Int J Pharm Bio Sci 2015 Oct; 6(4): (P) 530 - 539

Research Article **Analytical Chemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

A THERMODYNAMIC STUDY OF HOST-GUEST INCLUSION COMPLEX OF β-CYCLODEXTRIN AND LYSINE

SHUNMUGAKANI[1] AND DR. D.EASWARAMOORTHY[2*]

[1] Department of Chemistry, Agni College of Technology, OMR, Thalambur, Chennai-600 130, India
*[2 *] Professor, Department of chemistry, B.S.A.Rahman university, Vandalur, Chennai.*

ABSTRACT

The kinetics and oxidation of lysine by PMS in the presence of β-cyclodextrin was studied in acetic acid -sodium acetate buffer medium at 308 K. The rate constant n increased with increase in [Lysine]. In the addition of [beta cyclodextrin], the rate of the reaction increases. pH variation and solvent variation had no effect on the rate of the reaction. Thermodynamic parameters: free energy of activation (ΔG^0) enthalpy of activation (ΔH^0) and entropy of activation (ΔS^0) was calculated by studying the reactions at 303K, 308 K and 318K respectively. The positive value was obtained as enthalpy, entropy and free energy of activation. These entropy and enthalpy changes were favored through inclusions. The positive enthalpy values, positive entropic values are obtained, indicating that this inclusion was hydrophobic interaction. ∆G◦ obtained are also positive. It indicated that the inclusion process proceeded non-spontaneously at experimental temperature. The formation of inclusion complex was confirmed by UV-Visible absorption studies. The stability constant values of lysine are 3.7 L/mol. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 12.32 LM^{-1} and 37.33M^{-1} respectively. The method has been successfully applied to the determination of pharmaceutical formulation with good accuracy.

KEY WORDS: copper (II), glutamine, peroxomonosulphate (PMS), β-cyclodextrin (β-CD) catalyst, inclusion complex, kinetics

DR. D.EASWARAMOORTHY
Professor, Department of chemistry, B.S.A.Rahman university, Vandalur, Chennai.

INTRODUCTION

Amino acids act not only as the building blocks in protein synthesis but they also play a significant role in metabolism. Amino acids can undergo many types of reaction depending upon whether a particular amino acid contains non-polar groups or polar substituents. The oxidation of amino acids is of interest as the oxidation products differ for different oxidants[1,2] The kinetics of Os (VIII) catalysed oxidation of L-lysine by diperiodatoargentate (III) (DPA) in alkaline medium at T = 298 K and a constant ionic strength[3] of 0.50 mol .dm^{-3} and diperiodatocuprate (III) (DPC) in alkaline medium at a constant ionic strength of 0.15 mol/dm3 was also studied spectrophotometrically[4] A kinetic and mechanistic study on the oxidation of arginine and lysine by hexacyanoferrate (III) catalysed by iridium (III) in aqueous alkaline medium[5] . In cyclodextrins (CDs) are a family of cyclic oligosaccharides composed of glucopyranose units linked by a-(1, 4)-glycosidic bonds to form a cylindric structure. On account of their hydrophobic cavities which could include or incorporate hydrophobic compounds, it has been used as host molecules, solubilizing agents, inhibitor blocking agents and molecular chelating agents[6]. Kinetic studies on the thermal dissociation of β-cyclodextrin and ethyl benzoate inclusion complexes[7]. The kinetics of cleavage of phenyl phenyl acetates (PPA) and several para-substituted PPAs in basic aqueous sodium carbonate–bicarbonate buffer contains β-cyclodextrin (β-CD)[8] The effects of β-cyclodextrin on the kinetics of the oxidation of bis ferrocenyl cationic complexes by bis (pyridine -2,6-dicarboxylato)-cobalt (III) in aqueous solution[9] . Comparative kinetic investigation of oxidation of 3-methyl lindole by peroxomonosulphate and peroxodisulpahte using ethanol medium[10]. Kinetics and mechanism of oxidation of L-arginine by sodium periodate in alkaline medium[11] .The interactions between the hydrophobic cavities of cyclodextrins and pullulanase[12] was reported. We are using β-Cyclodextrin as a catalyst which functions as an oxidation process of lysine by peroxomonosulphate in acetic acid-sodium acetate buffer medium. It provides inclusion complex of hydrophobic interaction due to guest molecule (lysine) inside the cavity of host (β-cyclodextrin). It is also provided for the reaction mechanism and the result shows that the rate of the reaction was enhanced.

