CHAPTER 1

INTRODUCTION

1.1 PORPHYRINS AND METALLOPORPHYRINS: AN OVERVIEW

Porphyrrins are a set of organic compounds of which some of them are naturally occurring. Porphyrrins are the conjugate acids of ligands that bind metals to form complexes. The central metal ion of porphyrin usually has a charge of 2+ or 3+. An example of porphyrin is pigment in red blood cells (heme). Metallloporphyrins in alliance with protein globule undergo several significant biochemical tasks in nature. Some of the important porphyrin based natural systems are heme enzymes, hemoglobin, myoglobin, chlorophyll, cytochromes, catalase and peroxidase. The study of metallloporphyrin reveals the oxidation, transportation, storage and activation of molecular oxygen. Over the years attempts have been made to reveal the structure-reactivity relationship in natural porphyrins. During the last four decades synthetic porphyrins have been widely studied for various applications in chemical and biological fields Rezaeifard et al (2007), In et al (2003), Ruef et al (1992). Metallloporphyrins are greatly explored in the area of catalysis, as models and mimics of enzymes like peroxidase, cytochromes P450 and chlorophyll.
1.2 THE UBIQUITOUS PORPHYRIN SYSTEM

Porphyrins are heterocyclic compounds composed of four tailored pyrrole subunits united at their $\alpha$ carbon atoms through methine bridges (=CH-). They are having $4n+2$ $\pi$ electrons delocalized over the macrocycle. Thus porphyrin macrocycles are highly conjugated systems. The macrocycle in aromatic system has 22 $\pi$ electrons. The parent porphyrin is called porphine, and substituted porphines are called porphyrins.

![Figure 1.1 Structure of a simplest porphyrin](image)

1.3 PORPHYRINS IN LIFE PROCESS

The role of heme proteins are involved in the transport, storage and reactions with dioxygen. In the blood, hemoglobin binds with dioxygen and helps in transportation. In the tissues the structurally similar myoglobin traps the oxygen from hemoglobin and stores for reduction by cytochrome C oxidase in mitochondria. Important porphyrin based natural systems are heme enzymes, hemoglobin, myoglobin, cytochrome and chlorophyll. The chemistry on manganese(III) porphyrin Spasojevic et al (2006) showed further improvement in therapeutics for shielding mitochondria from oxidative damage.
1.4 ROLE OF PORPHYRINS IN SOLAR CELLS

Porphyrrins act as a photosensitizer on dye sensitized solar cells. Porphyrrin of LUMO and HOMO energy levels show very strong absorption of the soret band in the 400-450 nm region, as well as the Q-bands in the 500-700 nm region. Porphyrin derivatives can be suited as panchromatic photosensitizers for dye sensitized solar cells and are potential runners to replace ruthenium dyes. Introducing appropriate substituents in four meso and eight beta positions of the porphyrin, allows tailoring of the spectroscopic response as well as electrochemical potentials, which in turn, could be reflected in the efficiency of solar cells Panda et al (2012).

Photovoltaic solar cells consist of a low band gap material that converts electromagnetic radiation into electricity. The second generation materials such as cadmium-telluride and copper indium gallium selenide solar cells have low efficiencies and short lifetimes. The third generation based on porphyrin organic photovoltaics (OPV), dye sensitized solar cells (DSSC) and organic–inorganic hybrid cells are budding as suitable alternatives, both in terms of stability and cost. Therefore, porphyrin based DSSC have huge potential in future photovoltaic market. A number of reviews, articles on porphyrins and their applications in photovoltaics have been reported in recent years Nazeeruddin et al (2011), Imahori et al (2012).

1.5 OXYGENASES AND PEROXIDASES

In the life process the biological reactions are directed by enzymes. The enzymes are organic biological catalysts. Various natural enzymes such as metalloporphyrins (especially heme enzymes) comprise this prosthetic group.
In some of the enzymatic reactions one or both the oxygen atoms are inserted into the organic substrate. Enzymes catalyzing such type of reactions are called oxygenase. The enzymes dioxygenase catalyze for the insertion of both the atoms of oxygen into the substrate but the enzymes monooxygenase insert only one atom of oxygen into the substrate Hayashi et al (1963).

