CHAPTER 1

INTRODUCTION

1.1 IMPORTANCE OF AMINO ACIDS

Amino acids initiate metabolic activities which are critical to life. One important function is that, they serve as the building blocks for proteins, which are linear chains of amino acids. They also function as chemical messengers in bringing about communication between cells. Amino acids can also be used in biochemical research, microbiology, nutrition, pharmaceuticals and fortification of foods and feeds.

Protein is a nutrient needed by the human body for growth and maintenance. During digestion, proteins are broken down by enzymes known as proteases into smaller polypeptides to provide amino acids for the body. Next to water, proteins are the most abundant molecules in the body. Proteins are the major structural component of all cells in the body, which includes muscles, organs, hair and skin. Protein is also needed to form blood cells.

When high dietary protein is consumed, there is an increase in urea excretion, which is indicative of increase in oxidation of amino acids (as the body is unable to store excess protein). As a result, oxidation is facilitated and the amino group of the amino acid is excreted to the liver (Tarnopolsky et al 1992, Ten Have et al 2007). Excess amino acids are converted to other usable molecules by the liver in a process called deamination. Deamination converts nitrogen from the amino acid into ammonia, which is converted by the liver
into urea in the urea cycle. Excretion of urea is performed by the kidneys. These organs can normally cope with any extra workload but, if a kidney disease occurs, a decrease in the level of protein intake will often be prescribed.

Hence, oxidation of amino acids is of great importance both from a chemical point of view and its bearing on the mechanism of amino acids metabolism.

1.2 IMPORTANCE OF BASIC AMINO ACIDS

Basic amino acids such as arginine, histidine, lysine etc., are polar and positively charged at pHs below their pKₐs and are hydrophilic. They exhibit acidic as well as basic properties, and hence they are amphoteric.

Arginine, an essential basic amino acid, is needed to remove toxic ammonia from the body, used in muscle contraction and the construction of cartilage. It also plays an important role in cell division, immune function and in the release of hormones. Arginine is important to life, especially for the growth of children.

Histidine is useful in manufacturing glycogen and in the control of mucus. It has relevance in biological metabolic processes and hence it forms strong chelates with divalent and trivalent metal ions (Andrews and Grundemeier 1966). The presence of an α-amino group in the side chain and pyridine-type nitrogen in the imidazole ring of the histidine molecule, each with a centre of high electron density, provides one of the primary means by which metal ions may be bound to proteins (Sundberg and Goutam Gupta 1973).

Ornithine is a non-protein amino acid, derived from the breakdown of arginine during the citric acid cycle. It helps to build muscle and reduce
body fat, especially when combined with amino acids like arginine and carnitine. It is also needed for the formation of citrulline, proline and glutamic acid. Ornithine helps to remove toxic ammonia from the liver, and reduce the effects of cirrhosis of the liver and disorders associated with malfunctioning of the liver. Ornithine is the major source of polyamines in mammalian physiological systems.

Ornithine, a non-coded amino acid, is frequently added as a modifier in bioactive peptides, including drugs obtained industrially, to improve their biological properties.

1.3 OXIDATION STUDIES OF BASIC AMINO ACIDS BY DIFFERENT OXIDANTS

1.3.1 Haloamine

Mahadevappa et al (1980) reported the kinetic and mechanistic studies on the oxidation of arginine and histidine by chloramine-T (CAT) in hydrochloric acid medium at 30°C. The reaction indicated simultaneous catalysis by \( \text{H}^+ \) and \( \text{Cl}^- \) ions in \([\text{HCl}]\) range of 0.04-0.12 M. The reaction was first order with respect to [CAT], \([\text{H}^+]\) and [arginine], but zero order with respect to [histidine]. A suitable mechanism was proposed.

Mahadevappa et al (1988) investigated the kinetics and mechanism of oxidation of arginine, glutamine, histidine and lysine by bromamine-T [BAT] in acid and alkaline media at 30°C and 20°C respectively. Proton inventory studies in \( \text{H}_2\text{O}-\text{D}_2\text{O} \) mixtures with arginine as a probe revealed that the rate increased in the order: histidine > lysine > arginine > glutamine. In alkaline media, the rate showed a first order dependence on [BAT] and was fractional order in [amino acid] and [hydroxide ion]. Para-toluene sulphonamide retarded the rate and the mechanism proposed by them is given below.
Ivan Pinto et al (1990) studied the oxidation of L-histidine using electrolytically generated manganese(III) sulphate in aqueous sulphuric acid spectrophotometrically. Oxidation followed second order kinetics in [Mn(III)], first order in [histidine] and inverse first order in [H⁺]. The reduced product of the oxidant, Mn(II), retarded the rate of reaction. Evidence for the transient existence of the free radical intermediate was given. Effects of ionic strength, solvent composition, HSO₄⁻ and certain complexing agents like P₂O₇⁴⁻, Cl⁻, F⁻ on the rate were also studied. From the kinetic studies, they observed that the complexing agents when added, decreased the redox potential of the Mn(III)/Mn(II) couple, leading to a low rate of oxidation.