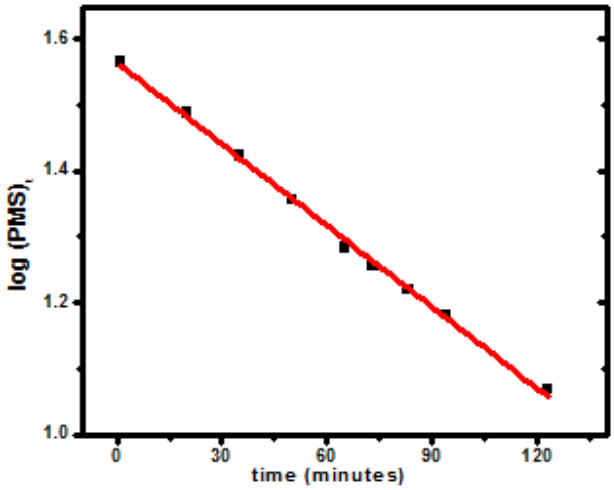
EXPERIMENTAL METHODS

1. Materials and Reagents

β- Cyclodextrin was purchased from SD-Fine chemicals, India. Lysine was obtained from Merck, India, and used as received. PMS was obtained from Aldrich, USA, and the purity of the sample was found to be 98% when tested by iodometric estimation and hence used without further purification. PMS solution was freshly prepared every day, stored in a blackened vessel to prevent photodecomposition, and standardized iodometrically. Acetic acid (E Merck, India Ltd.) was distilled and a stock solution of 8N acetic acid was prepared and standardized using sodium hydroxide (E Merck, India Ltd.). 4N acetic acid was prepared from the stock solution and used to make the buffer solution. Analar grade solvents such as acetonitrile and 2-methyl-2-propanol were distilled and used for the reactions.

2. Kinetic Measurements

The kinetics studies of effect of β– cyclodextrin on the oxidation of lysine by PMS, in acetic acid–sodium acetate buffered medium (pH 3.6-5.2) at 308K was studied under pseudo first order conditions i.e., [lysine] >> [PMS] at various time intervals. A known volume of PMS solution, thermostated at the desired temperature, was a pipette out into the reaction mixture and simultaneously a timer was started. Consumption of PMS in this reaction mixture was monitored by iodometric method. The rate of the reaction followed first-order kinetics as shown (Fig.1).

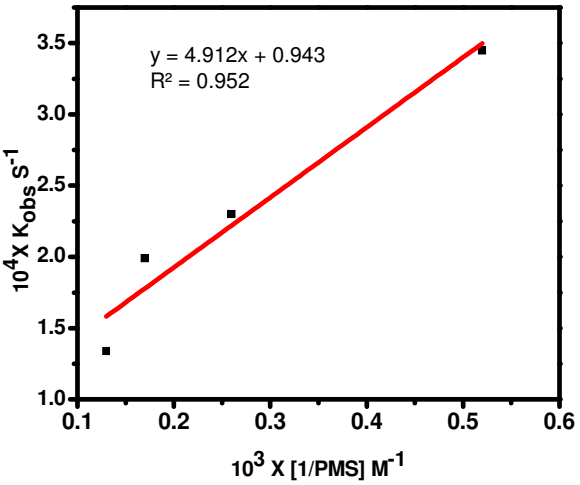


RESULTS AND DISCUSSION

1*. Effect of [PMS] on k_{obs}*

The effect of [PMS] on k_{obs} was studied by determining the rate constant for different concentrations of [PMS] and also by keeping the other parameters at predetermined values. The kinetic results showed that the rate constant decreased with an increase in [PMS] as shown Table 1. The plots of k_{obs} vs. [1/PMS] were linear, as shown (Fig.2).

