8-1-2013

Selective Catalytic Oxidation of Organic Sulfides by Iron (III) Porphryin Catalysts and Generation of Iron (IV)-OXO Prophyrin Radical Cations

Nawras A. Asiri
Western Kentucky University, nawras.asiri197@topper.wku.edu

SELECTIVE CATALYTIC OXIDATION OF ORGANIC SULFIDES BY IRON(III) PORPHRYIN CATALYSTS AND GENERATION OF IRON(IV)-OXO PROPHYRIN RADICAL CATIONS

A Thesis
Presented to
The Faculty of the Department of Chemistry
Western Kentucky University
Bowling Green, Kentucky

In Partial Fulfillment
Of the Requirements for the Degree
Master of Science in Chemistry

By
Nawras Asiri

August 2013

SELECTIVE CATALYTIC OXIDATION OF ORGANIC SULFIDES BY IRON(III) PORPHRYIN CATALYSTS AND GENERATION OF IRON(IV)-OXO PROPHYRIN RADICAL CATIONS

Date Recommended 07-11-13

Dr. Rui Zhang, Director of Thesis

Dr. Chad Snyder

Dr. Eric Conte

8-21-13

Dean, Graduate Studies and Research Date

ACKNOWLEDGEMENT

First of all, I would like to express the deepest appreciation to my committee chair Dr. Rui Zhang. Without his guidance and persistent help this thesis would not have been possible. Also, I would like to thank my committee members, Dr. Chad Snyder and Dr. Eric Conte. Also, I dedicate this thesis to my mother, my father, my husband, my daughter, and my brothers and sisters.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF SCHEMES

SELECTIVE CATALYTIC OXIDATION OF ORGANIC SULFIDES BY IRON(III) PORPHRYIN CATALYSTS AND GENERATION OF IRON(IV)-OXO PROPHYRIN RADICAL CATIONS

Nawras Asiri August 2013 51 Pages

Directed by: Dr. Rui Zhang, Dr. Chad Snyder, and Dr. Eric Conte

Department of Chemistry Western Kentucky University

Macrocyclic ligand-complexed transition metal-oxo intermediates are the active oxidizing species in a variety of important biological and catalytic oxidation reactions. Many transition metal catalysts have been designed to mimic the predominant oxidation catalysts in nature, namely the cytochrome P450 enzymes. Iron porphyrin complexes have been the center of research as catalysts. In this study 5,10,15,20-tetramesitylporphyrin (H_2TMP) and its corresponding iron complexes $Fe^{III}(X)TMP$ (X= Cl, ClO_4, ClO_3, NO_3, NO_2, and BrO_3) have been successfully synthesized and fully characterized by UV-vis and NMR spectroscopies.

For the catalytic selective oxidation of organic sulfides, the potential of iron(III) porphyrin complexes with iodobenzene diacetate [$PhI(OAc)_2$] have been investigated. Iodobenzene diacetate was found to be an efficient oxygen source in the iron(III) porphyrin-catalyzed oxidation of sulfides to sulfoxides. Iron(III) porphyrin catalysts show an excellent conversion and selectivity for the sulfoxidation reactions. Reaction conditions and environments that effect the catalytic sulfoxidation including solvent, catalytic amount, axial ligand, water, and thioanisole substrates, have been investigated to identify the optimal conditions and the substrate scope. Under optimized conditions, excellent substrate conversions (up to 100%) as well as product selectivies (sulfoxide:sulfone > 95:5) have been achieved.

To probe the nature of the oxidizing species in above catalytic sulfoxidations, iron(IV)-oxo porphyrin radical cations model of Compound I were chemically produced from the corresponding iron(III) tetramesitylporphyrin precursors with excess amounts of $PhI(OAc)_2$ (20-50 equivalents) in CH_3CN solvent. All $O=Fe^{IV}(X)TMP^{\cdot+}$ (X= Cl, ClO_4, ClO_3, and NO_3) show weaker Soret band and broader Q band that are characteristic of Compound I analogues. A new photochemical method that led to generation of the iron(IV)-oxo porphyrin radical cations was also successfully developed. Iron(IV)-oxo porphyrin radical cations were generated by irradiation of iron(III) porphyrin chlorate or bromate complexes that result in heterolytic cleavage of the O-X bond in the axial ligand.

CHAPTER 1

INTRODUCTION

1.1 General

In the production of many commodity-type chemicals, one of the most commonly utilized technologies is catalytic oxidation. The oxidation is significant in many fundamental natural transformations.[1] Up to now, many reactions that entail oxidation are commonly carried out in solvents that are environmentally undesirable. Characteristically, the solvents are made of halogenated hydrocarbons, with reagents that are appreciably priced and that give rise to wastes containing heavy-metal residues.[2] The formulation of novel processes, which make use of transition metals serving as catalysts that are substrate-specific, is one of the principal aims within oxidation chemistry settings.

An ultimate aim is the using of stoichiometric molecular oxygen, which are eco-friendly and most abundant in developing the processes.[1] Molecular oxygen are significantly atom-efficient. The sole by-product that they give off is water. More and more, the sources are growing in their significance in the production of fine chemicals.[2, 3] In living systems, oxidation reactions that are catalyzed by varied oxidative enzymes constitute the foundations of numerous processes that are either biodegradative in nature or of a biosynthetic character.[4]

Some early reports that Hayaishi and his co-workers published, found that there are varied ways in which nature makes use of atmospheric dioxygen for purposes of functionalizing molecules via the employment of different cofactors' sets. Complexes of

metalloporphyrin, flavin, copper, and non-heme iron have in the past been used in metabolizing the dioxygen within oxygenase-related catalytic cycles. The conscription of the complexes in the catalyzed metabolic processes enables the integration of a single or many atoms of oxygen into the substrates.[2] Notably, catalytic oxidations ensure the annual production of millions of oxygenated products.

Such products have wide-ranging uses and applications ranging from pharmaceutical drugs to industrial commodities.[5] Numerous stoichiometric oxidants with heavy metals remain costly. They are also toxic; therefore, impractical. Ideally, the green processes involving catalytic oxidation involve the use of hydrogen peroxide or molecular oxygen as the fundamental oxygen sources. Such sources also serve as catalysts that are recyclable within non-toxic solvents. Moreover, the sources serve as a cheap source of energy.[6] Largely, this research has been motivated by a category of enzymes that contain heme core structure, namely cytochrome P450s (P450s). Although the enzymes in the category are considered as being typical oxygenases, they play a number of crucial biological roles.

1.2 Overview of Cytochrome P-450 Enzymes (CYP450)

Cytochrome P450s are of significance in various crucial roles within biochemical types of reactions within living systems. More and more enzymes under the P450s' family have since been discovered. The P450s' numbers continue to rise as increasing numbers of genomes get sequenced. Certainly, as of now in excess of 8,100 separate genomes of P450s are recognized. Of these, however, only a few have been comprehensively studied. The P450s are commonly found in human beings, bacteria,

insects, plants, fungi, and other living systems. A good number of them are easily isolated from the tissues of mammals like intestines, kidney, lung, and liver.[3]

The enzymes play two principal functions within the body of a person. First, the P450s are critical in the processes in which xenobiotics, as well as drugs, are metabolized. Xenobiotics are compounds that to a given organism are exogenous. In the metabolisms, the P450s' role is largely protective, relating to degradation in readying for excretory processes. Second, P450s play crucial roles in processes that entail the biosynthesizing of molecules that are critical in signaling for the purposes of controlling homeostasis, as well as development.[7] Apart from being critical in the metabolism of xenobiotics as well as drugs, P450s serve crucial functions in the metabolism of vitamins that are soluble in fats, and the steroid hormones' synthesis.

P450s are also critical in converting fatty acids that are polyunsaturated into molecules that are metabolically active within the tissues of mammals.[3] Toxicologists along with pharmacologists stress on the P450s' bearing to the health of persons. In all P450s there are metal centers. Such centers and the linked distinctive spectral characteristics attract both chemists in bioinorganic disciplines as well as biophysicists. The challenging transformation of hydrocarbons that are yet to be activated to products that are oxygenated has attracted the attention of many of the chemists.[3, 8] A persistent difficulty is to appreciate the ways in which different substrate-specificities' sets as well as metabolism-driven transformations are impacted upon by the actual characters of heme-oxygen species of oxygen and structures of the related proteins.[7]

Both the electronic arrangement and structure of the intermediates of the active oxygen, which are effectual oxidants, constitute an area that many researchers are

focusing on.[3] One of the highly common groups of heme-prosthetics within P450s is referred to as Iron Protoporphyrin IX (*heme b*) Complex (Figure 1).[8] In various sources, the complex is presented as being the P450s' active site.[3, 4, 8] Notably, the enzymes are called cytochrome P450s owing to the actuality that the protein, which is reduced, perfectly binds molecules of carbon monoxide, with a band of absorption that is strong. The 450nm band is of a Soret π-π* type. This spectroscopic character has proved helpful in traditional researches on P450s, in monitoring their being there within microsomal sections of tissues extracted from livers.[7]

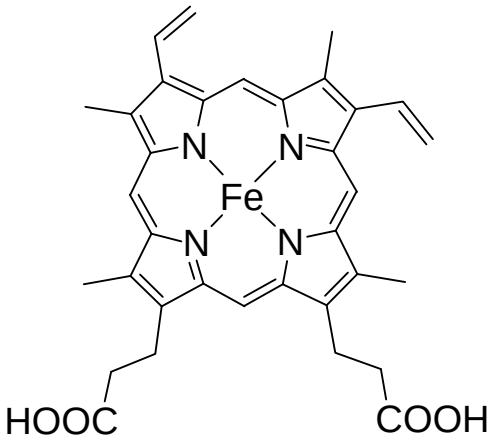


Figure 1. Structure of iron protoporphyrin IX (Heme *b*)

Gunsalus and co-workers discovered P450 CAM in *Pseudomonas putida.* The P450 CAM is a P450 monooxygenase derived from bacteria and that is soluble.[8] The monooxygenase was easily purified in large amounts as it is wholly soluble. The puzzle the structure of P450s was unraveled in the mid of 1986 by Poulos and others. They made available the foremost 3D P450 CAM structure (Figure 2). They established that the structure speeds up the hydroxylation of camphor's exo C_5-H bond in a stereospecific

manner (Scheme 1).[9] This project zeroes in on the mechanistic aspects, and characterization that is spectroscopic, for the catalyzed oxidation of sulfides, which is sulfoxidation-type of reactions. Such reactions are enabled by complexes of metalloporphyrin immersed in iodobenzene diacetate that serves as the source of the required sacrificial type of oxygen.

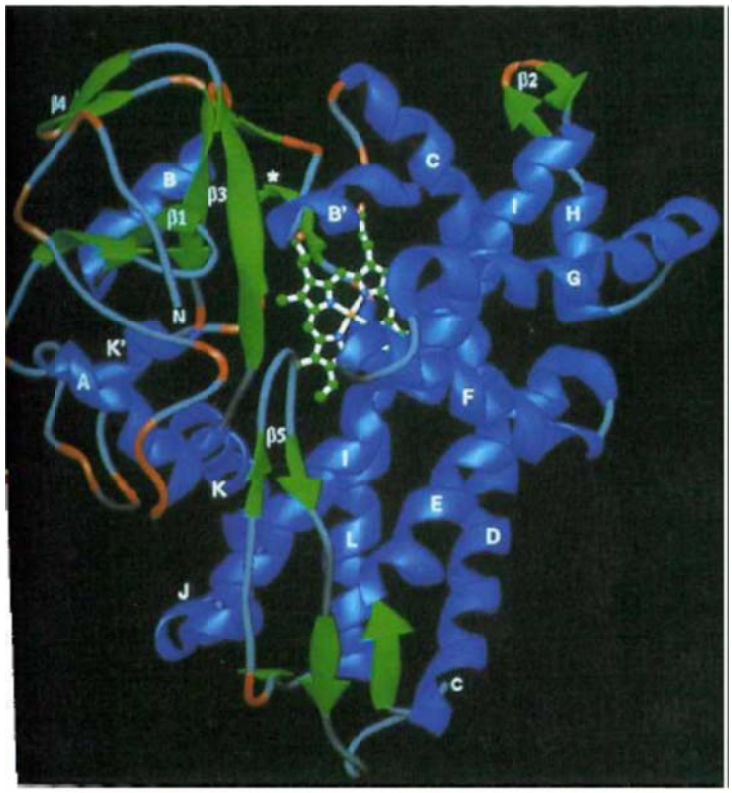
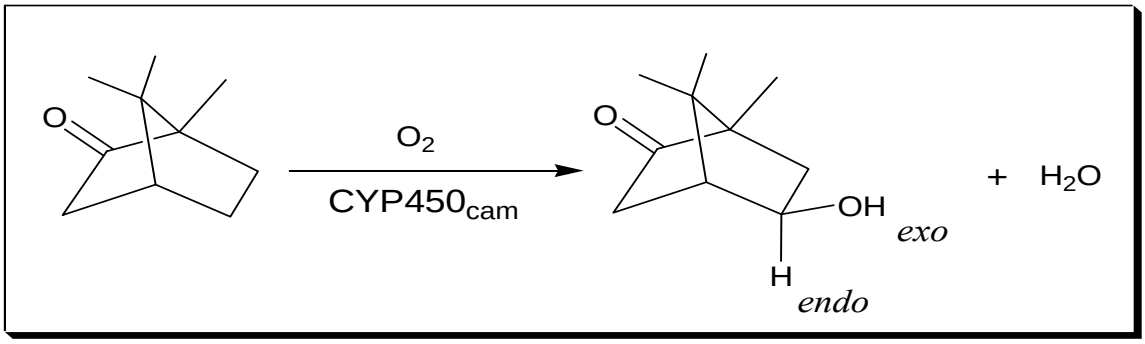


Figure 2. X-ray structure of cytochrome $P450_{cam}$



Scheme 1. Stereospecific hydroxylation of the *exo* C-H bond at position 5 of camphor by cytochrome $P450_{cam}$

Usually, P450s are present in every living system, including human beings, fungi, insects, and bacteria, among others. Additionally, they can be easily isolated in many tissues of mammals. Notably, monooxygenases need two electrons for the purpose of reducing dioxygen's 2nd atom to a molecule of water. P450s benefit in an appreciable way from the keenness that organic, physical, and inorganic chemists deal with them. The keenness has colored the P450s from the moment they were first isolated owing to their exceptional spectral characteristics along with their potential for effectually catalyzing different challenging biotransformations.[7]

Numerous oxygenases that contain heme move through complexes of ferrous-dioxygen. The complexes are principal intermediates within their cycles of catalytic type of reactions. Additionally, P450s easily use NADPH (nicotinamide adenine dinucleotide phosphate), and in some instances NADH (nicotinamide adenine dinucleotide) as donors of electrons in the catalysis of reactions that involve mono-oxygenation.[10] Electrons can be donated by agents such as NADH, which is highly reducing in its nature, or can be

given off by the concerned substrate. Comparatively, the sub-categorization of dioxygenases is done on the basis of whether the donated electrons get incorporated within distinct substrates or into just one molecule.