1.3.2 Hexacyanoferrate (HCF)

The kinetics of oxidation of amino acids such as lysine, arginine, and histidine by alkaline hexacyanoferrate(III) was studied by Didcy Laloo and Mahanti (1990). The rate was dependent on the first powers of the concentrations of amino acid and hexacyanoferrate, but independent of the
concentration of the alkali. They suggested that the reaction proceeded through formation of $\alpha$-imino acid, in a rapid step, which then hydrolysed to give the corresponding $\alpha$-keto acid, which mimics the oxidation of amino acids in the body.

\[
\begin{align*}
R\text{H} & \text{C} - \text{COO}^- + \text{OH}^- \\
& \xrightarrow{\text{slow}} R\text{H} & \text{C} - \text{NH}_3 \\
& \xrightarrow{\text{fast}} R\text{C} & \text{COO}^- + \text{HOH}
\end{align*}
\]

The kinetics of Ir(III) catalysed oxidation of some amino acids like arginine and lysine by hexacyanoferrate(III) (HCF) ions in aqueous alkaline medium was studied spectrophotometrically (Anjali Goel and Ruchi Sharma 2012). The reactions exhibit 2:1 stoichiometry and follow first order kinetics in [HCF(III)] and [alkali]. The dependence of the rate on amino acid concentration has been found to be of Michaelis-Menten type. A mechanism involving the complex formation between catalyst and the amino acid has been proposed. $\varepsilon$-guanidino-$\alpha$-oxo valeric acid and 6–amino-$\alpha$-oxo caproic acid have been identified chromatographically and spectroscopically as the final product of oxidation of arginine and lysine, respectively.

1.3.3 Periodate

Kinetics and mechanism of oxidation of chromium(III)-L-arginine complex by periodate ($\text{IO}_4^-$) was investigated by Khalek et al (1997). They observed that $[\text{Cr}^{\text{III}}(\text{Arginine})_2(\text{H}_2\text{O})_2]^+$ was oxidized by $\text{IO}_4^-$ and the electron transfer proceeded through an inner-sphere mechanism via coordination of $\text{IO}_4^-$ to chromium(III).
The spectrophotometric study on the kinetics of oxidation of L-arginine by periodate in alkaline medium monitored at wavelength 280 nm revealed that the reaction was first order with respect to [Arginine], [alkali] and [periodate] (Sridevi and Vani 2010). The oxidation product of the reaction was found to be α- keto acid. The anionic species of arginine was considered to be the reactive species and a suitable mechanism was proposed.

The electrochemical oxidation of glycine and lysine in a strong alkaline solution (Ogura et al 1998) was studied, and the nature of the adsorbed species was disclosed by means of an in situ FT-IR spectroscopic method. The oxidation was strongly suppressed by the adsorption of the amino acids, followed by oxidative decomposition. The adsorption of amino acid into the electrode was achieved through the terminal carboxylate ion group of fully unprotonated anions from +0.4 V vs Ag/AgCl, and the concentration of the adsorbent attained the maximum at + 0.9 V. Beyond this potential, the adsorption strength was weakened, and the oxidative decomposition to carbon dioxide, ammonia etc., occurred from +1.1 V.

Ionita et al (2000) reported the kinetics of oxidation of amino acids such as serine, proline, leucine, tryptophan, threonine, phenylalanine, methionine, histidine by sodium salts of 2-p-phenylsulphonic acid-2-phenyl-1-picrylhydrazyl and 2, 2-di-p-phenylsulphonicacid-2-phenyl-1-pylhydrayzyl at isoelectric point of amino acids. They studied the rate under pseudo-first order conditions with an excess of amino acid over the oxidant. The kinetics was followed spectrophotometrically by monitoring the disappearance of the oxidants. They observed that the aromatic amino acids such as histidine, tryptophan, and phenylalanine were oxidised more rapidly than the others. The following mechanistic pathway was proposed.
1.3.4  Permanganate

The kinetics and mechanism of Ru(III) catalysed oxidation of L-arginine by alkaline permanganate was reported (Halligudi et al 2001). The oxidation proceeded via formation of a complex between the active Ru(III) species and L-arginine, which then reacted with one mole of permanganate in a slow step to yield a L-arginine free radical, followed by a fast step to form aldehyde as the product.

1.3.5  N-bromobenzenesulphonamide (BAB)

Yathirajan et al (2003) reported the kinetic studies of the oxidation of L-isoleucine (ISL) and L-ornithine hydrochloride (ORH) by sodium N-bromobenzenesulphonamide (BAB) in aqueous perchloric acid medium. The rate showed first-order dependence on both [BAB] and [amino acid] and inverse first order dependence on [H]\(^+\) for [ORH]. The rate of the reaction decreased with a decrease in the dielectric constant of the medium. The rate remained unchanged in the ionic strength of the medium for ISL, whereas the rate decreased with an increase in the ionic strength of the medium for ORH. Isovaleronitrile and 3-(methylamino)propionitrile were identified as the products.
1.3.6 Tetrachloroaurate

The oxidation of L-histidine by tetrachloroaurate(III) ion in HClO₄ (Vimal Soni et al 2005) was first order in both [AuCl₄⁻] and [histidine] and the oxidation product was β-imidazolylpyruvic acid. The $k_{obs}$ decreased with an increase in [H⁺] and [Cl⁻]. The rate dependence on [Cl⁻] was due to the equilibrium between the reactive AuCl₄⁻ and AuCl₃OH⁻ species of Au(III); the reaction was in the order: AuCl₃OH⁻ $\gg$ AuCl₄⁻ ion. The rate dependence on [H⁺] was attributed to the reactive histidine species, RCH₂-CH (NH₃⁺) COO⁻ which was in equilibrium with the non-reactive R-CH (NH₃⁺) COOH where R is the imidazole ring. An inner-sphere mechanism based on the NMR study on the complex formed between [AuCl₄⁻] with histidine was suggested. The outer-sphere mechanism was ruled out because the $\Delta S^\#$ values were very different for the similarly charged species (AuCl₄⁻ and AuCl₃OH⁻).

1.3.7 Diperiodatocuprate (DPC)

The kinetics of oxidation of L-lysine by DPC in alkaline medium at a constant ionic strength of 0.15 M was studied spectrophotometrically (Kiran et al 2007). The reaction was first order in [DPC] and less than first order in [L-lysine] and [alkali]. The oxidation reaction was shown to proceed via a DPC-lysine complex. Oxidation of L-lysine by DPC was reported by Hiremath et al (2008).

