ S}^{-1}$	2.5	4.6	6.6	8.9

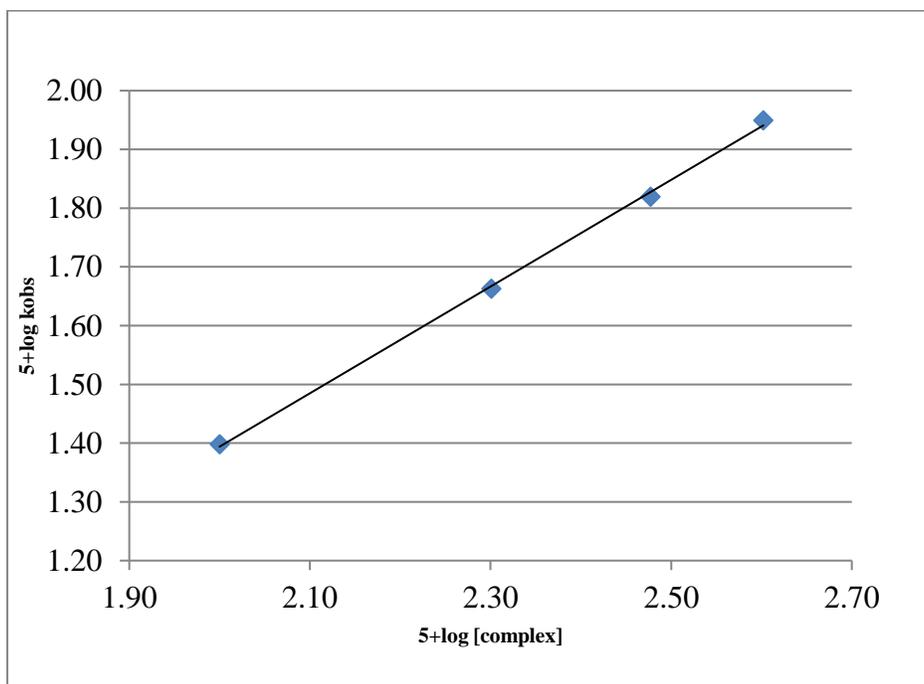


Fig. 1 Plot of  $5 + \log [\text{complex}]$  versus  $5 + \log k_{\text{obs}}$

E. Effect of Concentration of Acid on the Rate of Reaction at 313K

The effect of variation of added mineral acid concentration on the rate of oxidation was studied by varying the concentration of added sulphuric acid. The rate constant was found to be increasing as the concentration of hydrogen ion increases. The plot of  $\log k_{\text{obs}}$  versus  $\log [\text{H}_2\text{SO}_4]$  was linear with a unit slope indicating first order on  $[\text{H}^+]$  (Table IV & Fig. 2).

TABLE IV  
EFFECT OF VARYING  $[\text{H}_2\text{SO}_4]$  ON THE RATE OF OXIDATION  
[Nicotinic Acid] =  $2.0 \times 10^{-2} \text{mol dm}^{-3}$  Solvent = Water  
[Peroxo Complex] =  $2.0 \times 10^{-3} \text{mol dm}^{-3}$  Temperature = 313K  
[ $\text{Na}_2\text{SO}_4$ ] =  $2.5 \times 10^{-2} \text{mol dm}^{-3}$

$10^2 [\text{H}_2\text{SO}_4]$ ( $\text{mol dm}^{-3}$ )	$10^4 k_{\text{obs}} \text{ S}^{-1}$	$4+\log[\text{H}_2\text{SO}_4]$	$4+\log k_{\text{obs}}$	Slope
2.0	2.3	2.3010	0.3617	0.9026
4.0	4.6	2.6021	0.6628	
6.0	6.1	2.7782	0.7853	
8.0	8.2	2.9031	0.9138	

