Chapter 1

A General Introduction to Bioinspired High Valent Metal Complexes

1.1 Introduction

In nature, metalloenzymes carry out a wide range of biological and chemical reactions such as oxygen transport, radical formation, redox reactions, rearrangements, signal transduction proteins, storage and transport of proteins.[1] Metalloenzyme such as oxalate oxidase, catalase, superoxide dismutase, cytochrome P450, Rieske dioxygenases involves manganese/iron-peroxo.[2–7] While isopenicillin, cysteine dioxygenases, peptidylglycine-α-amidating monooxygenase, and dopamine β-monooxygenase have iron/copper-superoxo[8–13] as reactive intermediates, by the help of these intermediates many reactions are carried out such as hydroxylation, epoxidation, halogenation, and N-dealkylation.[14] High valent metal-oxo species are involved in oxidation reactions occurring in heme and non-heme iron systems and also in water oxidation in photosystem-II.[14-28]

Metalloenzymes are involved in dioxygen activation to form metal-oxygen intermediates, and these act as a reactive intermediate in metal-mediated catalytic transformation in biological and industrial processes.[14,29–32] Cytochrome P450 is a heme enzyme; it plays an important role in natural product biosynthesis, degradation of xenobiotics, steroid biosynthesis, and drug metabolism. In the liver of the human body, cytochrome P450 is involved in metabolism of xenobiotics and also involved in synthesis of estrogen and other hormones.[15-20] It is an important biocatalyst in nature because of substrate structure and it catalyzes many regio and stereo selective reactions such as hydroxylation, epoxidation, nitration, C-C bond coupling, or cleavage.[33,34] Side-on manganese(III)-peroxo intermediate is involved in catalytic cycles of a biological system such as photosystem-II and superoxide dismutase.[35–37] In photosystem-II manganese(III)-peroxo catalyze photolysis of water and produce molecular oxygen and in SOD these are involved in the biodegradation of toxic superoxide and lead to the formation of hydrogen peroxide and water. In a catalytic cycle of Rieske dioxygenase, a non-heme iron(V)-oxo intermediate is also an important reactive intermediate, and catalyzes many

reactions such as *cis*-dihydroxylations, O/N-demethylations, and C-C bond formation.[31,38–41] Binuclear, non-heme iron enzymes carry out many reactions by dioxygen activation, most-studied enzymes such as RNR1[42] (ribonucleotide reductase) which initiates radical chemistry to generate DNA building blocks, methane monooxygenase[43] and helps in the hydroxylation of methane to methanol. Desaturase[44] inserts a double bond into fatty acids to produce lipid precursors. Many metal ions such as Mg, Mn, Fe, Co, Ni, Cu, and Zn are involved as a reactive intermediate in the hydrolysis process, radical-based rearrangement, electron transfer reactions, oxidation-reduction process, and DNA processing.[8,33,35]

These intermediates are short-lived and experimental evidence are available for their existence. For understanding the catalytic mechanism of these enzymes there is a requirement for the development of synthetic model complexes that mimic their catalytic activity and also investigate electronic structures, and mechanistic pathways.[45-61] In biological studies, bioinorganic chemists are dedicated to develope biomimetic model complexes which mimic the reactivity of many catalytic reactions. All these provide a deeper insight into structures and mechanistic details of metalloenzymes under analysis.