Abbar et al (2009) reported the oxidation of DL-ornithine monohydrochloride(OMH) by DPC both in the absence and presence of ruthenium(III) catalyst in aqueous alkaline medium. In both the catalyzed and uncatalyzed reactions the order of the reactions with respect to [DPC] was unity while the order with respect to [OMH] was less than unity. The rate increased with an increase in [OH⁻] and decreased with an increase in [IO₄⁻] in both cases. The order with respect to Ru(III) was unity. The reaction rates revealed that Ru(III) catalyzed reaction was eight-fold faster than the
uncatalyzed reaction. Kinetic experiments suggested that [Cu (H₂IO₆) (H₂O)₂] was the reactive copper(III) species and [Ru(H₂O)₅OH]²⁺ was the reactive Ru(III) species.

1.3.8 Diperiodatoargentate (DPA)

The kinetics of oxidation of L-lysine by diperiodatoargentate(III) (DPA) in aqueous alkaline medium was studied spectrophotometrically (Munavalli et al 2008). The reaction was first order with respect to [diperiodatoargentate(III)], whereas the order with respect to [L-lysine] and [alkali] changed from first order to zero order as [L-lysine] and [alkali] were increased.

The mechanistic aspects of uncatalyzed and ruthenium(III) catalyzed oxidation of DL-ornithine hydrochloride by silver(III) periodate complex in aqueous alkaline medium was investigated by Malode et al (2010). The reaction was first-order in both catalyzed and uncatalyzed cases, with respect to [DPA] and was less than unit order in [ornithine] and negative fractional order in [alkali]. The order with respect to Ru(III) was unity. The uncatalyzed reaction in alkaline medium was shown to proceed via a DPA-ornithine complex, which decomposed in the rate determining step to give the products. Whereas in catalyzed reaction, it was shown to proceed via a Ru(III)-ornithine complex, which further reacted with two molecules of DPA in a rate determining step to give the products.

1.3.9 Au (III)–alkyldiamine

Reactions of Au(III)–alkyldiamine complex with L-histidine and imidazole were monitored by ¹H and ¹³C NMR. (Maythalony et al 2010) Kinetics for the [Au(en)Cl₂]⁺ reaction with L-histidine was determined by initial rate method at constant pH at 25°C using UV-vis absorption technique, and was found to be first order with respect to each component. Reaction rates
of L-histidine and imidazole reactions with the [Au(en)Cl$_2$]$^+$ complex was found to be strongly dependant on pD. The pD also had profound effect on the stability of the complex. It was observed that concurrent redox reactions also take place in solution, in which Au(III) was reduced to metallic Au(0), while L-histidine and imidazole were oxidized to oxy and hydroxyl products.

1.4 PEROXO OXIDANTS

Peroxo oxidants such as peroxomonosulphate (PMS), peroxomonophosphate (PMP), peroxydisulphate (PDS) and peroxomonocarbonate (PMC) have gained paramount importance due to their utilization as auxiliary reagents in organic synthesis (Swern 1971, Sosnovsky and Rawlison 1971 and Adam et al 1992). These peroxo oxidants are considered as the derivatives of hydrogen peroxide (H-O-O-H), formed by the replacement of hydrogen atom by groups such as sulphate, phosphate and carbonate. There is a great variety of inorganic peroxo compounds possessing O – O group. Typical inorganic hydroperoxides are peroxomonophosphoric acid (H$_3$PO$_3$), peroxomonosulphuric acid (H$_2$SO$_5$) and their salts.

1.4.1 Peroxomonosulphate (PMS)

PMS is a derivative of hydrogen peroxide, replacing one of the hydrogen atoms in H$_2$O$_2$ by sulphate group. Peroxomonosulphuric acid is commonly known as Caro’s acid. Stable salt of the acid was prepared as KHSO$_5$ in admixture with K$_2$SO$_4$ and KHSO$_4$.

The structure of H$_2$SO$_5$ is

\[ \text{H}_2\text{SO}_5 \]

\[ \text{H} - \text{O} - \text{S} - \text{O} - \text{O} - \text{H} \]

\[ \text{O} \]
Peroxomonosulphuric acid is a dibasic acid having two ionisable protons in which one proton is highly acidic and the second is weakly acidic. Its first pKₐ value is equivalent to that of sulphuric acid (-3 ± 0.1) and the second pKₐ value is 9.4 ± 0.2 (Ball and Edwards 1956). IR studies revealed that the O-O stretching frequency is higher than that of H₂O₂ and the two OH groups are structurally different (Arnau and Giguere 1970). Hence, PMS will exist as HSO₅⁻ at pH 4.0.

The structure of HSO₅⁻ is

![Structure of HSO₅⁻](image)

Peroxomonosulphate has high oxidation potential (−1.8 V) (Hu and Dryhurst 1993, Spiro 1979) and propensity to react through oxygen transfer. Hence, it has gained importance as one of the potential oxidants for organic compounds. It has also been proved to be a strong oxidizing agent compared to other peroxo oxidants like peroxodisulphate and peroxomonophosphoric acid (Sundar et al 2008, Meenakshisundram and Sathiyendran 2000, Shailaja and Ramachandran 2011). The predominant reactive species of PMS in acidic medium is HSO₅⁻ and it is more reactive than SO₅²⁻. The higher reactivity of HSO₅⁻ is due to both electrostatic effect and weakening of peroxide bond by the proton. The HSO₅⁻ frequently acts as a two electron oxidant in redox reactions that involve heterolytic cleavage of peroxo bond (Thompson 1981, Gilbert and Stell 1990).

Oxidative decarboxylation of α-amino acids is a known and documented biochemical reaction. Kinetics and mechanism of
decarboxylation of α-amino acids by peroxo oxidants is an area of intensive research because peroxo oxidants are environmentally benign oxidants and do not produce toxic compounds during their reduction.