The most essential enzyme monooxygenase is cytochrome P450. These enzymes are found in the microsomes of the liver cells. The reduced Fe(II) form of cytochrome P450 reacts with molecular oxygen in such a way that one of the oxygen is reduced to water while the other oxygen is inserted into the substrate like steroids, fatty acids and certain amino acids. They also undergo hydroxilations in a variety of drugs such as phenobarbital, morphine, codine and carcinogenic hydrocarbons like methyl cholanthere. Peroxidase enzymes catalyze the oxidation of variety of a organic and inorganic compounds by $\text{H}_2\text{O}_2$ and related compounds. Peroxidase in plants also contains hemine group (Fe(III) photoporphyrin). An example for peroxidase is horseradish peroxidase. The biomimetic systems using synthetic metallloporphyrins have offered a great contribution to illustrate the structure of monoxygenases and peroxidases Mansuy et al (2000).

1.6 HEMOGLOBIN AND MYOGLOBIN

The best example of porphyrin is the hemoglobin which is a transporter of oxygen in blood. Hemoglobins are highly potential to trap oxygen molecules spontaneously from the places where there are abundance of oxygen, and they release them when there is a shortage of oxygen.

Hemoglobin and myoglobin serves as oxygen transport and storage in higher animals. Hemoglobin transports oxygen from lungs to the muscle cells where the oxygen is transferred to myoglobin for use. Myoglobin
facilitate oxygen within the cell. Hemoglobin and myoglobin have similar structures having iron as a central metal atom. Hemoglobin and myoglobin are two oxygen binding proteins that contain iron porphyrins. Various cytochromes are also hemoproteins. Some of the iron-containing porphyrins are called hemes. Heme-containing proteins, or hemoproteins, are found widely in nature. The hemoglobin has a structure in which the porphyrin part called heme is linked to a big protein called globin. When hemoglobin acts as an oxygen carrier, a molecule of oxygen binds to it as an axial ligand. The heme refers to iron(II) porphyrin and hemin refers to iron(III) porphyrin.

Biomimetic oxidative systems using tetraphenylporphyrins have been widely studied as models of the natural heme prosthetic group. The highly reactive electrophilic oxidants in cytochrome P450 enzymes have eluded detection for many years. But strong evidence of Newcomb et al (2005) supports the content on two distinct types of electrophilic oxidants formed in P450 enzymes.

The system revealed catalyzed oxidation method with cytochromes P450 and contributed to an understanding of the mechanisms of the cytochromes P450 dependent reactions when using oxygen donors Rueff et al (1992).

### 1.7 CHLOROPHYLL

The chlorophyll is responsible for the green pigment in plants. The chlorophyll is a porphyrin with magnesium as a central metal atom. It is a magnesium complex of substituted chlorine. Heme and chlorophyll are naturally occurring metalloporphyrins and metallochlorins, respectively. Metalloporphyrins mainly functions as a key co-factor in enzymes and oxygen transporting proteins. In some cases, metalloporphyrins are also found in photosynthetic chlorophyllous molecules Yoshitaka Saga et al (2010).
1.8 HEMOPROTEIN

A heme protein or hemoprotein, is a metalloprotein containing a heme prosthetic group - an organic compound that allows a protein to carry out a function. Heme remains bound to the protein permanently, either covalently or non-covalently bound or both.

1.9 THE CYTOCHROME P450

In cytochromes P450 the letter ‘P’ represents the pigment (enzymes due to their heme group) and the number ‘450’ represents the wavelength of the absorption maximum of the enzyme. The cytochrome P450 is a group of enzymes that catalyze the oxidation reaction in organic substance. Cytochrome P450 are the major enzymes involved in 75 percent of the total number of different metabolic reactions (Guengerich 2008). The most common reaction catalyzed by cytochromes P450 is a monooxygenase reaction (insertion of one atom of oxygen into an organic substrate (RH) while the other oxygen atom is reduced to water)

\[
\text{RH} + \text{O}_2 + \text{NADPH} + \text{H}^+ \rightarrow \text{ROH} + \text{H}_2\text{O} + \text{NADP}^+
\]

