MODELING THE CATALYTIC EFFECT OF TRANSITION METAL COMPLEXES IN WATER OXIDATION AND HETERO-DIELS-ALDER REACTIONS

by

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ABSTRACT

MODELING THE CATALYTIC EFFECT OF TRANSITION METAL COMPLEXES IN WATER OXIDATION AND HETERO-DIELS-ALDER REACTIONS

This dissertation is composed of two parts, the catalytic effect of transition metals on chemical reactions in the fields of inorganic and organic chemistry has been handled by utilizing Density Functional Theory.

In the first part, mononuclear ruthenium-based water oxidation catalysts (WOC) and their operative water oxidation mechanisms have been modeled by means of DFT calculations. Computational comparison of the reaction mechanistic cycles for the mononuclear ruthenium based catalysts are investigated in order to understand which factors can affect their reaction pathways and in particular favor one of the two mechanisms. By taking geometrical and electronic factors into account, the structure/activity relationship has been discussed.

In the second part, the effect of transition metal catalysis in inverse electron demand Diels-Alder (IEDDA) reactions, focusing on silver-catalyzed IEDDA reaction of phthalazine and siloxy alkyne, were modeled utilizing DFT calculations. Along with detailed elaboration of proposed operative mechanisms for the silver-catalyzed system, uncatalyzed reaction has been modeled to emphasize the effect of transition metalbased catalyst. In addition, the mode of action for the silver-based catalyst as well as its effect on the regioselectivity/specificity of the reaction have been demonstrated.

ÖZET

SU OKSİDASYONU VE HETERO DIELS-ALDER TEPKİMELERİNDE GEÇİŞ METAL KOMPLEKSLERİNİN KATALİTİK ETKİSİNİN MODELLENMESİ

İki bölümden oluşan bu tezde, inorganik ve organik kimya alanlarında geçiş metallerinin kimyasal reaksiyonlar üzerindeki katalitik etkisi Yoğunluk Fonksiyonel Teorisi kullanılarak ele alındı.

Ilk bölümde, mononükleer rutenyum bazlı su oksidasyon katalizörleri ve bunların operasyonel su oksidasyon mekanizmaları Yoğunluk Fonksiyoneli Teorisi (DFT) hesaplamaları ile modellendi. Mononükleer rutenyum bazlı katalizörler için reaksiyon mekanizma döngülerinin hesaplamalı karşılaştırması, hangi faktörlerin reaksiyon yollarını etkileyebileceğini anlamak amacıyla ele alındı. Geometrik ve elektronik faktörler göz önüne alınarak yapı ve aktivite ilişkisi tartışıldı.

Ikinci bölümde, ftalazin ve siloksi alkilin gümüş ile katalizlenmiş ters elektron talebi Diels-Alder(IEDDA) tepkimesi, geçiş metal komplekslerinin bu tepkime üzerindeki etkisi gösterilerek Yoğunluk Fonksiyoneli Teorisi (DFT) hesaplamaları ile modellendi. Gümüş(I) tarafından katalizlenen sistem için önerilen operasyonel mekanizmaların detaylı bir şekilde incelenmesinin yanı sıra, katalize edilmemiş reaksiyon, geçiş metali bazlı katalizörün etkisini vurgulamak için modellendi. Ek olarak, gümüş bazlı katalizörün etki şekli ve bunun reaksiyonun bölgesel seçiciliği ve özgüllüğü üzerindeki etkisi gösterilmiştir.

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LIST OF SYMBOLS

E_{el}	Electronic Energy
$E_c[ho]$	Correlation Energy
$E_x[\rho]$	Exchange Energy
Н	Hamiltonian Operator
$h_{ m KS}$	Kohn-Sham Hamiltonian Operator
${ m J}[ho({ m r})]$	Coulomb Energy
$T[\rho(r)]$	Kinetic Energy of Interacting Electrons
$\mathbf{T}_{ni}[\rho(r)]$	Kinetic Energy of Non-Interacting Electrons
$V_{ext}(r)$	External Potential
$V_{ee}[\rho(r)]$	Electron-Electron Interactions
Ζ	Atomic Number
ΔG_{hind}	Binding Free Energy

ΔG_{bind}	Binding Free Energy
ΔG^{\ddagger}	Gibbs Free Energy of Activation
ΔG^{o}	Standard Gibbs Free Energy
$ ho({ m r})$	Electron Density
ψ_i	Kohn-Sham Orbitals
Ψ	Wavefunction

LIST OF ACRONYMS/ABBREVIATIONS

B3LYP	Becke-3-parameter Lee-Yang-Par functional
DFT	Density Functional Theory
ECP	Effective core potential
FMO	Frontier molecular orbital
GGA	Generalized Gradient Approximation
GTO	Gaussian Type Orbital
HF	Hartree-Fock theory
НОМО	Highest Occupied Molecular Orbital
I2M	Interaction of Two Metal Oxo Pathway
IEDDA	Inverse electron demand Diels-Alder
IEF-PCM	Integral equation formalism polarizable continuum model
IRC	Intrinsic reaction coordinate
LC	Long-range Corrected
LCAO	Linear Combination of Atomic Orbitals
LDA	Local Density Approximation
M06-2X	Empirical exchange-correlation functionals
M06-L	Empirical local functionals
MPW1K	Modified Perdew-Wang 1 Parameter Method for Kinetic
NHE	Normal Hydrogen Electrode
NPA	Natural population analysis
LANL2DZ	Los Alamos National Laboratory ECP plus DZ basis set
LUMO	Lowest Unoccupied Molecular Orbital
PBE0	Parameter-free Global Hybrid funtional
PCM	Polarizable Continuum Model
SDD	Stuttgard-Dresden Effective Core Potential
SMD	Solvation Model Based on Density Model
STO	Slater Type Orbital
WNA	Water Nucleophilic Attack Pathway

WOC	Water Oxidation Catalyst			
XC	Exchange-Correlation			
ω B97XD	Long-Range Corrected Hybrid Functional with Dispersion			
	Correction			

1. INTRODUCTION

Computational chemistry is a subfield of chemistry that uses computer modeling and simulation techniques to serve in solving chemical problems. Computational chemists use the aspects of theoretical chemistry, quantum mechanics and thermodynamics, incorporated into computer programs allowing to extract valuable information from huge amount of data, to calculate and accordingly characterize the structures of atoms, molecules and chemical reactions. Its field of application covers in many research areas such as material science, drug development and catalysis.

Interest in computational chemistry has started to rise gradually since Walter Kohn and John Pople was awarded 1998 Nobel Prize in Chemistry for their development of Density Functional Theory (DFT) and development of computational methods in quantum chemistry, respectively. Thereafter, Martin Karplus, Michael Levitt and Arieh Warshel recieved 2013 Nobel Prize in Chemistry for their expertise on multiscale modeling for complex chemical systems. These developments in computational chemistry have been attracted attention since then.

In this dissertation, the use of theoretical modeling to scrutinize catalytic and binding effects in organic and inorganic systems will be discussed by employing Density Functional Theory (DFT) which is the most widely used quantum mechanical method. More specifically, the reaction mechanisms assisted by transition metal-based catalysts for water oxidation which is one of the two half reactions of water splitting, and for inverse electron demand Diels-Alder (IEDDA) reaction which considered a counterpart of conceptual Diels-Alder, have been elucidated in order.

In the first part, catalytic performance and its effect on the reaction catalyzed by experimentally-studied [1] two ruthenium-based water oxidation catalysts (WOC) are examined through computational modeling tools in the light of water oxidation reaction, which is thought to be operated by two different mechanisms, depending on ligand environment around transition metal: water nucleophilic attack (WNA) and interaction of two metal-oxo (I2M). The pathways are named according to the type of formation of the oxygen-oxygen bond in water oxidation catalytic cycle.



Figure 1.1. Chemical structures of water oxidation catalysts studied in Part I.

In the second part, catalytic effect of silver (Ag(I)-bipyridine) on inverse electron demand Diels-Alder reaction (IEDDA) of 1,2-diazines and siloxy alkynes has been discussed. Along with modeling catalyzed reaction which is experimentally thought to be taken place via concerted or stepwise pathway [2]; uncatalyzed version of the reaction aiming to compare energetic effect of the catalyst on activation barriers, and mode of action for silver catalyst have been probed via computational tools.



Figure 1.2. Silver-catalyzed 1,2-diazine and siloxy alkyne [4+2] cycloaddition reaction studied in Part II.

2. METHODOLOGY

2.1. Density Functional Theory

The Density Functional Theory (DFT) [3], which is the quantum mechanical approach of the electronic structure of atoms and molecules, is enounced in 1964 by Kohn and Hohemberg [4, 5]. DFT is based upon two fundemental theorems known as Hohenberg–Kohn theorems. The first theorem states that the external potential $V_{ext}(\mathbf{r})$, and therefore the total energy, is a unique functional of the electron density $\rho(\mathbf{r})$. In other words, the electron density $\rho(\mathbf{r})$ determines the external potential $V_{ext}(\mathbf{r})$, and consequently the total energy.

The electron density is defined as:

$$\rho(r): N \int \dots \int |\Psi(r_1, r_2, \dots r_n)|^2 dr_1 dr_2 \dots dr_n$$
(2.1)

where $r_{\rm i}$ represents both spin and spatial coordinates of electrons.

The second theorem states that ground state energy of the system gives the lowest energy if and only if the input density is the true ground state density [6]. The ground state electronic energy can be expressed as a functional of the electron density in Equation 2.2:

$$E[\rho(r)] = \int V(r)\rho(r)dr + T[\rho(r)] + V_{ee}[\rho(r)]$$
(2.2)

where $T[\rho]$ is the kinetic energy of the interacting electrons and $V_{ee}[\rho]$ is the interelectronic interaction energy.

The ground state electronic energy may be rewritten by using the theory developped by Kohn and Sham [7] and Equation 2.2 becomes :

$$E[\rho(r)] = \int V(r)\rho(r)d(r) + T_{ni}[\rho(r)] + J[\rho(r)] + E_{XC}[\rho(r)]$$
(2.3)

The coulomb energy $(J[\rho])$, the kinetic energy of non-interacting electrons $(T_{ni}[\rho])$ and the exchange-correlation energy functional $(E_{XC}[\rho])$ are the revised component terms of the ground state electronic energy. The Coulomb energy $(J[\rho])$ describes the unfavorable electron-electron repulsion energy and therefore disfavors the total electronic energy. It can be represented as:

$$J[\rho(r)] = -\sum_{A=1}^{M} \int \frac{Z_A}{|r - R_A|} \rho(r) dr + \int \frac{\rho(r_1)\rho(r_2)}{|r_1 - r_2|} dr_1 dr_2$$
(2.4)

where M is the total number of nuclei.

The kinetic energy term describes the measure of the freedom for non-interacting electrons, it can be expressed as below:

$$T_{ni}[\rho(r)] = \sum_{i=1}^{N} \int \psi_i(r) - \frac{\nabla^2}{2} \psi_i(r) dr$$
 (2.5)

in which N is the total number of electrons.