The subcategories entail intramolecular as well as intermolecular classifications. Terms such as monooxygenase along with dioxygenase are clearly only linked to stoichiometries of reactions that involve the incorporation of oxygen as opposed to the activation mechanism for dioxygen.[10, 11] Save for P450s that are microbial, most of the P450s are bound to membranes, being linked to internal mitochondrial membranes, or microsomal type of membranes. In actuality, most substrates with physiological characters like fatty acids, molecules of xenobiotics, and with steroids are markedly hydrophobic. In excess of half a century when since the discovery of P450s, the precise character of related species that are active remains highly contested.[12]

Even then, the oxidative nature of P450s is associated with the possible presence of iron (IV)-oxo porphyrins radical cation. The species is commonly referred to as Compound I, analogically to various intermediates generated in catalase as well as peroxidase type of enzymes.[13] As novel processes continue to be developed, transition type of metals such as ruthenium, manganese along with iron are continually used as catalysts that are substrate-specific for P450s' biomimic models. Over time, numerous complexes of metalloporphyrin have been presented as being model-compounds in relation to enzymes as well as catalysts containing heme for different reactions that involve oxidation and that are selective.[12] Largely, this project is persuaded by a longing for enhanced appreciation of the elaborate biochemical oxidation mechanisms, utilizing straightforward biomimetic type of models.

1.3 Biomimetic Models of Cytochrome P450 Enzymes

Iron porphyrins that are appointed by nature for the purpose of mediating inherently challenging oxidations that involve P450s heme-centers are having dioxygen.[16] Scientists, over time, have stressed on the effective systems of oxidation catalysis. The oxidation is hinged on catalysts made of metalloporphyrin with manganese, or ruthenium, or iron complexes. Different models of P450s have been synthesized and employed in order to develop useful oxidation catalysts as well as probe the reaction mechanisms.[12] Numerous enzymes, which contain heme, have oxo-metalloporphyrins with high valences serving as active oxidizing intermediates within their cycles of catalysis. Additionally, the metal-oxo porphyrins serve as centers within reactions that involve oxidation and whose mediation is enabled by various synthetic types of metalloporphyrins.[9, 14]

Within biomimetic catalytic oxidations, catalysts made of transition metals are usually oxidized by sacrificial oxidants, to form the high-valent metal-oxo compounds. The high-valent metal-oxo intermediates consequently oxidize organic substrates.[15] Researches utilizing models made of synthetic forms of metalloporphyrins, for P450s have allowed noteworthy insights so as to biomimic characters of processes involving enzymes.[12, 16] Groves along with others,[14] isolated the foremost high-valent iron-oxo porphyrin by oxidizing Fe^{III}(Cl)TMP with *m*-chloroperbenzoic acid under low temperature.[9]

Over time, ruthenium porphyrins have been comprehensively studied as oxidation catalysts. The studies have been aimed at exploring biological mechanisms and processes

as well as formulating catalysts that resemble enzymes owing to the highly comparable periodic linkages to iron its rich redox as well as coordination chemistry.[7, 15]

The research is of marked significance as it expands the appreciation of catalyzed oxidations by complexes of porphyrin-iron, as well as the various biochemical P450s' reactions. Selective hydrocarbon oxygenation is a highly important technology for converting derivatives of petroleum into valuable commodity chemicals.[14] There has been continuous scrutinizes in present technologies, owing to the harm that they cause the environment. The invention of new alternatives that are more effective with environment and eco-friendly oxygen source such as O_2 and H_2O_2 of great signfice .[5, 17] Even then, the elevated kinetic hurdle of dioxygen's triplet condition inhibits the straightforward oxidation by hydrogen peroxides or molecular oxygen species. Transition type of metals might be assistive in this regard, if they are in suitable oxidation states.

The complexes may constitute dioxygen type of adducts when they come into contact with dioxygen in triplet condition. Consequently, they can undergo monooxygenase-facilitated reactions when mixed with the fitting substrates.[10] In mediating inherently challenging oxidations using molecular oxygen, iron-porphyrins that are nestled within P450 monooxygenases' centers of heme are chosen by nature.[18] Therefore, vast efforts and energies have been lend to the generation of biomimetic transition catalysts for regioselective and stereoselective oxidations of organic.[19] Metalloporphyrin-based catalysts including manganese, ruthenium, and iron continue to receive considerable attention as they promise effectual systems for catalyzing the oxidation of hydrocarbons. Manganese type of porphyrins show exceptionally high reactivity regarding the epoxidation of olefins and hydroxylation of alkanes.[12]

1.4 Sulfoxidation Reactions

Selective oxidations of sulfides are quite important in the synthetic chemistry and in varied applications.[20] The catalytic selective sulfoxidation are commonly used in the synthesis of organic species. These reactions are important from green chemistry and industrial viewpoints because organosulfur materials are major pollutants.[21] Moreover, organosulfoxides are employed as forerunners for compounds that are active biologically, and important as chemicals. Organosulfoxides are also critical in the generation of the synthetic intermediates that are employed in the generation of numerous biologically and chemically active molecular species, including agents that are therapeutic, like antiulcer, antifungal, antibacterial, cardiotonic, anti-atherosclerotic and antihypertensive agents along with psychotropics together with vasodilators.[22]

The mounting interest in the synthetic approaches for selective sulfoxidation has persuaded research works into fresh synthesis' approaches. Sulfoxidation is commonly presented as being a direct way of generating sulfoxides.[23] Although varied reagents can be used in sulfoxidation, most of them may prove to be unsatisfactory owing to their costliness, or toxicity, or straightforward methods are inadequate owing to sulfoxides' over-oxidation to form sulfones.[20] Managing the conditions where the sulfoxidation takes place can help in stemming the formation of oxidation byproducts and products. The conditions include relative quantities of the oxidants used, time, as well as temperature. Even then, the meeting of such requirements is commonly challenging. Consequently, there are still appreciable emphases on the formulation of suitable selective sulfoxidation approaches to actualize the desired transformations.[23, 24]

Given that hydrogen peroxide is an effective oxidant, sulfoxidation reactions catalyzed by metalloporphyrins with sacrificial oxidants have attracted little attention. In recent year, there have been detailed studies on hydrocarbons' hydroxylation as well as epoxidation by various *trans*-dioxoruthenium (VI) porphyrins. The study of iodobenzene diacetate a mild oxygen source has been scanty. The iodobenzene diacetate has scarcely been studied in relation to catalytic sulfoxidation by iron and ruthenium porphyrins.

In this work, we aim to fully explore the potential of iron porphyrins toward catalytic sulfoxidation reactions with iodobenzene diacetate $PhI(OAc)_2$ as a mild oxygen source under different conditions.

CHAPTER 2

EXPERIMENTAL SECTION

2.1 Materials and Chemicals

Sulfide substrates for catalytic oxidation including thioanisole, 4-methoxy thioanisole, 4-fluorothioanisole, 4-chlorothioanisole, and 4-bromothioanisole were obtained from the Aldrich Chemical Co. All organic solvents including dichloromethane, chloroform, aceton, acetonitrile, methanol, ethanol, were of analytical grade, and utilized without additional purification. Triethylamine, 2,3-dichloro-5,6-dicyano-*p*-benzequinone (DDQ), *N*,*N*-dimethylformamide (DMF), boron trifluoride diethyl etherate ($BF_3.OEt_2$), mesitaldehyde, iodobenze diacetate [$PhI(OAc)_2$], *meta*-chloroperoxybenzoic acid (*m*-CPBA), chloroform-d, silver perchlorate, silver chlorate, silver nitrate, silver nitrite, silver bromate, iron chloride, sodium sulfate, were purchased from Sigma-Aldrich and also used as received. Pyrrole was bought from Sigma-Aldrich and thoroughly distilled prior to its use.

2.2 Physical Measurments

UV-vis spectra was recorded on an Agilent 8453 diode array spectrophotometer. The ^{1}H-NMR spectra was conducted on a JEOL CA-500 MHz FT-NMR spectrometer at 298 K with tetramethylsilane (TMS) as internal standard. Chemical shifts (ppm) are reported relative to TMS.

2.3 Distillation of Pyrrole

The pyrrole was purified through distillation. Approximately 25 mL of the pyrrole was transferred in a 50 mL round-bottom flask. That amount of pyrrole was measured by a graduated cylinder. The flask contained a magnetic spin bar. The apparatus include a water-jacketed condenser. The distillation was carried out at approximately 130^{o}C, with the foremost distillate coming out before that temperature was reached. The solution was heated by a regulated heater. Given that pyrrole boils at approximately 129^{o}C at 1 atm, all the pyrrole distillate that was collected before reaching 129^{o}C was discarded.

2.4 Synthesis and Spectroscopic Characterization of Iron Porphyrin Complexes

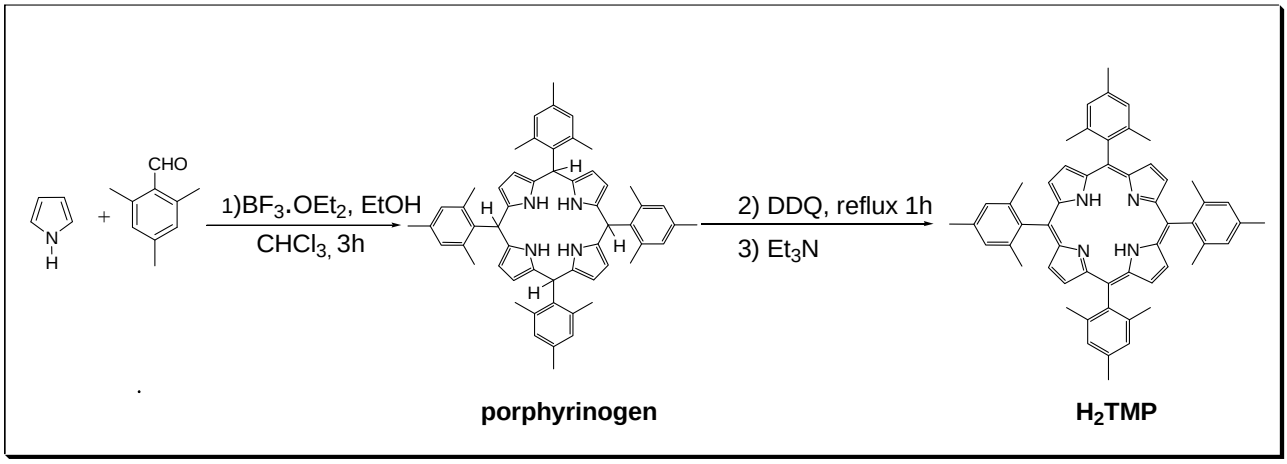
2.4.1 Tetramesitylporphyrin [H2TMP]

A free ligand of porphyrin was prepared in accordance to a renowned procedure reported by Lindsey along with others (Scheme 2).[25] A reflux condenser was fitted onto a round-bottom flask. Freshly prepared pyrrole (347 μL , 5 mmol) and mesitaldehyde (736 μL , 5 mmol) were dissolved in 500 mL solution of chloroform. Notably, the pyrrole was purified through distillation. In the solution, 3.47 mL of ethyl alcohol (0.5% v/v) was added as a co-catalyst. Argon was used to purge the solution for approximately 5 min. Boron trifluoride diethyl etherate (660 μL, 1.65 mmol) was added in a dropwise manner into the solution using a syringe. Under room temperature, the reaction solution was thoroughly stirred for about 3 h.

Following porphyrinogen's formation, DDQ (957 mg) was added into the solution, which was then gently refluxed for about an hour. The solution was allowed to cool to the room temperature. One equivalent of triethylamine (230 μL, 1.65 mmol) was added for the purpose of neutralizing the solution. The solution was evaporated to dryness. The resulting solid residue was washed by using methanol under vacuum conditions. The cleaning process resulted in a colorless filtrate. The crude product was further purified by column chromatography using silica gel. The product was eluted out by using dichloromethane. Solvent was removed by rotary evaporation, giving the purplish solid of H_2TMP (240 mg). The structure of H_2TMP was confirmed by UV-Vis (Figure 3) and ^{1}H-NMR (Figure 4), matching those literature reported.[25]

[H_2TMP] Yield = 24.5%. ^{1}H-NMR (500 MHz, $CDCl_3$) δ, ppm: -2.50 (s, 2H, NH), 1.81 (s, 24H, *ortho*-CH_3), 2.62 (s, 12H, *para*-CH_3), 7.26 (s, 8H, *m*-ArH), 8.61 (s, 8H, *β*-pyrrole). UV-vis($CHCl_2$) λ_{max}/nm, 418 (Soret), 441, 513, 546, 594, 645.