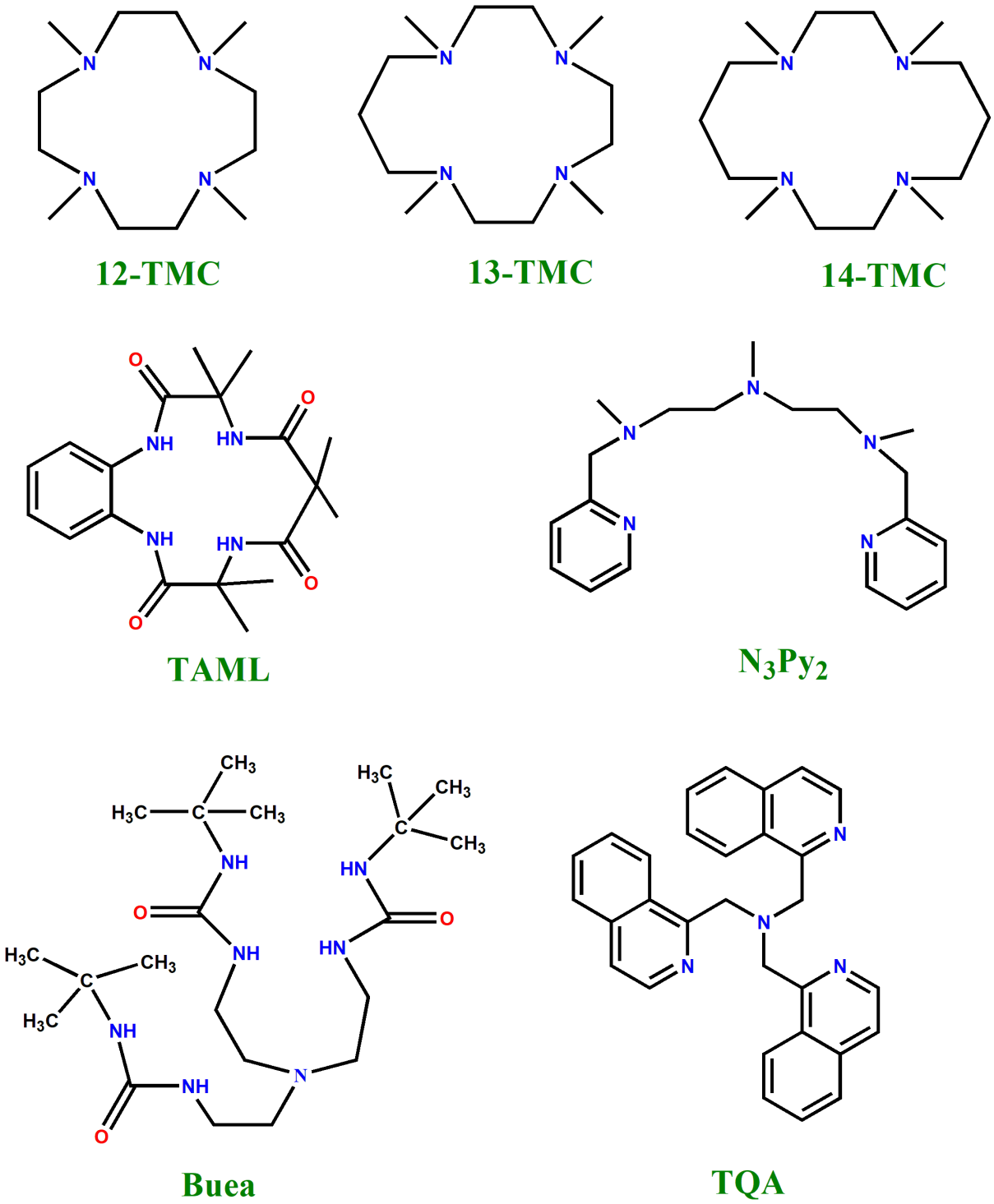
1.2 Biomimetic Catalysts

Chemical catalysis that mimics certain key characteristics of enzymatic systems are known as "biomimetic catalysis".[62] In bioinorganic chemistry, structure of active sites, reactive intermediates, mechanism of dioxygen activation, oxygenation reactions occurring at the active site, and factors that affect catalytic transformation reactions are studied.[14,63] Natural phenomena and reactive nature of intermediates involved in reactions such as water splitting, biosynthesis of DNA, organic hydroperoxides[64,65] cyt P450 and Rieske dioxygenase enzymes[66,67] have inspired scientist to develop synthetic biomimetic models which help us in understanding the nature of active sites and mechanism of catalytic intermediates of these

important enzymes and proteins. The catalytic mechanism of these enzymes can be investigated by the development of a synthetic biomimetic model studying the structural, electronic, and mechanistic pathways.[43-59] Several attempts have been undertaken towards the development of synthetic complexes.[50-57]

Fortunately, several biomimetic complexes have been synthesized and characterized. Some of the representative ligands which are functional models of mononuclear non-heme enzymes are given in Scheme 1.1. "Biomimetic catalysis" refers to chemical catalysis that mimics the main key features of enzymatic systems.[68–72] Theoretical studies help to understand the electronic structures of biomimetic complex and mechanism of metal-mediated catalytic transformation reactions and can tune the reactivity and product selectivity of dioxygen activation which can be governed by the interaction between metal and substrate. Understanding the mechanism of C-H/O-H bond activation remains a key consideration, and computational modeling provides insight into the process. Computational modeling of mechanism pathway provides characteristics of the transition state (TS) and intermediate on potential energy surface. It provides the assessment of energy barrier ($E^{\#}$) and activation barriers ($G^{\#}$). Transition state determination provides a better understanding of the reaction mechanism and suggests rate-limiting steps and provides insight into the reaction mechanism. Many reaction cycles have been proposed based on transition state and understanding of mechanism provides helps to generate new reaction conditions and reagents. The electronic structure of transition states facilitates the characterization of reaction mechanisms in terms of bonds that are broken and which are formed.

Understanding of the biomimetic system not only enhances scientific knowledge but also broadens the scope of cheap, efficient, selective, and environment friendly oxygenation catalysts.



Scheme 1.1. Representative examples of ligands employed in biomimetic non-heme model complexes.

Where, 12-TMC= 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclododecane, 13-TMC= 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclotridecane; 14-TMC=1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane, TAML= tetramidomacrocyclic ligand, N_3Py_2= N,N′-dimethyl-N-(2-(methyl(pyridin-2-ylmethyl)-amino)ethyl)-N′-(pyridin-2-ylmethyl-)ethane-1,2-diamine,

buea=tris[(N'-tert-butylureayl)-N-ethyl]-(6-pivalamido-2-pyridylmethyl)aminato], TQA=tris(2-quinolylmethyl)amine.