The latter term of the Equation 2.3, $(E_{\rm XC}[\rho])$ being the exchange-correlation energy functional, is expressed as the sum of an exchange functional $(E_{\rm X}[\rho])$ and a correlation functional $(E_{\rm C}[\rho])$ along with the kinetic energy correction term arising from the kinetic energy difference between the interacting and non-interacting electrons [8]. The exchange correlation energy is:

$$E_{XC}[\rho(r)] = \int \rho(r)\epsilon_{XC}(\rho(r))dr \qquad (2.6)$$

The derivative of Equation 2.6 with respect to the electron density, the following equation is obtained:

$$V_{XC}[\rho(r)] = \rho(r) \frac{d\epsilon_{XC}(\rho(r))}{d\rho(r)} + \epsilon_{XC}(\rho(r))$$
(2.7)

In Kohn-Sham density functional theory, a set of independent reference orbitals ψ_i are also known as Kohn-Sham orbitals and obtained by solving the following Kohn-Sham equations specified as:

$$h_{KS}\psi_i = \varepsilon_i\psi_i \tag{2.8}$$

in which the h_{KS} is the hamiltonian operator of Kohn-Sham, can be written in more detail as:

$$h_{KS} = -\frac{\nabla^2}{2} - \sum_{A=1}^{N} \frac{Z_A}{|r - R_A|} + \int \frac{\rho(r_1)\rho(r_2)}{|r_1 - r_2 dr_1 dr_2} V_{XC}[\rho(r)]$$
(2.9)

where $V_{XC}[\rho(r)]$ is the exchange correlation potential that is represented in the Equation 2.7. If the exact form of the exchange-correlation functional is known, the independent orbitals ψ_i give the exact electron density by the following equation:

$$\rho(r) = \sum_{i=1}^{N} |\psi_i|^2 \tag{2.10}$$

Since the exact form of exchange-correlation functional can not be known, approximate forms of functionals are developed.

2.2. Functionals

The first approximation is the local density approximation (LDA) that gives the energy of a uniform electron gas, depending on the value of the uniform distribution of electronic density at each point in the given system and the uniformly sprawled positive charge is associated with making the system neutral. The energy expression is as follow:

$$E[\rho] = T_{ni}[\rho] + \int \rho(r)v(r)dr + J[\rho] + E_{xc}[\rho] + E_b$$
(2.11)

where E_b is the electrostatic energy of the positive field. Since the positive charge density is the negative of the electron density due to uniform distribution of particles, Equation 2.11 can be reduced to:

$$E[\rho] = T_{ni}[\rho] + E_{xc}[\rho] \tag{2.12}$$

Since E_{xc} term can be divided into two terms: an exchange and a correlation functional. The Equation 2.12 can be rewritten by replacing the E_{xc} term with these functionals:

$$E[\rho] = T_{ni}[\rho] + E_x[\rho] + E_c[\rho]$$
(2.13)

The kinetic energy functional can be written as:

$$T_{ni}[\rho] = C_F \int \rho(r)^{5/3} dr$$
 (2.14)

where C_F is a constant that is equal to 2.8712.

The exchange functional can be written as follow:

$$E_x[\rho] = -C_x \int \rho(r)^{4/3} dr$$
 (2.15)

where C_x is a constant that is equal to 0.7386. The correlation energy, $E_c[\rho]$, for homogeneously distributed electron gas is obtained from the parametrization of the results of a set of quantum Monte Carlo calculations. However, LDA method underestimates the exchange energy since electron density cannot spread out uniformly in a molecule. Therefore, it can be said that LDA is not a suitable approximation in order to determine the exact form of the exchange-correlation functional.

Generalized gradient approximaton (GGA) methods [9], on the other hand, take into account the non-uniform nature of electron density. It is assumed that the exchange and correlation energies depend not solely on the density but also on the gradient as seen in the following equation:

$$E_{XC}^{GGA}[n] = \int n(r)\epsilon_{XC}(n(r), |\nabla n(r)|)dr \qquad (2.16)$$

An alternative method is the hybrid functionals that are a class of approximations to the exchange–correlation energy functional in DFT. This method incorporates a portion of exact exchange from Hartree–Fock theory with the rest of the exchangecorrelation energy from GGA method. The exact exchange energy functional is expressed in terms of the Kohn–Sham orbitals rather than the density. One of the most commonly used versions is B3LYP [5, 10], which stands for Becke, 3-parameter, Lee-Yang-Parr. It is composed of a mixture of LDA and GGA functionals as illustrated:

$$E_{XC}^{B3LYP} = (1-a)E_X^{LSDA} + aE_X^{HF} + b\Delta E_X^B + (1-c)E_C^{LSDA} + cE_C^{LYP}$$
(2.17)

where the empirical coefficients are determined to be 0.20, 0.72 and 0.81, respectively [11].

Another approch is the long-range corrected (LC) hybrid density functionals that use 100% Hartree Fock exchange for long-range electron-electron interactions. A long range corrected hybrid of a density functional approximation (LCDFA) is described as:

$$E_{XC}^{LCDFA} = E_X^{SR-DFA}(\omega) + E_X^{LR-HF}(\omega) + E_C^{DFA}$$
(2.18)

Accurate results can be obtained with such LC partitioning in terms of the longchain polarizability, reproduction of atomization energies, barrier heights, reaction enthalpies, optical and geometrical properties, excitation energies and dissociation of two-centered three electrons bonds [12–14]. ω B97-XD [15] is one of the (LC) hybrid density functionals, having a small fraction around 22% for short-range exact exchange.

2.3. Basis Sets

A basis set is a set of functions that is used to describe the orbitals by defining the electronic wave function. Basis sets are first developed by John C. Slater [16]. Basis functions are expanded as a linear combination of atomic orbitals (LCAO) approximations in order to define molecular orbitals from atomic orbitals.

There are two types of basis sets: Slater-type orbitals (STOs) and Gaussian-type orbitals (GTOs). In spite of the suitability of STOs which have the correct shape of the orbitals, the latter (GTOs) is extensively preferred in modern DFT because GTOs allow practical computation of molecular integrals with a simpler formula. GTOs have been developed by S. Francis Boys [17] and are the approximated analogues of STOs.

Valance electrons principally take part in the chemical bonding, so it is important to represent valence orbitals by more than one basis function. For that purpose, split valence basis sets, where the core and valence orbitals are treated differently, have been developed by Pople *et al.* Since core electrons are less affected by the chemical environment than the valence electrons, core electrons are treated with a minimal basis set while the valence electrons are treated with a larger basis set. Examples of the split valence basis sets are 3-21G, 6-21G, 6-31G^{*}, 6-311G^{**} and 6-31++G^{**}, which the number specified in the left side of the dash stands for the number of Gaussian functions for inner shell orbitals and the latter numbers which placed in the right side of the dash are for the valence electrons.

Polarization and diffuse functions can be added into the basis sets in order to get closer to the exact electronic energy. Polarization functions add higher angular momentum orbital to all heavy atoms represented with a * or (d). Hydrogen atoms can be polarized as well, this would be done by ** or (d,p). Diffuse functions, represented by a "+", allow orbitals to occupy larger spaces. One '+' means only 'p' orbitals are taken into account and '++' means both 'p' and 's' orbitals are considered.

In the case of transition metals, since the inner core of these atoms is very large and therefore the number of basis functions used to describe it would be very big; those basis functions can be replaced by an Effective Core Potential (ECP) [18]. Nuclear point charge is reduced by metal's core electrons and pseudopotential is defined for core electrons of the metal. One of the most commonly used versions is Stuttgart-Dresden ECPs, designated as SDD [19] along with Los Alamos National Laboratory (LANL) ECPs, designated as LANL1DZ and LANL2DZ [20]. (DZ) stands for double zeta quality and the overall combination of ECP and valence basis set is thus referred to as "LANL1DZ" or "LANL2DZ" basis.

2.4. Continuum Solvation Models

In quantum chemical calculations, continuum solvation models are used to simulate the solvent environment of molecular system where the reactions take place [21]. In order to obtain more realistic results, solvent effects can be either taken implicitly and/or explicitly. In explicit solvation models, molecular details of each solvent molecules are explicitly added into the model. In implicit solvation models, on the other hand, solvent is considered as a uniform polarizable medium of fixed dielectric constant having a solute molecule placed in a suitable shaped cavity. The total solvation free energy is defined as:

$$\Delta G_{solvation} = \Delta G_{cavity} + \Delta G_{dispersion} + \Delta G_{electrostatic} + \Delta G_{repulsion} \tag{2.19}$$

In this equation, ΔG_{cavity} is the free energy required to form the solute cavity. $\Delta G_{dispersion}$ is the energy of interaction between solvent and solute, stabilizes the system by lowering the solvation free energy. $\Delta G_{electrostatic}$ is the electrostatic component that refers to the electrostatic interaction energy between solute and solvent induces charges distribution, and $\Delta G_{repulsion}$ is the exchange solute-solvent interactions that are not included in the ΔG_{cavity} .

Polarizable Continuum Model (PCM) is one of the polarizable continuum solvation models developed by Tomasi *et al.* [22]. In this model, cavity is formed by union spheres centered on each atom, having radii identified by the van der Waals radii of the atoms multiplied by a constant factor. The polarization charges are placed into small domains that is produced by subdividing of the cavity surface.

Three different approaches are considered to perform PCM calculations: Dielectric PCM (D-PCM) which is the first formulation method of PCM, the second one is Conductor-like PCM (C-PCM) [23] in which solvent is treated as a conductor not dielectric and lastly, Integral Equation Formalism of PCM (IEF-PCM) that is an implementation whereby the PCM equations are reformed [24, 25].

A relatively new and an alternative model is Solvation Model Based on Density, denoted as SMD [26]. In SMD, cavity is determined by using full solute charge density instead of partial atomic charge. This model separates the solvation free energy into two main components: the bulk electrostatic contribution and the cavitydispersion-solvent-structure contribution. The former component term arises from a self-consistent reaction field and the latter one comes from short-range interactions between the solute and solvent molecules in the first solvation shell.

3. WATER OXIDATION ASSISTED BY RUTHENIUM BASED CATALYSTS

3.1. Introduction

The energy crisis caused by overconsumption of fossil fuels leads us to find alternative sources of energy. Solar energy draws attention as a most abundant energy source as well as its clean and renewable nature. In order to use this energy appropriately, many experimental and computational studies have been carried out in recent years. Among these studies, solar-driven water splitting to produce hydrogen is one of the best strategies for the production of clean and renewable energy to cover increasing societal demand [27].

Obtaining hydrogen as a clean fuel just from water would have a great impact on green environment, since its combustion gives nothing but water vapor. Although water splitting is a brilliant idea for future energy problems, there are several challenges that need to deal with.

Water splitting consists of two half reactions; water oxidation $(2H_2O \rightarrow O_2 + 4H^+ + 4e^-)$ and proton reduction $(4H^+ + 4e^- \rightarrow 2H_2)$ as shown in Figure 3.1. Coupling of the two half reactions take place in molecular assemblies, nanostructured arrays, or photoelectrochemical cells (PECs) that use light absorption, electron transfer in excited states, directed long range electron transfer and proton transfer [28].