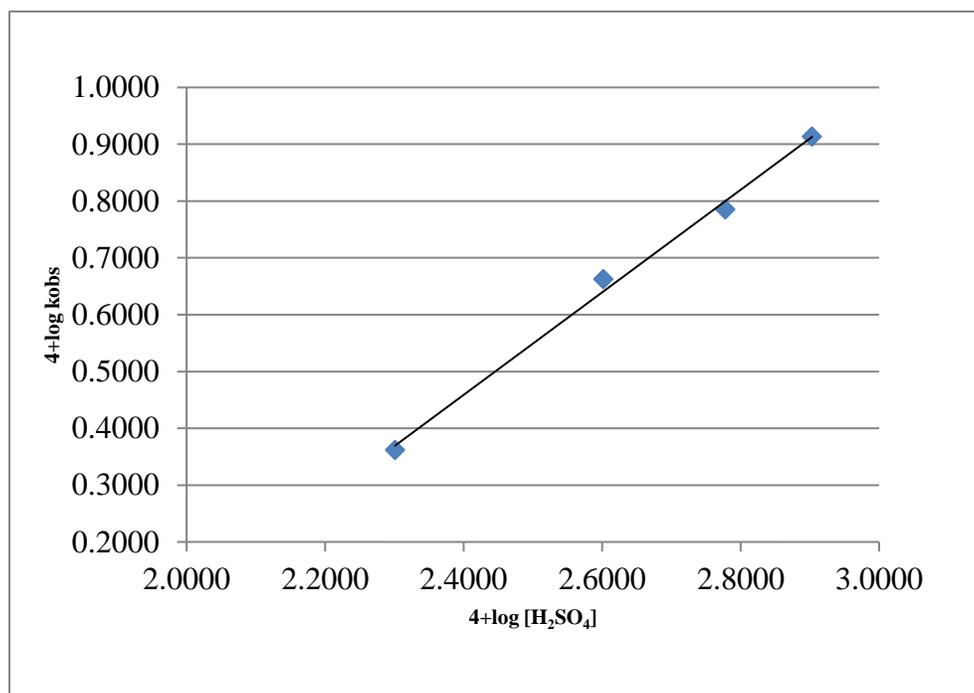


Fig. 2 Plot of  $4+\log [\text{H}_2\text{SO}_4]$  versus  $4+\log k_{\text{obs}}$

F. Effect of Temperature on the Oxidation of Nicotinic Acid

The reactions were studied at 313, 318, 323 and 328 K. The activation parameters ( $E_a$  &  $A$ ) and the thermodynamic parameters  $\Delta H^\ddagger$ ,  $\Delta G^\ddagger$  &  $\Delta S^\ddagger$  have been evaluated (Table V). The Arrhenius plot of  $\log k_{obs}$  versus  $1/T$  and the Eyring plot of  $\log (k/T)$  versus  $1/T$  were found to be linear (Fig. 3 & Fig. 4). The negative values of entropy of activation ( $\Delta S^\ddagger$ ) reflect that the transition state is more rigid than initial state. The nearly constant  $\Delta G^\ddagger$  value indicates that similar mechanism is operative for the oxidation of nicotinic acid.

TABLE V

THE ACTIVATION PARAMETERS FOR THE OXIDATION OF NICOTINIC ACID BY  $\mu$ -PEROXO COMPLEX

[Nicotinic Acid] =  $2.0 \times 10^{-2} \text{ mol dm}^{-3}$       [Na<sub>2</sub>SO<sub>4</sub>] =  $2.5 \times 10^{-2} \text{ mol dm}^{-3}$   
 [Peroxo Complex] =  $2.0 \times 10^{-3} \text{ mol dm}^{-3}$       Solvent = Water  
 [H<sub>2</sub>SO<sub>4</sub>] =  $4.0 \times 10^{-2} \text{ mol dm}^{-3}$

$10^4 k_{obs} \text{ S}^{-1}$				$E_a$ KJ mol <sup>-1</sup>	$\Delta H^\ddagger$ KJ mol <sup>-1</sup>	$\Delta G^\ddagger$ KJ mol <sup>-1</sup>	$\Delta S^\ddagger$ JK mol <sup>-1</sup>	log A
313K	318K	323K	328K					
4.6	6.2	7.9	11.1	49.3	46.6	56.6	-31.4	8.9