The cytochrome P450 are hemoproteins and they catalyze many chemical reactions. They catalyze in the biotransformation of drugs, bioconversion of xenobiotics and the metabolism of chemical carcinogens. They also play an important role in the synthesis of compounds such as steroids, fatty acids, fat-soluble vitamins, and bile acids. They also catalyze in the conversion of alkanes, terpenes, and aromatic compounds. There are also reactions catalysed by cytochromes P450 such as carbon hydroxylation, heteroatom oxygenation, dealkylation, epoxidation, aromatic hydroxylation, reduction and dehalogenation. The structure and function relationships of cytochromes P450 are far from being well understood and their catalytic
activity has so far hardly been used for biotechnological (Bernhardt 2006) and pharmacogenetic approach (Macphee 2012). Heme plays an important role in a component of the enzyme cytochrome P450 in organs like liver. In hemoglobin, only a molecule of oxygen gets attached. But in the case of cytochrome P450 even a single atom of oxygen gets attached to the central metal atom. When cytochrome P450 approaches a target compound the enzyme oxidizes it by shifting the oxygen atom to it. In biological aspects cytochrome P450 enzyme plays different catalytic role in many places. There are various kinds of cytochrome P450 enzymes in liver. Usually the drugs taken by a person are first taken up to the liver to get metabolized by the cytochrome P450 enzymes. For cytochrome P450 the model robust catalyst metalloporphyrins could be used as the intermediate of oxygen carrier in biological systems Spasojevic et al (2006). In the modeling of cytochrome P450, high valent metal-oxo species have been extended as active intermediates in numerous different oxidation reactions using an iron porphyrin catalyst and oxygen atom donors like PhIO, NaOCl, KHSO$_5$, peracetic acid as an oxygen source.

1.10 MODEL METALLOPORPHYRINS: BIOMIMETIC CHEMISTRY

1.10.1 Advantages of Model Systems

The advantages of using metalloporphyrins as model system is to understand the following oxidation process in drug metabolism (Prakash and Francisca Mary 2005), Yun-jing et al (2007), Othman et al (2000).

(i) The forecasting of the oxidative metabolism of drugs, agrochemicals or other xenobiotics.
(ii) Metabolites of drugs and other compounds of biological interest can be prepared in sufficient amounts for further study.

(iii) Candidate metabolites which are available in huge amounts can be identified and used for oxidation.

(iv) Drug samples for pharmacological oxidation and testing can be done.

(v) The technique of metabolism through oxidation can be clarified, for example, instable metabolites can be prepared under controlled conditions.

(vi) The use of experimental animals can be reduced.

(vii) The catalysis of selective oxidations in organic synthesis.

1.10.2 Catalytic Cycle of Cytochrome P450

Under optimum conditions, cytochrome P450 catalyzes the monooxygenation of variety of substrates by utilizing dioxygen and a reducing agent (NADPH or NADH). The catalytic cycle is schematically shown in (Prakash and Francisca Mary 2005) Figure 1.2. It involves

(i) The reduction of Fe(III) to Fe(II) state.

(ii) The binding of oxygen to the Fe(II) state.

(iii) The one-electron reduction of the Fe(II)-O₂ intermediate.

(iv) The formation of the active oxygen complex (high-valent iron-oxo complex)

(v) Fe(V)=O or Fe(IV)=O delivers its oxygen atom into substrates.
It is not easy to mimic by employing simple metalloporphyrin catalysts. However, it has been recognized that cytochrome P450 may perform similar oxidations by using single oxygen atom donors such as peroxymonosulphate, perborates, peroxides or perbenzoic acids, instead of $O_2$ and NADPH. This shortened catalytic cycle is easier to mimic. It is clear that the construction of a catalytically active model system for cytochrome P450 is critically dependent upon the oxygen atom donor that is used.

![Reaction scheme for the catalytic cycle of cytochrome P450](image)

**Figure 1.2** Reaction scheme for the catalytic cycle of cytochrome P450

### 1.11 HISTORY OF BIOMIMETIC SYSTEMS

Chemists have compensated a great deal of attention towards modeling of cytochrome P450 monooxygenase using synthetic metalloporphyrins as they have a strapping resemblance to heme in both structures and catalytic property. The metalloporphyrin complexes are widely
used as mimic compounds simulating the catalytic behavior of cytochrome P450 enzymes in life growth. The model iron porphyrins are very useful in the determination of the catalytic cycle of cytochrome P450 acting in monooxygenases (Hrycay and Bandiera 2012). Cytochrome P450 on iron porphyrin models in 1980s has directed to a good reorganization on the cytochrome P450 catalytic cycle. It also led to an indepth mechanism of the oxidation of its various substrates. Mansuy et al (1982), Dolphin et al (1983), (Traylor and Miksztal 1987), (Mansuy 1993). They have also revealed the reality of the rich coordination chemistry of hemeproteins. In 1990s, well organized chemical model systems were able to imitate the catalytic functions of cytochrome P450 dependent monooxygenases (Gilmartin and Smith 1995), Havranek et al (1999). Researches were made by many scientists to develop efficient model systems based on metalloporphyrin catalysts in order to mimic cytochrome P450 (Lane and Burgess 2003), Meunier et al (2004), (Mansuy 2007). These systems were connected with a Fe(III) or Mn(III) meso-tetraphenylporphyrin with an oxygen atom donor like tetra-n-butylammonium periodate, iodosyl benzene, hydrogen peroxide, perchlorate, or molecular oxygen.