Figure 2
Plot of log $[PMS]_t$ vs. time at 308K

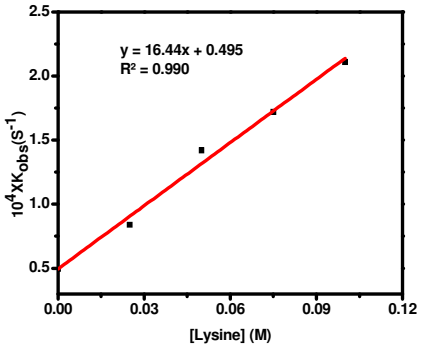


[lysine]= 0. 05 mol dm^{-3}; pH =4.0 ± 0.1; β Cyclodextrin = 0.3g

2. Effect of [Lysine] on k_{obs}

The rate constant k_{obs} were calculated for different concentrations of [Lysine] by keeping all other parameters at constant values. The kinetic results showed that the rate constant increased with increase in [Lysine] Table 1.The plots of log k_{obs} vs. [Lysine] were linear, as shown (Fig.3). Further, the plots of k_{obs} vs. [Lysine] were linear with positive intercepts. This result indicated first order dependence of rate on [Lysine]. The positive intercept obtained in the above plots revealed that the reaction proceeded in two steps: one dependent on [amino acid] and the other independent of [Lysine]. The amino acid independent step was due to the self-decomposition of PMS under the experimental conditions employed in this study[15].

Figure 3
Plot of k_{obs} vs. [Lysine] at 308 K

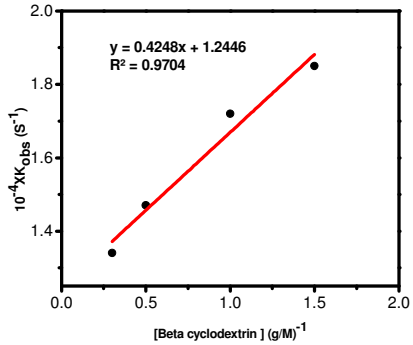


pH =4.0 ± 0.1; [PMS] =3.98× 10^{-3} mol $dm^{-3;}$; β Cyclodextrin=0.3g

3. Effect of k_{obs} vs. [β-CD]

The values of k_{obs} were calculated for different quantities of [β-cyclodextrin] by keeping the other parameters as constant. Kinetic results for variation of β-cyclodextrin showed that the rate constant k_{obs} increased with increase in [β-cyclodextrin][13] Table 1 .The plots of k_{obs} vs. [β-cyclodextrin] were linear with positive intercepts in all the cases (Figure 4). This linear plot indicated that the formation of inclusion complex between β- cyclodextrin and lysine. The same phenomenon has been observed by[16]. In the addition of β-cyclodextrin catalyst was 10^2 times faster than the absence of β-Cyclodextrin catalyst.

Figure 4
Plot of k_{obs} vs. [β-CD] at 308 K



[lysine]= 0. 05 mol dm^{-3};; pH =4.0 ± 0.1; [PMS] =3.98× 10^{-3} mol dm^3

4. Effect of Temperature on k_{obs}

The rate of the reaction was studied by varying the temperature, viz., 303, 308, and 318 K. and also by keeping other parameters at constant values. The k_{obs} increased with the increase in temperature[14] (Table 1) . The plot of log k_2 vs. 1/T was a straight line (Arrhenius plot) and a plot of log k_2 /T vs. 1/T was also linear (Eyring's plot). From the slope and intercept of the straight line, Figure.6 & Figure.7 the thermodynamic parameters were calculated (Table 2). ΔG^o obtained are positive, which indicated that the inclusion process formed non-spontaneously at the experimental temperature. The positive ΔH^o and positive ΔS^o was obtained.

