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Catalytic Water Oxidation by Molecular Ruthenium Complexes Bearing Multifunctional Ligands

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Catalytic Water Oxidation by Molecular Ruthenium Complexes Bearing Multifunctional Ligands

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy

in

Chemistry

By

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2017
The dissertation of Jayneil Mukesh Kamdar is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

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Chair

University of California, San Diego
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2017
DEDICATION

To my family without whom none of my success would have been possible
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In 2009, I quit my job as a production chemist at SAFC (Sigma-Aldrich Fine Chemicals) in beautiful (but cold) Madison, WI and made my way to sunny San Diego for graduate school. While my time in industry was a tremendous learning experience (thanks Rick and Randy for whipping me into shape), I chose to pursue graduate studies so that I could delve deeper into the science.

First and foremost, I would like to wholeheartedly thank my advisor Doug Grotjahn for training me to be a skilled chemist. Rumor has it that Doug is one of a rare breed of advisors that works equally hard in the lab alongside his graduate students as he does in a managerial capacity. His intuition as a synthetic chemist is remarkable. He really pushed me to think critically about chemistry and his work ethic and genuine enthusiasm for all things chemistry have been a great inspiration. In addition to all that, he is very patient and kind-hearted - qualities that make him a great mentor.

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Studies in Synthesis and Organometallic Catalysis
Professor Douglas B. Grotjahn
ABSTRACT OF THE DISSERTATION

Catalytic Water Oxidation by Molecular Ruthenium Complexes Bearing Multifunctional Ligands

by

Jayneil Mukesh Kamdar

Doctor of Philosophy in Chemistry

University of California, San Diego, 2017
San Diego State University, 2017

Professor Douglas B. Grotjahn

Global concern about the long-term sustainability and environmental impact of burning fossil fuels has prompted widespread research on alternative fuels. Hydrogen is attractive as a chemical fuel because it is carbon-free and therefore its exothermic reaction with oxygen does not generate CO₂ as a byproduct. Large scale implementation of hydrogen, however, depends on efficient and clean production of hydrogen from non-fossil sources. Splitting water with sunlight is often considered the “Holy Grail” of a sustainable hydrogen economy, however the greatest challenge towards achieving this goal is in lowering the high kinetic barrier of the water oxidation half reaction. With the right electronics and geometry of coordinated ligands, transition metals can effectively mediate the loss of 4 e⁻ / 4 H⁺ required to oxidize water. This dissertation details
the syntheses, characterization, and reactivities of three novel catalytic systems containing multifunctional ligands that appear to have a marked effect on catalysis.

Chapter 2 details the synthesis and reactivity of novel ruthenium complexes bearing 2,2’-bipyridine ligands with various pyrazolate groups in the 6,6’-positions. The structures of these complexes were characterized by NMR spectroscopy and x-ray crystallography and for one of the complexes, the unique solvatochromic and acid-base properties involving the uncoordinated nitrogen atoms of the ligand were investigated by non-aqueous and aqueous UV-visible spectroscopy and electrochemistry. Rapid O₂ evolution was witnessed under acidic conditions in the presence of Ce⁴⁺. While the apparent rates (between 3 and 4 s⁻¹) are in the upper range of rates observed for ruthenium-based molecular catalysts, lag periods observed for 1 – 1.5 min prior to O₂ production may be indications of slow catalyst dissolution or activation, or of catalyst modification. Alternatively, Ce⁴⁺ may have a non-innocent role during catalysis by interaction with the uncoordinated nitrogen.

Chapter 3 details the synthesis and catalysis-relevant properties of two novel ruthenium complexes, [Ru(2,2′-bipyridine-6,6’-diphosphonato)(pic)2] (pic=4-picoline) and [Ru(6,6’-diisopropyl-2,2′-bipyridine-6,6’-diphosphonato)(pic)2]. These complexes are the first examples of water oxidation catalysts deliberately bearing phosphonate groups positioned to serve as metal-bound ligands. They have been characterized by NMR spectroscopy, elemental analyses, x-ray crystallography, cyclic voltammetry, and UV-visible spectroscopy. From electrochemical data, we have discovered that charge states of P-OH/P-OR groups have a significant influence on redox and catalytic properties, features that are absent in much more commonly studied carboxylate analogs.
Chapter 4 details the synthesis and reactivity of a series of ruthenium complexes bearing novel 2,2’-biimidazole-4,4’-phosphonate ligands. Surprisingly, the new ligands did not participate in the intended tetradentate coordination, but instead bidentate N,N’-coordination, placing the phosphonate groups in the secondary coordination sphere to engage in hydrogen bonding interactions with two aquo ligands. The presented complexes have been characterized by NMR spectroscopy, x-ray crystallography, and cyclic voltammetry. Qualitative and quantitative oxygen evolution studies (from cyclic voltammetry and addition of excess CeIV, respectively) have shown a dramatic improvement in catalytic rates compared to those of previously reported Ru diaquo complexes. Our working hypothesis to explain the superior catalytic activity includes involvement of the phosphonates in the secondary coordination sphere potentially as basic proton-relaying functionalities.
Chapter 1