Metalloprotein is a common term for a protein that includes a metal ion cofactor. In the last two decades different biomimetic approaches to cytochrome P450 activity have been attained with metallocorphyrins and various oxidants SaeedZakavi et al (2011), Rezaeifard et al (2007), Latifi et al (2011), (Davoras and Coutsolelos 2003). The first system mimicked was a short catalytic cycle of cytochrome P450 with iodosylbenzene as oxidant in the presence of catalyst “iron tetraphenylporphyrin chloride”. This scheme was able to replicate most reactions formed by cytochrome P450. meso-Iron tetraphenylporphyrin chloride catalyst is called as a first generation catalyst. The difficulty in the system was the fast oxidative degradation of their porphyrin ring in meso-iron tetraphenylporphyrin chloride under tough
oxidizing conditions. The utilization of metalloporphyrins in the presence of different oxygen atom donors to many systems reproduces the catalyst in most oxidation reactions catalysed by cytochromes P450. Though chromium, cobalt porphyrin are able to catalyze alkene epoxidation the metalloporphyrins having iron and manganese porphyrin gave the most excellent outcome for cytochromes P450 type oxidations Singh et al (2011), Claudia et al (2011). The application of iron porphyrins was of great help to understand the nature of intermediates of cytochrome P450 substrates. These chemical catalysts may be useful in drug metabolism prediction (Sheldon and Dakka 1994).

Models in the field of cytochrome P450 and oxidation catalysis are anxious with the understanding of,

(i) The structure and reactivity of the iron complexes involved in the P450 catalytic cycle,

(ii) The nature of the iron metabolite complexes that are formed upon reaction of some substrates with cytochrome P450.

They are also concerned with the development of metalloporphyrin-based systems that catalyze typical P450 reactions such as the hydroxylation of alkanes or aromatic compounds, the epoxidation of alkenes, N-, S- and O-oxidative dealkylations, N-oxidations, and sulfoxidations. Such systems have been successfully applied to the preparation of oxidized metabolites of drugs (Mansuy 2007).

DNA damage is a critical factor in carcinogenesis. The ames assay is a short-term test that screens for DNA-damaging agents. To be detected in the assay, most carcinogens require oxidation by cytochrome P450, a component of the liver homogenate preparation (S9 mix) that is traditionally
used to metabolize promutagens to an active form in vitro. A combination of iron(III) porphyrin plus, an oxidant activates many promutagens by mimicking cytochrome P450 metabolism (Inami and Mochizuki 2002).

### 1.12 DEVELOPMENT OF BIOMIMETIC SYSTEMS

The first work of biomimetics was done by Groves et al (1979), using iodosyl benzene as oxidant and tetraarylporphyrin iron(III) chloride. The performance of the catalyst was same as catalyzed by cytochrome P450. (Scheme 1.3)

![Reaction scheme for the Performance of catalyst using iodosyl benzene as oxidant](image)

Figure 1.3 Reaction scheme for the Performance of catalyst using iodosyl benzene as oxidant

Iron-tetraphenylporphyrin chloride which was used as a catalyst was degraded in the oxidation reaction. So it became difficult to use them in oxidation reactions. So the catalytic activities were improved using Fe(III) or Mn(III) complexes of polyhalogenated tetraarylporphyrins like tetra-2,6-dichlorophenylporphyrin Traylor et al (1984). For instance, the oxidation by H$_2$O$_2$ catalyzed by 5,10,15,20-tetraarylporphyrinatoiron(III) chlorides provides a suitable chemical model of natural cytochrome P450 enzymes and gives products very similar to its in vivo metabolites (Chauhan 2007). Even more robust catalyst polyhalogenated with central Mn(III)- and Fe(III)-porphyrins, like iron(tetrakis-2,6-dichlorophenyloctabromoporphyrin) chloride, have been
isolated and used as an efficient catalyst for hydrocarbon oxidation (Traylor and Xu 1987).