According to Lindsey and others[25], mesitaldehyde and pyrolle condensation rate and yield in the formation of sterically hindered H_2TMP are dependent on several factors: co-catalysts, temperature, catalysts, type of solvent, and the ratios of concentration of reacting agents. Present literature reports that a H_2TMP yield of up to 24.5% is attainable. The procedure that is reported in this section proved to be convenient in the synthesis of the sterically encumbered porphyrin (H_2TMP) with > 95% purity.



Scheme 2. Two-step and one-pot synthesis of H_2TMP

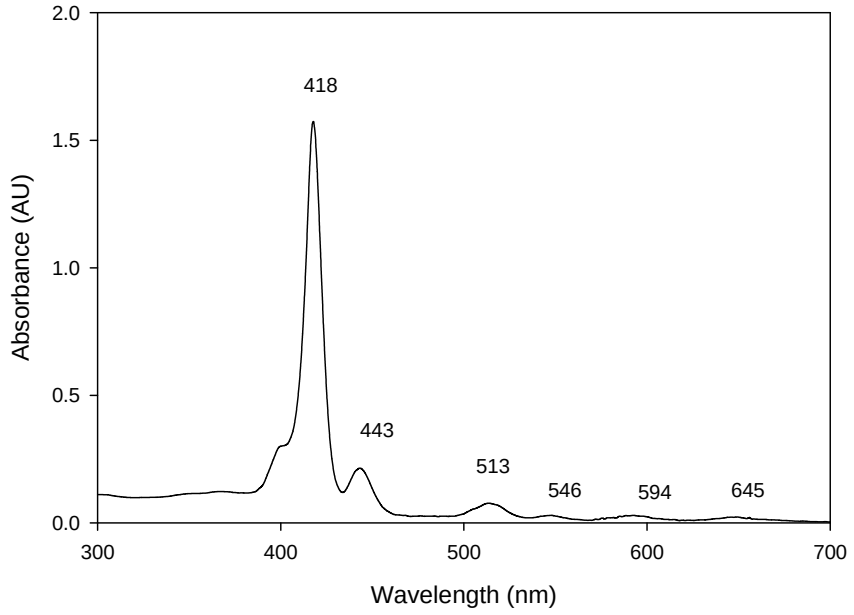


Figure 3. The UV-vis spectrum of H_2TMP in CH_2Cl_2

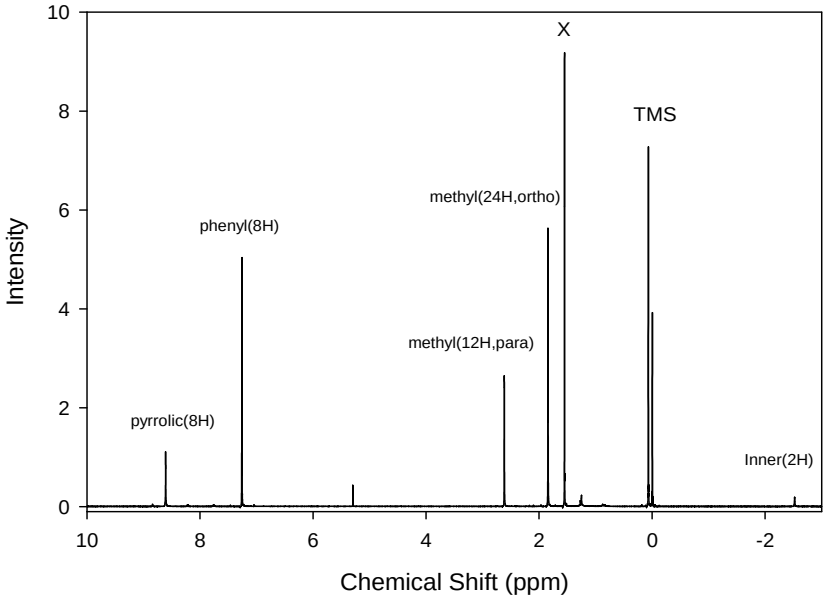
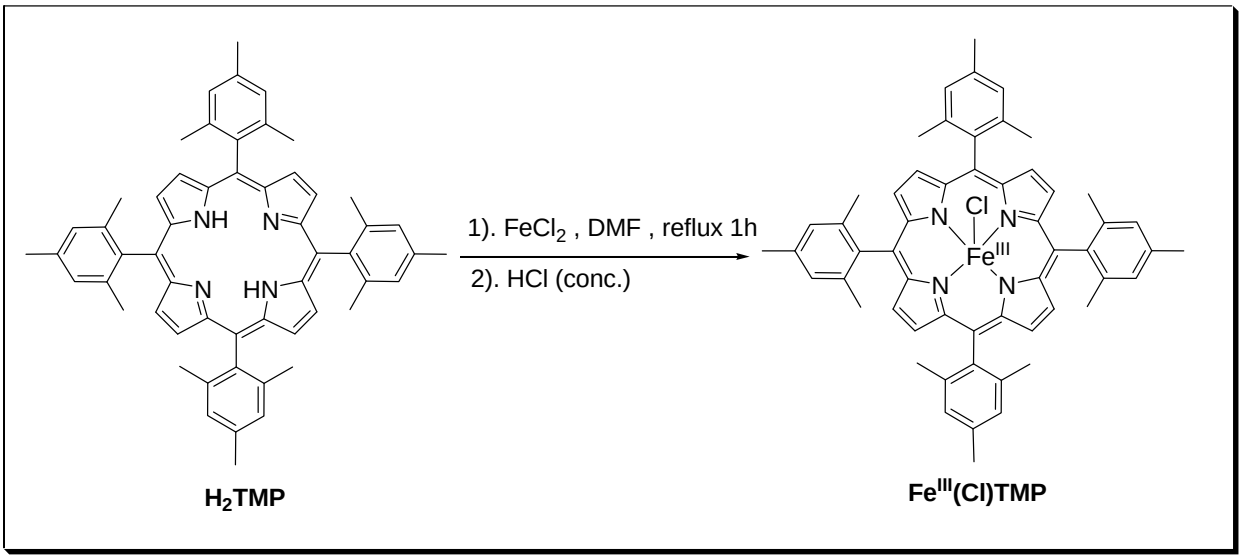


Figure 4. The ^{1}H-NMR spectrum of H_2TMP in $CDCl_3$

2.4.2 Iron(III) Tetramesitylporphyrin Chloride [FeIII(Cl)TMP]

A reflux condenser was fitted onto a 100 mL round-bottom flask. 100 mg of H_2TMP along with excess amount of $FeCl_2$ (500 mg) were mixed in a solution of DMF (30 mL). The mixture was purged with Argon for 5 min to remove the atmospheric oxygen. The mixture was then refluxed for approximate 1 h. UV-vis spectroscopy was employed in monitoring the entire process. The mixture was cooled down to room temperature. 30 mL of deionised water was added into the flask to precipitate the formed product. The solid was collected through vacuum filtration and the resulting crude residue was thoroughly washed with deionized water (500 mL).

The resulting clear solid was dried in open air and then dissolved in approximate 25 mL of CH_2Cl_2. Concentrated HCl (30 mL, 3 M) was added into the resulting organic solution. The solution was continuously stirred for 15 min. The organic part of the mixture was separated and dried over excess anhydrous sodium sulfate (Na_2SO_4). The product was further purified by wet column chromatography using silica gel. In the column purification, CH_2Cl_2 was used as eluent. The green solid product (57 mg) was obtained. UV-Vis (Figure 5) and ^{1}H-NMR (Figure 6) with a typical pattern expected for paramagnetic complexes were used to characterize the structure of final product. [Fe^{III}(Cl)TMP] Yield = 45.3%. ^{1}H-NMR (500MHz, $CDCl_3$): δ, ppm: 82 ppm, 17 ppm, 18 ppm. UV-vis (CH_2Cl_2) λ_{max}/nm: 378, 415, 510.



Scheme 3. Synthesis of Fe^{III}(Cl)TMP

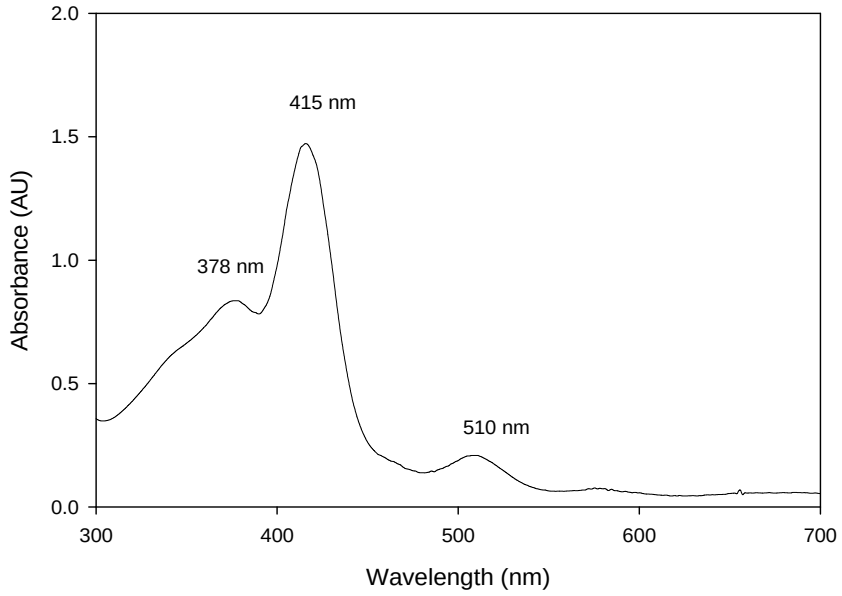


Figure 5. The UV-vis spectra of Fe^{III}(Cl)TMPin CH_2Cl_2

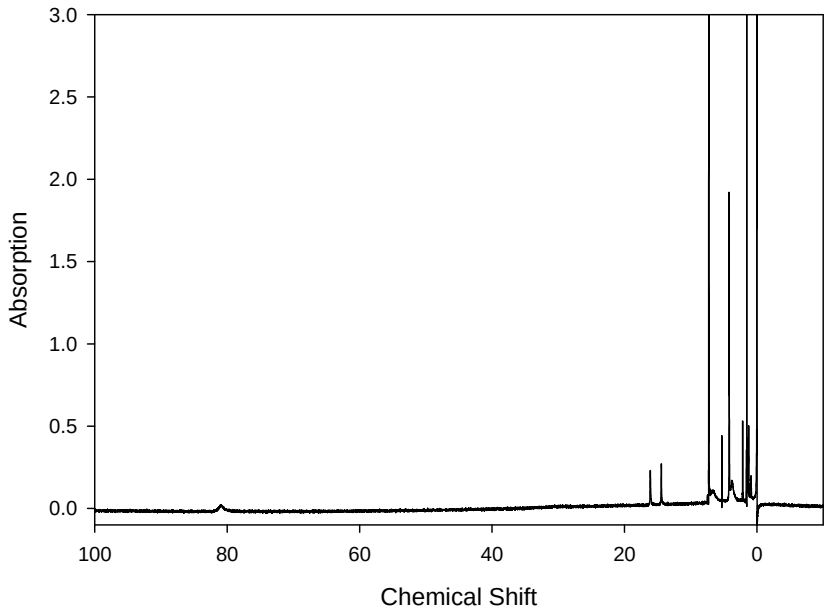
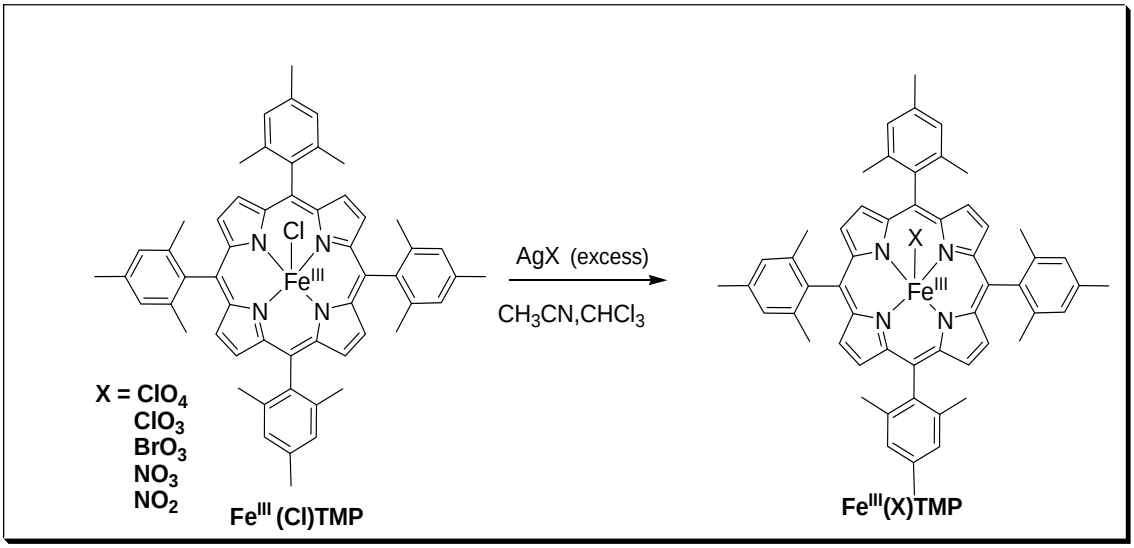


Figure 6. The ^{1}H-NMR spectrum of Fe^{III}(Cl)TMP in $CDCl_3$

2.4.3 Iron(III) Tetramesitylporphyrin Perchlorate [FeIII(ClO4)TMP]

The stock solution of $Fe^{III}(ClO_4)$TMP was readily prepared by a facile ligand exchange with corresponding silver salts. 2 mg of Fe^{III}(Cl)TMP was added into a solution containing $CHCl_3$ (0.5 mL) and CH_3CN (0.5 mL). The mixture was stirred until all the Fe^{III}(Cl)TMP had dissolved. Excess amount of $AgClO_4$ (1 mg) was added into the resulting solution. Immediately, AgCl precipitate was formed and was filtered, leaving the desired $Fe^{III}(ClO_4)$TMP filtrate. The entire transformation was monitored by UV-vis spectroscopy (Figure 7).