Biomimetic chemistry covers the synthesis and study of artificial enzymes. Metal-superoxo/peroxo/hydroperoxo/oxo species have been synthesized and these acts as, a reactive intermediate in metal-mediated catalytic transformation and industrial processes.

1.3 Metal-Superoxo

Metal-superoxo/peroxo are involved as an important intermediate in dioxygen (O_2) activation by enzymes and metal-containing proteins, and dioxygen formation by photosystem-II.[9,31,54] In Rieske dioxygenases iron-peroxo is proposed as an active intermediate, which carries *cis*-dihydroxylation of aromatic compound whereas manganese-peroxo helps water oxidation in photosystem-II.[39,40,60,73] Metal-superoxo species are also reactive intermediates in enzymatic reactions, like non-heme iron enzymes such as isopenicillin N synthase, 2,3-dioxygenase, myo-inositol oxygenase, homoprotocatechuate, and cysteine dioxygenase along with copper-containing enzymes peptidylglycine-α-amidating monooxygenase and dopamine β-monooxygenase.[8–12,74] Iron(III)-hydroperoxo species is involved as a key intermediate and involved in the catalytic cycle of bleomycin and Rieske dioxygenase.[75–79] Metal-superoxo species have gained more attention as iron(III)/copper(II)-superoxo, are active oxidants in hydrogen atom abstraction reactions.[8,10-12,74] Dioxygen binding metal-complexes such as superoxo (η^1; end on) and peroxo (η^2; side on) have been synthesized with the help of X-ray crystallography and several spectroscopic techniques binding nature of dioxygen and nature of metal ions have been intensively investigated.[39,60,80–85] Metal-superoxo species carried out wide range of chemical reactions which play an important role in pharmaceutical industries and environmental applications.[60,82,86-100] Non-heme iron(III)-superoxo species, is also a

precursor of iron-oxo which is an oxidant in enzymatic reactions.[8,9,14,101] Both iron-oxo and iron-superoxo complexes are biologically important.[10-12] Many iron containing heme mononuclear enzymes use high-spin iron(II) ions and react with dioxygen (O_2) and form the iron(III)-superoxo species and they are converted to iron(III)-peroxo by one-electron reduction. In heme system, iron(III)-superoxo complexes were well characterized and their crystal structure was also studied.[102,103] Nam *et al.*[97,104,105] proposed iron(III)-superoxo as a short-lived 'putative' intermediate during dioxygen activation by non-heme iron(II) complexes, while Goldberg *et al.*[105] proposed that iron(III)-superoxo species formation is ease by sulfur ligand at the axial position of iron(II) complex. Evidence for the existence of side-on manganese(III)-peroxo species are also found as a reactive intermediate in biological catalytic cycle for example in photosystem-II and superoxide dismutase.[35–37]

Inspired by these natural processes, for understanding the catalytic intermediates involved in proteins and enzymes, synthetic biomimetic models have been developed. Iron(III)-superoxo complex with TAML (tetramido macrocyclic ligand) is reported, and it is characterized as side on (η^2) iron(III)-superoxo complex, both structurally and spectroscopically,[106] $[(TAML)Fe^{III}(O_2)]^{2-}$. Bakac and co-workers reported mononuclear chromium(III)-superoxo complex as chemical models in dioxygen activating metalloenzymes and acts as a reactive intermediate in the oxidation of substrates.[107,108] Chromium(III)-superoxo complex, $[Cr^{III}(O_2)(TMC)(Cl)]^+$ has been reported and characterized by X-ray and spectroscopic studies along with C-H bond activation.[109-111] A rare thiolate-ligated cobalt-superoxo species $Co(O_2)$ has been synthesized and characterized by spectroscopic techniques.[112] Cu(II)-superoxo is also synthesized and also participitate in C-H/O-H bond activation.[94,113–115] Formation of nickel(III)-peroxo is characterized by UV-vis, electrospray ionization mass spectrometry, resonance Raman, electron paramagnetic resonance and X-ray analysis.[116] In literature studies, it is found that supporting ligands also play an important role in tuning the

geometric and electronic structures, stabilities, and reactivities of oxygen-coordinating metal complexes. One notable example among such types of ligands is N-tetramethylated cyclam (TMC) and its derivatives.[117] It has been proved as an accomplished ligand in the biomimetic chemistry of dioxygen activation by metal complexes.

First row-transition metal-peroxo/superoxo (TMC) complexes have been synthesized and they are involved in many oxidation reactions.[109,118–128] It is also found that the nature of metal ions and the size of the TMC ring alter the electronic structure of $[M(n\text{-}TMC)(O_2)]^{n+}$ complexes.