	2H ₂ O	\rightarrow	2H ₂ + O ₂	Water Splitting	
(1)	2H ₂ O		O ₂ + 4H ⁺ + 4e ⁻	Water Oxidation	<i>E</i> ° = 1.23 V vs NHE
(2)	4H ⁺ +	4e ⁻	► 2H ₂	Proton Reduction	<i>E</i> ° = 0.0 V vs NHE



Water oxidation reaction, which is the most challenging and critical step of water splitting, must be accomplished in order to obtain hydrogen at the end of the full process of water splitting. O-O bond formation step as well as multiple intermediates require many electron/proton transfer steps, making water oxidation reaction difficult to achieve, resulting in slow kinetics. The need for an effective water oxidation catalyst (WOC) arises to stabilize these intermediates, thus lower the kinetic energy barrier, and consequently increase the reaction rate.

Photocatalytic water splitting is also called artificial photosynthesis, because nature performs this reaction with an excellent efficiency and high rate for over two billion years with the aid of Mn_4O_5 cluster as a natural catalyst at the oxygen evolving center [29]. All efforts in water splitting field are to design highly efficient water oxidation catalysts (WOCs) with high turnover frequency (TOF) and low overpotential by inspiring from the nature.

Various approaches are used to synthesize WOCs, such as aid with metal oxides/hydroxide, mononuclear/multinuclear transition metal complexes and, recently, metal organic frameworks [30–32]. The monomeric transition metal complexes are popular in research, due to their structural simplicity, and therefore convenience of mechanistic investigation. A number of transition metal based water oxidation catalysts including manganese, iridium, iron, cobalt and ruthenium metals are synthesized and studied to understand natural oxygen evolving complexes and applications of lightdriven water splitting [33]. In early research, Meyer *et al.* introduce an oxo-bridged dinuclear ruthenium complex cis,cis-[(bpy)₂(H₂O)Ru^{III}ORu^{III}(H₂O)(bpy)₂]⁴⁺, known as blue dimer, to the scientific community in 1982, which is the first designed molecule to catalyze water oxidation [34]. Based on this ground-breaking development, initially believed that polynuclearity is key requirement for WOCs but later studies reveal that mononuclear Ru complexes also capable of catalyzing the water oxidation reaction [35]. In recent years, Ru-based complexes have been in the spotlight, hence understanding their full mechanistic properties is of increasing interest. Two different mechanisms are considered for water oxidation enabling oxygen oxygen bond formation initiatied from high valent metal-oxo active species : water nucleophilic attack (WNA) and interaction of two metal-oxo (I2M) [36]. More specifically, O-O bond formation occurs through water nucleophilic attack to the highly oxidized metal-oxo complex in the case of water nucleophilic attack mechanism (WNA). For the other well-accepted mechanism (I2M), two metal-oxo species couple and eventually the O-O bond is formed between two approaching water oxidation catalysts. These mechanisms are depicted briefly in Figure 3.2.





Figure 3.2. O-O bond formation mechanisms promoted by transition metal complexes in high oxidation states : (top) Water Nucleophilic Attack (WNA) pathway and (bottom) Interaction of Two Metal-Oxo (I2M) pathway.

In this part of this thesis, experimentally synthesized [1] two water oxidation catalysts (WOC) are selected as prototypes: $[Ru^{II}(tpc)(pic)_2]^+$, $(tpc^-=2,2':6',2''-terpyridine-$ 6-carboxylate, pic = 4-picoline) and the $[Ru^{II}(bda)(pic)_2]$, $(bda^{2-}=2,2'-bipyridine-6,6'$ dicarboxylate, pic = 4-picoline). In short, Ru-tpc and Ru-bda will be used throughout the dissertation in order to avoid complexity and therefore to make a brief nomenclature. The structural difference between that two is following: while Ru-tpc carries pyridine moiety in horizontal ligands around ruthenium, which forms terpyridine; Rubda has two carboxylates instead. The structures are depicted in Figure 3.3.



Figure 3.3. Chemical structures of Ru-tpc and Ru-bda catalyst.

It has been experimentally reported that Ru-tpc and Ru-bda water oxidation catalysts (WOCs) show different disposition in the catalytic water oxidation cycle, despite their structural similaries [1]. Therefore, studying such Ru-based water oxidation catalysts that share structural similarities but show different mechanical trend will help to understand the structure/activity relationships.

In early research, Sun *et al.* reported that oxygen evolution was occuring via second-order kinetics for Ru-bda catalyst, indicating O-O bond formation goes through with coupling of two metal oxo as known as I2M pathway [37,38], and it is a bimolecular process. More recently, they synthesized Ru-tpc and kinetic measurements reveal that this time O_2 evolution is first-order reaction in catalyst and therefore they proposed that O-O bond formation goes through WNA pathway, meaning water molecule nucleophilicly attacks to the metal oxo center of the single catalyst in order to make oxygen-oxygen bond, and it is considered as single molecular pathway [1]. Computational investigations were mainly focused on spin densities and orbital energies in $Ru^V=O$ state of the catalysts in order to explain the different pathway preferences for these two catalysts.

The factors affecting the water oxidation mechanism that water oxidation catalysts (WOC) follow are not yet fully understood. Important aspects affecting the mechanism are: i) structure and electronic properties of ligands surrounding ruthenium, ii) coordination number and coordination geometries at different oxidation states, iii) hydrogen bond network [39] iv) redox properties in catalytic cycle, and more recently proposed v) size or interior of the cavity in supramolecular catalyst [40] are shown to influence the mechanism that will be followed. Understanding ligand-dependent characteristics clearly will help to rationalize the full catalytic cycle for water nucleophilic attack mechanism (WNA) and interaction of two metal oxo mechanism (I2M).

In this part, the purpose of this work is firstly to evaluate the viability of water nucleophilic attack (WNA) path for selected Ru-based water oxidation catalysts and at a later stage, the interaction of two metal oxo (I2M) pathway will also be investigated on the same catalysts.

The full water oxidation cycle of Ru-bda and Ru-tpc catalysts, particularly by investigating their tendency to follow WNA and I2M path, will be investigated. Focusing on each intermediate, O-O bond formation and possible O_2 evolution step in the catalytic cycle are all equally important to elucidate the different trends that the two catalysts display, especially since the two Ru based WOC are structurally very similar. Comparing the effect of these catalysts on different mechanisms will give us valuable mechanistic perspective. From a theoretical point of view, geometrical and electronic tendencies of the two catalysts in the full water oxidation cycle will help to understand the ligand-activity relationships in a better way with the aid of Density Functional Theory (DFT) calculations.

3.2. Computational Details

Density functional theory (DFT) was performed within the Gaussian09 program package [41] throughout the study. In this part, all stationary points including geometry optimizations, frequency calculations, and transition states were were fully optimized at the PBE0 [42] level of density functional theory in gas phase and the solvent. For ruthenium, Los Alamos LANL2DZ effective core potential [20] as a pseudopotential and for the rest of the atoms 6-31+G(d,p) basis set were employed. Frequency analyses were performed on the optimized geometries to characterize each minima (with zero imaginary frequencies) and each transition state structure (with only one imaginary frequency) [43].

The integral equation formalism polarizable continuum model (IEF-PCM) [44] has been utilized implicitly to take into account the solvent effect during the geometry optimizations. As a solvent, water ($\varepsilon = 80.37$) has been used to be consistent with the experimental conditions.

3.3. Results and Discussions

As laid out in the introduction, the main objective of this work is to gain a better understanding of water oxidation reaction which carried on via either water nucleophilic attack (WNA) or interaction of two metal oxo (I2M) mechanism/pathway. These mechanisms were named due to the differences in the formation of the oxygen oxygen bond in the water oxidation reaction assisted by transition metal catalysts.

In the catalytic cycles, the steps are usually categorized into three phases: water activation which covers the steps starting from water-bounded intermediate $[M^{II}-OH_2]$ to higly oxidized metal oxo intermediate $[M^V=O]$; secondly oxygen–oxygen bond formation at the stage $[M^V=O]$, which describes which mechanism will be favored (either WNA or I2M); and finally oxygen evolution [45].

The computational study in this part begins with the corresponding reaction mechanism (water oxidation) proceeded with water nucleophilic attack (WNA) cycle by focusing on single-center catalysts, $[Ru^{II}(tpc)(pic)_2]^+$ and the $[Ru^{II}(bda)(pic)_2]$, shortly Ru-tpc and Ru-bda. The coordination of the central Ru atom is pseudo-octahedral, as shown in the introduction in Figure 3.3, and catalysis takes place in water bound site.

Kinetic studies have revealed that the rate of water oxidation is first-order in the catalyst concentration for Ru-tpc, which indicates that there is one metal center during and also after oxygen-oxgen bond formation in the catalytic cycle [1]. Thus, Sun *et*

al. proposed that O-O bond formation on the Ru-tpc proceeds via WNA mechanism, water molecule attacks to the electrophile and highly oxidized site [Ru^V=O] of the catalyst.

For other catalyst, Ru-bda, the reaction favors second-order kinetics, indicating two metal centers are involved in the oxygen-oxygen formation step (possibly rate determining step), which is equivalent definition for interaction of two metal oxo (I2M) mechanism of water oxidation. Ru-bda catalyst has been investigated for many years since its discovery due to its catalytic activity with high turnover number [38]. Later study revealed [Ru^{II}(bda)L₂] type catalyst can also prefer WNA mechanism when it is in the supramolecular catalyst form [40].

3.3.1. Proposed Water Nucleophilic Attack (WNA) Mechanisms for Rubased Catalysts

Water nucleophilic attack (WNA) pathway is studied in recent years because of its increasing trend as a promising operative mechanism among Ru based water oxidation catalysts [28,40]. Taking reference to this, complete WNA mechanism will be investigated in this thesis in order to understand full picture of metal catalysis in water oxidation. Main focus is to primarily elucidate the effect of $[Ru^{II}(tpc)(pic)_2]^+$ catalyst on water oxidation since it experimentally favors WNA mechanism. For comparison, the mononuclear $[Ru^{II}(bda)(pic)_2]$ has also been studied under the same theoretical conditions.

A key concern in this part of the thesis is to be able to have insight why two structurally similar mononuclear catalysts prefer different path (i.e. either WNA or I2M) for O-O bond formation in the catalytic cycle, and secondly, why Ru-bda has better catalytic activity than Ru-tpc [1]. This should be addressed this question (i.e. ligand effect on reactivity) by modeling and investigating the reactivity of each intermediate in the proposed WNA mechanisms in Figure 3.4 and 3.5, for Ru-tpc and Ru-bda respectively, by mainly focusing on high valent and highly oxidized [Ru^V=O] intermediate.



Figure 3.4. Proposed water nucleophilic attack (WNA) mechanism for Ru-tpc catalyst.



Figure 3.5. Proposed water nucleophilic attack (WNA) mechanism for Ru-bda catayst.

The catalytic cycle corresponding to water oxidation reaction $(2H_2O \rightarrow O_2 + 4H^+ + 4e^-)$ is starting with water association to the single center catalyst Ru-tpc, resulting $[Ru^{II}-OH_2]^+$ as first intermediate as shown in Figure 3.4. Same trend can be confirmed for Ru-bda in Figure 3.5. This initial step of mechanism (i.e. association of water ligand) is investigated in several studies with different ligand framework of Ru catalyst since the catalyst itself does not bear water ligand [45]. In this dissertation, this very early step will not be discussed since the focus is to investigate ligand/activity relationship in the O-O bond formation step in the corresponding mechanism.