1.5 OXIDATION STUDIES OF AMINO ACIDS BY PEROXO OXIDANTS

1.5.1 Oxidation with Hydrogen Peroxide (H₂O₂)

Kinetics and mechanism of oxidation of some amino acids by hydrogen peroxide in the presence of Fenton’s reagent (FeSO₄ + H₂O₂) was studied extensively by Muhammed Ashraf et al (1979, 1980). The mechanism involved the formation of hydroxyl radical as given below.

\[ \text{Fe}^{2+} + \text{H}_2\text{O}_2 \rightarrow \text{Fe}^{2+}(\text{OH}) + \cdot \text{OH} \quad (1.1) \]

The hydroxyl radical reacted with the α-amino acids through the abstraction of α-hydrogen as represented below:

\[ \text{R} - \text{H} - \text{C} = \text{COOH} + \cdot \text{OH} \rightarrow \text{R} - \text{C} = \text{O} - \text{OH} + \text{H}_2\text{O} \]

\[ \text{R} - \text{H} - \text{C} = \text{COOH} + \cdot \text{OH} \rightarrow \text{R} - \text{C} = \text{OH} + \cdot \text{OH} \]

\[ \text{NH}_4^+ + \text{R} - \text{C} = \text{O} - \text{COOH} \rightarrow \text{R} - \text{C} = \text{COOH} + \cdot \text{OH} \]

\[ \text{RCHO} + \text{CO}_2 \]

R= Methyl or Benzyl
Studies on the kinetics of Mn(II) and Fe(II) catalysed oxidation of amino acids by hydrogen peroxide in HCO$_3^-$/CO$_3^{2-}$ buffer (Berlett et al 1990) showed that the amino acids facilitate the dismutation of H$_2$O$_2$.

Stadtman and Berlett (1991) reported the bicarbonate-dependent oxidation of amino acids by Fenton’s reagent (H$_2$O$_2$ + Fe(II)). Oxidation was dependent on the presence of bicarbonate ion and was stimulated by iron chelators at levels which were sub-stoichiometric with respect to the iron concentration but was inhibited at higher concentrations. The metal ion catalysed oxidation of amino acids was like a “caged” process, as the oxidation was not inhibited by hydroxyl radical scavengers.

Murahashi et al (1994) studied oxidative decarboxylation of N-alkyl amino acids with hydrogen peroxide using tungstate catalyst under phase transfer conditions to get the corresponding nitrones.

The biomimetic oxidation of L-arginine with hydrogen peroxide catalysed by the resin-supported iron(III) porphyrin was reported by Monalisa Mukherjee and Ray (2007). Unsupported iron(III) porphyrin complex was not stable in the presence of peroxides and the porphyrin groups were oxidized.
with the separation of iron ions. To overcome this decomposition, anionic porphyrin complex was immobilized on a counter ionic resin matrix. The supported catalyst was efficient for the release of nitric oxide (NO.) on oxidation with hydrogen peroxide. This resin-supported iron(III) porphyrin catalyst was easily recovered after the reaction and reused without loss of activity.

The catalytic decomposition of hydrogen peroxide by Cu(II) complexes with polymers bearing L-alanine and glycylglycine in their side chain was studied in alkaline media (Spyridon Skounas et al 2010). They reported that Cu(II)/Cu(I) redox pair, was involved in the kinetics and was found to have more catalytic efficiency due to differences in modes of complexation and in the conformation of the macromolecular ligands.

1.5.2 Oxidation with Peroxy Disulphate (S$_2$O$_8^{2-}$)

Anticatalytic effect of Mn(II) in the silver catalyzed oxidations of oxalate, citrate, tartrate, malonate and arsenious acid by peroxydisulphate was reported by Sengar and Gupta (1968).

The kinetics of the silver ion catalyzed oxidation of dl($\alpha$) alanine by peroxy disulphate was studied by Chandra and Srivastava (1972). The reaction was first order with respect to peroxy disulphate and silver ion concentration and was almost independent of alanine concentration.

Oxidative decarboxylation of $\alpha$-amino acids by peroxydisulphate in the presence of Ag(I) was reported (Bacon et al 1966). Minisci et al (1983) and Zelechonok and Silverman (1992) showed that aldehyde was formed through radical intermediates during oxidation. This reaction was considered as a model system for the reaction catalysed by monoamine oxidase (Gates and Silverman 1990 and Silverman 1992). Oxidative kinetics of amino acids by peroxydisulfate and the effect of dielectric constant were reported by Khalid (2008).
These results stimulated interest for several scientists to study the kinetics and mechanism of oxidative decarboxylation of amino acids by PDS and also in the presence of various metal ions. (Chandra and Srivastava 1971 and 1973, Kumar and Saxena 1970, Ram Reddy et al 1978 a,b and 1979).

\[ \text{S}_2\text{O}_8^{2-} \rightarrow 2\text{SO}_4^- \quad (1.2) \]

### 1.5.3 Oxidation with Peroxomonophosphate (PMP)

Anand Rao (1987) reported the Ru(III) catalysed oxidation of amino acids by peroxodiphosphate in acid medium. Kinetics and mechanism of oxidation of amino acids by PMP was reported by Panigrahi and Paichha (1990). The reaction path included oxidation steps due to $\text{H}_2\text{PO}_5^-$ and $\text{HPO}_5^{2-}$.