1.4 Effect of Ligands

Dioxygen reacts with the metal to form either metal-superoxo or metal-peroxo species. From the literature studies, it is found that some metals form superoxo species or some forms peroxo species. As $[Cr^{II}(14\text{-}TMC)(Cl)]^+$ reacts with dioxygen (O_2) or H_2O_2 in the presence of a base such as triethylamine (TEA) or tetramethylammonium hydroxide (TMAH) to form $[Cr^{III}(14\text{-}TMC)(O_2)(Cl)]^+$ species and it is characterized by spectroscopic methods. Single crystal structure of $[Cr^{III}(14\text{-}TMC)(O_2)(Cl)]^+$ revealed that mononuclear end-on chromium-superoxo complex is distorted octahedral geometry, in which N-methyl groups of 14-TMC are oriented anti to the superoxo moiety and syn to chlorine ligand.[109-111] By substiting methylamino at pyridine ring of PDP ligand (2-((R)-2-[(R)-1-(pyridine-2-ylmethyl)pyrrolidin-2-yl]pyrrolidin-1-ylmethyl) pyridine) the catalytic reactivity, enantioselectivity towards asymmetric epoxidation increases.[129]

Spin state of complex is affected by ligand, for it consider octahedral iron(IV)-oxo complex, where spin state of complex is determined by the energy gap between orbitals d_{xy} and $d_{x^2-y^2}$.[130] This energy gap is larger than the spin-pairing energy, then S=1 complex is formed, and

if the equatorial ligand is weak then it will give S=2 complex.[131] From ortho hydroxylation of aromatic compounds with $[Fe^{II}(BPMEN)(CH_3CN)_2]^{2+}$ and $[Fe^{II}(TPA)(CH_3CN)_2]^{2+}$ (where TPA = tris(2-pyridylmethyl)amine and BPMEN = N,N'-dimethyl-N,N'-bis(2-pyridylmethyl)ethane-1,2-diamine), it is found that complex $[Fe^{II}(BPMEN)(CH_3CN)_2]^{2+}$ is more reactive than the $[Fe^{II}(TPA)(CH_3CN)_2]^{2+}$, and it because of ligand design as in complex $[Fe^{II}(TPA)(CH_3CN)_2]^{2+}$ pyridine ring is parallel to Fe(V)=O bond that is formed during reaction by which it mix with the $\pi_{Fedxy\text{-}Opy}$ which in turn reduces the electrophilicity of ferryl oxygen atom, whereas in $[Fe^{II}(BPMEN)(CH_3CN)_2]^{2+}$ pyridine ring is perpendicular to the Fe(V)=O bond.[132] For adopting the trigonal bipyramidal geometry d_{xy} and $d_{x^2\text{-}y^2}$ orbital will be degenerate. Reactivity of cobalt(III)-nitrosyl complexes bearing TMC ligands are studied in NO-transfer and deoxygenation reactions are significantly influenced by the spin state of cobalt(II) center, caused by ring size of TMC ligands.[124,133-135] From earlier studies, it is also found that non-heme iron(IV)-oxo complexes with smaller TMC ligand it is more reactive in both the HAT and OAT reactions.[136]

1.5 Formation of High Valent Metal-oxo Species

Transition metals in higher oxidation states either co-ordinates to oxygen or nitrogen by multiple bonds to form high valent metal-oxo or imido complexes. Metal-oxo are involved as active intermediates in the catalytic cycles of enzymes and biomimetic compounds to carry out oxidation reactions of organic substrates and water.[14,22,66,137–139] These also help in C-H/N-H/O-H bond activation and oxygen atom transfer reactions, mediated by a biological and chemical catalysts[14,32,43,60,140–153] and also play a very important role in pharmaceutical industries. Studies of high valent metal centers have been a subject of great interest because of their biological relevance and help to understand the structural and spectroscopic properties of metal-containing enzymes. Modeling active sites of enzymatic systems and

developing biomimetic alkane hydroxylation catalysts have become important and emerged as a vast area.[146-153]

Mononuclear heme and non-heme enzymes have metal ions at active sites. Metal ions bind with dioxygen, to produce metal-superoxo species, and by one-electron reduction, it gets converted to metal-peroxo species, and protonation of peroxo species results in the formation of hydroperoxo species. Alternatively, superoxo species can be directly converted to hydroperoxo species by abstracting hydrogen atoms. This direct conversion occurs only in non-heme iron enzymes. Heterolytic O---O bond cleavage in hydroperoxo species produce metal(V)-oxo species[66] whereas homolytic O---O bond cleavage produces high valent metal(IV)-oxo species. In the non-heme system metal(III)-hydroperoxo species gets converted to metal(II)-hydroperoxo species by one-electron reduction and then via heterolytic O---O bond cleavage it gets converted to metal(IV)-oxo species.[9,88,154]

From the last decades, in biomimetic complexes, high valent metal-oxo species have been intensively studied and synthetic terminal high valent iron-oxo and manganese-oxo complexes have been reported.[155,156] Heme and non-heme iron enzymes, terminal as well as bridging high-valent iron-oxo are found as important oxidizing intermediates in activation of molecular oxygen and these have spectroscopically characterized and found to be responsible for a wide number of oxidative transformations such as, in catalytic cycles of monooxygenase heme enzymes e.g. cytochrome P450, catalase,[14,66,137] and peroxidase high valent iron(IV)-oxo π-cationic radical intermediate is involved is supported by spectroscopic evidence by UV-vis, EPR, and M*ö*ssbauer.[157] Iron(IV)-oxo carries aliphatic hydroxylation, substrate epoxidation, aromatic hydroxylation, desaturation, and heteroatom transfers such as sulfoxidation reactions.[158,159] The capacity of iron to exist in multiple redox states and its availability in abundance makes it one of the common transition metals acting as a key