In water activation phase of the catalytic cycle, after water is attached to the catalyst to obtain the first intermediate of the cycle, which is $[Ru^{II}-OH_2]^+$, next steps of the reaction mechanism involve sequential proton-coupled electron transfer (PCET) steps and oxidations. These prepare water molecule to form oxygen-oxygen bond at the stage in which highly oxidized metal oxo $[Ru^V=O]$ is formed, obtaining from $[Ru^{IV}-O]$ with the aid of proton-coupled electron transfer (PCET). PCETs consequently allow oxidation of ruthenium in a complex, starting from oxidation state II to III, III to IV and as a last step of water activation phase of water oxidation cycle, IV to V as shown in Figure 3.4 and 3.5.

After reaching $[\operatorname{Ru}^{V}=O]$ intermediate in both cycle, oxygen-oxygen bond formation phase begins. This may be considered as a key phase of the reaction mechanism since it is subject to debate whether it is a rate determining step or not. In literature, it has been suggested that an essential step in the cycle that may prove turnover limiting is O–O bond formation step, characterized by the kinetic constant k_{O-O}, supporting the study that oxygen kinetic isotope effect shows O-O bond formation is irreversible and turnover limiting the catalytic cyle [46, 47]. However, Wasylenko *et al.* attributed the final step (i.e oxygen evolution) releasing molecular oxygen as rate determining depending on the nature of the ligand [48]. Theoretical studies support the idea that O-O formation is rather energy demanding and therefore rate determining step [49]. In the case of Ru-tpc and Ru-bda catalyst, it has been reported experimentally that the rate-determining step is O–O bond formation step, supported by the kinetic data that shows electron transfer steps are much faster than O-O bond formation step [1]. First, O-O bond formation will be discussed via water nucleophilic attack (WNA) in this thesis. As it is represented in the proposed catalytic cyles for both catalyst in Figure 3.4 and Figure 3.5, water attacks to the metal bound, electrophilic oxo group in $[Ru^V=O]$, and thus forms $[Ru^{III}-OOH]$ by losing its one proton (H⁺). This picture (i.e WNA) is thought to describe oxygen-oxygen forming bond in the oxygen-evolving complex (OEC) of photosystem II [50].

In the final phase of the water oxidation cycle (i.e oxygen evolution), another water molecule attacks to the metal whose oxidation state IV [Ru^{IV} -OO], which was obtained from [Ru^{III} -OOH] via one more electron/proton transfer step, and kicks off the oxygen as a molecule. During the liberation of molecular oxygen, water makes bond with the metal and then the first intermediate [Ru^{II} =OH₂] is obtained after finalization of the catalytic cycle.

For both catalyst, calculated geometry optimizations of each intermediates, transition states and redox potentials of PCET steps in the catalytic cycle will be discussed in the next sections of this part.

3.3.2. Ground State Geometry Optimizations

After proposing operating water nucleophilic attack mechanism (WNA) for both catalyst, geometry optimizations for each oxidative species (intermediates) in both mechanisms for the catalysts, Ru-tpc and Ru-bda, have been modeled by DFT calculations employing implicit solvent model (IEFPCM) to the system, and depicted in Figure 3.6 and Figure 3.7, respectively. In both figures, changing of ruthenium-oxygen distances in all oxidative species in the catalytic cycle that covers from water activation phase to oxygen liberation phase are highlighted as well as specific atomic interactions observed specifically in [Ru^{II}-OH₂], [Ru^{III}-OH] and [Ru^{III}-OOH] oxidative species in both WNA cycles.

As it is seen in Figure 3.6, all intermediates are modeled in accordance with the proposed WNA mechanism (Figure 3.4) for Ru-tpc catalyst. After water association

to the metal center, which is preliminary phase and therefore not included in the cycle; first complex of the cycle is $[Ru^{II}-OH_2]^+$, designated as (A), where water is bounded to the ruthenium as in 2.19 Å. Since catalysis takes place through water bounded site of the catalyst, ruthenium-oxygen distances have reached significance on the optimized structures. Starting from (A) $[Ru^{II}-OH_2]^+$ to (D) $[Ru^V=O]^{2+}$, that distance is gradually decreasing in conjunction with becoming stronger bonds as well as increasing oxidation number until the end of water activation phase.



Figure 3.6. Geometry optimizations (PBE0/LANL2DZ,6-31+G(d,p)) for the oxidation steps of Ru-tpc catalyst in WNA mechanism; ruthenium-oxygen distances (highlighted) and specific atomic interactions (in dash) in Å.

After reaching highly oxidized oxo species (D) $[Ru^V=O]^{2+}$, oxygen-oxygen bond is detected on the next intermediate which is designated as (E) $[Ru^{IV}-OOH]^+$. This bond formation in WNA mechanism will be elucidated in the next sections where transition state calculations are discussed in order to understand the preferences of
Ru-tpc and Ru-bda catalysts during the mechanism since this is the crucial phase of water oxidation. Subsequently, the oxygen, which is still bonded to ruthenium (in 2.03 Å), in (F) $[Ru^{IV}-OO]^+$ structure will be liberated as a molecule after approaching another water molecule to the ruthenium in order to complete and start new WNA cycle by forming first intermediate (A) $[Ru^{II}-OH_2]^+$.



Figure 3.7. Geometry optimizations (PBE0/LANL2DZ,6-31+G(d,p)) for the oxidation steps of Ru-bda catalyst in WNA mechanism; ruthenium-oxygen distances (highlighted) and specific atomic interactions (in dash) in Å.

Another significant result is the coordination number around ruthenium that changes based on atomic interaction caused by hydrogen bonding between hydrogen of water and the carboxylate, particularly observed in (A) $[Ru^{II}-OH_2]^+$, (B) $[Ru^{III}-OH]^+$ and (E) $[Ru^{IV}-OOH]^+$ intermediates. While coordination number is six for these oxidative species; the rest, (C) $[Ru^{IV}-O]^+$, (D) $[Ru^V=O]^{2+}$ and (F) $[Ru^{IV}-OO]^+$, have seven coordination around ruthenium since lacking of hydrogen due to proton coupled electron transfer (PCET) steps throughout the mechanism. Even forcing to make seven coordination for (A), (B) and (E) species, attempts failed because of the strong interaction, and resulted in energetically more stable six coordination complexes during geometry optimization calculations.

In Figure 3.7, same observations had been noticed regarding ruthenium oxygen distances and coordination number fashion for other catalyst (Ru-bda). Since this catalyst has symmetric nature compared to Ru-tpc, hydrogen bond formation takes place through one of the two carboxylates randomly in the first place.

3.3.3. Spin Density Analysis

Spin densities have been calculated in order to understand the effect of electronic spin factors on water oxidation mechanism that Ru-tpc and Ru-bda are going to favor (either WNA or I2M) after reaching highly oxidized oxo species, (D) $[Ru^V=O]^{2+}$ for Ru-tpc, and (D)' $[Ru^V=O]^+$ for Ru-bda. Noted that, spin density calculations were carried out by considering low-spin state for Ru complexes, since second row transition metals prefer to rest in low-spin state due to larger splitting energy between $d_{t_{2g}}$ and d_{e_g} orbitals. That Δ splitting is large enough that these complexes do not exist in high-spin state, even when the metal center is coordinated to weak field ligands. Based on this, spin density plots are embedded on each oxidative species for both catalyst system and depicted in Figure 3.8 and Figure 3.9.

As shown in Figure 3.8, there is no spin density in singlet (A) $[Ru^{II}-OH_2]^+$, while doublet (B) $[Ru^{III}-OH]^+$, triplet (C) $[Ru^{IV}-O]^+$, doublet (D) $[Ru^V=O]^{2+}$, doublet (E) $[Ru^{IV}-OOH]^+$, and triplet (F) $[Ru^{IV}-OO]^+$ exhibit spin density delocalized over Ru and O on the Ru-tpc catalyst. Same trend can be confirmed for other catalyst (Ru-bda) as shown in Figure 3.9. Along with qualitative approach, quantitative value of spin density on oxygen at the oxo species (D) $[Ru^V=O]^{2+}$ for Ru-tpc and (D)' $[Ru^V=O]^+$ for Ru-bda may give important perspective about which mechanism (either WNA or I2M) will be favored.



Figure 3.8. Spin density plots (0.02 au isovalue) for the optimized oxidation steps for Ru-tpc catalyst in WNA mechanism.



Figure 3.9. Spin density plots (0.02 au isovalue) for the optimized oxidation steps for Ru-bda catalyst in WNA mechanism.

Since I2M mechanism requires two radicaloid oxo species to couple in order to make oxygen-oxygen bond by definition, unpaired spin should appear on singly occupied orbitals of ruthenium-oxygen bond having π^* character. Regarding to this, spin density values on oxygen of [Ru^V=O] species for both catalysts have also been reported in Table 3.1.

Table 3.1. Spin density located on oxygen of [Ru^V=O] species for Ru-tpc and Ru-bda catalyst.

Complex	Spin density on $O_{Ru=O}$
$[{ m Ru}^V({ m tpc})({ m pic})_2({ m O})]^{2+}$	0.673
$[\mathrm{Ru}^{\mathrm{V}}(\mathrm{bda})(\mathrm{pic})_2(\mathrm{O})]^+$	0.682

It is already expected that Ru-bda catalyst, which is suggested to favor I2M mechanism, should has a bigger spin density, indicating this catalyst has more radical character when compared to Ru-tpc catalyst that favors WNA mechanism. Accordingly, as seen in Table 3.1 and in spite of the similar values, spin density located on oxygen in $[Ru^{V}(bda)(pic)_{2}(O)]^{+}$ complex for Ru-bda has slightly higher (0.682) than in $[Ru^{V}(tpc)(pic)_{2}(O)]^{2+}$ complex for Ru-tpc (0.673). This supports compatibility with experimental results suggesting different preferences of two catalysts.

3.3.4. Frontier Molecular Orbital Analysis

The frontier orbital analysis has been discussed by focusing on the $[Ru^V=O]$ species since it is the active species controlling the O–O bond formation pathways via either I2M or WNA. Therefore, both HOMO and LUMO isosurface plots and related numeric values (in eV) that belong to $[Ru^V=O]$ species are demonstrated for both catalyst in Table 3.2 and Table 3.3.

From an orbital point of view, an orbital having σ character (HOMO) approaches to the LUMO, which is π^* -orbital of [Ru^V=O] in this case. The combination leads to the formation of an O-O σ bond while breaking one of the Ru-O π bonds, indicating $2e^{-}$ reduction of the metal center.

Since LUMO of the species are playing an important role while accepting HOMO of water to make oxygen oxygen bond in water nucleophilic attack (WNA) pathway, comparing LUMO energies for both catalyst can give an insight about the mechanism that the catalysts favor. Based on the LUMO orbital results in Table 3.2, $[Ru^V=O]$ species for Ru-tpc has more stabilized LUMO energy, which is -4.39 eV, and closer to the HOMO of the water molecule (HOMO_{water} = -9.15 eV) when considering LUMO energy for Ru-bda (-4.17 eV), indicating Ru-tpc catalyst is more inclined to accept HOMO electrons of water and consequently more prone to undergo WNA pathway over I2M pathway, which is consistent with the experimental studies.