The next objective in the growth of model catalysts is to use simple oxidants which are more easily available than iodosylbenzenes. The results obtained on oxidation based on Fe- or Mn- porphyrins and ClO⁻ or KHSO₅ were found different from PhIO and the same catalysts (Mansuy et al 1982). When a robustic catalyst Mn(TDCPP)Cl was used using hydrogen peroxide as oxidant, the reaction was found to be effective to mimic cytochrome P450 reactions Segrestaa et al (2002), Battioni et al (1988).

The final step is the development of better models of cytochrome P450 systems using molecular oxygen itself as oxygen atom donor as in the long catalytic cycle of cytochrome P450. Several model systems using molecular oxygen and various oxidants in the presence of Mn(III)- and Fe(III)- porphyrins as catalysts have been described in the literature of the last thirty years.

1.13 FEATURES OF PORPHYRINS

Electrophilic substitution reactions are often made on porphyrins. Further, substituents on a porphyrin molecule can be altered. This leads to a range of different porphyrins. The metal in a porphyrin can be removed or inserted. A number of metals such as Fe, Zn, Cu, Ni and Cr can be introduced into the porphyrin cavity by using various metal salts. Elimination of the metal (demetalation) can usually be attained by treating the porphyrin with acids of different concentrations.
1.14 SPECTRAL PROPERTIES OF PORPHYRINS

Functional groups of porphyrins in IR studies get absorbed in the expected regions. The band for the -NH group in porphyrin occurs around 3300 cm$^{-1}$. It is unaffected in CCl$_4$, which is a strong evidence for intramolecular hydrogen bonding.

The visible spectra of metal-free porphyrins usually have four absorption bands between 500 and 650 nm. Apart from these four bands, there is another band observed in the region of 400 nm. This is called as the ‘soret band’ and is specific to conjugated tetrapyrroles. The soret band obtained is very intense and can be used to characterize porphyrins.

Porphyrins have appropriate LUMO and HOMO energy levels and very strong absorption of the Soret band in the 400–450 nm region, as well as the Q-bands in the 500–700 nm region Panda et al (2012).

1.15 METALLOPORPHYRIN CATALYZED OXIDATIONS

Metalloporphyrin is the active site of number of enzymes like hemoglobin, myoglobin, cytochromes, chlorophyll, guanylate cyclase, catalase, peroxidase, vitamin B$_{12}$, chlorophyll etc., due to the following reasons

(i) The ability of the central metal atom to bind with smaller molecules like oxygen, oxides of carbon and nitrogen and other small molecules like protein amino acid residues (cysteine, methionine, histidine etc.) and

(ii) The electron-transfer (redox) properties of the metal, i.e. the ability to accept and donate electrons (Walker and Simonis 1994), (Brown 2005), (Larkum and Kuhn 2005)

A variety of oxidants were used as oxidants to metalloporphyrins (Meunier 1992) which comprise iodosyl benzenes, hydrogen peroxide, peroxy acids, hypochlorite, chlorite, hydroperoxides, chloroperbenzoic acid, monoperoxyphthalate and potassium monopersulfate (oxone). Iodosylbenzene was one of the first and the best oxidant which is used in many substrates than other alternatives. Reductants such as borohydrides with oxygen have also been used for substrate oxidation. Porphyrins have more advantage with substrates of electron withdrawing substituents with respect to the rate of the reactions.

Metalloporphyrins have proven to be highly efficient catalysts for the epoxidation of electron-rich double bonds with various monooxygen donors like hydrogen peroxide (H$_2$O$_2$), potassium monopersulfate (KHSO$_5$) and iodosylarenes (ArIO) Collman et al (2000).

1.16 INTERMEDIATES IN METALLOPORPHYRIN-OXIDATION

In metalloporphyrin mediated oxidation reactions the intermediate formed is supposed to be a high-valent metal-oxospecies Zhou et al (2007), frequently formed by the reaction of iron(III) porphyrin complex with oxidants such as iodosyl benzene, oxone and persulphate. Groves et al (1996) also proved that an oxygen atom is shifted from an oxygen donor to the
metalloporphyrin to form a high-valent metal-oxo species. Other possible intermediates have also been revealed Collman et al (1998).

Disagreement is also there in the formation of intermediates of other oxidation reactions such as epoxidation, N-oxidation and S-oxidation by metalloporphyrin catalysts Traylor et al (1995). The intermediates proposed for the oxygen transfer from an oxidant to the porphyrin is shown in the Figure 1.4. As discussed later that there are in fact multiple pathways possible in these oxidations, which explains, in part, the lack of agreement in these complex mechanistic issues. The nature of the transition state also remains open Prakash et al (2005).