The synthetic process of $Fe^{III}(ClO_3)$TMP , $Fe^{III}(NO_3)$TMP, $Fe^{III}(NO_2)$TMP, and $Fe^{III}(BrO_3)$TMP are similar to the procedure described for $Fe^{III}(ClO_4)$TMP as shown in Scheme 4. UV-Vis (Figure 8) was used to characterize the products.



Scheme 4. Synthesis of $Fe^{III}(X)TMP$

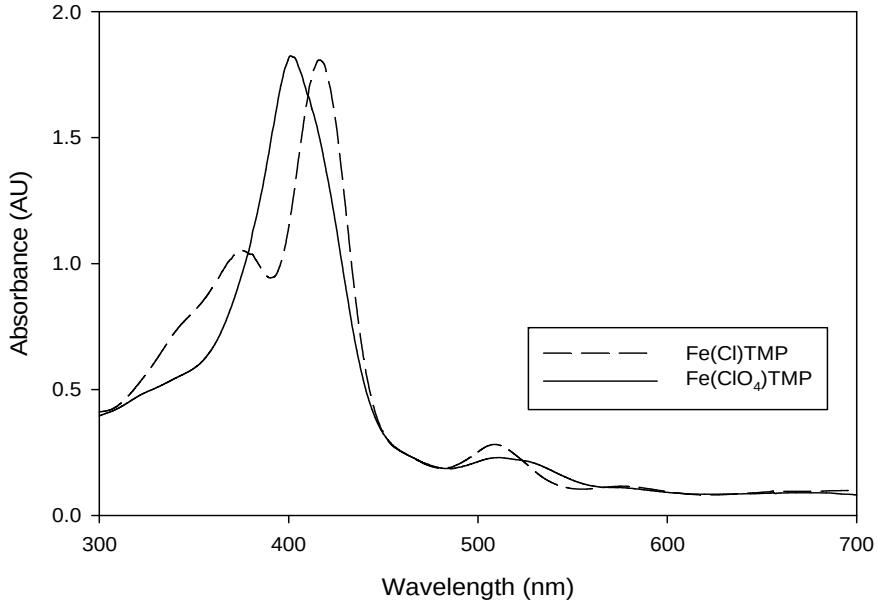


Figure 7. UV-vis spectra of the generated of $Fe^{III}(ClO_4)TMP$(solid line) from $Fe^{III}(Cl)TMP$(dash line)

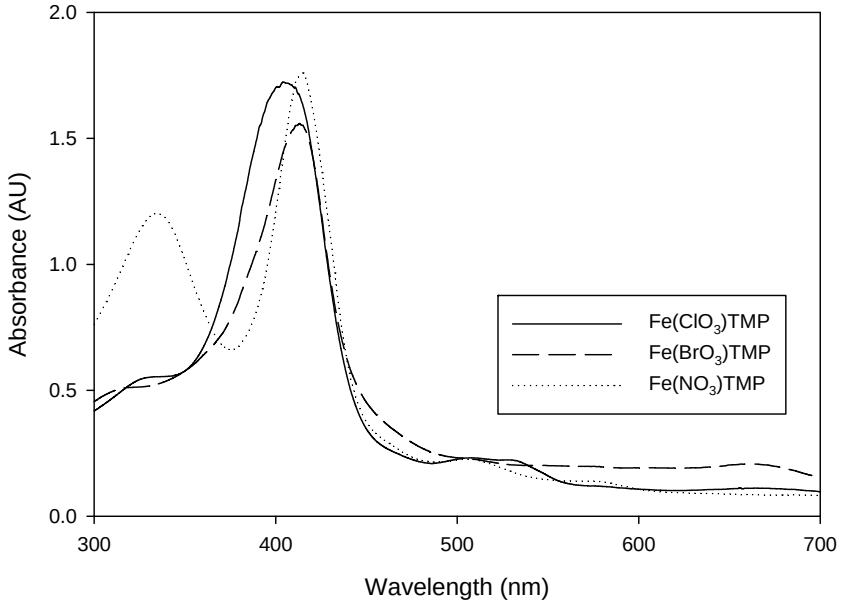


Figure 8. UV-vis spectra of $Fe^{III}(ClO_3)TMP$(solid line), $Fe^{III}(BrO_3)TMP$(dash line), and $Fe^{III}(NO_3)TMP$(dotted line)

CHAPTER 3

CATALYTIC SELECTIVE OXIDATION OF ORGANIC SULFIDES BY IRON(III) PORPHYRIN COMPLEXES

3.1 Introduction

The selective oxidation of sulfides to sulfoxides (sulfoxidation) is one of great importance in organic synthesis.[20] Organic sulfoxides are valuable reagents for the production of a variety of chemically and biologically significant molecules. Optically active sulfoxides are also useful intermediates in medicinal and pharmaceutical chemistry to prepare the therapeutic, antihypertensive and cardiotonic agents, as well as psychotonics and vasodilators.[20] A large variety of electrophilic reagents such as perasids, hypochlorite, sodium periodate, iodosobenzene peracids, and highly toxic oxo metal oxidants have been utilized for the oxidation of conventional sulfides with the aim of obtaining high selectivity for sulfoxide over sulfone.[20, 22] However, the methods that are currently reported rarely provide the ideal combination of selectivity, fast reaction kinetics, and high product yields. The search for efficient and selective catalytic oxidation methods for the sulfoxide preparation has continued to be the interest of chemical research.

In this work, we aim to fully explore the potential of iron porphyrins toward catalytic sulfoxidation reactions with iodobenzene diacetate [$PhI(OAc)_2$] as a mild oxygen source. In contrast to the common sacrificial oxidants used for metalloporphyrin-catalyzed reactions, $PhI(OAc)_2$ does not show appreciable reactions

towards organic substrate or does not damage the porphyrin catalyst under the usual catalytic conditions. Due to the mild oxidizing ability, $PhI(OAc)_2$ has been less often employed in the metalloporphyrin-catalyzed oxidations. To the best of our knowledge, using $PhI(OAc)_2$ for the sulfoxidation of organic sulfides catalyzed by iron porphyrin complexes is unprecedented.

3.2 General Procedure for Catalytic Oxidation of Sulfides by Iron Porphyrin Catalysts

A typical catalytic reaction experiment was carried out in a vial at room temperature (23±2ºC). To the mixture of Fe^{III}(Cl)TMP (1 μmmol) and oxygen source $PhI(OAc)_2$ (0.75 mmol) in 2 mL of $CDCl_3$ was added thioanisole (0.5 mmol). The reaction process was followed by ^{1}H-NMR analysis directly on the crude mixture. To identify the most efficient systems and optimal conditions, the thioanisole was chosen as standard substrate in the screening reactions.

3.3 Results and Discussions

With $PhI(OAc)_2$ as mild oxygen source, we have evaluated iron(III) porphyrins as catalyst in the oxidation of thioanisole under different conditions. Note that iron(III) porphyrins catalyze the selective oxidation of sulfide to the corresponding sulfoxide (> 95%), which was the only identifiable product in all runs. All reactions have been run at least three times.

Solvent effect on the catalytic oxidation of thioanisole by Fe^{III}(Cl)TMP has been investigated as shown in Table 1and Figure 9. Chloroform, methanol, and acetonitrile were tested as solvent for the sulfoxidation reactions. In Table 1, it could be observed that solvent played an important role in the oxidation reactions. Methanol gave the highest conversion of 71%, but when chloroform and acetonitrile were used, lower conversions were obtained. Methanol was much more favorable to the oxidation of sulfide to sulfoxide, presumably due to its polar nature.

Table 1. Solvent effect on the catalytic oxidation of thioanisole by Fe^{III}(Cl)TMP

Solvent	Substrate	Product	Time (h)	Conversion (%)	Selectivity (Sulfoxide:Sulfone)
$CDCl_3$			17	49	> 95:5
CD_3OD			17	71	> 95:5
CD_3CN			17	51	> 95:5

All reactions were performed under the following conditions: thioanisole(0.5 mmol) , iron(III) chloride porphyrin catalyst(1 μmmol), solvent (2 mL), Iodobenzene diacetate [$PhI(OAc)_2$] (0.75 mmol).

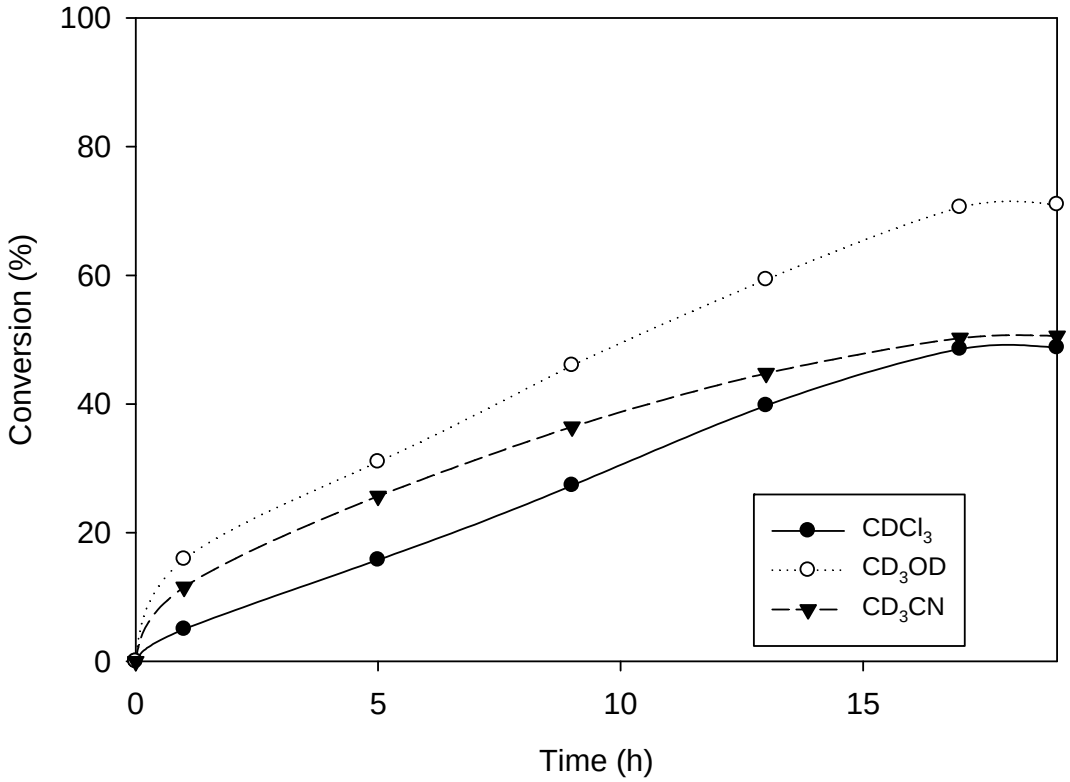


Figure. 9 Time courses of the catalytic oxidation of thioanisole by Fe^{III}(Cl)TMP with different solvents

The effect of the amount of iron porphyrin catalyst on the sulfoxidation reaction was investigated as shown in Table 2 and Figure 10. Three different amounts of the catalyst were used to understand the effect of catalyst amounts in the oxidation reactions. From Table 2, it can be found that the higher amount of catalyst shows a higher conversion of the oxidation of thioanisole within the same time.

Table 2. The effect of amount of Fe^{III}(Cl)TMP on sulfoxidation reactions

Fe^{III}(Cl)TMP (μmol)	Substrate	Product	Time (h)	Conversion (%)	Selectivity (Sulfoxide:Sulfone)
0.5			17	19	> 95:5
1.0			17	49	> 95:5
2.0			17	61	> 95:5

All reactions were performed under the following conditions: thioanisole (0.5 mmol) , iron(III) chloride porphyrin catalyst, $CDCl_3$ (2 mL), Iodobenzene diacetate [$PhI(OAc)_2$] (0.75 mmol).

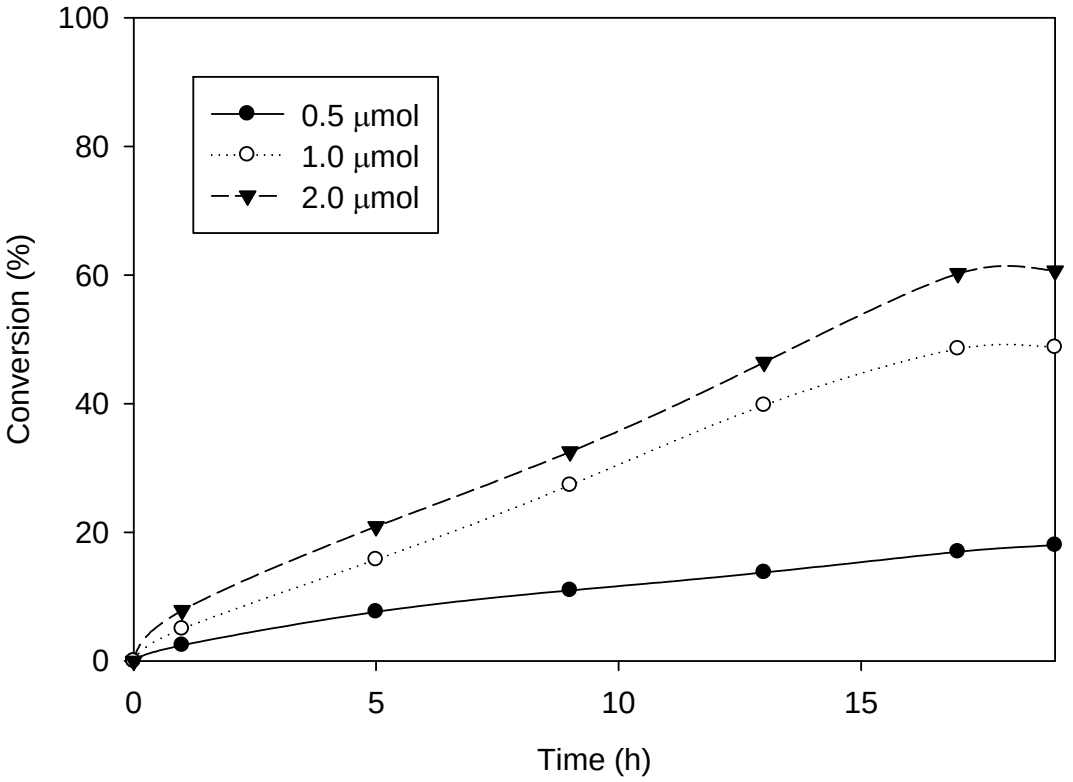


Figure. 10 Time courses of catalytic oxidation of thioanisole with different amount of Fe^{III}(Cl)TMP

We have carried out the catalytic sulfoxidations by $Fe^{(III)}$(X)TMP with different axial ligands (X= Cl^-, ClO_4^-, ClO_3^-, NO_3^-, and NO_2^-) and the results are summarized in Table 2 and Figure 11. Quite surprisely, under identical conditions the axial ligand on the iron metal has a significant effect. It seemed that $Fe^{III}(ClO_4)$TMP was the best catalyst for the sulfoxidation reactions, which gave the highest yield of 73% within 17 h. Much lower yields were obtained when $Fe^{III}(NO_3)$TMP and $Fe^{III}(NO_2)$TMP were used instead. Among all axial ligands that we studied, ClO_4^- had the weakest coordinating ability to iron, indicating a rapid reaction with $PhI(OAc)_2$ to generate the active oxidizing species.