On the other hand, if a catalyst performs water oxidation via the I2M mechanism, its LUMO energy should not be too close to the highest occupied molecular orbital of water, which matches with frontier molecular orbital calculation results for Ru-bda catalyst in this study. Not only its relatively high lying LUMO energy but also its higher spin density on oxygen atom in $[Ru^V=O]$ species supports the idea that this catalyst undergoes I2M pathway during water oxidation.



Table 3.2. LUMOs of [Ru^V=O] species for Ru-tpc (left) and Ru-bda (right) catalysts.

In Table 3.3, highest occupied molecular orbitals (HOMO) are also demonstrated for the purpose of showing full picture of frontier molecular orbital calculations employed on $[Ru^V=O]$ species for both catalysts.



Table 3.3. HOMOs of [Ru^V=O] species for Ru-tpc (left) and Ru-bda (right) catalysts.

3.3.5. Transition State Analysis

In this section, oxygen-oxygen bond formation step in WNA mechanism will be discussed in detail, which is considered as crucial step of water oxidation reaction. As stated earlier, the water molecule attacks nucleophilicly to the highly oxidized electrophilic metal-oxo center $[Ru^V=O]$ of the catalyst in order to make oxygen-oxygen bond in the case of WNA pathway. Higher oxidation state (commonly in oxidation state V) is essential for O-O bonding since there is no evidence for stable O-O bonded structure involving $[Ru^{IV}-O]$ [51]. In the light of such information, transition state calculations are employed on studied water oxidation catalysts; and as a result, optimized transition state geometries as well as required energy barriers to form oxygen-oxygen bond are indicated in Figure 3.10. The effect of solvent environment was also taken into consideration by means of continuum solvation model IEFPCM in transition state optimization calculations.



Figure 3.10. Transiton state geometries (PBE0/LANL2DZ,6-31+G(d,p)) of O-O bond formation step; water attack to high valent [$Ru^{V}=O$] state of Ru-tpc (left) and

Ru-bda (right) catalysts. Energies in kcal/mol, distances in Å.

As shown in Figure 3.10, required energy to form oxygen-oxygen bond is 30.5 kcal/mol for Ru-tpc catalyst, whereas activation barrier of this step is higher by almost 3 kcal/mol for Ru-bda (33.4 kcal/mol). The higher barrier indicates that Ru-bda does not undergo the WNA pathway as easily as Ru-tpc, which is completely consistent with experimental kinetic results that reported oxygen evolution is a first-order reaction with Ru-tpc but second-order with Ru-bda catalyst as proposed to go through I2M pathway to obtain oxygen-oxygen bond.

Note that, the barriers are measured by taking the energy difference between the separated reactants and the transition state, rather than from the pre-reactive complex of $[Ru^V=O]$ and attacking H₂O. In modeling, the use of separate reactants can prevent multiple geometric conformation problems, which are frequently observed in a relatively nonrigid systems. However, a relatively larger barrier may occur this way with respect to the use of reactive complex as a reference point to calculate the barrier.

3.3.6. DFT Calculations on Redox Events

The redox potentials for oxidative species in the catalytic cycle have been calculated by utilizing the polarizable continuum model for solvent effects. The redox potentials are related to the calculated standard free energy of the reduction in solution represented in the equation as follows:

$$\Delta G_{sol}^{\circ EA} = -nFE^{\circ} \tag{3.1}$$

where $\Delta G_{sol}^{\circ EA}$ is the standard free energy change associated with reduction in solution; E° is the standard electrochemical potential and F is the Faraday constant along with n the number of electrons involved in each step. $\Delta G_{sol}^{\circ EA}$ is formulated from two other components specified in Equation 3.2.

$$\Delta G_{sol}^{\circ EA} = \Delta G_{gas}^{\circ EA} + \Delta G_{solv} \tag{3.2}$$

where $\Delta G_{gas}^{\circ EA}$ is the standard free energy of reduction in gas phase, and ΔG_{solv} is the solvation free energy.

The free energy of the reduction, also defined as electron affinity (EA, $M^{n+} + e^- \rightarrow M^{(n-1)+}$), in solution ($\Delta G_{sol}^{\circ EA}$) can be calculated from $\Delta G_{gas}^{\circ EA}$ and ΔG_{solv} by referring Born–Haber cycle, which is an approach to analyze reaction energies and was named after the two German scientists Max Born and Fritz Haber developed it in 1919 [52]. The Born-Haber cycle is shown in Figure 3.11.

The theoretical standard redox potentials in solution are predicted with the help of Born-Haber cycle by employing the following equation:

$$\Delta G_{sol}^{\circ EA} = \Delta G_{gas}^{\circ EA} + \Delta G_{solv}^{\circ} (\text{Red}) - \Delta G_{solv}^{\circ} (\text{Ox})$$
(3.3)



Figure 3.11. Born-Haber cycle.

In equation 3.3, the free energy change of the half reaction in solution, $\Delta G_{sol}^{\circ EA}$, consists of the free energy change in the gas phase, $\Delta G_{gas}^{\circ EA}$, and the solvation free energies of the the reduced and the oxidized species, $\Delta G_{solv}^{\circ}(\text{Red})$ and $\Delta G_{solv}^{\circ}(\text{Ox})$, respectively.

Computational investigation of reduction/oxidation (redox) events in monomeric species in the catalytic cyle was performed according to the procedure developed by Cramer *et al.* [53]. First, the geometry optimizations were performed with the system in the gas phase and second, the optimized structures were reoptimized in the solvent phase to obtain consistency. So, there are two different calculated energetic values for one species: free energy obtained in gas phase as well as in solvent phase utilizing SCRF method.

The majority of oxidation events are characterized by proton-coupled electron transfer (PCET), where electron transfer (ET) is accompanied by proton transfer (PT) to the solvent [51]. Therefore, in order to calculate redox potential of the each step involving electron/proton transfer, the standard free energy of a proton in solution must be included. There are commonly used values that have been used in literature. In this dissertation, a widely accepted value for the free energy of solvation of a proton is used as $G_{(aq)}^{\circ H+} = -265.9$ kcal/mol [54]. The equation giving calculated redox potential,

 E° , of each step in the catalytic cycle is as follows:

$$E^{\circ} = -\frac{1}{F} \times \left(\Delta G_{gas}^{\circ EA} + \Delta G_{solv} - n_{H_{+}} \times G_{(aq)}^{\circ H_{+}}\right) - 4.24 \text{V}$$
(3.4)

where -4.24V stands for the referenced potential to the normal hydrogen electrode (NHE) which is corrected for experimental conditions in the proton transfer steps.

After obtaining calculated electrochemical potentials (in V) for required steps in the WNA cycle, the results were compared with experimental values that change according to pH of the environment. Calculated potentials are reported for both catalysts, Ru-tpc and Ru-bda, in Table 3.4 and Table 3.5.

In Table 3.4, calculated redox potentials (in V) of all proton-coupled electron transfer (PCET) steps leading stepwise oxidation of ruthenium which is in agreement with proposed mechanism for Ru-tpc catalyst (Figure 3.4) are compared with corresponding experimental values [1] as follows.

	Calculated Redox Potentials
$\mathbf{E}_{1/2}(\mathbf{III}/\mathbf{II})$	1.07
$\mathbf{E}_{1/2}(\mathbf{IV}/\mathbf{III})$	1.36
$\mathbf{E}_{1/2}(\mathbf{V}/\mathbf{IV})$	1.52
$\boxed{\mathbf{E}_{1/2}(\mathbf{IV}/\mathbf{III})}$	1.25

Table 3.4. Calculated (PBE0/LANL2DZ,6-31+G(d,p)) electrochemical potentials (V vs NHE) for stepwise oxidation of Ru in the Ru-tpc catalyst in WNA cycle.

The first calculated oxidation potential from $[\mathrm{Ru}^{\mathrm{II}}-\mathrm{OH}_2]^+$ to $[\mathrm{Ru}^{\mathrm{III}}-\mathrm{OH}]^+$ is 1.07 V, but reported experimentally observed oxidation potential of $\mathrm{Ru}^{\mathrm{II/III}}$ process is 0.91 V, and below 4.0 pH, it involves only electron transfer $([\mathrm{Ru}^{\mathrm{II}}]^+ \rightarrow [\mathrm{Ru}^{\mathrm{III}}]^{2+} + \mathrm{e}^-)$. As Fan *et al.* reported, under basic conditions, the first redox potential becomes pH dependent and follows $n\mathrm{e}^-/n\mathrm{H}^+$ process as presented in this work.

The calculated second oxidation potential from $[Ru^{III}-OH]^+$ to $[Ru^{IV}-O]^+$ is reported as 1.36 V, wheras Ru (IV/III) could not be detected by cyclic voltammograms (CV) and square wave voltammograms (SWV) techniques due to slow kinetics and thus, experimental value for this step could not be shown. Instead, Fan *et al.* stated that $[Ru^{IV}-O]^+/[Ru^{II}]^+$ redox event might occur with $2e^-/2H^+$ process.

When proceeded to the next oxidation step, $\operatorname{Ru}^{IV/V}$ requires only electron transfer and thus, $[\operatorname{Ru}^{IV}-O]^+/[\operatorname{Ru}^V=O]^{2+}$ oxidation process was calculated by considering without H⁺ loss, resulted in 1.52 V, in accordance with its experimental value reported as 1.27 V. The last PCET step involving oxidation from $[\operatorname{Ru}^{III}-OOH]^+$ to $[\operatorname{Ru}^{IV}-OO]^+$ is calculated as 1.25 V, and its experimental value is not reported since no information for this step was obtained in experiments. Studies have mainly focused on highly oxidized intermediate $[\operatorname{Ru}^V=O]^{2+}$ instead of full water nucleophilic attack (WNA) mechanism.

	Calculated Redox Potentials
$\mathbf{E}_{1/2}(\mathbf{III}/\mathbf{II})$	0.90
$\mathbf{E}_{1/2}(\mathbf{IV}/\mathbf{III})$	1.15
$\mathbf{E}_{1/2}(\mathbf{V}/\mathbf{IV})$	1.22
$\boxed{\mathbf{E}_{1/2}(\mathbf{IV}/\mathbf{III})}$	0.90

Table 3.5. Calculated (PBE0/LANL2DZ,6-31+G(d,p)) electrochemical potentials (V vs NHE) for stepwise oxidation of Ru in the Ru-bda catalyst in WNA cycle.

As for the second catalyst (Ru-bda), the same procedure was carried out and the results has been reported in Table 3.5 in accordance with the proposed mechanism for Ru-bda catalyst shown in previous section. The calculated potentials for the Ru-bda catalyst indicated $E([Ru^{III}-OH]/[Ru^{II}-OH_2])$, $E([Ru^{IV}-O]/[Ru^{III}-OH])$, $E([Ru^V=O]^+/[Ru^{IV}-O])$ and $E([Ru^{IV}-OO]/[Ru^{III}-OOH])$ redox couples are 0.9, 1.15, 1.22 and 0.9 V, respectively. According to the data provided by experimental studies, $[Ru^{III}-OH]$ is not stable at pH 7, which undergoes disproportionation to form $[Ru^{II}-OH_2]$ and $[Ru^{IV}-O]$ [55]. For this reason, 2e⁻ process of $[Ru^{II}-OH_2]/[Ru^{IV}-O]$ redox event has been detected experimentally and its electrochemical potential was noted as 0.7 V. The next oxidation step ($\operatorname{Ru}^{\operatorname{IV/V}}$) forming the active species of the cycle, which is $[\operatorname{Ru}^{V}=O]^{+}$, is 1.10 V as presented in the experimental study by Fan *et al.* [1].