![Figure 1.4](image_url)  

**Figure 1.4** Reaction scheme for the intermediates proposed for the oxygen transfer from an oxidant to the porphyrin

### 1.17 IRON PORPHYRINS AS CATALYSTS

1.18 SIGNIFICANCE OF THE STUDY

Metalloporphyrin catalyzed oxidations are governed by several mechanisms and are also influenced by various factors like the oxidants (various types of oxygen atom donors can be used), the central metal atom (iron, manganese etc.), the porphyrin ligand (substituents modifying steric and electronic effects), the proximal ligand (halide anion, pyridine or imidazole) and the substrate (with various substituents). Decisions based on specific cases cannot be used to set up a unifying mechanism in these oxidation reactions catalyzed by metalloporphyrins. The work in such an area may create a new application for metalloporphyrin chemistry. For example in the field of medicine, the metabolism of drugs can be broadly studied based on the oxidation and biosynthetic ways. The metalloporphyrins are very useful oxidation catalysts, which can be used in different oxidation reactions such as olefin epoxidations, alkane hydroxylations, pollutant oxidations, drug metabolism, DNA cleavage etc. (Prakash 2005). Synthetic porphyrins are useful in an interdisciplinary area such as inorganic chemistry, catalysis, pharmacology and molecular biology. Combined efforts may create new applications in chemistry.

1.19 SELECTION OF THE CATALYST

The catalyst meso-tetraarylporphyriniron(III) chlorides are not efficient catalysts, which are easily oxidized in the reaction medium. Those catalysts are called by Meunier (1992) ‘first generation catalysts’. To study the hindrance in the catalytic activity due to degradation of the first generation catalyst (Figure 1.5) meso-tetraphenylporphyriniron(III) chloride (5,10,15,20-tetraphenyl-21h,23h-porphineiron(III) chloride) has been selected for the study. Artificial metalloporphyrin oxidation catalysts were only able to oxidize the substrate in the presence of a fifth axial ligand such as imidazole or pyridine. In order to use any catalyst for oxidation of hydrocarbons, the
catalyst must be oxidatively compared to the substrate. Simple metalloporphyrins are easily degraded under oxidizing conditions (Prakash and Francisca Mary 2005). This oxidative degradation occurs readily at the meso-ring position (the methine carbons), and the same mechanism was utilized for the metabolism of heme in vivo.

![Structure of meso-tetraphenylporphyriniron(III) chloride](image)

**Figure 1.5 Structure of meso-tetraphenylporphyriniron(III) chloride**

Both electronic and steric factors can be inclined to develop the oxidative robustness of metalloporphyrins. The electron withdrawing substituents on the porphyrin particularly halogenated and perhalogenated phenyl porphyrins (Ellis and Lyons 1990), Bartoli et al (1991), (Mansuy 1993) have shown very fruitful in generating the robust catalysts.

### 1.20 ORIGIN OF THE RESEARCH PROBLEM

Preparation of porphyrin with its substituents artificially is relatively simple, and many methods were identified. Porphyrins are anticipated to have fascinating photochemical and electrochemical properties. Chemists can vary these characteristics by changing the substituents, or by changing the central metal atom. The potential of the heme group is the ability to combine with tiny ligands (including molecular oxygen) in enzymatic oxidations. The contribution of heme in these oxidation processes aggravated chemists to turn-over from these naturally occurring catalysts and operate them into
industrial processes. In order to learn, the core of the heme group, the porphyrin ring with iron as the central metal iron atom, has been selected. These complexes can catalyze the oxidation of aniline in simulating the function of P450. Metalloporphyrin iron complexes have been the subject in a number of findings as they can be added as catalysts in selective oxidation of aniline. The iron complexes with meso-tetraphenyl groups are expansively considered as models of the natural ironporphyrins due to their constructive properties such as catalytic and semi conducting properties. Iron complexes of tetraphenylporphyrins, which can be regarded as macrocyclic ligands has an intermediate structure sandwiched between common natural iron porphyrins with cytochrome P450. Massive efforts have been taken for the learning of iron metalloporphyrin chloride complexes as catalysts for oxidation of aniline. It is a known factor that metalloporphyrin chlorides catalyze for the oxidation of saturated and unsaturated hydrocarbons. So the research was focused towards catalyst meso-tetraphenylporphyriniron(III) chloride. To complement the studies in the field of the catalytic oxidation of aniline, the oxidation of aniline by a range of oxidants catalysed by first generation catalyst meso-tetraphenylporphyriniron(III) chloride (5,10,15,20-tetraphenyl-21h,23h-porphineiron(III) chloride) was taken for the study.