intermediate in many biotransformation reactions, occurring via C-H/O-H bond activation, including biological O_2 activation.[32-37] The chief interest in high valent iron chemistry is due to its ubiquitous nature, low toxicity, inexpensive, and its ability to carry out green catalytic oxidations.[38-40] The first, biomimetic metalloporphyrins catalysts, high valent iron(IV)-oxo porphyrin π-radical intermediate was synthesized and characterized by Groves and co-workers in 1981.[144] [(TMP)Fe^{III}(Cl)] (TMP = meso-tetramesityl porphinate dianion) reacts *m*-chloroperbenzoic acid at -78˚C in a dichloromethane-methanol mixture, to produce a green colored species, which was spectroscopically characterized as iron(IV)-oxo coordinated with a porphyrin-π radical, $[(TMP)Fe^{IV}(O)(CH_3OH)]^+$. These species have the characteristic features of cpdI present in P450, and found that it is an olefin epoxidation and alkane hydroxylation.[142,143,145] After that many iron(IV)-oxo porphyrin π radicals having electron-rich and electron-deficient porphyrins with different axial ligands have been reported to make understanding of the effect of electronic effects of porphyrin and axial ligands. The first time, non-heme iron(IV)-oxo intermediate was reported in 2000, during the reaction of $[Fe^{III}$(cyclam-acetato)$(CF_3SO_3)]^+$ and O_3 in acetone and water at -80˚C, spectroscopically detected by Wieghardt and co-workers. M*ö*ssbauer analysis characterized it as an intermediate-spin Fe(IV)-oxo (S=1).[160] The First, well-characterized mononuclear $[Fe^{IV}(O)(TMC)(NCCH_3)]^{2+}$ was reported in 2003. It is characterized by many spectroscopic methods such as and features a short Fe=O bond distance of 1.646(3) Å.[161–163] Most of the synthetic non-heme iron(IV)-oxo complexes have a triplet spin state (S=1) as the ground state while a small number of complex have quintet spin state (S=2) as a ground state.[164-166] Along with Fe^{IV}=O species, Fe^{V}=O species also acts as a reactive intermediate in many biological reactions. First, iron(V)-oxo complex was reported with TAML ligand. First time, TAML ligand was characterized by the collines group in 2002. TAML systems have gained importance as green catalysts because the chemistry mimicking these system performances is

comparatively greener than the current technological chemistry based upon environment degrading chemicals.[43] Capacity of TAML to stabilize diverse iron-oxo species in the high valent state such as: iron(IV) complex in the high spin state (S=2), iron(IV) complexes in the intermediate spin state (S=1), diiron(IV) dimers having an oxo-bridge and iron(III) (TAML-radical-cation) complex in a singlet state (S=0) and Fe(V)-oxo has been reported.[50] Synthetic Fe(V)-oxo complex with the tetra-amido ligand is well characterized by spectroscopic techniques e.g. electronic, magnetic circular dichroism, Raman, electron paramagnetic resonance (EPR), and Mössbauer spectroscopy. It also acts as a reactive intermediate in selective hydroxylation of aliphatic compounds, and carries reactions such as C-H and C=C oxidation reactions. Many iron complexes carry out regio-selective hydroxylation reactions.[167] The first example, published by Que and co-workers is $[Fe^{II}(TPA)(CH3CN)_2]^{2+}$ (TPA = tris(2-pyridylmethyl)amine) and it is capable of performing stereoselective C-H bond hydroxylation.[51] Reactivity of alkane hydroxylation and olefin epoxidation are greatly affected by several factors, such as by nature of supporting and axial ligands, spin states of metal ions.[23,28,63,143,156,168–174]

Along with, high valent iron-oxo, manganese-oxo complexes have also investigated and spectroscopically characterized[14,66,137] and these are involved in various oxidation reactions, such as C-H bond activation, oxygen atom transfer (OAT), and electron-transfer (ET) reactions.[173-174] Terminal manganese-oxo complex with buea (tris(N'-tert-butylureaylato)-N-ethylene) aminato) ligand in a tetragonal environment is stabilized by hydrogen bonding with it is notable for its elegant and concise design.[27,175–179] Terminal or bridging manganese-oxo is transient but not separable is supposed to be involved in a critical part of the energy demanding O-O bond formation step. Terminal vanadium/chromium-oxo complexes have also been synthesized to provide an additional chemical basis to understand the reaction mechanism of metalloenzymes and also help to develop artificial oxidation catalysts.[119] For a