Since Ru-bda type catalysts, $[Ru(bda)L_2]$ (bda=2,2'-bipyridine-6,6'-dicarboxylate, L = typically nitrogen heterocycles), have been reported to favor by coupling two metal oxo mechanism, as known as I2M, after reaching highly oxidized state $[Ru^V=O]$, no information for $E([Ru^{III}-OOH]/[Ru^{IV}-OO])$ process was reported in experiments, including studied $[Ru^{II}(bda)(pic)_2]$ catalyst in this work.

Based on the DFT calculations for the redox events of WNA mechanism, catalytic performance of Ru-tpc might not good as much as Ru-bda catalyst during the water oxidation, because Ru-tpc requires larger potential in total for electron/proton transfers compared to Ru-bda. Since this is just a preliminary investigation to have an insight about the catalytic performance of the catalysts, more elaborated studies in conjunction with kinetic experiments needs to be carried out. Indeed, on the basis of their kinetic experiments, Sun *et al.* argued that Ru-tpc was not a state-of-the-art catalyst compared to Ru-bda.

3.4. Conclusion and Future Work

The sunlight-driven splitting of water into oxygen and hydrogen is a promising long-term source of clean and renewable energy to mitigate the fossil fuel dependence in our society. Water oxidation, as one of the half reaction of water splitting, is especially challenging due to four-electron oxidation, coupled to the transfer of four protons and the formation of O-O bond. Therefore, highly efficient water oxidation catalysts (WOCs) is required for this process, and investigations on WOCs have a great importance in terms of the development of light-driven water splitting.

In the first part of the thesis, two mononuclear ruthenium-based water oxidation catalysts (WOCs), $[Ru^{II}(tpc)(pic)_2]^+$ and $[Ru^{II}(bda)(pic)_2]$, and their water oxidation mechanisms by focusing on water nucleophilic attack (WNA) pathway, modeled by means of DFT calculations. Computational comparison of the catalytic reaction cycles

for the mononuclear ruthenium based catalysts are presented in order to understand which factors can affect their reaction pathways and in particular favor one of the two mechanisms. The structure/activity relationship has been discussed by taking geometrical and electronic factors into account.

According to the kinetic measurements in the experimental studies, while Ru-tpc catalyzes the O-O bond formation with WNA pathway like most of the Ru complexes, Ru-bda has been reported to favor I2M pathway. Since WNA mechanism is preferred by most of the WOCs along the water oxidation, this mechanism was prioritized in this study. So that, WNA pathway has been modeled for both catalysts, and computational results in this dissertation support experimental studies in the literature. To be more precise, the pathway preference that one catalyst will proceed is controlled by [Ru^V=O] which is the highly active species in the water oxidation catalytic cycle. Therefore, investigations on spin density and frontier molecular orbital (FMO) calculations have been based on this intermediate. Based on the results of these calculations, Ru-tpc has shown slightly lower spin density on $O_{[Ru^V=O]}$, as well as lower $LUMO_{[Ru^V=O]}$ compared to Ru-bda. In addition, transition states calculations aiming to reveal O-O bond formation, which is thought to be rate-determining step, were handled and revealed that Ru-tpc has shown smaller energy barrier to obtain O-O bond compared to Rubda. In the light of these findings, Ru-tpc prefers WNA mechanism along the water oxidation reaction when compared to Ru-bda, which endorses the experimental studies. DFT calculations on redox events for each oxidation step along the WNA pathway have been also presented and reported that Ru-tpc requires larger electrochemical potential for the electron/proton transfers during the water oxidation.

As future work, oxygen evolution phase for both catalyst in water nucleophilic attack (WNA) cycle will be investigated in order to present full picture of WNA pathway. The other operative mechanism of water oxidation which is coupling mechanism of two metals (I2M, interaction of two metal centers) will also be scrutinized because ultimate goal is to design and offer efficient water oxidation catalyst (WOCs) by understanding water oxidation mechanisms.

4. CATALYTIC EFFECT OF SILVER IN INVERSE ELECTRON DEMAND DIELS-ALDER REACTION OF 1,2-DIAZINES AND SILOXY ALKYNES

4.1. Introduction

The Diels-Alder (DA) reaction is a cycloaddition reaction under the broad title of pericyclic reactions in organic chemistry. Due to its simplicity of operation, rapid convergence and broad applicability, Diels-Alder (DA) reaction is widely used synthetic method for unsaturated six-membered rings since its discovery in 1928 [56, 57]. The efficiency of the DA reaction can be improved by electron-donating and withdrawing groups on diene and dienophile, which ease the interaction between the highest occupied molecular orbital (HOMO) of diene and the lowest unoccupied molecular orbital (LUMO) of dienophile. This substituent effect is one of the methods in DA reactions to make this reaction more efficient, but catalysis is essential for some reactions due to low reactivity of the reaction partners. In this case, Lewis acid catalysis and transition-metal catalysis, which provide better HOMO-LUMO matching, are used.

Diels-Alder reactions with normal electron demand, which takes place between electron-rich dienes and electron-deficient dienophiles, are comprehensively studied throughout the years. On the other hand, the complementary process of DA, inverse electron-demand Diels-Alder (IEDDA) reaction, involving electron-poor dienes and electron-rich dienophiles, has been in the spotlight for the last 50 years.

The electron movement is reversed by switching from normal to inverse electron demand Diels-Alder reactions. In normal DA, electrons move from HOMO of diene to LUMO of dienophile, whereas in inverse electron demand DA, electron motion is in the direction from HOMO of dienophile to LUMO of diene. Frontier molecular orbital depictions for normal and inverse electron demand DA reactions are illustrated in Figure 4.1.



Figure 4.1. Frontier molecular orbital diagrams for normal and inverse electron demand Diels-Alder reactions.

From a theoretical point of view, the catalyst effect on such DA reactions is considered through stabilization of the frontier molecular orbitals, which is achieved by using strong electron acceptors like Lewis acids and transition metals. The coordination of the catalyst to the diene or dienophile lowers their energetically high lying LUMOs by transition state stabilization compared to uncatalyzed reaction.

IEDDA reactions could be carried out with the same catalysis strategies just as normal DA reactions, i.e. Lewis acid catalysis and transition-metal catalysis, in the case that substitution of electron donating group (EDG) or electron withdrawing group (EWG) on the diene/dienophile do not yield a cycloadduct. Nevertheless, Lewis acid catalysis has showed limited success in IEDDA reactions, and transition-metal catalyzed IEDDA reaction mechanisms have not been fully understood. [58, 59].

Heterocyclic azadienes (e.g. 1,2-diazines) are used for the synthesis of heterocyclic compounds in IEDDA reactions [60, 61]. As this type of azadienes have high LUMO energy, they do not easily react with dienophiles. This also requires rough reaction conditions. Since only a few dienophiles react with unsubstituted phthalazines, activity

of such azadienes are improved by various substituents [62–64]. Oishi *et al.* have shown the effect of electron-withdrawing groups substituted on phthalazine, and reported IEDDA reactions of 1-substituted phthalazines with enamines or ynamines at high temperatures [65].

IEDDA reactions of 1,2-diazines catalyzed by Lewis acids were introduced by Wegner *et al.* [66–68]. The dihydroborantherene was synthesized as a bidentate Lewis acid catalyst and it activates the phthalazine by lowering the energy of its LUMO. In that study, unsubstituted phthalazines were reported to be reactive towards several enamines and enol ethers, but unreactive towards alkynes. Bidentate Lewis acid catalysis allowed this reaction to be used within a broad range of substrates under mild conditions at lower temperatures. In the case of using monodentate Lewis acid, such as BF_3 , it has been noted that the reaction could not be catalyzed.

Transition metal catalysis, on the other hand, allows different modes of activity in organic reactions [69–72] and has been used in some IEDDA reactions. As an example, silver catalysis has found great use in alkyne-based organic reactions, including cycloaddition reactions, owing to the π coordination ability of silver with the carbon–carbon triple bond [73].

Kozmin *et al.* introduced silver-based catalysis for [2+2] cycloadditions of siloxy alkynes with various unsaturated carbonyl compounds for the first time [74]. They proposed two plausible mechanistic pathways: traditional Lewis acid activation through LUMO-lowering of the diene and silver-based activation of siloxy alkyne. However, deuterium labeling studies have shown that the reaction proceeded with a stepwise mechanism. It supports silver-based activation of siloxy alkyne with 1,4-addition and the formation of the ketenium ion.

In later studies, Rawal *et al.* reported the development of highly effective silvercatalyzed IEDDA reaction of siloxy alkynes with 1,2-diazines [2]. This reaction is represented in Figure 4.2.



Figure 4.2. 1,2-diazine and siloxy alkyne [4+2] cycloaddition reaction in the presence of silver-bipyridine catalyst.

It has been noted that little amount or none of the cycloadduct was obtained when this reaction was carried out in the presence of traditional Lewis acids (such as MgCl₂, ZnBr₂, Sc(OTf)₃, TiCl₄, and BF₃.OEt₂). However, as shown in previous studies, gold- and silver-based catalysts were alternatively used since these metals are known to have high affinity for alkynes. In spite of both gold and silver salts such as AuCl and AgOTf with no multidentate coordinated ligands gave the cycloadduct, the yields were low. The desired cycloadduct can be obtained in high yields in the presence of Ag(I) salts coordinated with bidentate ligands such as 2,2'-bipyridine. It is noteworthy that the importance of bidentate ligands are required for effective catalysis.

Subsequently, Rawal *et al.* have broaden their work by using of copper(I) and nickel(0) complex catalysts, which are isoelectronic with Ag(I) [75]. It was expected that copper(I) and nickel(0) complexes behave differently. Neutral nickel(0) center is sterically crowded since Ni(CO)₂(PPh)₃ is hindered; whereas Cu(I) acts as a soft Lewis acid, coordinates more strongly and thus leads to noticeably faster reaction, experimentally. Although the copper catalyst was also effective on the corresponding cycloaddition, yields and the reaction times are still in favor of Ag(I) catalyst.

The IEDDA reactions are commonly known as [4+2] cycloaddition reactions, however, there is a debate about the operative mechanism. Both concerted and stepwise mechanisms have been shown to be operative in different reactions depending on the steric and electronic factors. The proposed mechanism by Turkmen *et al.* for the IEDDA reaction of diazines and siloxy alkynes is shown in Figure 4.3.



Figure 4.3. Proposed mechanism indicating concerted and stepwise pathway.