1.21 ANILINE

Aniline, phenylamine or aminobenzene is an aromatic organic compound holding a phenyl group attached to an amino group. Aniline was first prepared by the destructive distillation of indigo by Otto Unverdorben. Its name is taken from indigo-yielding plant Indigoferaanil (Indigofera Suffruticosa). Aniline is a weak base because of the electron-withdrawing effect of the phenyl group. Aniline reacts with strong acids to form anilinium (or phenylammonium) ion (C₆H₅-NH₃⁺). Aniline is a colourless liquid having an unpleasant odour. It burns with a sooty flame showing the property of
aromatic compounds. Aniline slowly oxidizes in air. It is used in the production of polyurethane, methylene diphenyldiisocyanate, rubber processing chemicals, herbicides, dyes and pigments. Aniline derivatives such as diphenyl amine are used as antioxidants. An important medicine prepared from aniline is paracetamol (acetaminophen [active ingredient], tylenol [Brand name]). The other use of aniline in the dye industry is a precursor to indigo, the blue of blue jeans Kahl et al (2000).

The oxidation of aniline is an essential reaction for the synthesis of its oxygenated derivatives such as hydroxylamine, nitroso, nitro, azo and azoxy compounds. Among these, the preparations of nitroso and azoxy compounds have a special importance as synthetic useful intermediates (Jagtap and Ramasamy 2006). Aromatic nitroso compounds are used in the vulcanization of rubber, stabilization of halogenated materials and as antioxidants in lubricating oil (Zengel and Hans 1983). Some derivatives of azoxybenzenes are used as liquid crystals in electronic display and therapeutic medicines Sakuae et al (1993). A variety of oxidation methods transition metal complexes in homogenous (Sheldon and Dakka 1994), Huang et al (2001), Tollari et al (1993) and heterogenous medium (Selvam 1996, Waghmode et al 2001) have been reported. Mesoporous silica containing nanometric dispersed titanium oxide (Tuel and Hubert-Pfalzgraf 2003) is also been used to catalyze the oxidation of aniline to azoxybenzene.

Many factories, such as coal conversion, petroleum refining, iron and steel, textiles, dyes, resins, plastics and agrochemicals, discharge waste water which containing aniline compounds Emtiazi et al (2001). These compounds are dangerous to human health, and suspected to be pollutants. Advanced oxidation methods are helpful in destroying harmful organic pollutants. Advanced oxidation processes are defined as the oxidation processes in which the hydroxyl radicals are derived in sufficient quantity to
effect waste water treatment Anotai et al (2010). In the recent trends enzymes are widely used to eliminate aniline compounds Simmons et al (1987).

Aniline when released into the environment is harmful to aquatic organisms as it may cause damage to central nervous system, cardiovascular system, liver and kidney of animals Ye et al (2009). It has been listed as one of the 129 priority pollutants by U.S. Environmental Protection Agency (Li and Xie 2007).

Aniline in solution is strongly adsorbed on the colloidal organic matter. Transferring aniline from soil to groundwater is a typical route for the environmental pollution, a risk factor for human health and aquatic environment Morales-Torres et al (2011).


The oxidation of anilines into the respective azoxybenzene was catalyzed meso-porous silica containing cobalt oxide using $\text{H}_2\text{O}_2$ as the oxidant (Chang and Liu 2009). Paramagnetic iron oxide nanoparticles were used as catalysts for the oxidation of aniline compounds Zhang et al (2009) where aniline may be decomposed by the hydroxyl free radicals. Peroxidase activity of iron oxide nanoparticles combined with its distinct property, such as easy preparation, high stability and convenient separation from solution by external magnetic field, gives a suitable method for the removal of aniline from waste water Blinova Natalia et al (2009).
1.22 OXIDANTS

The oxidants selected for the study were potassium peroxomonosulphate (oxone), *meta*-chloroperbenzoic acid, magnesium monoperoxyphthalate, sodium perborate and tertiary butyl hydroperoxide.

Potassium peroxomonosulphate in acetic acid medium exists as \( \text{HSO}_5^- \) is a versatile anionic oxidant which is usually represented as oxone, \( \text{KHSO}_3.\text{KHSO}_4.\text{K}_2\text{SO}_4 \) Chandramohan et al (2002).

1.23 STRUCTURE REACTIVITY RELATIONSHIP

Structural factors controlling the reactions may be obtained by the application of the linear free energy relationships. A substituent can influence a distant reaction center at least by five different processes (Karunakaran 1993).