Table 3. Axial ligand effect on catalytic sulfoxidation reaction with $PhI(OAc)_2$.

Fe^{III}(X)TMP Cat.	Substrate	Product	Time (h)	Conversion (%)	Selectivity (Sulfoxide:Sulfone)
$Fe^{III}(Cl)$TMP			17	49	> 95:5
$Fe^{III}(ClO_4)$TMP			17	73	> 95:5
$Fe^{III}(ClO_3)$TMP			17	54	> 95:5
$Fe^{III}(NO_3)$TMP			17	19	> 95:5
$Fe^{III}(NO_2)$TMP			17	15	> 95:5

All reactions were performed under the following conditions: thioanisole (0.5 mmol), iron(III) porphyrin catalyst Fe^{III}(X)TMP (1 μmmol) in $CDCl_3$ (2 mL), Iodobenzene diacetate [$PhI(OAc)_2$] (0.75 mmol).

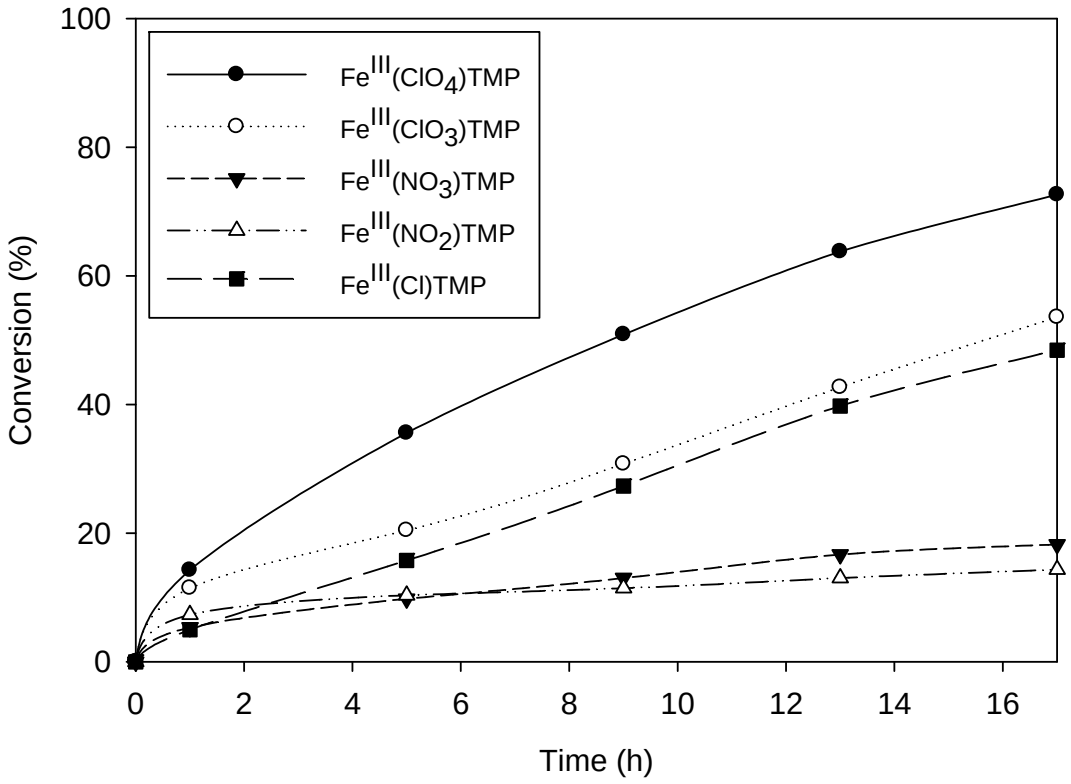
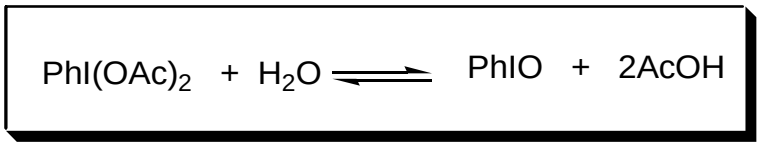


Figure. 11 Time courses of catalytic sulfoxidation reaction with different axial ligands

Consistent with the literature known report, [26] we have observed a significant water effect on the rate of sulfoxidation reaction. The time course of thioanisole oxidation by carrying out the reactions in the absence and presence of H_2O was shown in Figure 12. The results in Table 4 and Figure 12 show that the sulfoxidation proceeded vary rapidly in the presence of small amount of H_2O (4.5 μL) and 100% conversion was obtained within 60 min. The fast reaction in the presence of H_2O is rationalized with the generation of more oxidizing PhIO from the reaction of $PhI(OAc)_2$ and H_2O (eq. 1)



Eq 1. PhIO formation from the reaction of $PhI(OAc)_2$ and H_2O

Table 4. Water effect on the catalytic oxidation of thioanisole by Fe^{III}(Cl)TMP

H_2O (μL)	Substrate	Product	Time (h)	Conversion (%)	Selectivity (Sulfoxide:Sulfone)
0			1	12%	> 95:5
2.0			1	46%	> 95:5
4.0			1	69%	> 95:5
4.5			1	100%	> 95:5

All reactions were performed under the following conditions: thioanisole (0.5 mmol), iron(III) chloride porphyrin catalyst(1 μmmol), methanol solvent (2 mL), Iodobenzene diacetate [$PhI(OAc)_2$] (0.75 mmol).

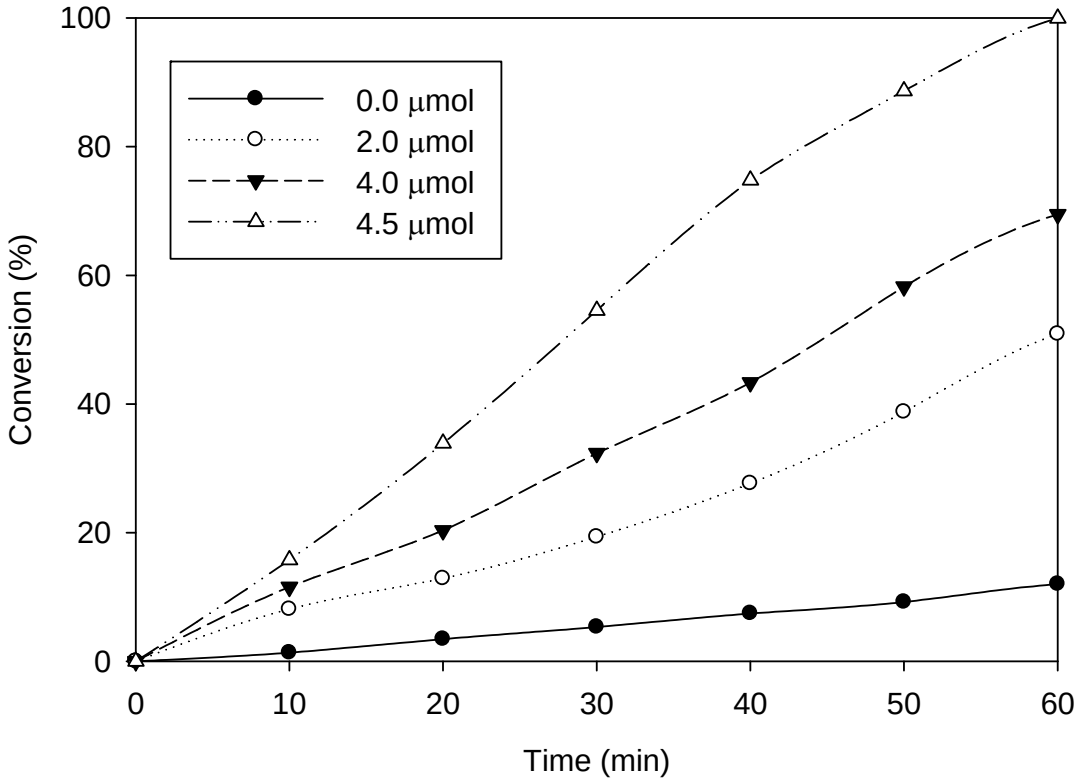
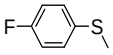
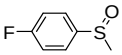
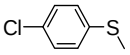
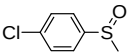
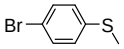
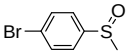
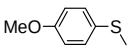
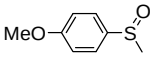


Figure . 12 Time courses for the catalytic sulfoxidation by Fe^{III}(Cl)TMP with $PhI(OAc)_2$ in the presence (0,2.0, 4.0, and 4.5 μL) of water

With Fe^{III}(Cl)TMP as catalyst, different thioanisole substrates were examined for the oxidation of sulfide to sulfoxide and the results are shown in Table 5 and Figure 13. The different substrates that were examined include thioanisole, 4-methoxythioanisole, 4-fluorothioanisole, 4-chlorothioanisole, and 4-bromothioanisole. Table 5 shows that thioanisole and 4-methoxy thioanisole are more reactive substrates giving higher conversions within 17 h. The reactions show much faster oxidation rates in the presence of water, which give up to 100% conversions within 1 h as shown in Table 6 and Figure 14. Although the rate of the sulfoxidation was markedly influenced by the addition of H_2O, the product selectivity was not affected by the presence and absence of H_2O.

Table 5. Catalytic oxidation of thioanisole and substituted thioanisole by Fe^{III}(Cl)TMP with $PhI(OAc)_2$ as oxygen source

Fe^{III}(Cl)TMP Cat.	Substrate	Product	Time (h)	Conversion (%)	Selectivity (Sulfoxide:Sulfone)
1			17	71	> 95:5
2			17	46	> 95:5
3			17	52	> 95:5
4			17	14	> 95:5
5			17	63	> 95:5

All reactions were performed under the following conditions: thioanisole or substituted thioanisole(0.5 mmol), Fe^{III}(Cl)TMP catalyst(1 µmmol) in $CDCl_3$ (2 mL), Iodobenzene diacetate [$PhI(OAc)_2$] (0.75 mmol).

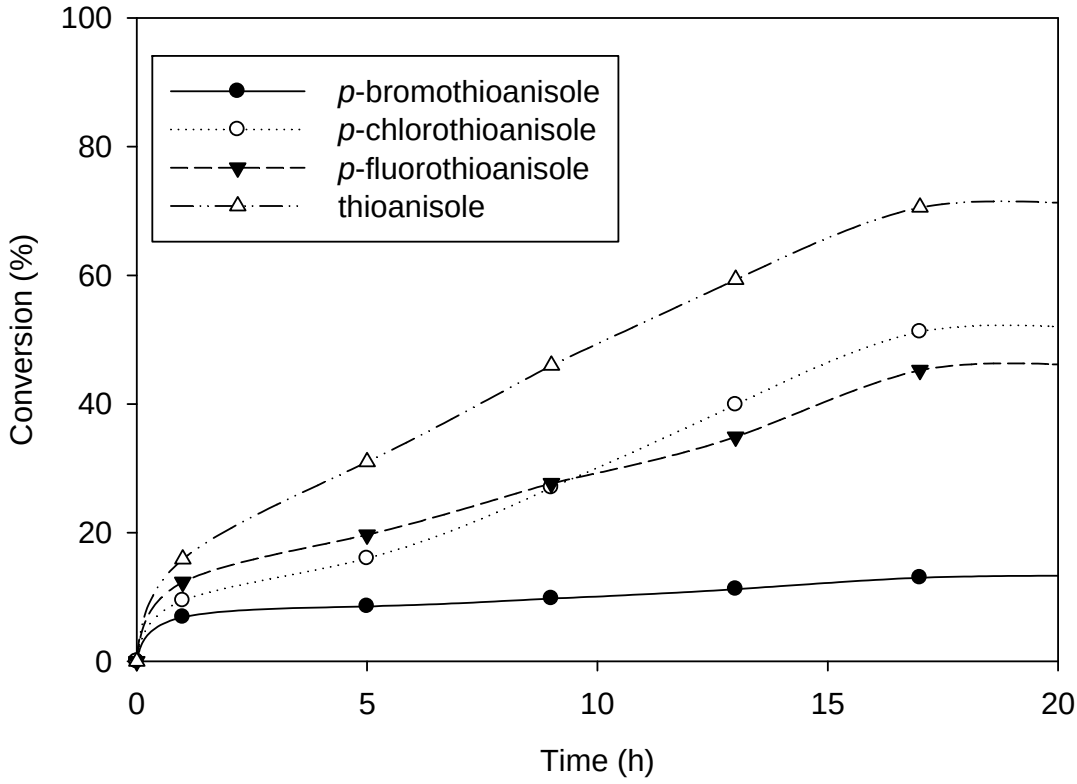
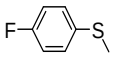
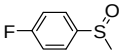
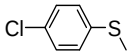
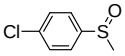
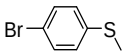
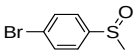
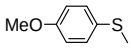
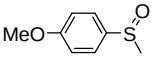


Figure. 13 Time courses of catalytic oxidation of thioanisole and *p*-halogenated thioanisoles by Fe^{III}(Cl)TMP with iodobenzene diacetate.