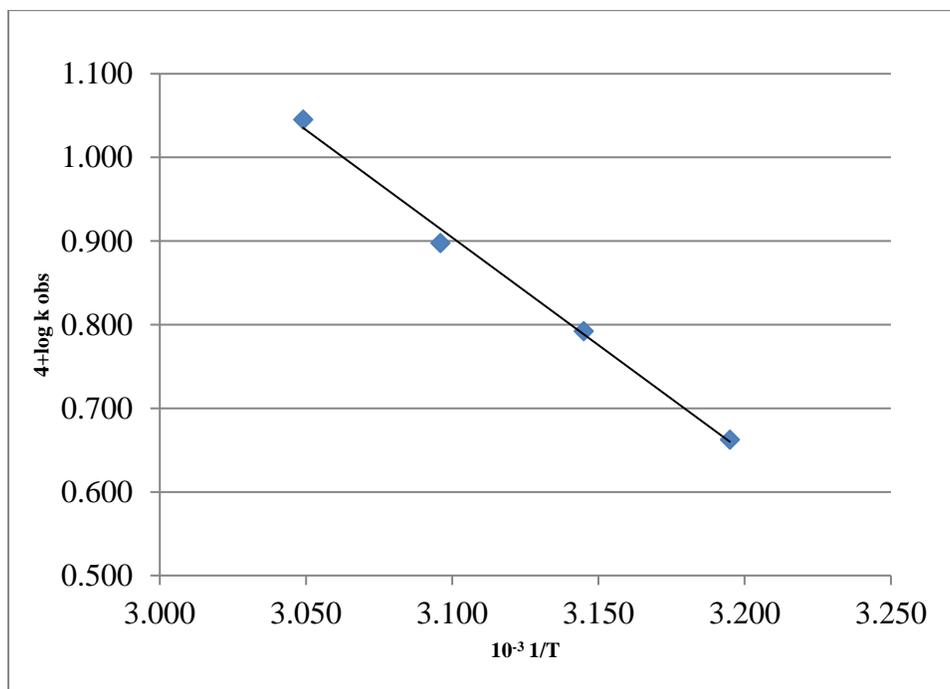


Fig. 3 Arrhenius Plot of  $\log k_{obs}$  versus  $1/T$

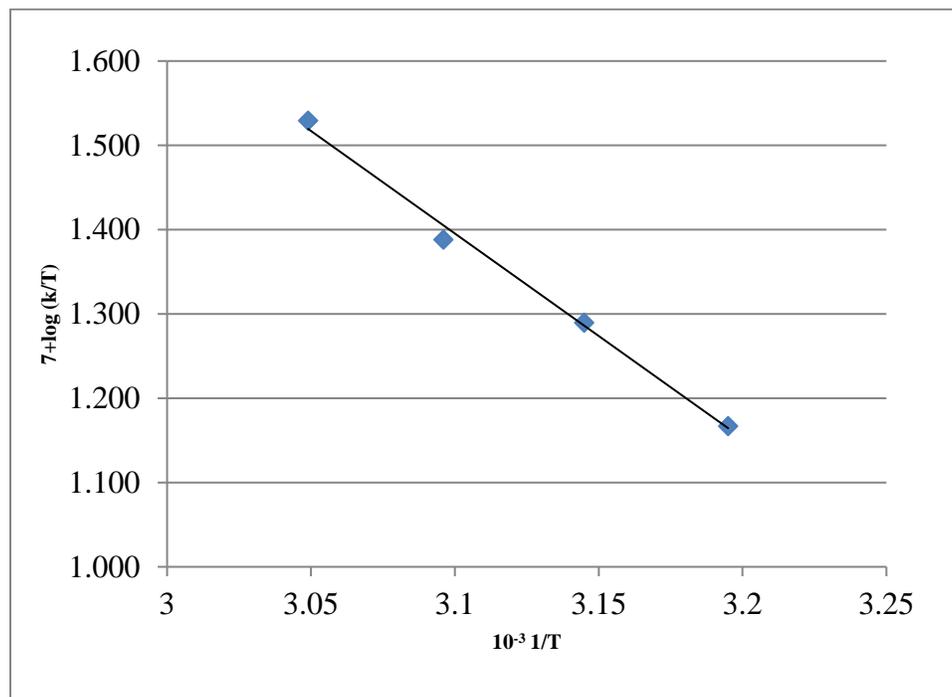


Fig. 4 Eyring Plot of  $\log(k_{obs}/T)$  versus  $1/T$

G. Mechanism and Rate Law

The mechanism of oxidation reaction may be divided into two steps. The first step is the release of caged oxygen molecule from a  $\mu$ -peroxo cobalt (III) complex along with the reduction of Co (III) complex to Co (II) complex [10]-[12]. In the second step, the released oxygen molecule attacks the substrate leading to the final products. From the above results the most probable mechanism for the oxidation behavior of  $\mu$ -peroxo complex is given as



where L = bis(bipyridyl)



(S= Nicotinic Acid)