Figure 6
Plot of 1/T Vs. log k_2 /T

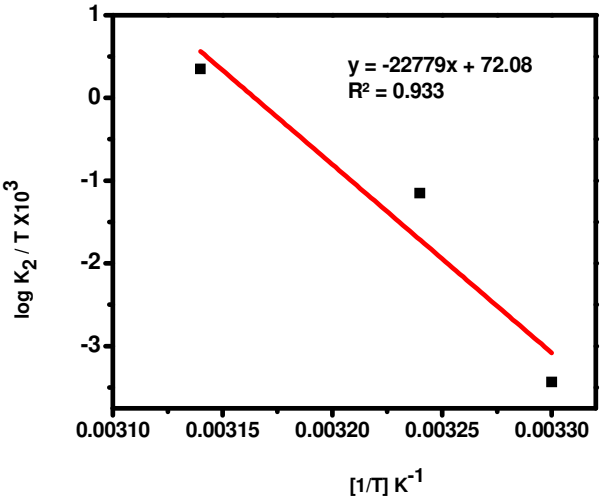
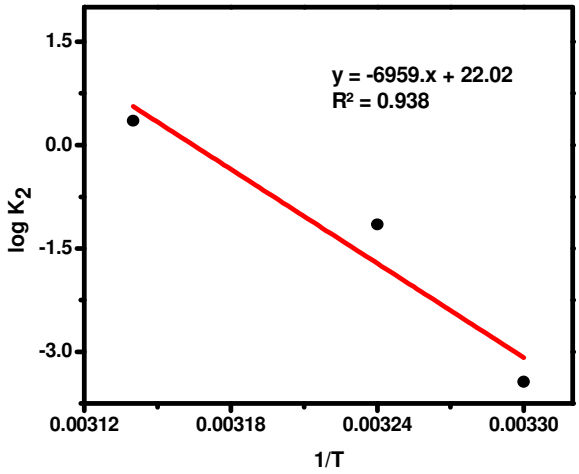
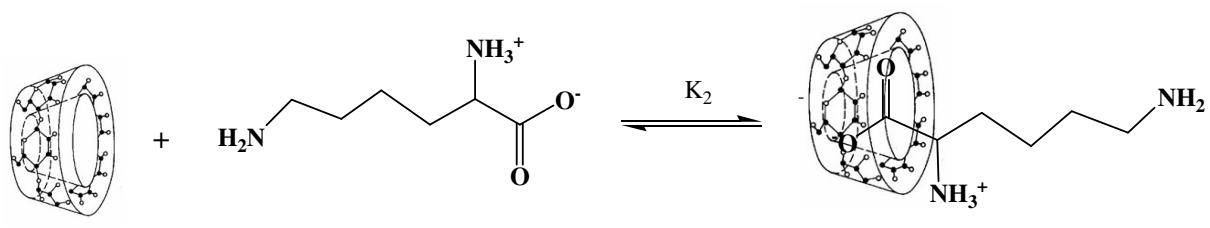


Figure 7
Plot of 1/T vs. log k_2



The thermodynamic parameter: enthalpy changes (ΔH^0) and entropy changes (ΔS^0) of the binding reaction are important to confirm the force of interactions of lysine with β-cyclodextrin. Hydrophobic interaction essentially involves favorable positive entropy together with a slightly positive enthalpy change, whereas the other forces involve negative ΔH^0 and ΔS^0. Upon complexation both positive enthalpic changes and positive entropic values are obtained, indicating that this inclusion is mainly entropically driven. The positive ΔH^0 together with positive ΔS^0 suggested that the inclusion process was an enthalpy controlled process in this case [15]

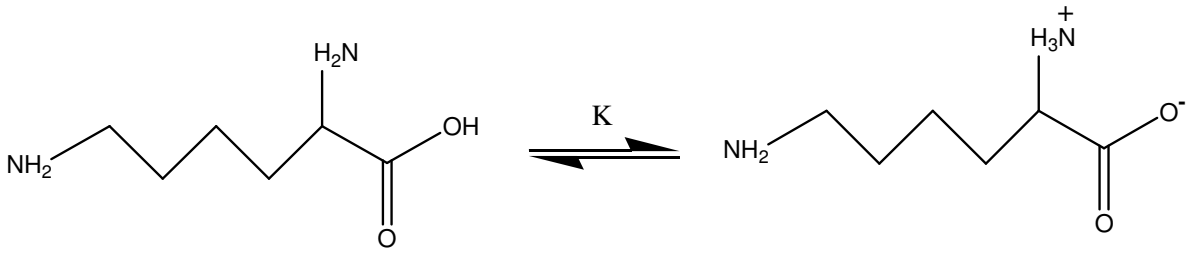


Inclusion complex

Eq (1)