Table 6. Catalytic oxidation of thioanisole and substituted thioanisole by Fe^{III}(Cl)TMP with $PhI(OAc)_2$ in presence of H_2O.

Fe^{III}(Cl)TMP Cat.	Substrate	Product	Time (h)	Conversion (%)	Selectivity (Sulfoxide:Sulfone)
1			1	100	> 95:5
2			1	99	> 95:5
3			1	94	> 95:5
4			1	65	> 95:5
5			1	98	> 95:5

All reactions were performed under the following conditions: thioanisole (0.5 mmol) or substituted thioanisole(0.5 mmol), Fe^{III}(Cl)TMP catalyst(1 µmmol) , methanol (2 mL), Iodobenzene diacetate [$PhI(OAc)_2$] (0.75 mmol), H_2O(4.5µl).

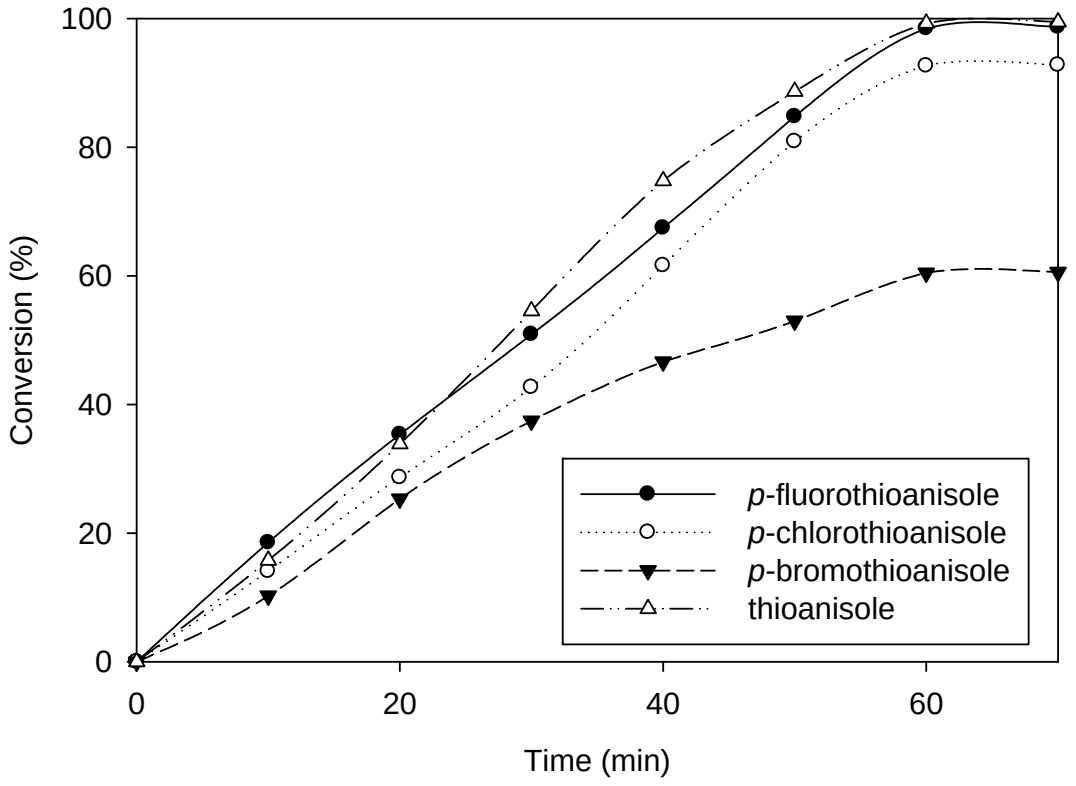


Figure. 14 Time courses of catalytic oxidation of thioanisole and *p*-halogenated thioanisoles by Fe^{III}(Cl)TMP with $PhI(OAc)_2$ in presence of H_2O (4.5µl)

In summary, our results have demonstrated that $PhI(OAc)_2$, which is soluble in organic solvents, safe to use and readily available is an efficient oxygen source in iron(III) porphyrin-catalyzed oxidation of sulfides to sulfoxides. Under optimal conditions, excellent substrate conversions (up to 100%) as well as product selectivies (sulfoxide:sulfone > 95:5) were obtained within 60 min.

CHAPTER 4

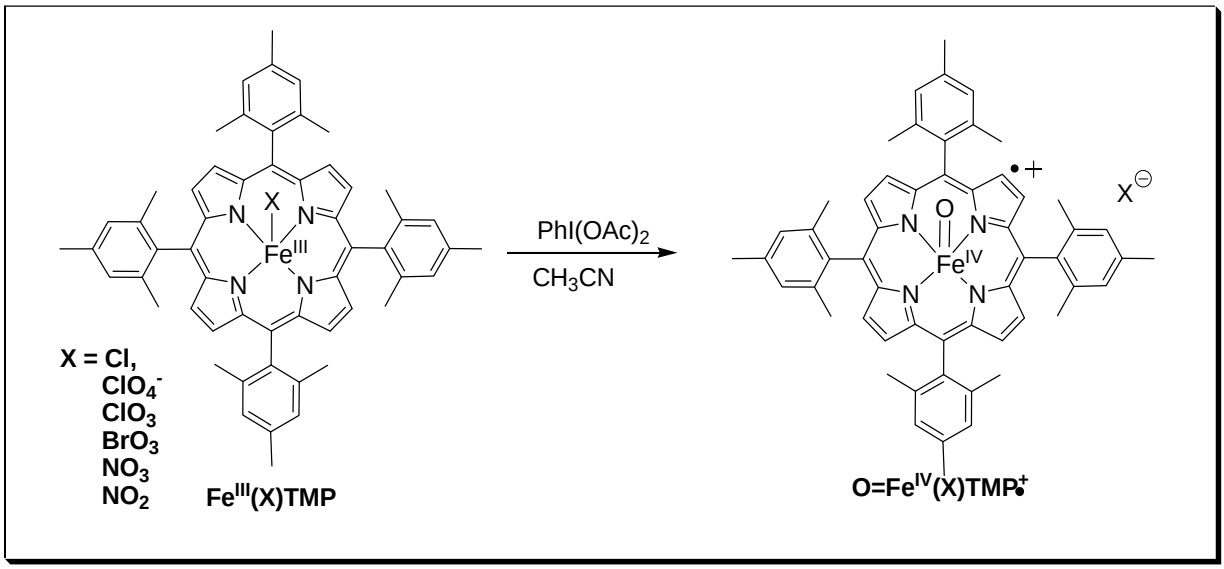
CHEMICAL AND PHOTOCHEMICAL GENERATION OF IRON(IV)-OXO PORPHYRIN RADICAL CATIONS (COMPOUND I ANALOGUES)

4.1 Introduction

Iron(IV)-oxo porphyrin radical cations occur as oxidizing intermediates in catalase and peroxidase enzymes, where they are referred to Compound I species, and the putative oxidative species in P450s, enzymes.[27] Two-electron oxidation of porphyrin-iron(III) precursors gives off observable of iron(IV)-oxo porphyrin radical cations within the enzymes and model systems.[28] Iron(IV)-oxo porphyrin radical cations as models of Compound I have been known for more than two decades as the reactive intermediates in iron porphyrin-catalyzed oxidation reactions.[28] Axial ligands in Compound I have marked impacts on their reactivities. To probe the nature of the transient oxidizing intermediates in the iron porphyrin-catalyzed oxidations with $PhI(OAc)_2$, the well-known iron(IV)-oxo porphyrin radical cations containig different axial ligands, i.e. $O=Fe^{IV}(X)TMP^{\cdot+}$ (X = Cl^-, ClO_4^-, ClO_3^-, NO_3^-, NO_2^-, and BrO_3^-) were generated with the mild sacrificial oxygen source, namely $PhI(OAc)_2$, as shown in scheme 5. To the best of our knowledge, using $PhI(OAc)_2$ for the generation of iron(IV)-oxo porphyrin radical cations is unprecedented.

The iron(IV)-oxo porphyrin radical cations were of different forms: iron(IV)-oxo tetramesitylporphyrin radical cation perchlorate [$O=Fe^{IV}(ClO_4)TMP^{\cdot+}$], iron(IV)-oxo tetramesitylporphyrin chloride [$O=Fe^{IV}(Cl)TMP^{\cdot+}$], iron(IV)-oxo tetramesitylporphyrin

radical cation chlorate[$O=Fe^{IV}(ClO_3)TMP^{\cdot+}$] , iron(IV)-oxo tetramesitylporphyrin radical cation nitrate [$O=Fe^{IV}(NO_3)TMP^{\cdot+}$], iron(IV)-oxo tetramesitylporphyrin radical cation nitrite [$O=Fe^{IV}(NO_2)TMP^{\cdot+}$], and iron(IV)-oxo tetramesitylporphyrin radical cation bromate [$O=Fe^{IV}(BrO_3)TMP^{\cdot+}$]. Compared to the corresponding iron(III) precursors, these Compound I analogs show a characteristic weaker Soret band and broader Q band.



Scheme 5. Chemical generation of iron(IV)-oxo tetramesitylporphyrin radical cations with $PhI(OAc)_2$

4.2 Time-Resolved Spectra for the chemical formation of O=FeIV(X)TMP·+

$Fe^{IV}(O)TMP^{\cdot+}$ with different axial ligands were prepared by reaction of the corresponding $Fe^{III}TMP$ salts with 20-50 equivalents of $PhI(OAc)_2$ in CH_3CN solutions. Time-resolved spectra of $Fe^{IV}(O)TMP^{\cdot+}$ are shown in Figures 15, 16, 17, and 18. For the purpose of comparison, the conventional oxidant, i.e. meta-chloroperoxybenzoic acid (*m*-CPBA) was also used to generate the same Compound I analogue under similar conditions. $Fe^{IV}(O)TMP^{\cdot+}$ with axial ligands (Cl^-, ClO_4^-, and ClO_3^-) were generated with $PhI(OAc)_2$ and with *m*-CPBA consistently showing a weaker Soret band and broader Q

band that are characteristic of Compound I (Figure 15, 16, and 17). Of note, $Fe^{IV}(O)TMP^{\cdot+}$ with NO_3 as the axial ligand was generated with 40 equivalent of *m*-CPBA over 80 seconds, but when $PhI(OAc)_2$ was used instead of *m*-CPBA we did not observe the formation of Compound I.

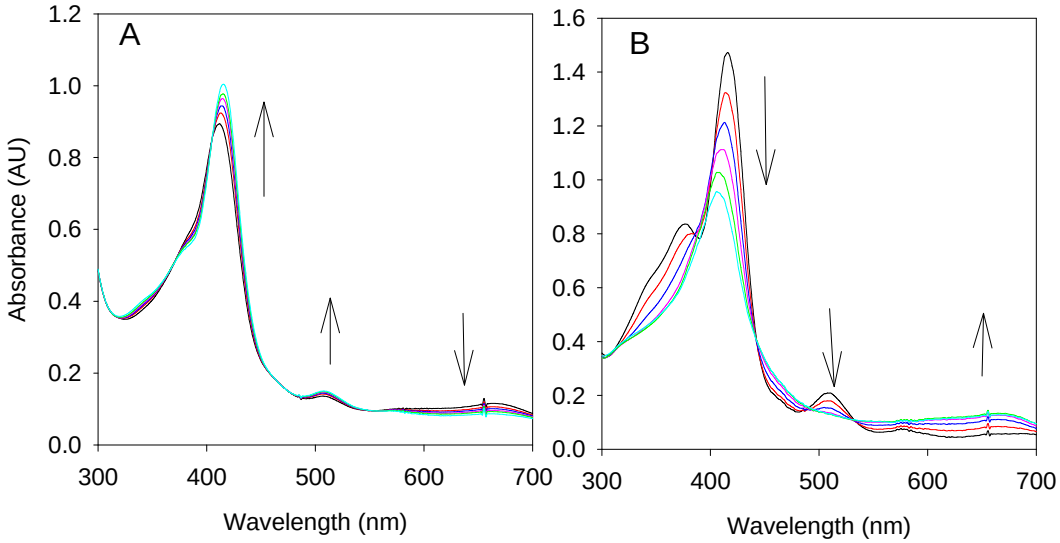


Figure 15. Time-resolved spectra of the generation of iron(IV)-oxo tetramesitylporphyrin radical cation chloride [$O=Fe^{IV}(Cl)TMP^{\cdot+}$] in CH_3CN. (A) 50 eq of $PhI(OAc)_2$ over 50 s; (B) 25 eq of *m*-CPBA over 80 s

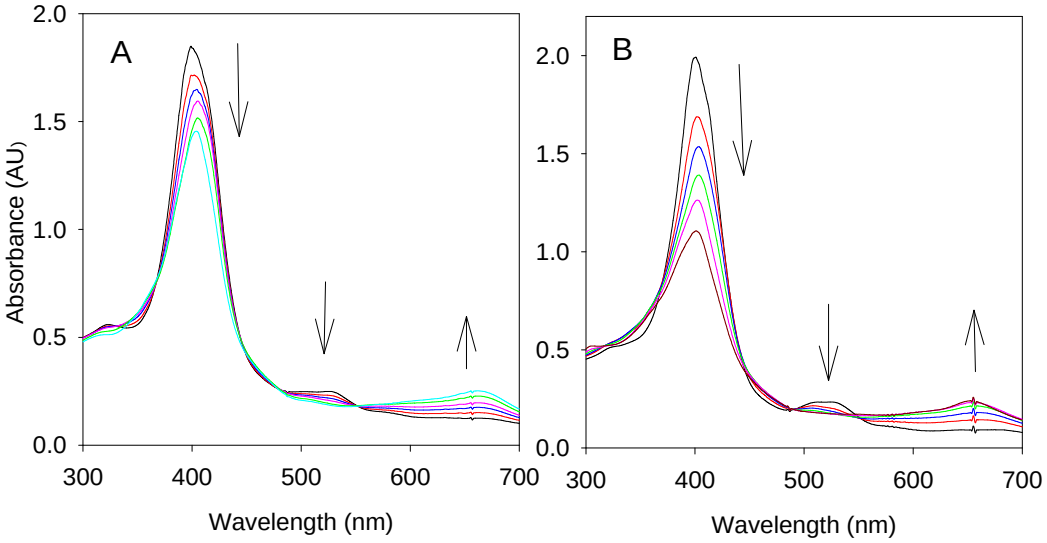


Figure 16. Time resolved spectra of the generation of iron(IV)-oxo tetramesitylporphyrin radical cation perchlorate [O=Fe^{IV}(ClO_4)$TMP^{\cdot+}$] in CH_3CN. (A) 25 eq of $PhI(OAc)_2$ over 300 s; (B) 25 eq of *m*-CPBA over 100 s.