1. The electronic dipole field of the polar substituent substrate bond influencing the reaction center across space.

2. The primary inductive effect can be transmitted to the reaction center by successive polarization of the intervening sigma bonds.

3. The electrostatic charge setup at a conjugate atom to the substituent may polarize the corresponding \( \pi \) - electron system.

4. The \( \pi \)-electron system can be polarized by resonance interaction with the substituent.
5. The electromeric effect, has importance when there is mutual
conjugation between the substituent and the reaction center.
The importance of these various effects can be understood
from many examples.

1.24 THE HAMMET EQUATION

The Hammet linear free energy relationships is commonly assessed
by calculating the correlation coefficient ‘r’ and the standard deviation ‘SD’
of the estimated values of ‘logk’ or ‘logK’ of the equations

$$\log k = \log k_o + \sigma \rho$$

$$\log K = \log K_o + \sigma \rho$$

(Jaffe 1953) investigated about 400 reaction series, and stressed the
importance of correlation coefficient as a measure of the achievement of the
Hammet equation. The parent of all the relationships of this kind was founded
by Bronsted and Pederson (1924) of the general acid base catalysis. Pederson
obviously revealed that there is a relationship between the rate of the reaction
and equilibria of the same series of the reactions. Hammet and Pfluger (1933)
extended the idea by finding a linear relation between the logarithms of the
specific rates of the reactions and those of the equilibrium constants of the
reactions

$$\text{RCOOCH}_3 + \text{N(CH}_3)_3 \rightarrow \text{RCOO}^- + \text{N(CH}_3)_4^+$$

$$\text{RCOOH} + \text{H}_2\text{O} \rightarrow \text{RCOO}^- + \text{OH}_3^+$$

(Burkhardt 1935) and Hammet reported many free energy
relationships (LFER), in the reactions of substituted benzene derivatives and
Hammet systematised relationships in the form of two parameter equations.
By computing Hammet equation and Eyring’s equation, we can show that

\[-\Delta G^\# / RT = -\Delta G_0^\# / RT + \sigma \rho\]

This is often called as linear free energy relationship and implies that there is a linear free energy relationship between the free energies of activation (in rate processes) for one homologous series (\(\Delta G^\#\)) of reaction and those for another (\(\Delta G^\#\)). Thus,

\[\Delta G^\# = \rho / \rho' \times \Delta G^\# + \text{constant}\]

Here \(\rho\) and \(\rho'\) are constants for the first and second reactions respectively. In the above equation (Laidler 1963) reveals that the linear free energy relationship is embedded in the Hammet equation. In the case of para- and meta– substituted benzene derivatives there is no steric effect.

1.25 SCOPE AND OBJECTIVES OF THE PRESENT INVESTIGATION

The scope and objectives of the present investigation are as detailed given below:

- To study the mimic of cytochrome P450 monooxygenase and heme using synthetic metalloporphyrins as they have a strapping resemblance in both structures and catalytic property.

- To study the catalytic activity of meso-tetraphenylporphyriniron(III) chloride complex which can be regarded as macrocyclic ligands having an intermediate structure sandwiched between common natural iron porphyrins with cytochrome P450.
To analyse the oxidation of aniline using different oxidants like oxone, magnesium monoperoxyphthalate, meta-chloroperbenzoic acid, tertiary butylhydroperoxide and sodium perborate catalysed by meso-tetraphenylporphyriniron(III) chloride.

To study the contribution of heme and cytochrome P450 (by mimicking with meso-tetraphenylporphyriniron(III) chloride) in the oxidation of aniline and to merge them from these naturally occurring catalysts in industrial processes.

To study the kinetics on oxidation of aniline, by varying the concentration of aniline, oxidants, meso-tetraphenylporphyriniron(III) chloride, solvent, $\text{H}^+$, substituents and by varying temperature.

To study the free energy relationship in the meso-tetraphenylporphyriniron(III) chloride catalysed oxidation of aniline and its substituents by different oxidants.

To determine various thermodynamic parameters and to correlate using Hammet, isokinetic and Exner relationships.

To study and find out the cause for the short comings of Hammet equation constants in substituent effect (lack of free energy relationship) with anilinium ions and finding out the corrective measures by correlating with biparametric or triparametric equations.

To propose suitable mechanisms and rate laws for the oxidation of aniline by different oxidants catalysed by meso-tetraphenylporphyriniron(III) chloride.