5. Formation of zwitterions

Zwitterions arising from transfer of a proton from the carboxyl to the amino group of lysine. It exists as a dipolar ion in aqueous solutions. The dissociation of lysine depends on the pH of the medium. The pKa value was suggested that in acidic medium, lysine exists both in the protonated form and as zwitterions as shown below.



Lysine

Eq (2)

6. Stoichiometry

The stoichiometry of the reactions was determined for the reaction mixtures containing a large excess of [PMS], [β-cyclodextrin] over [lysine]. Then the reaction mixture was kept for 48 h and the unconsumed PMS was estimated iodometrically. Corrections for the self-decomposition of PMS were made from the value obtained from the control experiments. The observed stoichiometry of the reaction in the mixture of β-cyclodextrin and lysine: PMS was 1:1. This is clearly indicated that the formation of inclusion complex.

7. Product Analysis

The reaction mixture containing a large excess of β-cyclodextrin, PMS over lysine in acetic acid- sodium acetate buffer was kept for 48 h in a blackened vessel at room temperature. The organic layer was separated, dried and given for IR analysis. Further the inclusion complex was confirmed by UV Spectral analysis. The values of stability constant were calculated by varying [β-cyclodextrin] keeping the parameters as [sodium acetate]; [H^+]; [lysine] was kept constant. The concentrations of [β-CD] have been assigned as 500 mg and concentrations of [lysine] have been assigned as 50 mg. There was a linearly decrease in the absorbance with the series of 0.5ml,1.0 ml,1.5ml,2.0ml) by the successive addition of β-CD. (Figure 8) The inclusion complex had a decreased intensity at all points of wavelength due to the interaction of β-CD and lysine. It is observed that, the absorbance value decreased with increasing β-CD concentrations while the concentration of lysine remains the same. It indicates that the solubility of lysine increases upon forming the inclusion complex. Eq. (4) is also known as the Benesi-Hildebrand. The inclusion complex can be proved that the plots of 1/A vs. [1/ β-CD] were linear, in both cases as shown in (Figure 9). A very good linear relationship was obtained for 1/A vs. [1/ β-CD]. This linear plot clearly indicates that the stability constant values of lysine are 3.7 L/mol.[1] and the stoichiometry ratio for the inclusion complex formation between lysine and β-CD is 1:1.

$$\frac{1}{A} = \frac{1}{\varepsilon [G]_0 K[CD]} + \frac{1}{\varepsilon [G]_0} \quad (3)$$

Figure 8
Absorption spectra of glutamine with various concentration of β-CD in presence of Cu (II) Catalyst

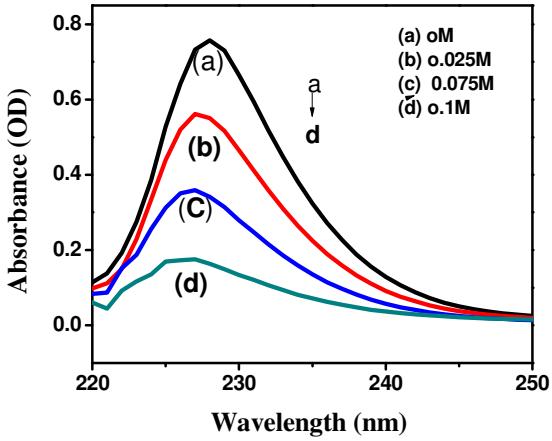
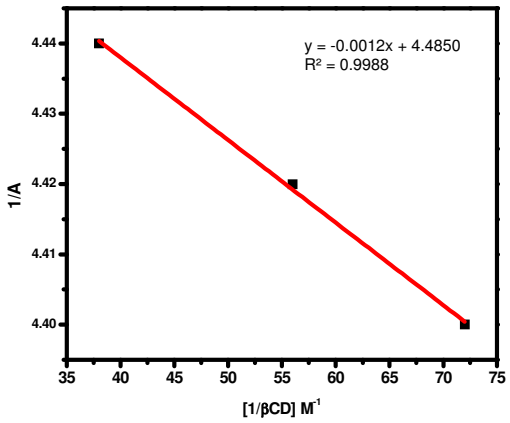