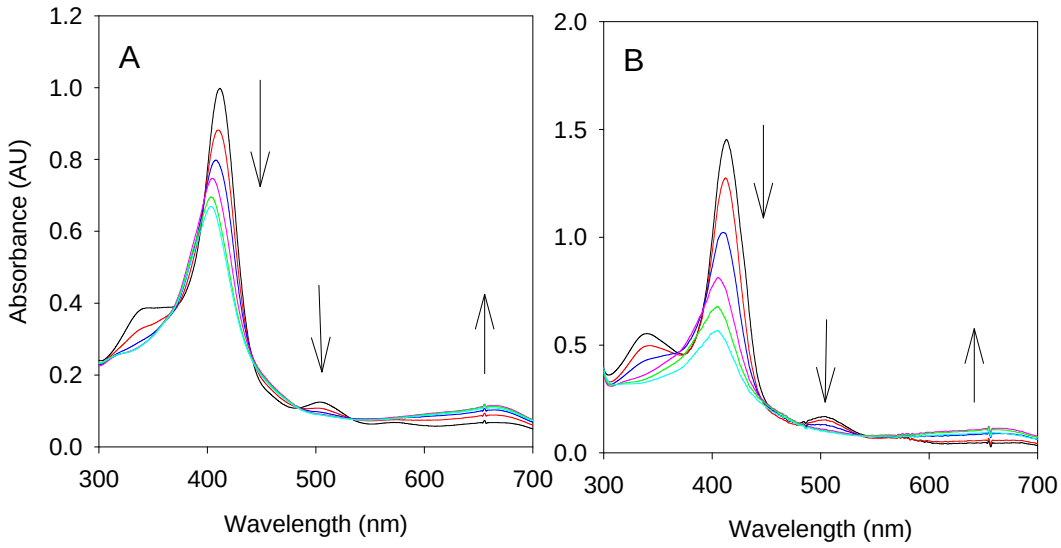


Figure 17. Time resolved spectra of the generation of iron(IV)-oxo tetramesitylporphyrin radical cation chlorate [O=Fe^{IV}(ClO_3)$TMP^{\cdot+}$] in CH_3CN. (A) 50 eq of $PhI(OAc)_2$ over 600 s; (B) 25 eq of *m*-CPBA over 70 s.

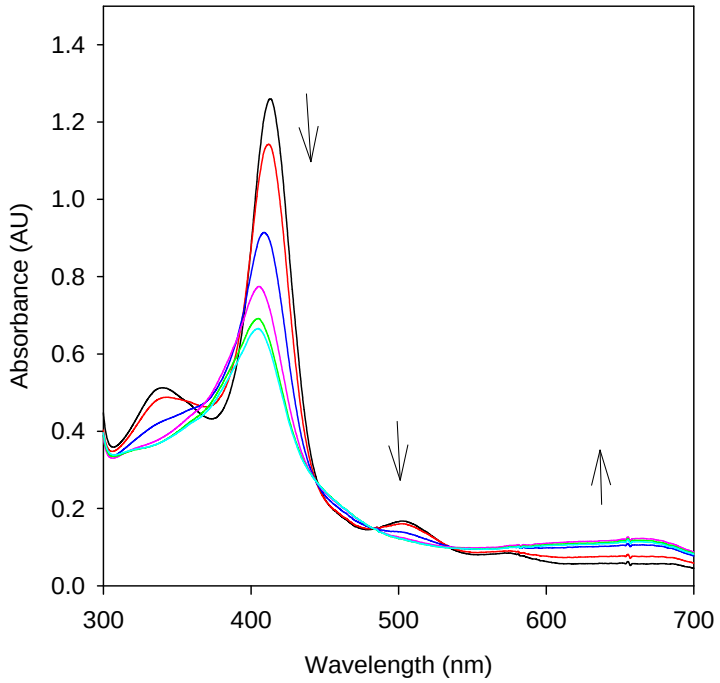
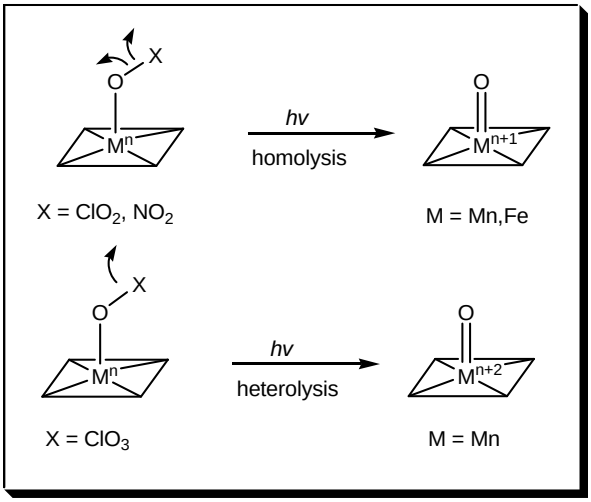


Figure 18. Time-resolved spectra of the generation of iron(IV)-oxo tetramesitylporphyrin nitrate [O=$Fe^{IV}(NO_3)TMP^{\cdot+}$]in CH_3CN with 40 eq of *m*-CPBA over 80 s.

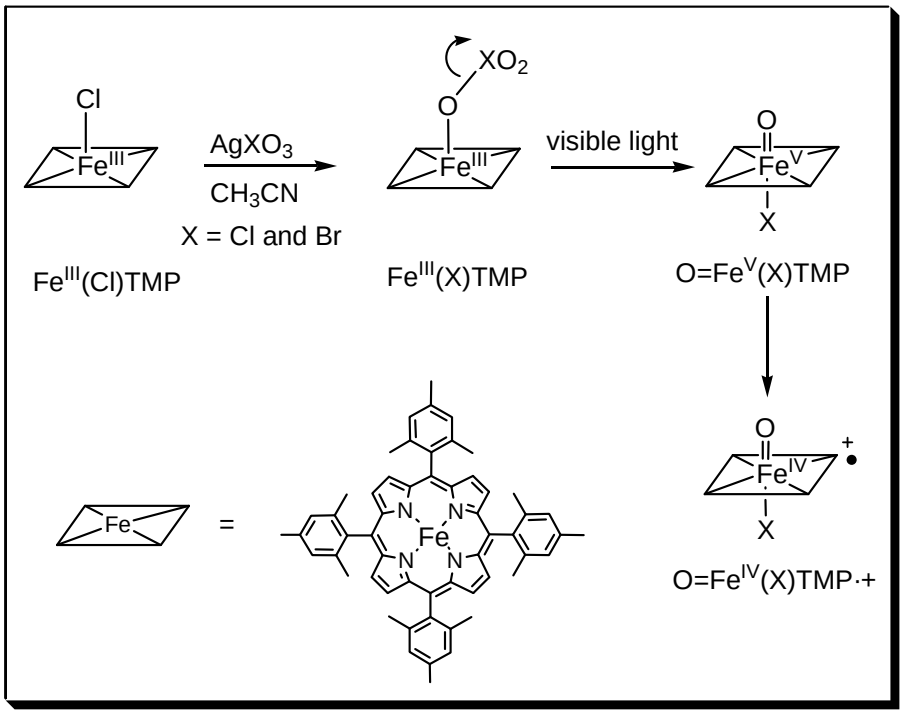
4.3 Photochemical Generation of Iron(IV)-oxo porphyrin radical cations

Recently, photo-induced ligand cleavage reactions have been developed to generate a variety of metal-oxo species.[30,31] The concept of photo-induced ligand cleavage reactions is very straightforward, as illustrated in Scheme 6. The precursors are metal complexes with the metal in the oxidation state and an oxygen-containing ligand such as perchlorate, chlorate, or nitrate. Photolysis can result in homolytic cleavage of the O–X bond in the ligand to give an (n + 1) oxidation state metal-oxo species (one electron photo-oxidation) or heterolytic cleavage of the O–X bond in the ligand to give an (n + 2) oxidation state metal-oxo species (two electron photo-oxidation).



Scheme 6 . Photochemical generation of high-valent metal-oxo species by photo-induced ligand cleavage reactions

In this work, a new photochemical method that led to generation of the iron(IV)-oxo porphyrin radical cations was successfully developed. The new photo protocol is shown in Scheme 7. Iron(IV)-oxo porphyrin complexes can be generated by irradiation of iron(III) porphyrin chlorate or bromate complexes that result in heterolytic cleavage of the O-X bond in the axial ligand as shown in Scheme 7.



Scheme 7. Photosynthesis of $O=Fe^{IV}(X)TMP^{\cdot+}$ by photo-induced ligand cleavage reactions

4.3.1 Photolysis of iron(III) porphyrin chlorate [$Fe^{III}(ClO_3)TMP$]

Exchange of the counterion Cl in $Fe^{III}(Cl)TMP$ with $AgClO_3$ readily gave the corresponding photo-labile chlorate salt, i.e. $Fe^{III}(ClO_3)TMP$ which was subsequently used for photochemical reactions. Irradiation of $Fe^{III}(ClO_3)TMP$ in anaerobic CH_3CN with visible light from tungsten lamp (100W) resulted in a heterolytic cleavage of O-Cl bond in the axail ligand to generate $O=Fe^{IV}(Cl)TMP^{\cdot+}$. In Figure 19, the chlorate precursor was decayed and a new species was formed displaying a weaker Soret band at (400 nm) and broader Q band at (650 nm) that is characteristic for $O=Fe^{IV}(Cl)TMP^{\cdot+}$.

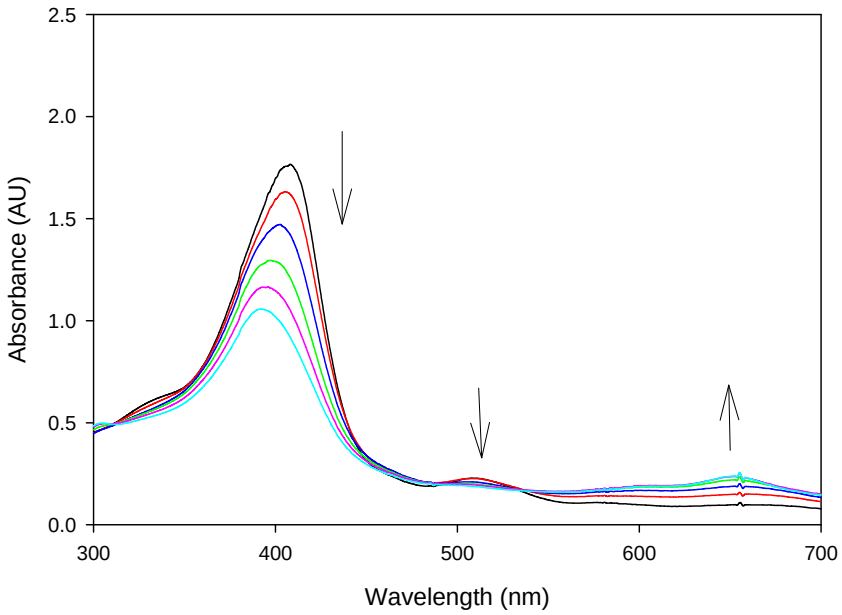


Figure 19. UV-vis specral change of $Fe^{III}(ClO_3)TMP$ upon irradiation with a 100W tungsten lamp in anaerobic CH_3CN solution over 50 min.

4.3.2 Photolysis of iron(III) porphyrin bromate [$Fe^{III}(BrO_3)TMP$]

In a fashion similar to that describe for $Fe^{III}(ClO_3)TMP$, irradiation of $Fe^{III}(BrO_3)TMP$ complex was also possible, to produce $O=Fe^{IV}(Br)TMP^{\cdot+}$ in anaerobic CH_3CN with visible light from a tungsten lamp (100W). The photolysis also gave a heterolytic cleavage of O-Br bond in the axial ligand. In the time-resolved spectra of Figure 20, $Fe^{III}(BrO_3)TMP$ was decayed to form a new spaecies with weaker Soret band at (400 nm) and broader Q band at (650 nm), which are characteristics of $O=Fe^{IV}(Br)TMP^{\cdot+}$ Figure 20. Under similar conditions, irradiation of iron(III) porphyrin perchlorate $Fe^{III}(ClO_4)TMP$ and iron(III) porphyrin nitrate $Fe^{III}(NO_3)TMP$ did not generate any metal-oxo species.