Introduction

The second industrial revolution from 1870 to 1914 was a period of unprecedented innovation and technological growth. Fundamental advances in manufacturing methods allowed for the mass production of oil and steel, bolstering the expansion of an enormous range of industries. Invention of the steam turbine led to the development of power stations for centralized generation and distribution of electricity. Internal combustion engines were developed and gasoline-powered automobiles were mass-produced for the first time. With the ensuing metamorphosis in the global economy, the demand and consumption of fossil fuels (coal, natural gas, and oil) skyrocketed. Today, nearly every facet of life as we know it depends on fossil fuels. Gasoline derived from crude oil allows us to effortlessly commute to work on a daily basis or fly across the country in a matter of hours. Coal-burning power plants provide unlimited electricity to illuminate our homes at any hour. Even common luxuries such as clothes, plastic bags, cosmetics and medicines are made widely available by mass manufacturing in factories that are powered by electricity derived from fossil fuels. Nearly 80% of the world’s primary energy needs are met by fossil fuels.\(^1\) However, modern society is now met with a profound dilemma concerning the inherent issues associated with continued fossil fuel usage.

1.1. Disadvantages of fossil fuels

Fossil fuels are remnants of buried prehistoric organisms that were chemically altered from millions of years of geological decomposition; thus, the first issue is that by their very nature – *fossil fuels are finite resources*. In one study, depletion of conventional supplies is calculated to
occur as early as 2044, 2046, and 2116 for oil, natural gas, and coal, respectively.\textsuperscript{2} The global population is projected to reach nearly 9.7 billion by 2050, which means an additional 2.3 billion people will require energy.\textsuperscript{3} The United States Energy Information Administration (EIA) projected a 48% increase in world energy consumption between 2012 and 2040.\textsuperscript{4} Predictive calculations such as these make it clear that the capability of fossil energy production to keep up with world energy consumption is dubious at most. Moreover, the availability (thus price) of oil is often at the mercy of the geo-political or geo-economic climate surrounding oil-rich areas of the world. Quintessential examples of such phenomena are the oil crises of 1973 and 1979 when many countries experienced great petroleum shortages due to politically-charged tensions in the Middle East.

Proponents of fossil fuels may argue that resource depletion is a non-issue due to the advent of new technologies and continued discovery of conventional and unconventional reserves, however even if this is true, impacts of fossil fuel \textit{extraction} cannot be ignored. In the case of oil, significant habitat degradation is associated with both on-shore and off-shore oil wells. For example, in 2010, a ruptured oil pipeline in Kalamazoo, MI spilled approximately 840,000 gallons of oil into the Kalamazoo River negatively impacting fish and wildlife and forcing the evacuation of local residents.\textsuperscript{5} In the same year, the disastrous BP oil spill discharged approximately 210 million gallons of oil into the Gulf of Mexico causing devastating effects on local ecosystems that are still manifesting today.\textsuperscript{6} Spanning from 2010-2017 there have been 47 large spills that have discharged a total of nearly 12.4 million gallons of oil; in 2016 alone, more than 2 million gallons of oil were lost through tanker incidents. Similarly, the coal industry has numerous issues related to land use, waste management, water pollution and occupational health that cannot be ignored. Although coal mining has become considerably more advanced in developed countries, safety
concerns remain high in lesser developed countries. Coal workers’ pneumoconiosis (black lung disease) is the main occupational lung disease in China with nearly ~14,000 new diagnoses in 2013 alone. The United States Department of Labor reported that an average of 26 coal miners per year died between 2005 and 2014 in the United States. The statistics listed above merely graze the surface of the controversial impacts of fossil fuel extraction.

The second issue is that fossil fuels are composed primarily of carbonaceous compounds ranging from pure carbon to hydrocarbons with various molecular weights and C:H ratios (e.g. coal, alkanes, cycloalkanes, aromatic hydrocarbons, etc.) and their combustion yields CO$_2$ as a major by-product. In the midst of the industrial revolution, Svante Arrhenius was the first to propose that anthropogenic CO$_2$ formed from burning fossil fuels could lead to global warming. However, concern for global warming did not begin to mount until the 1950s when Charles Keeling showed evidence that CO$_2$ levels in the atmosphere were indeed increasing rapidly. More evidence accumulated in the 1970s and by the late 1980s, there was a scientific consensus that man-made atmospheric pollution is likely causing global temperatures to rise and that efforts are needed to significantly reduce emissions. In 2013, the Intergovernmental Panel on Climate Change projected that increases in average global temperatures could be as high as 4.3 °C by 2100. Such a dramatic change in the atmospheric temperature can result in disastrous consequences, as a report by Molina et al. eloquently states that we may be “faced with serious and largely irreversible changes to large components of the Earth’s climate system.”