### 1.6 TRANSITION METAL ION CATALYZED OXIDATION OF AMINO ACIDS BY PEROXO OXIDANTS

Zwart et al (1981) reported the accumulation and reactions of $\text{H}_2\text{O}_2$ during the copper ion catalyzed auto oxidation of cysteine in alkaline medium. Products of this oxidation reaction were cystine, $\text{H}_2\text{O}_2$ and $\text{H}_2\text{O}$. The $\text{H}_2\text{O}_2$ generated, reacted with cysteine, selectively, to form cystine and $\text{H}_2\text{O}$. The reaction between $\text{H}_2\text{O}_2$ and cysteine was not catalyzed by the copper complex which was present during the catalytic auto oxidation reaction. On the other hand, experiments carried out in the absence of oxygen show a marked catalytic effect ascribed to the presence of a copper(I) complex. Reaction pathway is given below.
Valodkar et al (2004) carried out the anchoring of an amino acid L-valine on cross-linked styrene-divinyl benzene in the presence of a base. The reaction of cupric acetate with the polymeric ligand resulted in chelate formation with copper(II) ion. They observed that the supported copper(II) complexes behaved as versatile catalysts during the oxidation of various substrates such as benzyl alcohol, cyclohexanol and styrene in the presence of t-butyl hydroperoxide as oxidant. They also found that the conversion matrix could be recycled for about four times with no major loss in activity.

Lin and Wu (2005) investigated the activation of hydrogen peroxide by different copper(II)–amino acid complexes and compared them by using quinaldine blue as an oxidation indicator. The rate of the reaction was first order in copper(II)-amino acid complexes and was with varying order in hydrogen peroxide. This indicated that the ligand-copper(II)-peroxide complex formed was responsible for the activation of hydrogen peroxide. A mechanistic pathway that included the formation of ligand-copper(II)-peroxide complex and hydroxyl radical was proposed. For glycine, alanine and lysine the maximum activation efficiencies appeared at a ligand/copper molar ratio of 1.5-2.0, regardless of the change in pH values or ligand concentrations. According to the stability constants for copper(II)-amino acid complexes, it was predicted that CuL, and not CuL$_2$, was the dominant species forming the active copper complex catalyst.

The reactions of CH$_3$OO$^-$ radicals with Cu$^{II}$(glycine)$_2$ and Cu$^{II}$ (glycylglycylglycine), in aqueous solutions were studied by weiss et al (2005). The results showed that the peroxyl radicals oxidized the copper complexes forming relatively stable intermediates of the type L$_m$Cu$^{III}$ – OOCH$_3$. These intermediates decomposed via oxidation of the ligand, glycine and glycylglycylglycine, respectively. Substituents on the alkyl of the peroxyl radical affected the kinetics of reaction but not the mechanism of oxidation.
They also suggested that the analogous reactions were contributing to the radical-induced deleterious biological processes.

Sayee Kannan et al (2008) reported the kinetics and mechanism of oxidation of β-alanine by PMS in the presence of copper(II) ion at pH 4.2 (acetic acid-sodium acetate buffered medium). Autocatalysis was observed only in the presence of copper(II) ion, and this was explained due to the formation of hydroperoxide intermediate. The rate constant for the catalyzed ($k_{2}^{\text{obs}}$) and uncatalyzed ($k_{1}^{\text{obs}}$) reactions were calculated. The kinetic data obtained, revealed that both the reactions were first order with respect to [PMS].

$k_{1}^{\text{obs}}$ values initially increased with the increase in [β-alanine] and reached a limiting value, but $k_{2}^{\text{obs}}$ values decreased with the increase in [β-alanine]. $k_{1}^{\text{obs}}$ values increased linearly with the increase in [Cu(II)], whereas $k_{2}^{\text{obs}}$ values increased with [Cu(II)]². Furthermore, $k_{1}^{\text{obs}}$ values were independent of [acetate], but $k_{2}^{\text{obs}}$ values decreased with the increase in acetate and they suggested the following mechanism.

\[
\begin{align*}
\text{Cu}^{2+} + \text{HSO}_5^- & \xrightleftharpoons{\text{rds}}^{\text{H}_2\text{O}} \text{CuO}_2 + \text{H}^+ + \text{SO}_4^{2-} \\
\text{CuO}_2 + \text{H}_2\text{N}-\text{COOH} & \xrightarrow{\text{fast}} \text{HO}-\text{COOH} + \text{Cu}^{2+} + \text{NH}_4^+ 
\end{align*}
\] (1.3) (1.4)

The kinetics of the Ru³⁺-(edta) (where, edta⁴⁻ = ethylenediaminetetraacetate) catalyzed oxidation of L-arginine by H₂O₂ mimicking the action of nitric oxide synthases (NOSs) was studied spectrophotometrically (Debabrata Chatterjee et al 2011). Formation of NO in the reacting system was confirmed with an isolated nitric oxide free radical analyzer.
1.7 OXIDATION STUDIES OF VARIOUS COMPOUNDS (BOTH ORGANIC AND INORGANIC) BY PEROXOMONOSULPHATE

The kinetics of the redox reaction between oxovanadium(IV) and peroxodisulphate ions in weakly acidic aqueous solution were studied by Frennesson and Fronaeus (1972). The overall second-order rate constant, expressing an increased rate of concentration of vanadium(V), was determined. The rate determining step was the hydrogen-ion catalyzed decomposition of peroxodisulphate ion, to form the active oxidizing agent, $\text{HSO}_5^-$.

The oxidation of halide (Fortnum et al 1960), nitrite (Edwards and Mueller 1962) and chlorite ion (Johnson et al 1966) by PMS was reported. The rate limiting step was nucleophilic attack on the peroxide oxygen.

Sharma et al (1992a) carried out the oxidation of nitrite by PMS and identified the product as nitrate.

$$\text{HSO}_5^- + \text{NO}_2^- \rightarrow \text{SO}_4^{2-} + \text{NO}_3^- + \text{H}^+ \quad (1.5)$$

The oxidation of bisulphate ion by PMS was studied by Connick et al (1993). The overall reaction was given as

$$\text{HSO}_5^- + \text{HSO}_3^- \rightarrow 2\text{SO}_4^{2-} + 2\text{H}^+ \quad (1.6)$$

They proposed a mechanism involving the formation of pyrosulphate ion, $(\text{S}_2\text{O}_7^{2-})$ as intermediate, which underwent hydrolysis to form sulphate and hydrogen ions.