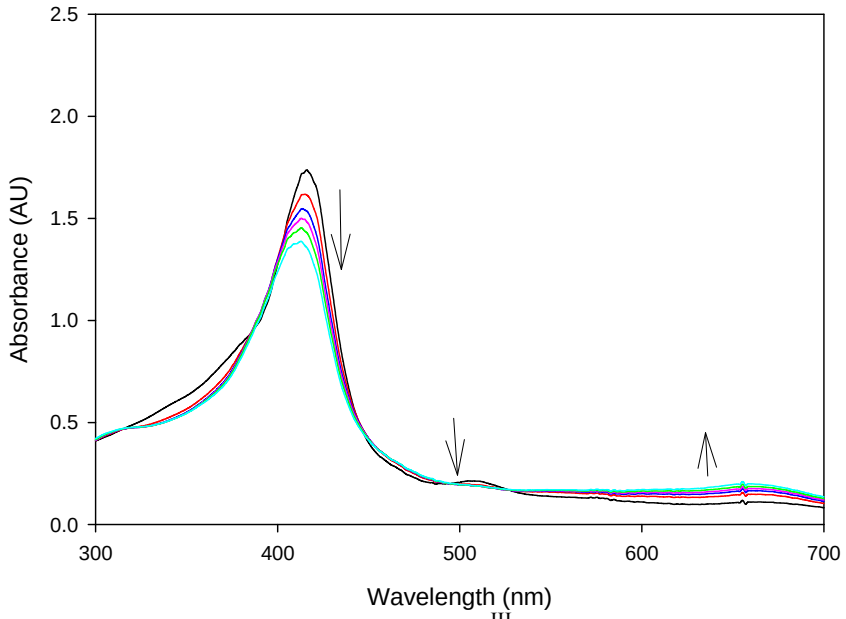


Figure 20. UV-vis specral change of $Fe^{III}(BrO_3)TMP$ upon irradiation with a 100W tungsten lamp in anaerobic CH_3CN solution over 10 min.

In conclusion, we have developed a new preparation of iron(IV)-oxo porphyrin radical cations through a photochemical approach. With this method, we have produced the iron(IV-oxo porphyrin radical cations by photolysis of the corresponding iron(III) chlorate or bromate precursors with visible light. The characteristic UV-vis spectral features of the formed $O=Fe^{IV}(X)TMP^{\cdot+}$ (X= Cl, Br) are matching those reported.

CHAPTER 5

CONCLUSION

The sterically hindered macrocyclic compound 5,10,15,20-tetramesitylporphyrin (H_2TMP) and its iron(III) complexes were successfully synthesized and spectroscopically characterized in accordance to the literature known methods. All the characterization data including UV-vis and ^{1}H-NMR are matching literature values.

Catalytic oxidation of organic sulfides by a series of iron(III) porphyrin complexes was studied with $PhI(OAc)_2$ as mild oxygen source. $PhI(OAc)_2$, which is soluble in organic solvents, safe to use and readily available is an efficient oxygen source in iron(III) porphyrin-catalyzed oxidation of sulfides to sulfoxides. Different factors including solvent effect, catalyst amount, axial ligands of the catalytic and substrate scope that effect the catalyst oxidation reactions have been evaluated to identify the optimal conditions. The sulfoxidation was found to proceed very rapidly in the presence of small amounts of H_2O (4.5 μL) and 100% conversion was obtained within 60 min. Under optimized conditions, excellent substrate conversions (up to 100%) as well as product selectivies (sulfoxide:sulfone > 95:5) were obtained.

To understand the mechanism of above catalytic oxidations, the proposed iron(IV)-oxo porphyrin radical cations were chemically generated of different forms: iron(IV)-oxo tetramesitylporphyrin radical cation perchlorate [$O=Fe^{IV}(ClO_4)TMP^{\cdot+}$], iron(IV)-oxo tetramesitylporphyrin radical cation chloride [$O=Fe^{IV}(Cl)TMP^{\cdot+}$], iron(IV)-oxo tetramesitylporphyrin radical cation chlorate [$O=Fe^{IV}(ClO_3)TMP^{\cdot+}$], and iron(IV)-oxo tetramesitylporphyrin radical cation nitrate [$O=Fe^{IV}(NO_3)TMP^{\cdot+}$] with 20 to 50

equivalents of $PhI(OAc)_2$ or *m*-CPBA. All these oxidizing species show weaker Soret band and broader Q band. Notably, a new photochemical approach to generate iron(IV)-oxo porphyrin radical cations is discovered by photolysis of iron(III) chlorate or bromate precursors with visible light that result in heterolytic cleavage of the O-X bond in the axial ligand.

REFERENCES

1. Backwell, J.-E.; Piera J . Catalytic oxidation of organic substrates by molecularoxygen and hydrogen peroxide by multistep electron transfer – A biomimetic approach. *Angew. Chem. Int. Ed*. **2008,** *47*, 3506-3523.
2. Brink, G. J.; Arends, I. W. C. E.; Sheldon, R. A. Green, catalytic oxidation of alcohols in water. Science **2000** , *287* , 1636-1639
3. Denisov, I. G.; Makris, T. M.; Sligar, S. G.; Schlichting, I., Structure and chemistry of cytochrome P 450. *Chem. Rev.* **2005,** *105*, 2253-2277.
4. Zhang, R. "Asymmetric organic oxidation by chiral ruthenium complexes containing D2- and D4- symmetric porphyrinato ligands." *Ph. D. Thesis* **2000,** 1-235.
5. Sheldon, R.A.; Dekker, M. “Metalloprophyrins in Catalytic Oxidations” *New York*, **1994.**
6. Punniyamurthy, T.; Velusamy, S.; Iqbal. “Recent Advances in Transition Metal Catalyzed Oxidation of Organic Substrates with Molecular Oxygen”*J. Chem. Rev*. **2005**, *105*, 2329-2363.
7. Meunier, B. Metal-oxo and metal-peroxo species in catalytic oxidations. Academic Press: New York, 2000.
8. Masanori, M.; Roach, M. P.; Coulter, E. D.; Dawson, J. H., Heme-Containing Oxygenases. *Chem. Rev.* **1996,** *96* , 2841-2887.
9. Ullrich, V., Cytochrome P450 and Biological hydroxylation Reaction. **1979**, *83*, 67-104.

10. Newcomb, M.; Zhang, R.; Chandrasena, E. P.; Halgrimson, J. A.; Horner, J. H.; Makris, M. T.; Sligar, S. G. Cytochrome P450 Compound I. *J. Am.Chem. Soc* . **2006**, *128*, 4580-4581
11. Hamilton, G.A. *In molecular mechanisms of oxygen activation;* Hayaishi, O., Ed.; Academic: New York, **1974**; Chapter 10,405 - 451.
12. Meunier B. "Metalloporphyrins as versatile catalysts for oxidation reactions and oxidative DNA cleavage." *Chem. Rev.* **1992**, *92,* 1411-1456.
13. Zhang, R.; Nagraj, N.; Lansakara-P.,D.S.P.; Hager, L.-P.; Newcomb, M. "Kinetics of two-electron oxidation by the Compound I derivative of chloroperoxidase, a model for cytochrome P450 oxidants." *Org. Lett.* **2006,** *8*, 2731-2734.
14. Groves, J. T. "Reactivity and mechanism of metalloporphyrin-catalyzed oxidations." *J. Porph. Phthal*. **2000**, *4*, 350-352.
15. Abebrese, C.; Thompson, H. Y.; Pan, A.; Yuan, Z. B.; Zhang, R, Kinetic studies of oxygen atom transfer from *trans*-dioxoruthenium(VI) porphyrins to sulfides. *J. Inorg. Chem.* **2011,** *105*, 1555-1561.
16. Davies, J., *Selective hydrocarbon activation: Principle and progress.* VCH: New York, **1994**.
17. Simandi, L. "Dioxygen activation and homogeneous catalytic oxidation."*Elsevier: Amsterdam*, **1991**.
18. Wang, C.; Shalyaev, K.V.; Bonchio, M.; Carofiglio, T.; Groves, J.T. "Fast catalytic hydroxylation of hydrocarbons with ruthenium porphyrins." *Inorg.Chem.* **2006**, *45*, 4769-4782.

19. Che, C.-M.; Zhang, R.; Yu, W.-Y. "Catalytic enantioselective oxidation of aromatic hydrocarbons with D4-symmetric chiral ruthenium porphyrin catalysts."*Tetrahedron: Asymmetry* **2005**, *16*, 3520-3526.
20. Kowalski, P.; Mitka, K.; Ossowska, K.; Kolarska, Z. Oxidation of sulfides to sulfoxides. Part1: Oxidation using halogens derivatives. *Tetrahedron* **2005,** *61*, 1933-1953.
21. Nehlsen, J. P.; Benziger, J. B.; Kevrekidis, I. G., Removal of alkanethiols from a hydrocarbon mixture by a heterogeneous reaction with metal oxides. *Ind. Eng.Chem. Res.* **2003,** *42*, 6919-6923.
22. Surendra, K.; Krishnaveni, N.S.; Kumar, V.P.; Sridhar, R.; Rao, K.R. 2005 , Selective and efficient oxidation of sulfides to sulfoxides with N-bromosuccinimide in the presence of β-cyclodextrin in water. *Tetrahedron lett.* **2005,** *46*, 4581-4583.
23. Chellamani, A.; Alhaji, N.M.I.; Rajagopal, S, Kinetics and mechanism of (salen)Mn(III)-catalyzed hydrogen peroxide oxidation of alkyl aryl sulphides. *J. Phys. Org. Chem.* **2007,** *20*, 255-263.
24. Golchoubian, H. Hosseinpoor, F., Mn(III)-catalyzed oxidation of sulfides to sulfoxides with hydrogen peroxides. *Tetrahedron lett.* **2006,** *47*, 5195-5197.
25. Lindsey, J.; Wagner, R. D. Investigation of the synthesis of ortho-substituted tetraphenylporphyrins. *J. Org. Chem.* **1989,** *54*, 828-836.
26. Zhen, L.; Xie, C.; Ji, M., Manganeseporphyrin-catalyzed alkenes epoxidation by iodobenzene diacetate in a room temperature ionic liquid. *Inorg. Chem. Acta*. **2003**, *343*, 373-376

27. Harischandra, D. N.; Zhang, R.; Newcomb, M., Photochemical Generation of a Highly Reactive Iron-Oxo Intermediate. A True Iron(V)-Oxo Species? *J. Am. Chem. Soc.* **2005,** *127*, 13776-13777.

28. Pan, Z.; Zhang, R.; Newcomb, M., Kinetic studies of reactions of iron(IV)-oxoporphyrin radical cations with organic reductants. *J. Inorg. Biochem.* **2006,** *100*, 524-532.

29. Vanover, E.; Huang, Y; Xu, L.-B.; Newcomb, M.; Zhang, R. "Photocatalytic aerobic oxidation by a bis-porphyrin-ruthenium(VI) p-oxo dimer: observation of a putative porphyrin-ruthenium(V)-oxo intermediate." *Org. Lett.* **2010,** 12, 2246 - 2249.

30. Suslick, K.S.; Watson, R.A. "Photochemical reduction of nitrate and nitrite by manganese and iron porphyrins." *Inorg. Chem*. **1991**, *30*, 912.

31. Zhang, R.; Newcomb, M. "Laser Flash Photolysis Generation of High-Valent Transition Metal-Oxo Species: Insights from Kinetic Studies in Real Time." *Acc. Chem. Res*. **2008**, *41*, 468-477.

ABBREVIATIONS AND SYMBOLS

$BF_3.(OEt_2)$	Boron trifluoride diethyl etherate
CYP450	Cytochrome P450
$CYP450_{cam}$	Cytochrome $P450_{cam}$
DDQ	2,3-Dichloro-5,6-dicyano-*p*-benzequinone
DMF	*N,N*-Dimethylformamide
$Fe^{III}(Cl)TMP$	Iron(III) tetramesitylporphyrin chloride
$Fe^{III}(ClO_4)TMP$	Iron(III) tetramesitylporphyrin perchlorate
$Fe^{III}(ClO_3)TMP$	Iron(III) tetramesitylporphyrin chlorate
$Fe^{III}(NO_3)TMP$	Iron(III) tetramesitylporphyrin nitrate
$Fe^{III}(NO_2)TMP$	Iron(III) tetramesitylporphyrin nitrite
$Fe^{III}(BrO_3)TMP$	Iron(III) tetramesitylporphyrin bromate
^{1}H-NMR	Pronton nuclear magnetic resonance
H_2TMP	*meso*-tetramesitylporphyrin
m-CPBA	*meta*-Chloroperoxybenzoic acid
$O=Fe^{IV}(Cl)TMP^{\cdot+}$	Iron(IV)-oxo tetramesitylporphyrin radical cation chloride
$O=Fe^{IV}(ClO_4)TMP^{\cdot+}$	Iron(IV)-oxo tetramesitylporphyrin radical cation perchlorate
$O=Fe^{IV}(ClO_3)TMP^{\cdot+}$	Iron(IV)-oxo tetramesitylporphyrin radical cation chlorate
$O=Fe^{IV}(NO_3)TMP^{\cdot+}$	Iron(IV)-oxo tetramesitylporphyrin radical cation nitrate
$O=Fe^{IV}(NO_2)TMP^{\cdot+}$	Iron(IV)-oxo tetramesitylporphyrin radical cation nitrite

$O{=}Fe^{IV}(BrO_3)TMP^{\cdot+}$	Iron(IV)-oxo tetramesitylporphyrin radical cation bromate
$PhI(OAc)_2$	Iodobenzene diacetate
UV-vis	Ultraviolet-visible