The above mechanism leads to the following rate law and this rate law explains all the observed experimental facts,

$$\text{Rate} = k_{obs} [\mu\text{-Peroxo complex}] [H^+]$$

## IV. CONCLUSIONS

The  $\mu$ -peroxo cobalt (III) complex has been prepared. The oxidation of biologically important substrate nicotinic acid by  $\mu$ -peroxo complex in presence of sulphuric acid was studied in the temperature range 313-328K. The rates were measured potentiometrically. It shows a first order dependence on [ $\mu$ -peroxo complex] and zero order dependence on [substrate]. The effect of added salt on the rate of oxidation was negligible. The rate of oxidation increases with increase in the initial concentration of sulphuric acid. The oxidation process did not induce the polymerization of the added acrylonitrile and confirmed the absence of free radical formation. The Arrhenius parameters ( $E_a$  &  $A$ ) and the thermodynamic parameters ( $\Delta H^\ddagger$ ,  $\Delta G^\ddagger$  and  $\Delta S^\ddagger$ ) have been evaluated. A plausible reaction mechanism consistent with the experimental observation has been proposed.

## REFERENCES

- [1] E. G. Kovaleva and J.D. Lipscomb, "Versatility of biological non-heme Fe (II) centers in oxygen activation reactions", *Nature Chemical Biology*, vol. 4, pp. 186-193, Jan. 2008.
- [2] D.O. Kennedy, "B Vitamins and the Brain: Mechanisms, Dose and Efficacy-A Review, *Nutrients*, vol. 8, p. 68, Jan. 2016.
- [3] JB. Kirkland, "Niacin requirements for genomic stability", *Mutation Research.*, vol. 733, pp. 14-20, May. 2012.
- [4] Chandrashekar, B.M. Venkatesha, and S. Ananda, "Kinetics of Oxidation of Vitamin-B3 (Niacin) by Sodium N-bromo benzene sulphonamide (Bromamine-B) in HCl Medium and Catalysis by Ru(III) ion", *Research Journal of Chemical Sciences*, vol. 2, pp. 26-30, Aug. 2012.
- [5] Chandrashekar, B.P. Siddaraju and K.C. Shivakumara, "Ruthenium (III) Catalysed Oxidation of Niacin by Chloramine-B in Hydrochloric acid Medium: A Kinetic Study", *International Journal of Current Research*, vol. 10, pp. 63806-63811, Jan. 2018.
- [6] Anju Agrawal, Riya Sailani, Beena Gupta, C.L. Khandelwal, and P.D. Sharma, "The Kinetics and Mechanism for the Oxidation of Nicotinic Acid by Peroxomonosulfate in Acidic Aqueous Medium", *Journal of the Korean Chemical Society*, vol. 56, pp. 212-216, Apr.2012.
- [7] A. Varale and N. Hilage, "Oxidation of Nicotinic acid hydrazide by Thallium (III) in Acidic Medium: A Kinetic and Mechanistic Study", *Int. J. Chem. Sci.*, vol. 7, pp. 2173-2182, 2009.
- [8] I.B. Anweting, J.F. Iyun, S.O. Idris, "Kinetics and mechanism of oxidation of nicotinic acid by potassium permanganate in aqueous acidic medium", *Scholars Research Library, Archives of Applied Science Research*, vol. 4, pp. 1628-1635, 2012.
- [9] R. MacArthur, A. Sucheta, F. F. S. Chong, O. Einarsdottir, "Photodissociation of a ( $\mu$ -peroxo)( $\mu$ -hydroxo)bis[bis(bipyridyl)Cobalt(III)] complex: A tool to study fast biological reactions involving  $O_2$ , *Proc. Natl. Acad. Sci. U.S.A.*, vol. 92, pp. 8105-8109, Aug. 1995.
- [10] M. Kikkawa, Y. Sasaki, S. Kawata, Y. Hatakeyama, F. Ueno, and K. Saito, "*Inorg. Chem*", 1985, vol. 24, pp. 4096-4100.
- [11] R. Annaleise, Howard-Jones, Virgile Adam, Andrew Cowley, Jack E. Baldwin and Dominique Bourgeois, "Cryophotolysis of a caged oxygen compound for use in low temperature biological studies", *Photochemical and photobiological sciences*, vol. 8, pp. 1150-1156, 2009.
- [12] N. Shinohara, S. Matsufuji, and W. Okubo, "Photochemistry of the  $\mu$ -hydroxo- $\mu$ -peroxo-[triethylenetetraamine) cobalt (III)] complex in basic aqueous solutions", *Polyhedron*, vol 10, pp. 107-112, 1991.