Thompson et al (1979) reported the oxidation of azide and azido pentammine chromium(III) by PMS in aqueous acidic medium and observed
that the reaction proceeded through transfer of terminal peroxide oxygen of HSO₅⁻ to the reductant, resulting in the formation of N₂ and N₂O in azide and [Cr(NH₃)₅NO]²⁺ in pentamineazidechromium(III)[Cr(NH₃)₅N₃]²⁺, respectively.

Studies on the oxidation of inorganic compounds such as tris-(1,10-phenanthroline)iron(II)sulphate, tris-(2,2'-bipyridyl)iron(II)sulphate (Somuthevan et al 1980), peroxovanadium, VO³⁺, (Thompson 1982), Mn(II) (Lawrence and Ward 1985), oxovanadium(IV) and its complexes (Anandkumar et al 1991) and thialato complexes of Ru(III) by PMS (Johnson and Nickerson 1992) were reported.

Kinetics of oxidation of simple inorganic compounds such as thiocyanate SCN⁻ (Smith and Wilson 1966a,b and 1967), SO₂ (Betterton and Hoffmann 1988), hydrogen sulphide (Betterton 1992), hydroxylamine, (Sharma et al 1992b) and hydrazine (Gupta et al 1993) by PMS have been reported.

Oxidation of peroxovanadium(V), VO₃⁺ by HSO₅⁻ and Co³⁺ in acidic aqueous solution was reported by Thompson (1982). They observed that the oxidation of VO₃⁺ by HSO₅⁻ was catalyzed by low concentrations of VO²⁺ in acidic solution.

Reactions of PMS were catalyzed in the presence of ketones (Montgomery 1974, Curci et al 1980, Galloplio and Edwards 1981). On the basis of experimental data, they suggested that dioxirane intermediate catalysed the reaction. The structure of dioxirane is given below.

\[ \text{H}_3\text{C}=\text{C}=\text{O} + \text{HOO}_3^- \rightleftharpoons \text{H}_{3}\text{C}==\text{C}==\text{O} \text{SO}_3^- \]

\[ \text{H}_3\text{C}=\text{C}=\text{O} \text{SO}_3^- + \text{OH}^- \rightleftharpoons \text{H}_2\text{O} \]

PMS ion in aqueous acetonitrile readily converts aryl, thio-benzoates to carboxylic acid and sulphonic acid (Bunton et al 1995).

Studies on the oxidative hydrolysis of phosphorous(V) esters of thiols (Blasko et al 1997) by PMS revealed that HSO$_5^-$ converts phosphorous(V) esters of thiols into the phosphorous(V) and sulfonic acids.

Janakiram et al (1998) investigated the oxidation of aliphatic acetals by PMS and suggested a mechanism involving hydride ion shift.

While studying the kinetics of oxidation of some sulfoxides with oxone in the presence of Ru(III), Meenakshi Sundaram and
Sathiyendran (2000) have explained the catalytic activity of Ru(III) with several diaryl, dialkyl and alkyl aryl sulfoxides, all of which were found to undergo oxidation under homogeneous conditions. They inferred that the rates increased substantially with increasing water content in aqueous acetic acid and also suggested a mechanism involving electron transfer from electrophilic perhydroxyl oxygen of oxone to sulfoxides.

Oxidation of Indole -3- acetic acid by PMS in acetonitrile medium was reported (Chandramohan et al 2002). The reaction followed a total second order, first order each with respect to [Indole -3- acetic acid] and [PMS]. The rate of the reaction was not affected by [H⁺]. Variation of ionic strength (μ) had no influence on the rate. An increase in the percentage of acetonitrile reduced the rate. The rate of the reaction proceeded through a non-radical pathway.

Kinetics and mechanism for the oxidation of hypophosphorous acid by PMS in acid medium was investigated by Dubey et al (2002) and they suggested a probable reaction mechanism which is given below.

\[
\begin{align*}
&\text{Oxidation of Indole -3- acetic acid by PMS in acetonitrile medium was reported (Chandramohan et al 2002). The reaction followed a total second order, first order each with respect to [Indole -3- acetic acid] and [PMS]. The rate of the reaction was not affected by [H⁺]. Variation of ionic strength (μ) had no influence on the rate. An increase in the percentage of acetonitrile reduced the rate. The rate of the reaction proceeded through a non-radical pathway.} \\
&\text{Kinetics and mechanism for the oxidation of hypophosphorous acid by PMS in acid medium was investigated by Dubey et al (2002) and they suggested a probable reaction mechanism which is given below.}
\end{align*}
\]
Mehrotra and Mehrotra (2008) reported the kinetics and mechanism of the oxidation of tris(1,10-phenanthroline)iron(II) by PMS ion. Formation of an ion pair between $M^+$ and $\text{HSO}_5^-$ ions was suggested with spectral evidence and accordingly, the intermediates $[\text{Fe(phen)}_3 \ldots \text{HSO}_5]^+$ and $[\text{Fe(phen)}_3 \ldots M\ldots\text{SO}_5]^+$ were assumed to be formed where $M^+$ ion acted as a bridge.

Murugavelu et al (2009) reported the kinetic studies on the reaction between nickel(II) lactate and PMS ion and also the effect of formaldehyde in the pH range 4.0-5.9. When formaldehyde concentration was greater than or equal to $[\text{Ni(II)}]$ the self-decomposition of PMS was observed. The turn over number, the number of PMS decomposed for each molecule of HCHO, was found to be four. Nickel lactate reacted with formaldehyde to give a hemiacetal intermediate. The reaction was unique in which the Ni(II)-hemiacetal formed an ion pair with $\text{SO}_5^{2-}$, which protected the $\alpha$- hydroxyl group of the lactate (Ni(II)), preventing the oxidation of nickel $\alpha$- hydroxyl carboxylate through the hydroperoxide intermediate.