Figure 9
Plot for 1/A against 1/[β–Cyclodextrin] of glutamine with Cu (II) ionsinclusion complex

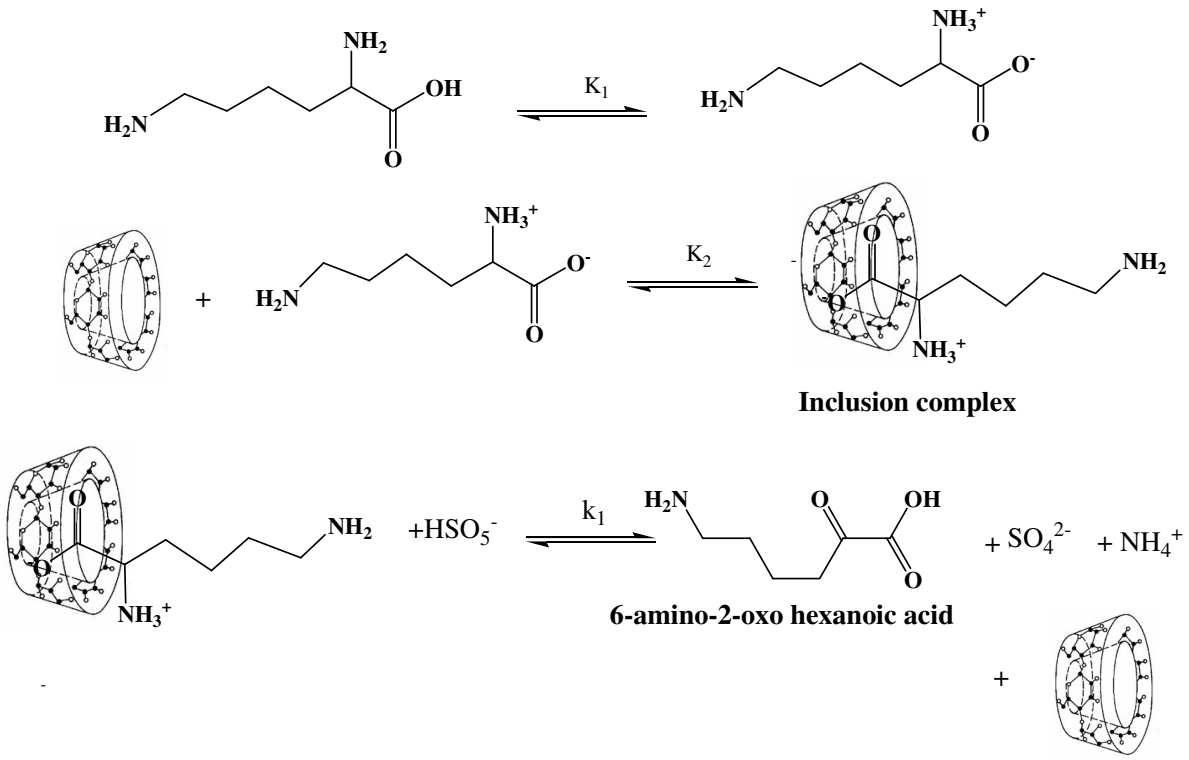


VALIDATION OF THE METHODS

Limit of detection

The limit of detection (LOD) or LOQ=KS.Da/b, where K= 3.3 for LOD and 10 for LOQ, S.Da is the standard deviation of intercept, and b is the slope[16]. The LODs value and LOQ values for the inclusion complex are 12.32 LM^{-1} and 37.33M^{-1}.