long time, many metal-oxo and imido complexes of the 7,8 group have isolated and characterized.[119,121,180–208] High valent metal-oxo of earlier transition metal series are well known, but in late transition series, a few are known. This is related to the "Oxo Wall" concept proposed by Wray and Wrinkler. According to which "The high valent metal-oxo of late transition series are not supported in tetragonal geometry". Whereas, a few metal-oxo species of late transition series are reported in other geometries. High valent metal-oxo species of late transition series, mainly the cobalt-oxo is a reactive transit species involved in the C-H bond activation and O-O bond formation.[209–211] Cobalt(IV)-oxo species are proposed as the reactive intermediate in many cobalt-mediated oxidation reactions.[186–190,192,193] Catalytic oxidation of water to give molecular oxygen, remain a topic of intensive research in developing artificial photosynthesis and water-efficient splitting catalyst (EPR), X-ray absorption, and time resolved Fourier-transform infrared spectroscopic methods provides the evidence for the involvement of terminal and bridging cobalt(IV)-oxo species as a key intermediate in water oxidation reactions. Proposed cobalt(IV)-oxo intermediates are short-lived and highly reactive it makes their chemical and physical properties in catalytic cycles of cobalt-based oxidation catalysts. Even though these are considered more reactive than iron-oxo species because of the weak bond between metal and oxygen,[153,212] reactivity of metal-oxo complexes is governed by the electronic environment about the metal center. Inspired by enzymes such as NOD (nickel oxide dismutase), and its potential towards the activation of small molecules such as H_2O_2,[213–216] mCPBA,[210,217] and NaOCl.[218–220] Synthetic nickel complexes have gained attention but these are less explored as compared to Fe/Mn-oxo intermediates. There, many high valent Ni(III),[213–215,221], and Ni(IV)[221,222] intermediates have been characterized spectroscopically, but the formation of Ni(III), Ni(IV) oxido complexes is controversial to Oxowall premise.[223,224] Although a few high valent Ni(II) and

Ni(III) oxido complexes formed with O_2 and H_2O_2 have been characterized at low temperature.[80,225–228]

1.6 Dinuclear Metal Complexes

Apart from mononuclear species, Fe, Mn, and Cu dinuclear species which are bridged via oxygen as {M-μ(O)-M} are found in enzymes such as tyrosinase, catechol oxidase, methane monooxygenase and play an important role in the biological system.[229] These enzymes use dinuclear metal centers for catalyzing biological transformations. Dinuclear μ-bridged complexes play a very important role in biological systems such as binuclear, non-heme iron enzymes carry out many reactions by dioxygen activation. In non-heme diiron enzymes such as methane monooxygenase (MMO) and ribonucleotide reductase (RNR) high valent non-heme intermediates are reported.[229–233] MMO catalyzes the hydroxylation of methane to methanol via diiron(IV) intermediate and the RNR catalyzes the conversion of ribonucleotides to deoxyribonucleotides to produce a via Fe(III)Fe(IV) intermediate and initiates radical chemistry to generate DNA building blocks. Dinuclear iron-oxo species acts as an active species in hydroxylating and dehydrogenating enzymes.[227] From last few years, many model complexes having dimeric μ-oxo bridged metal ions coordinated with ligands are investigated.

The coordination chemistry of Mn(II) complexes is also very important because Mn is involved in many metalloenzymes such as manganese peroxidase (MnP), manganese thiosulphate oxidase,[234] manganese catalase,[150] ribonucleotide reductase,[235] acid phosphase[236], and superoxide dismutase (MnSOD).[237] Along with manganese many dinuclear cobalt, nickel, and copper complexes, have been explored to mimic the various biological metalloenzyme.[238–244] From literature, the design, construction, and characterization of

dinuclear transition metal complexes has become important because of their intriguing structure and wide applications in magnetism, optics, electronics, catalysis, and fluorescence.[245–252] There has been also a great interest in polynuclear manganese and copper complexes because of their wide application in the field of bioinorganic chemistry and material science.