Shailaja and Ramachandran (2009) reported the kinetics of oxidation of glycolic acid (GLYCA), an $\alpha$-hydroxy acid, by PMS in the presence of Ni(II) and Cu(II) ions and in acidic pH range 4.05–5.89. The metal glycolate is oxidized by PMS. The rate is first order in [PMS] and metal ion concentrations. The oxidation of nickel glycolate is zero-order in [GLYCA] and inverse first order in $[\text{H}^+]$. The increase of [GLYCA] decreases the rate in copper glycolate, and the rate constants initially increase and then remain constant with pH. They suggested that the metal glycolate $\text{ML}^+$ reacts with PMS through a metal-peroxide intermediate, which transforms slowly into a hydroperoxide intermediate by the oxygen atom transfer to hydroxyl group of the chelated GLYCA. The effect of hydrogen ion concentrations on
$k_{\text{obs}}$ suggested that the structure of the metal-peroxide intermediates may be different in Ni(II) and Cu(II) glycolates.

Kinetics of degradation of acid red 88 in the presence of Co$^{2+}$-ion by PMS was studied by Madhavan et al (2009). Decolorization of the dye in the Co$^{2+}$/PMS system was observed to follow zero-order kinetics with respect to the dye. It was also found that the decolorization of the dye increased with an increase in the concentration of cobalt ions.

The kinetics of the redox reactions of PMS ion (HSO$_5^-$) with iron(II), vanadium(IV), cerium(III) ions were studied (Gabor Lente et al 2009). Cerium(III) was oxidized upon illumination by UV light itself and cerium(IV) was produced in a photoreaction. Iron(II) and vanadium(IV) were oxidized through one-electron transfer producing sulphate ion radicals as intermediates. The halide ions were oxidized in a formally two-electron process, which most likely included oxygen-atom transfer.

Kutti Rani et al (2009a) studied the oxidation of vanillin by PMS in acetic acid – sodium acetate buffered medium and reported that the rate was first order with respect to [vanillin] and [PMS]. They observed that rate increased with an increase in pH and the rate was too fast to be measured at pH 5.2. The rate increased with an increase in [acetate] and the plot of $k_{\text{obs}}$ vs [acetate] was a straight line with positive intercept. They also reported that the variation of ionic strength had no effect on the rate of the reaction. Effects of polarity were studied with five different solvents and in all the cases; log $k_{\text{obs}}$ versus $1/\epsilon$ were linear with negative slope. They carried out the reactions at four different temperatures and the activation and thermodynamic parameters were calculated. The product of oxidation was confirmed as vanillic acid by IR, $^1$H NMR and GC-MS spectral analysis.
Shailaja and Ramachandran (2011) reported the kinetics of oxidation of tartaric acid by PMS in the presence of Cu(II) and Ni(II) ions. They suggested that the initial reaction was the oxidative decarboxylation of the tartarate to an aldehyde. The aldehyde intermediate reacted with the $\alpha$-hydroxyl group of the tartarate to give a hemiacetal, which was responsible for the autocatalysis.

Fei Ji et al (2011) reported the performance of CuO/oxone system in the heterogeneous catalytic oxidation of phenol at ambient conditions CuO particles used to activate oxone for advanced oxidation of phenol in aqueous solution. The catalyst was demonstrated to have good stability and reusability. Radical quenching studies were conducted to classify the type of active radicals present in the reaction and X-ray photoelectron spectroscopy (XPS) was used to investigate the transformation of the chemical state of copper.

The kinetics of oxidation of L-ascorbic acid by PMS in the presence and absence of copper(II) catalyst has been studied by Riya Sailani et al (2011). Rate of the reaction is first order with respect to [PMS]. The rate constant decreases with increasing concentration of perchloric acid and the rate constant increases with increasing ionic strength. They calculated the energy of activation and entropy of activation in a conventional manner. The stoichiometry of the reaction is represented by the following equation:

\[ \text{H}_2\text{A} + \text{HSO}_5^{-} \rightarrow \text{A} + \text{HSO}_4^{-} + \text{H}_2\text{O} \]  \hspace{1cm} (1.7)

The order with respect to ascorbic acid and PMS is one each.

The kinetics of oxidation of nicotinic acid by peroxyomonosulphate (PMS) was reported by Anuj Agrawal et al (2012) in acetate buffers.
Stoichiometry of the reaction corresponds to the reaction of one mole of the oxidant with a mole of nicotinic acid. N→O product has been confirmed both by UV visible and IR spectroscopy. The reaction is second order viz. first order with respect to each reactant. Activation parameters have also been evaluated. A plausible reaction mechanism has been described and the derived kinetic rate law accounts for experimental observations. The mechanism is given below.

\[
\begin{align*}
\text{N} & \text{O} \\
+ \text{H}^+ & \quad \text{K}_1 \quad \text{N} \text{O} \\
\text{K}_2 & \quad \text{HSO}_5^- \quad \text{[Adduct]} \\
\text{[Adduct]} & \quad \text{k}' \quad \text{N} \text{O} \\
\end{align*}
\]
1.8 OXIDATION STUDIES OF AMINO ACIDS BY PEROXOMONOSULPHATE

In the study of kinetics and mechanism of the oxidation of $\alpha$-amino acids by PMS in acetic acid/sodium acetate buffered medium (pH 3.6 – 5.2), Ramachandran et al (1984c), Ramachandran and Vivekanandan (1984a, b and 1988) observed that $\text{SO}_3^{2-}$ was more reactive (six orders of magnitude higher than $\text{HSO}_3^-$) and this higher reactivity was attributed to nucleophilic attack of peroxide on the amino group.