The coordination of silver to phthalazine could activate it by making phthalazine less electron rich while lowering its LUMO energy, and thus promote the cycloaddition in a concerted way (concerted pathway). Alternatively, both reaction partners may be activated by Ag, leading to the nucleophilic attack of siloxy alkynes to phthalazines (stepwise pathway). The intermediate of this first step is a diaza-enolate bearing a highly reactive silylketenium; the intramolecular cyclization of the diaza-enolate to the silyl ketenium leads to the DA adduct and eventually, formation of siloxy naphthalene by extraction of N_2 .

In this part of the thesis, the mechanism of the IEDDA reaction between siloxy alkynes and 1,2-diazines catalyzed by Ag(I)-bipyridine will be elucidated. The complex structures of Ag(I)-bipyridine coordinated with 1,2-diazine and siloxy alkyne were modeled in order to understand the affinity of the catalyst to the reaction partners. Also, the uncatalyzed IEDDA reaction were modeled to serve as a reference point and to emphasize the role of the catalyst. NPA charges and frontier molecular orbitals were studied to show how the catalyst alters the mechanism and kinetics, and to better understand the basis of the reaction mechanism.

4.2. Computational Details

Geometry optimizations were performed within Gaussian 09 suite program using M06-2X [76] functional which is global hybrid with 54% HF exchange. For silver, Stuttgart/Dresden effective core potential (SDD), and for the rest of the atoms 6-31+G(d,p) basis sets were employed. Frequency analyses are performed on the optimized geometries to characterize each minima (with zero imaginary frequencies) and each transition state structure (with only one imaginary frequency). The integral equation formalism polarizable continuum model (IEF-PCM) has been utilized to take into account the solvent effect by using dichloromethane (ε =8.93) as the solvent.

The free energies include the thermal free energy corrections obtained from calculations done in solvent at the M06-2X/6-31+G(d,p) level at 298.15 K and 1 atm. The intrinsic reaction coordinate (IRC) [77] method was used to connect the transition structures with the corresponding reactants and products. A level of theory study was performed with ω B97X-D, MPW1K [78] and BMK [79] functionals in order to improve the energetic data via single point calculations on optimized geometries, since barriers calculated with M06-2X were large considering the mild experimental conditions necessary for the completion of the reaction (3 hours at room temperature). Throughout the thesis, results are reported at the ω B97X-D/6-311+G(d,p) level utilizing the SMD polarizable continuum model as they are more consistent with the experimental data.

Transition structures and products are named based on the type (catalyzed or uncatalyzed), the mechanism (stepwise or concerted), the regioselectivity of the reaction (a or b) as well as the conformation of the TMS group on the siloxy alkyne (I or II). For instance, $TS_{uncat}^{conc} - I$ is the transition structure of the concerted mechanism in the uncatalyzed cycloaddition reaction with a particular conformation of the TMS group, whereas $TS1_{cat}^{step} - IIa$ shows the first transition structure of the stepwise mechanism of the silver catalyzed cycloaddition reaction with a different conformation of the TMS group. Regarding the coordination sites of Ag(I)-bipyridine to phthalazine, a and b represent the coordination sites of Ag(I)-bipyridine with respect to the OSiMe₃ (TMS) group on siloxy alkyne that attacks phthalazine. (a: cross , b: same) Note also that the TMS group can occupy the "out" or "in" positions with respect to plane of the page. (I: out, II: in).

4.3. Results and Discussion

Experimental studies show that among the different metals considered, silver has a significant catalytic effect on inverse electron-demand Diels-Alder (IEDDA) reaction between 1,2 diazines and siloxy alkynes. The importance of bidentate chelating ligand that coordinates with Ag⁺ ion is emphasized for effective catalysis. Bipyridine was experimentally selected as a ligand due to its simplicity and high catalytic effect for further studies [2].

Experimentally, 1,2 diazines and siloxy alkynes bearing different R groups were shown to exhibit similar yields [2]. In this study, experimentally employed smallest R group (methyl) was selected as the R group for the siloxy alkyne for computational simplicity. However, larger aliphatic R groups on the siloxy alkyne have the potential to further increase the alkynes nucleophilic nature by donating electron density. In this study, Ag(I)-bipyridine complex is used as a catalyst to model the formal inverse electron demand Diels-Alder reaction (IEDDA) of phthalazine and trimethyl siloxy alkyne as shown in Figure 4.2.

4.3.1. Coordination of Ag(I)-bipyridine

In order to understand the preferred coordination of Ag(I) bipyridine to the reaction partners, two possible complexes of silver with phthalazine and siloxy alkyne were modeled as shown in Figure 4.4. It has been reported that Ag(I) salts, especially when coordinated with bidendate N-donor ligands, such as 2,2-bipyridine, catalyze the desired cycloadditon to yield silyl-protected 2-napthol [75]. 1,2 diazines show similarity with bipyridines due to their potential for bidentate chelation. Also, as previously mentioned, silver based catalysts have high affinity for alkynes. Thus, Ag(I) bipyridine was employed in IEDDA to activate both reaction partner in order to see the binding effect.



Figure 4.4. Ag(I)-bipyridine-phthalazine (A) and Ag(I)-bipyridine-siloxy alkyne complexes(B).

As shown in Figure 4.4, Ag(I)-bipyridine coordinates to phthalazine in two different ways; in an axial or equatorial with respect to phthalazine plane, resulting in two almost isoenergetic conformers. Ag(I)-bipyridine coordinates with only one of the diazine nitrogens of phthalazine, instead of both concurrently, which would have led to a ternary complex. Phthalazine does not prefer a bidentate coordination with Ag(I), possibly due to the respective positions of the N-lone pairs. Hence, the silver-phthalazine complex (A) exhibits monodentate coordination consistent with directional interaction with one of the nitrogen lone pairs.

In the case of the silver-siloxy alkyne complex (B), the axial conformer of this could not be located; Ag(I)-bipyridine coordinates to the siloxy alkyne with two slightly asymmetric C-Ag(I) bonds, enabling the π -coordination of silver to the triple bond of alkyne in accordance with the polarization of the triple bond. Both axial and equatorial silver-phthalazine complexes (A) are about 5 kcal/mol more stable than the silver-siloxy alkyne complex (B) in the solvent (CH₂Cl₂) environment. These findings show that Ag(I)-bipyridine prefers to coordinate with the phthalazine rather than the siloxy alkyne, energetically. Therefore, Ag(I)-bipyridine-phthalazine complex (A) is considered to form initially during the IEDDA reaction. Nevertheless, the affinity of Ag(I)-bipyridine catalyst to alkyne is also demonstrated with a negative calculated binding energy in accordance with the previous experimental studies. However, the affinity is higher for the diene when considering the binding energies.

4.3.2. Uncatalyzed IEDDA Reaction of 1,2 Diazine and Siloxy Alkyne

The reaction mechanism of the [4+2] cycloaddition reaction of 1,2 diazine and siloxy alkyne in the presence and absence of the catalyst was subsequently investigated. First, uncatalyzed cycloaddition reaction will be elucidated to compare the uncatalyzed and silver catalyzed reactions and to understand the effect of the silver catalyst on the reaction pathway.

<u>4.3.2.1.</u> Transition State Analysis. Transition state conformers of the uncatalyzed cycloadditon of phthalazine and siloxy alkyne are modelled as shown in Figure 4.5. These conformers, $TS_{uncat}^{conc} - I$ and $TS_{uncat}^{conc} - II$, are differentiated from each other according to the position of TMS group as indicated by I (out) or II (in). The second conformer, $TS_{uncat}^{conc} - II$, is 0.5 kcal/mol energy higher and the forming bond distances are similar

to the former structure. Since $TS_{uncat}^{conc} - I$ is energetically more stable, this transition state is employed on the free energy profile.



Figure 4.5. Concerted transition states of uncatalyzed-IEDDA reaction between phthlazine and siloxy alkyne and relative Gibbs free energies in kcal/mol. I-II: Positions of TMS group (out/in).

<u>4.3.2.2. Free Energy Profile.</u> The uncatalyzed cycloaddition reaction of phthalazine (1) and siloxy alkyne (2) results in the formation of cycloadduct (3), which further loses N_2 to yield silyl-protected 2-naphtol (4). Free energy profile of this reaction was demonstrated in Figure 4.6.

This reaction requires an energy barrier of 45.2 kcal/mol to reach cycloadduct (3), and is concerted in the absence of Ag(I)-bipyridine catalyst. It is noteworthy that relatively synchronous bond distances are observed when electron-rich siloxy alkyne is approached nucleophilicly to the vicinal carbon atoms of phthalazine during the transition state, $TS_{uncat}^{conc} - I$, where the two forming carbon-carbon bond distances are 2.16 and 2.22 Å. Besides, intermediate formation was not observed and efforts to locate a stepwise mechanism failed, indicating a concerted mechanism.



Figure 4.6. Free energy profile (kcal/mol) for uncatalyzed IEDDA reaction of phthalazine (1) and siloxy alkyne (2).

4.3.3. Silver-Catalyzed IEDDA Reaction of 1,2 Diazine and Siloxy Alkyne

Afterwards, the silver-catalyzed [4+2] cycloaddition mechanism of 1,2 diazine and siloxy alkyne has been investigated; which is the main concern of this study in order to reveal the proposed reaction mechanism by experimentalists.

<u>4.3.3.1. Proposed Reaction Mechanisms.</u> It was proposed that the silver-catalyzed reaction may follow two different pathways to yield the cycloadduct: either a concerted (one step) or a stepwise pathway with the formation of a diaza-enolate intermediate bearing a silylketenium (Int); depicted as catalytic cyle in Figure 4.7. Both concerted and stepwise mechanisms have been modeled in order to determine the most favorable pathway for the [4+2] cycloaddition of phthalazine (1) and siloxy alkyne (2) catalyzed by Ag(I)-bipyridine (5) catalyst.



Figure 4.7. Reaction mechanisms for silver-catalyzed cycloaddition of phthalazine (1) and siloxy alkyne (2).

<u>4.3.3.2. Transition State Analysis.</u> The transition states of the silver-catalyzed cycloadditon of phthalazine (1) and siloxy alkyne (2) are modelled in conformity with both concerted and stepwise pathway.

In concerted pathway, one transition step is required to obtain cycloadduct when considering conventional cycloaddition reactions under the title of pericyclic reactions. During the concerted pathway investigation in this study, $TS_{cat}^{conc}-Ib$ is located as transition state structure in accordance with the concerted fashion, depicted in Figure 4.8. Trimethyl silane (TMS) group on siloxy alkyne creates steric hindrance, and for that reason bond formation distance near to that group (2.22 Å) is a bit longer than the other forming bond (2.14 Å), exhibiting slightly asynchronous bond formation.



 $TS_{cat}^{conc} - Ib$

Figure 4.8. Concerted transition state, TS^{conc}_{cat} – Ib, of Ag(I) catalyzed-IEDDA reaction of phthalazine (1) and siloxy alkyne (2); distances are in Å. I-II: Positions of TMS group (out/in), a-b: Coordination site of the catalyst (5) with respect to TMS (cross/same).

When it comes to the stepwise pathway, multiple steps are considered throughout the reaction in order to obtain cycloadduct. Located first and second transition conformers are reported in Figure 4.9 and Figure 4.11, as well as the intermediate (Figure 4.10) that connects multiple transition states in consistent with the proposed reaction mechanism.