Scheme 1



$$2HSO_5^- \xrightarrow{k_2} 2HSO_4^- + O_2$$

$$\frac{-d}{dt}[HSO_5^-] = k_1[complex]\,[HSO_5^-] + k_2[HSO_5^-]$$

$$k_{obs} = \frac{k_1K_1K_2[Lysine]\,[\beta\text{-CD}]}{K_1 + [H^+]} + k_2$$

since $K_1 << [H^+]$

$$\text{Hence} \quad k_{obs} = \frac{k_1K_1K_2[Lysine]\,[\beta\text{-CD}]}{[H^+]} + k_2$$

Table 1
Effect of varying concentrations [Lysine] on the reaction rate at 308K

10^3 x [PMS] (mol dm^{-3})	10^2x [Lysine] (mol dm^{-3})	10^2x [sodium acetate] (mol dm^{-3})	pH± 0.1	β-Cyclodextrine (gram)	10^4x k_{obs} (s^{-1})	Temperature (K)
1.93	5.00	8.50	4.0	0.3	3.45	308
3.86	5.00	8.50	4.0	0.3	1.72	308
5.79	5.00	8.50	4.0	0.3	1.99	308
7.72	5.00	8.50	4.0	0.3	1.34	308
3.86	0.025	8.50	4.0	0.3	0.84	308
3.86	0.0375	8.50	4.0	0.3	1.42	308
3.86	0.05	8.50	4.0	0.3	1.72	308
3.86	0.0625	8.50	4.0	0.3	2.11	308
3.86	5.00	2.13	4.0	0.3	1.65	308
3.86	5.00	4.25	4.0	0.3	1.65	308
3.86	5.00	6.38	4.0	0.3	1.57	308
3.86	5.00	10.63	4.0	0.3	1.57	308
3.86	5.00	8.50	3.6	0.3	1.42	308
3.86	5.00	8.50	4.0	0.3	1.42	308
3.86	5.00	8.50	4.4	0.3	1.68	308
3.86	5.00	8.50	4.8	0.3	1.42	308
3.86	5.00	8.50	4.0	0.1	1.34	308
3.86	5.00	8.50	4.0	0.2	1.57	308
3.86	5.00	8.50	4.0	0.3	1.61	308
3.86	5.00	8.50	4.0	0.5	1.72	308
3.86	5.00	8.50	4.0	0.3	0.883	303
3.86	5.00	8.50	4.0	0.3	1.82	308
3.86	5.00	8.50	4.0	0.3	2.6	318

Table 2
Kinetic and thermodynamic parameters for the oxidation of lysine using β-cyclodextrin catalyst at 308 k

AMINO ACIDS	E_a kJ mol^{-1}	$\Delta H^{\#}$ KJ mol^{-1}	$\Delta S^{\#}$ J $K^{-1}mol^{-1}$	$\Delta G^{\#}$ kJ mol^{-1}
LYSINE	57.85	189.38	401.73	65.65

Table 3
Absorption spectra of amino acid with various concentration of β-CD

[1/β CD] M^{-1}	1/A M^{-1}
	Lysine
72	4.40
56	4.42
38	4.44

CONCLUSION

We are using β-Cyclodextrin as a catalyst which functions as an oxidation process of lysine by peroxomonosulphate in acetic acid-sodium acetate buffer medium. These are responsible for greater importance in terms of the rate constant value and thermodynamic parameters. It provides inclusion complex of hydrophobic interaction due to guest molecule (lysine) inside the cavity of host (β-Cyclodextrin). These inclusions were favored through entropy and enthalpy changes were calculated by thermodynamic parameters. ΔG^{o} obtained are positive, which indicated that the inclusion process formed non-spontaneously at

the experimental temperature. This linear plot clearly indicates that the stability constant values of lysine are 3.7 L/mol.[1] The limit of detection (LOD) or LOQ was calculated.

ACKNOWLEDGEMENT

The principal and the management of Agni College of technology, OMR, Thalambur, Chennai-600 130, India for their constant encouragement and support.

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