\[
\begin{align*}
\text{R-CH-CONH}_3^+ + \text{O-O-SO}_3^- & \rightarrow \text{R-CH-CONH}_2^- + \text{H}_2\text{O} + \text{SO}_4^{2-} + \text{CO}_2 \\
\text{RCHO} + \text{NH}_3 & \xrightarrow{\text{Hydrolysis}} \text{R-CH=NH}_2^+ + \text{H}_2\text{O} + \text{SO}_4^{2-} + \text{CO}_2
\end{align*}
\]

The kinetics of oxidation of amino acids (AA) by PMS in the presence and absence of formaldehyde were studied by Ramachandran and Vivekanandan (1984d). They showed that the reaction was autocatalysed by the aldehyde formed in the reaction. Perusal of the kinetic results showed that the formaldehyde catalyzed reaction occurs approximately $10^5$ times faster than uncatalyzed and this was attributed to the formation of Schiff base. Mechanism of the reaction was discussed in terms of the kinetic results. The mechanism is given below.
Ramachandran et al. (1994) reported the kinetics of oxidation of amino acids by PMS in aqueous alkaline medium and observed that the electrophilic attack on HSO$_3^-$ occurred at the amino acid nitrogen. The breakdown of the intermediate was influenced by the nature of the substituent on the amino carbon atom. The intermediate disintegrated to give either imine or imino acids, which hydrolysed to the corresponding aldehyde.

Kinetics and mechanism of decarboxylation of $\alpha$-amino acids by PMS in acetic acid/sodium acetate buffered medium was studied extensively with structurally different amino acids (Sayee Kannan and Ramachandran 2003). Comparison of the results in glycine and N-methyl glycine revealed that the autocatalytic effect was more pronounced in N-methyl glycine. This suggested that the formation of Schiff base was not the reason for the
autocatalysis as reported earlier. The authors suggested that the formation of hydroperoxide was responsible for autocatalysis.

\[
\begin{align*}
RCH(NH_3)COO^- + HOOSO_3^- & \overset{k_1}{\longrightarrow} RCHO + NH_4^+ + CO_2 + SO_4^{2-} \quad (1.8) \\
RCHO + HOOSO_3^- & \rightarrow \text{Hydroperoxide} + SO_4^{2-} + H^+ \quad (1.9) \\
RCH(NH_3)COO^- + \text{Hydroperoxide} & \rightarrow 2 \text{RCHO} + NH_4^+ + CO_2 \quad (1.10)
\end{align*}
\]

Sundar et al (2008) studied the kinetics and mechanism of Mn(II) catalysed decomposition of peroxomonosulphate (PMS) in highly alkaline medium and reported the formation of manganese peroxide (Mn(O_2)) as molecular intermediate, as given below.

\[
\begin{align*}
\text{Mn(OH)}_2 + \text{OH}^- & \rightarrow \text{HO}_2^-
\end{align*}
\]

Kutti Rani et al (2009b) reported the formation of Manganese peroxide (Mn(O_2)) as intermediate in their studies on the kinetics and mechanisms of Mn(II) catalyzed oxidative decarboxylation of five structurally different amino acids viz alanine, valine, leucine, phenyl alanine and 2-methyl alanine by PMS in alkaline medium.

Maria Rayappan et al (2010) investigated the kinetics of Ag(I) catalyzed oxidation of amino acids by PMS in aqueous perchloric acid medium.
From the foregoing discussions, it is understood that peroxy oxidants such as hydrogen peroxide, PDS, PMS and PMP have been widely used as an oxidizing agent for organic reactions. PMS has gained paramount importance due to its high oxidation potential.

Oxidation of α-amino acids has been carried out using these peroxidants especially PMS in order to design a model system for the enzymatic oxidation of α-amino acids. One of the oxidation products was the corresponding aldehyde which tends to condense with amino acids to form Schiff bases, an important intermediate in biological reaction.
In the α-amino acids, the authors observed autocatalysis of the product aldehyde. Initially it was explained due to the formation of Schiff base intermediate. Later with more detailed studies with different substituted α-amino acids, the authors explained the autocatalysis as the formation of hydroperoxide intermediate.

A few papers are available in literature regarding the oxidation of basic amino acids by PMS. Further, the autcatalytic effect was not observed in the oxidation of basic amino acids. It prompted the researcher to study the oxidation reaction in detail by using all spectroscopic techniques. Moreover in one of the basic amino acids, arginine, the formation of NO is observed as the biochemical oxidation mechanism.

In order to mimic the biological system, oxidation of basic amino acids with peroxomonosulphate was carried out. This thesis emphasizes uncatalyzed and copper(II) catalyzed oxidation of basic amino acids such as arginine, histidine and ornithine by PMS in acetic acid-sodium acetate buffered medium. Literature survey pertaining to the following was reviewed.

- studies on the oxidation of basic amino acids by different oxidants
- transition metal ion catalyzed oxidation of amino acids by peroxo oxidants
- studies on the oxidation of various compounds (both organic and inorganic) by PMS
- studies on the oxidation of α-amino acids by peroxo oxidants
- oxidation studies of amino acids by PMS
The following amino acids have been chosen for the present studies.

i. Arginine

ii. Histidine

iii. Ornithine

A systematic kinetic study of the oxidation of basic amino acids namely ornithine, histidine and arginine by peroxomonosulphate (PMS) in acetic acid-sodium acetate buffered medium was carried out to explain the mechanistic aspects of these oxidations and to understand the active form of PMS in aqueous acidic medium. The present study is carried out to mimic the oxidation in vitro to identify the rate of oxidation, the catalytic effect of copper(II) ions, product formed and to propose a suitable mechanism. The results have been discussed in the subsequent chapters.