Figure 4.9. First transition state conformers of Ag(I) catalyzed-IEDDA reaction of phthalazine (1) and siloxy alkyne (2). The relative free energies in kcal/mol and distances in Å. I-II: Positions of TMS group (out/in), a-b: Coordination site of the catalyst (5) with respect to TMS (cross/same).

In first transition state conformers shown in Figure 4.9, $\text{TS1}_{cat}^{step} - Ib$ and $\text{TS1}_{cat}^{step} - IIb$ are higher in energy than $\text{TS1}_{cat}^{step} - IIa$ by 3.1 and 3.5 kcal/mol, respectively. Correspondingly, coordination site of the catalyst with respect to trimethyl silane (TMS) group in the cross position (designated as a) is preferred when considering relative

energies. The steric hindrance is relieved by positioning the catalyst in cross position, consequently stabilizes the structure. The energy difference among the conformers will be clarified from a different viewpoint in the following sections where natural charges of atoms (NPA) are analyzed. More stabilized $TS1_{cat}^{step}-IIa$ is employed as first transition state of stepwise pathway in the free energy profile in the following section.

In addition to all these, asynchronicity is noticed in the first transition state, $TS1_{cat}^{step} - IIa$, where a single carbon-carbon bond formation is 1.80 Å. The first carboncarbon bond (1.64 Å) of silver-catalyzed cycloaddition is already formed in the intermediate structure in Figure 4.10.



Intermediate

Figure 4.10. Diaza-enolate intermediate bearing silvlketenium (Int) of Ag(I)-catalyzed IEDDA reaction of phthalazine (1) and siloxy alkyne (2).

After first carbon-carbon bond formation, the second bond formation was also examined through transition state calculations for second step of studied cycloaddition reaction. Located second transition state conformers are shown in Figure 4.11. $TS2_{cat}^{step} - IIa$ is stabilized by 1.7 kcal/mol compared to $TS2_{cat}^{step} - IIb$. Again, coordination site of the catalyst in the same orientation (b) with TMS led to the latter structure to be less stabilized due to the same steric reasons explained in the first transition state structures. TS2_{cat}^{step} -*IIa* is considered as second transition state of stepwise pathway, employed on the free energy profile in the following section.



Figure 4.11. Second transition state conformers of Ag(I) catalyzed-IEDDA reaction of phthalazine (1) and siloxy alkyne (2). The relative free energies in kcal/mol and distances in Å. I-II: Positions of TMS group (out/in), a-b: Coordination site of the catalyst (5) with respect to TMS (cross/same).

<u>4.3.3.3.</u> Free Energy Profiles for Concerted and Stepwise Pathway. In accordance with the proposed mechanism demonstrated in Figure 4.7, free energy profiles for concerted and stepwise pathways for Ag(I)-catalyzed IEDDA reaction of phthalazine (1) and siloxy alkyne (2) are shown in Figure 4.12.

In the concerted pathway, the nucleophilic attack of the siloxy alkyne to phthalazine follows a simultaneous bond formation resulting in the formation of cycloadduct (6) in a single concerted step. The transition state, $TS_{cat}^{conc}-Ib$, has 32.2 kcal/mol activation barrier by referring the corresponding reactants. The cycloadduct (6-b) forms in a single step and the process is exothermic by -26.0 kcal/mol.

In the stepwise pathway, the carbon-carbon bond formation occurs in two steps via the formation of the diaza-enolate intermediate bearing silylketenium (Int). The first step of the stepwise pathway is the nucleophilic attack of the siloxy alkyne to phthalazine. The transition state, $\text{TS1}_{cat}^{step}-IIa$, requires 25 kcal/mol activation energy and the forming bond distance (1.80 Å) is getting closer until it is reached to intermediate. The first carbon-carbon bond (1.64 Å) of silver-catalyzed cycloaddition between siloxy alkyne and phthalazine is already formed in the intermediate structure, which lowers the energy to 23.8 kcal/mol after stabilization. After the first bond formation, intramolecular cyclization takes place at the distance of 2.96 Å in the second transition state, $\text{TS2}_{cat}^{step}-IIa$, in order to form second carbon-carbon bond, and consequently to attain cycloadduct (6-*a*); that process is exothermic by -25.8 kcal/mol.



Figure 4.12. Free energy profile (kcal/mol) for concerted (black line) and stepwise (red line) pathways for Ag(I)-catalyzed IEDDA reaction of phthalazine (1) and siloxy alkyne (2).

4.3.4. Mode of Action for the Silver Catalyst

In this section, natural population analysis (NPA) for atomic charges and frontier molecular orbital (FMO) calculations have been implemented in order to understand how silver catalyst affects reaction kinetics when considering its mode of action. Accordingly, the effect of the catalyst on regioselectivity and the regiospecificity of the reaction will be discussed.

<u>4.3.4.1. Regioselectivity.</u> The regioselectivity is observed during first carbon-carbon bond formation (stepwise mechanism, first step) via $TS1_{cat}^{step} - IIa$ which is energeticaly favored by 3.1 and 3.5 kcal/mol energy compared to its conformers, $TS1_{cat}^{step} - Ib$ and $TS1_{cat}^{step} - IIb$, respectively. (Figure 4.9). This preference can be justified by charge analysis employed on reaction partners and Ag(I)-phthalazine complex (B) as shown in Figure 4.13. The first bond formation can take place either by the attack of C5 carbon of siloxy alkyne (2) to C1 carbon of complex (A), which is the case in $TS1_{cat}^{step} - IIa$, or attack of C5 carbon of siloxy alkyne to C4 carbon of complex (A) in $TS1_{cat}^{step} - Ib$ and $TS1_{cat}^{step} - IIb$, noted that these are energetically less stabilized conformers.

The NPA charge analysis of reaction partners (2) and complex (A) shows that the nucleophilic attack of C5 (-0.178e) to C1 carbon (0.127e) of complex (A) is preferred due to its higher electrophilic nature. It can be noticed that the electron withdrawing effect of Ag(I)-bipyridine is effective on the vicinal carbon atoms (C1 and C4) of complex A. However, the effect is more pronounced on C1, rendering this site more prone to accept the siloxy alkyne as a nucleophile.

<u>4.3.4.2. Regiospecificity.</u> The regiospecificity is also noticed in the formation of first C-C bond in stepwise fashion, meaning no nucleophilic attack through C6 carbon of siloxy alkyne (2) to the either C1 or C4 carbon of complex (A) is observed, which is expected when the charge on C6 (0.278e) is considered. (Figure 4.13). In the concerted fashion, since the vicinal carbon atoms (C1 and C4) of complex (A) are simultaneously open to nucleophilic attack by siloxy alkyne, there is no regioselectivity

for this mechanism. Besides, no concerted transition state conformer is located other than $TS_{cat}^{conc}-Ib$, indicating the regiospecificity instead.



Figure 4.13. a) NPA atomic charges of 1,2,A. b) LUMOs of 1,A and HOMO of 2 (isovalue = 0.05 au)

<u>4.3.4.3.</u> Frontier Molecular Orbital (FMO) Analysis. HOMO and LUMO analysis (Figure 4.13, b) was demonstrated in order to reveal the effect of Ag(I)-bipyridine catalyst when it is coordinated to phthalazine (1), lowering its energetically high lying LUMO (-0.090 eV) to -0.589 eV (Figure 4.13, b), and consequently increase the rate while taking electrons from HOMO of siloxy alkyne (2).

4.4. Conclusion

In the second part of this thesis, the mechanism of Ag-catalyzed inverse electron demand Diels-Alder (IEDDA) reaction of phthalazines with siloxy alkynes have been demonstrated by the aid of DFT calculations, and presented that silver catalyst can promote the corresponding reaction with two different pathways, which are concerted and stepwise fashion. More particularly, diaza-enolate intermediate bearing silylketenium confirms that the reaction can follow different direction in the presence of the silver catalyst. The results are important in modeling full reaction mechanisms of highly efficient silver catalyst in inverse electron demand Diels-Alder (IEDDA) reactions, and fully support the experimentally proposed mechanism [2] for transition metal based catalysis of the IEDDA reaction of phthalazine and siloxy alkynes.

When the results are evaluated in detail, effect of silver catalyst is noticeably seen when considering energy barriers between uncatalyzed and silver-catalyzed cycloaddition reactions, demonstrated with the free energy profiles of both reactions. Catalysis of this reaction in the presence of Ag(I)-bipyridine in concerted pathway endorses the cycloaddition by 13 kcal/mol energy in comparison to the uncatalyzed reaction. In the situation of stepwise pathway, the difference in energy barriers is even higher, 20.2 kcal/mol, between uncatalyzed and silver-catalyzed cycloaddition, which highlights the latter pathway is more likely to develop.

In addition, investigation of the mode of action for the catalyst revealed that the binding site of Ag(I)-bipyridine to reactive partners resulted in significant energetic effect on structures and in particular on transition states energies, which has rationalized by discussing regioselectivity/specificity of this reaction. Frontier molecular orbital (FMO) analysis gave valuable information about how the silver catalyst affects the reaction by binding to phthalazine and lowering its energetically high lying LUMO_{diene} and consequently increasing the reaction rate.

In the light of all the findings mentioned above, this study has been concluded by adhering to the initial purpose and shown that the silver catalyst has a significant effect on the energy barriers of the cycloaddition reaction when compared to the uncatalyzed reaction, which emphasizes the high efficiency of transition metal catalysis in IEDDA reactions.

5. CONCLUDING REMARKS

In this dissertation, two different projects involving significant chemical reactions in the fields of inorganic and organic chemistry have been presented by means of DFT applications in order to demonstrate the catalytic effect of transition metal-based complexes on those reactions.

Transition metals are considered to be good catalysts due to their ability to lend and withdraw electrons easily from the reagents and also to interchange between a variety of oxidation states while making complexes with the reagents, making transition metals good electron sources and ultimately effective catalysts. In order to address this affect, water oxidation and inverse electron demand Diels-Alder (IEDDA) reactions catalyzed by transition metal complexes have been probed throughout the dissertation.

In the first part, DFT applications have been utilized to model and investigate the ruthenium-based water oxidation catalysts (WOCs) and their operative mechanisms along water oxidation half reaction of water splitting by taking geometrical and electronic factors into account. Along with proposing water nucleophilic attack (WNA) mechanism for two catalysts; investigating each species in the catalytic cycles, spin density and frontier molecular orbital (FMO) analysis, oxygen-oxygen bond formation phase and the redox calculations have been presented throughout the water oxidation reaction.

As for the second part of the thesis, the aim was to reveal the effect of highly efficient transition metal catalysis in inverse electron demand Diels-Alder (IEDDA) reactions by means of DFT calculations, focusing on silver-catalyzed IEDDA reaction of 1,2 diazines and siloxy alkynes. Throughout this study, two different reaction pathways, concerted and stepwise, were explored as well as the uncatalyzed reaction to highlight the effect of transition metal-based catalyst. The mode of action for the silver-based catalyst has been revealed, and also its effect on the regioselectivity/specificity of the reaction has been presented.
Overall, throughout this dissertation it has been tried to address the effect of transition metal-based catalysts in some significant inorganic and organic reactions by focusing on various mechanistic assumptions. Most widely used quantum mechanical method, which is Density Functional Theory (DFT), have been employed in both studies to model the behavior of molecular systems.

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