1.7 C-H/O-H Bond Activation

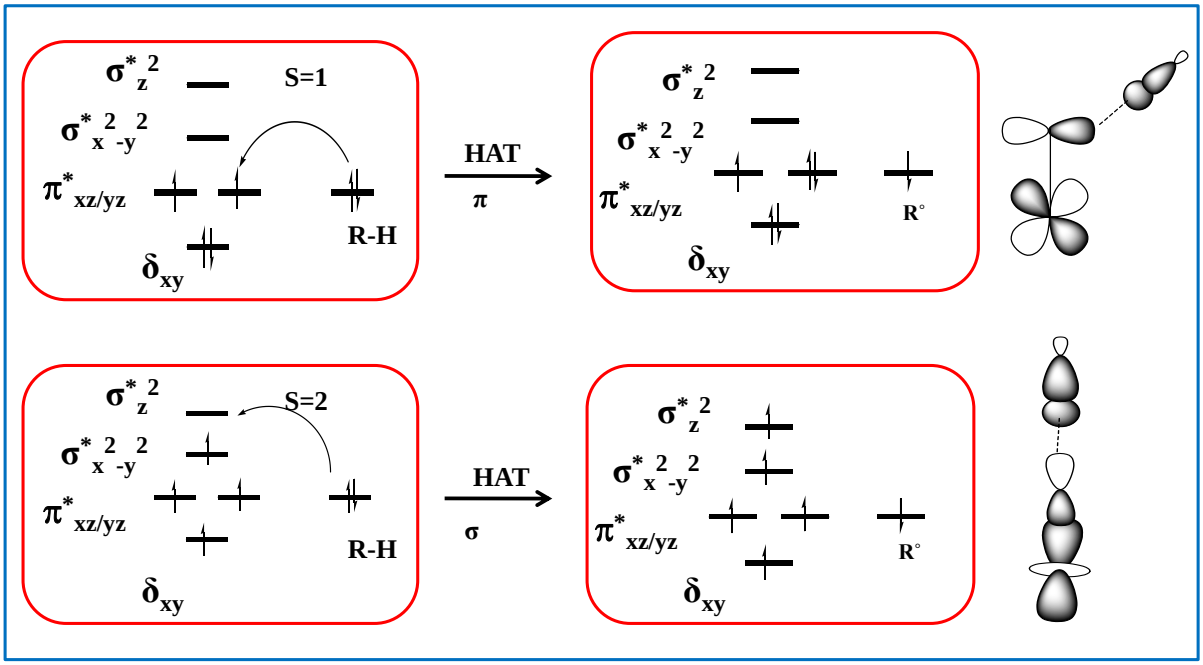
C-H/O-H bond activation in alkanes offers insertion of a functional group into a relatively inert hydrocarbon in a cost-effective manner and these have a wide application in industry.[60,63,240,253,254] Metal-oxo/superoxo/peroxo species play an important role in hydroxylation, epoxidation, halogenation etc. Understanding the mechanism of C-H/O-H bond activation remains a key consideration, and computational modeling provides insight into the process.[255]

From the last several decades, many affords have been made for the selective transformation of the C-H bond in other functional groups that have many practical implications. As the prosperity of C-H bond functionalization has a very great impact in the industry for the manufacturing of chemicals. Selective C-H bond activation affects the synthesis of chemicals, natural products, polymers, and agrochemicals and these have boosted the economy and efficiency.[256] The direct C-H bond activation can thoroughly shorten the possible routes in natural product synthesis by disconnecting the unknown steps and have the potential for smooth schemes, by eliminating the need for preparation and separation. Two factors regulate selective C-H bond activation one is inert and another one is selectivity control. Challenge in C-H bond cleaving is due to its strong, unpolar, and unreactive nature. The saturated alkanes are formed by C-C and C-H bonds, due to which neither empty orbital of low energy nor filled orbital of higher energy are present to participate in the chemical

reaction. This is different with alkenes, alkynes, and aromatics which provide π and π* orbitals for reactions.[257] Their underutilization in chemical synthesis is may be because of the higher thermodynamic stability of most of the C-H bonds. To overcome this thermodynamic barrier, one has to use the regents that are oxidizing, nonselective, and also incompatible with other functional groups. Some oxidants may have costly and toxic metal ions, their expensiveness and environment incompatibilities makes limit their use. Thus the development of new reagents which are efficient, environment friendly and easily accessible towards the specific C-H bond is an important area in chemical science.

There are two possible approaches for cleaving the C-H bond to attack iron-oxo either may attack from the top of the equatorial position. Both the possibilities have different electronic structures and have different pathways. From, the orbital occupancy evolution diagram, in triplet channel C-H bond electron, is transferred to d_{xz} orbital (π mechanism), for maximum orbital overlap in between electron donor and acceptor orbitals, the substrate may take a horizontal approach to iron-oxo reactive center. This orbital overlap and Pauli repulsion lead to the transition states having bent Fe-O-H angle. In the quintet state pathway, electron of the substrate is shifted to d_z^2 orbital (σ-mechanism). To, the upwards pointing lobe of the Op_z orbital, for overlapping there should be a vertical approach of the substrate; thus transition state has nearly collinear Fe-O-H-C arrangement (see Scheme 1.2).

C-H bond activation mechanism can occur in two possible ways, either by H-atom transfer (HAT) or proton-coupled electron transfer (PCET), these are the fundamental process in the biological and chemical process.[181,226,258] HAT reactions take place via a two-step mechanism, either proton transfer followed by electron transfer or electron transfer is followed by proton transfer, while in PCET proton and electron are transferred simultaneously such as in lipooxygenase and cytochrome P450 enzymes.[259–263]



Scheme 1.2. Schematic summary of the electronic structure changes along with the reaction Pathway in the triplet and quintet state of mononuclear non-heme iron(IV)-oxo complexes.

Sason Shaik has led the proponent notion of exchange-enhanced reactivity, where exchange stabilization favors the pathway in which at a metal center number of an unpaired electron during transition state increases.[264–267]As the reactivity of Fe^{IV}=O complexes towards C-H bond, is found that S=2 state is more reactive than the S=1 spin state. While Solomon favors the frontier molecular orbital (FMO) approach that states stereo electronic factors can affect the C-H bond approach towards the Fe=O unit, it depends upon that whether the target C-H bond interacts with σ* FMO or π* FMO of Fe=O unit.[264-267] The reaction may proceed via single state or multi-state reactivity. The fundamental characteristic of TSR/MSR is that the reaction proceeds at least on two potential energy surfaces with different spin multiplicity, either they may cross each other or they may have approximate energy, and different spin states produce different products.

Apart from C-H bond activation, O-H bond also play an important role. Diiron complex (*μ*-oxo)bis(m-carboxylato)) was proposed to cleave the strong O-H bonds of methanol and *t*-

butanol. Reactivity of methanol is studied by this complex, and found that it occurs at spin state of S=2, arised from the triplet state at individual iron center. Antiferromagnetic coupling spin state is the ground state but during the transition state it shows ferromagnetic coupling. It is due to enhance exchanged reactivity. It occurs via σ-π/π-π pathway through proton coupled electron transfer mechanism.

1.8 Importance of Present Thesis Work

The main motto of this thesis is to study the electronic structures and reaction mechanisms occurring during catalytic transformation reactions carried out by biomimetic model complexes using computational tools. For understanding the reaction mechanism, it is very important to study the structure and chemical bonding of the catalytic site. Rate of reactions are affected by the electronic and steric factor, therefore it is essential/important to study how these factors affect the rate of similar reactions. It is difficult to control the relative height of the activation energy barrier to tune their catalytic selectivity experimentally, but computationally it can be achieved. The computational study provides many ideas to understand the important biological process that occurs in nature with the help of high valent metal-oxo species. Additionally, it also helps the experimentalists to design new environment friendly and cheap catalysts.

1.9 Aim of Current Thesis

Metalloenzymes are involved in a wide number of reactions. Many model complexes are purposed that mimic the biological activity of metalloenzymes. The main aim is that these model complex help to understand the reactivity of enzymes and get a catalyst with very high efficiency, selectivity. In this context many heme and non-heme biomimetic models have

been reported, where several catalytic reactions, electronic structures, mechanistic study and reactivity pattern.

The second chapter presents an introduction to the methodology used in our investigations. This assists in understanding the basic computational approaches in calculations. Transition state theory provides a fundamental role in the analysis of chemical reactivity. In our third chapter, we have focused on the electronic structures of TAML ligated mono/dinuclear complexes. Mononuclear and dinuclear iron complexes are found as key intermediates in many synthetic and bio-catalytic reactions. By computing all the possible spin states for these species, we have predicted the ground state, structure-function relationships in their ground states, and analyzed the bonding aspects of these species by employing MO analysis. We have also discussed the shifting of iron centers out of the plane and magnetic coupling between iron and iron/oxygen centers. In our fourth chapter, we have studied the mechanistic study on allylic oxidation of aliphatic compounds cyclohex-2-enol to cyclohex-2-enone by tetraamido iron(V)-oxo. Metal catalyzed allylic oxidations of aliphatic compounds are attractive intermediates and these are very useful in pharmaceutical industries. We have reported electronic structures and also a first-time mechanistic detail of selective allylic oxidation of the cyclohex-2-enol by an oxidant non-heme iron-oxo species. The reaction can be feasible via O-H (***pathway a***) and C-H (***pathway b***) bond activation. We have found that the C-H bond activation is relatively preferable over the O-H and oxygen attack. Additionally, we have also performed the epoxidation of cyclohex-2-enol by iron(V)-oxo species.

In the fifth chapter, we have studied the metal-superoxo species, as it is of great interest because plays an important role in carrying many metal-mediated catalytic transformation reactions. Such catalytic reactivity is affected by many factors such as by nature of metal ions and the ring size of ligands. We have reported the electronic structures of a series of metal-

superoxo species (M=V, Cr, Mn, Fe, and Co) with two different ring size ligands i.e. 13-TMC/14-TMC, and a detailed mechanistic study of C-H bond activation of cyclohexa-1,4-diene followed by the effect of ring size of ligands. Our DFT results show that the electron density at distal oxygen plays an important role in C-H bond activation. Computing energetics of C-H bond activation and mapping potential energy surface, it is found that initial hydrogen abstraction is the rate-determining step, with both the TMC rings with all studied metal-superoxo species. A significant electron density at cyclohex-1,4-diene carbon indicates that the reaction proceeds via a proton-coupled electron transfer mechanism. Here, we have performed first and foremost theoretical studies on ring size, and found that TMC is more reactive towards C-H bond activation and is also supported by structural correlation.

In the sixth chapter, we have studied the formation of high valent metal-oxo species. High valent terminal metal-oxo species containing iron and manganese are involved in biological and catalytic reactions. Terminal metal-oxo of earlier transition metals are well known, whereas metal-oxo of late transition series are rare. This is related to the concept of the "Oxo wall". According to "Oxo Wall" late transition metals cannot support a terminal oxo ligand. Here, we have undertaken the first and foremost theoretical initiative for the formation of metal-oxo from metal hydroperoxo with 3*d* transition metal series (Metal= Cr, Mn, Fe, Co, Ni, Cu) by calculations of the transition state barrier height of O-O bond cleavage with two different octahedral and trigonal bipyramidal geometries. Our calculations show that the barrier height for the cobalt/nickel/copper-oxo is higher than the corresponding chromium, manganese and iron-oxo species, which is also supported by the concept of the "Oxo Wall".

1.10 References

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