1.2. Hydrogen

Interest in clean and renewable energy gained momentum in the 1970s amidst oil shortages and increasing concern for global warming. Technologies for harnessing wind, geothermal,
hydropower, and solar energy have reached incredible new heights and are beginning to play a formidable role in world energy production. Solar energy is particularly fascinating. The average solar flux that strikes the Earth’s surface – accounting for the Earth’s rotation, angle at which the rays strike, and influence of the atmosphere – is 174.7 W/m² or approximately 10.5 kJ/(m²·min). A simple calculation shows that merely ~3.5 weeks of sunlight in an area of land about the size of Arizona would be able to cover the total amount of energy consumed in the United States in 2016 (~1.03 × 10²⁰ J).

Despite the massive amount of energy that can be generated by renewable energy platforms, they are greatly dependent on Mother Nature. For example, geothermal energy is limited to areas near tectonic plate boundaries. Wind energy is at the mercy of the whims of geographical weather patterns. Harnessing solar energy depends on how many hours of daylight a geographical location receives and how cloudy it is on a certain day. Thus, it is important to find a way to efficiently store the energy harnessed by these technologies so that it can be accessed anywhere and anytime.

Historically our energy has been stored in chemical bonds. The C-H and C-C bonds of hydrocarbons in fossil fuels store energy derived from prehistoric photosynthetic mechanisms and this chemical energy is released as usable heat energy in a combustion reaction with oxygen. From the 1950s to the 1970s, the discussion of distancing mankind from carbonaceous fuel inspired the idea of a “hydrogen economy” which is based on the idea that the H-H bond of hydrogen gas can be used to store energy. From an environmental standpoint, hydrogen is an attractive fuel because the only by-product from its reaction with O₂ is pure H₂O (Eq. 1).

\[
2\text{H}_2(\text{g}) + \text{O}_2(\text{g}) \rightarrow 2\text{H}_2\text{O} (\text{l})
\]  
(Eq. 1)
Infrastructure for a hydrogen economy is expanding year by year with new hydrogen fueling stations emerging globally and major auto companies announcing production of vehicles with fuel cell technologies (e.g. Toyota Mirai, Honda Clarity). However, the critical problem with hydrogen is that 96% of it is produced from fossil fuels by processes such as steam reforming, partial oxidation of methane, or coal gasification.\textsuperscript{22–24} Thus, the hydrogen economy in its current state is not carbon-neutral.

1.3. Splitting water for hydrogen

Nearly 227 years ago, two Dutch scientists, Adriaan Paets van Troostwijk and Jan Rudolph Deiman, conducted an experiment where two thin gold wires connected to an electrostatic machine were inserted into a U-shaped glass tube that was sealed on one end.\textsuperscript{25,26} The first wire was inserted through the sealed end, while the second wire was inserted through the open end until it reached close to the sealed end and was separated by only a short distance from the first wire. The glass tube was then filled with degassed water and a potential difference was applied between the two wires via the electrostatic machine. Rapid evolution of gas bubbles was observed from both wires, and continued until volume displacement caused the first wire to cease contact with the water. Additional sparks applied to the headspace via the electrostatic machine led to an explosive reaction whereby the headspace was reconstituted with water. Based on these and previous results,\textsuperscript{27} Paets van Troostwijk and Deiman concluded that sparks applied from the electrostatic machine decomposed water to produce a gas containing a 2:1 ratio of hydrogen to oxygen. This was the first experimental report\textsuperscript{28,29} of water electrolysis, also known as “water splitting”, where two water molecules react to form hydrogen and oxygen gas (Eq. 2) upon application of an electrical potential difference.
\[ 2H_2O (l) \rightarrow 2H_2(g) + O_2(g) \quad (\text{Eq. 2}) \]

Today, about 4% of global hydrogen is derived from water electrolysis. Electrolysis is an attractive way to produce hydrogen because water is extremely abundant on the Earth’s surface and no greenhouse gases (e.g. CO\textsubscript{2}) are produced in the process. The challenge for widespread commercial adoption of this method lies in overcoming the inherent energetic costs associated with the reaction, which can be understood better by breaking down the reaction into its two half-reactions.

**anode:** \[ 2H_2O (l) \rightarrow O_2(g) + 4H^+ + 4e^- \quad (\text{Eq. 3}) \]

**cathode:** \[ 4H^+ + 4e^- \rightarrow 2H_2(g) \quad (\text{Eq. 4}) \]

A 4 e\textsuperscript{-} oxidation of two water molecules generates O\textsubscript{2} and protons at the anode, while at the cathode, protons generated at the anode are reduced to produce H\textsubscript{2} gas. Considering only thermodynamics at first, under highly acidic conditions (pH ~ 0), the standard oxidation potential for eq. 3 is \( E^\circ = 1.23 \) V and the standard reduction potential for eq. 4 is \( E^\circ = 0.0 \) V. Raising the pH will vary the standard potentials according to the Nernst equation (\( \Delta E = -59 \text{ mV} / \text{pH unit} \)) however the overall potential difference will remain \( \Delta E = -1.23 \) V which translates to an extremely endothermic reaction with a \( \Delta G \) value of \( \sim +475 \text{ kJ per mol of O}_2 \) formed. Thus, it is already apparent that from a thermodynamic standpoint splitting water is an uphill battle. In addition, one must overcome the kinetic barrier associated with each half reaction which manifests itself as “overpotential”. Appel and Helm defined “overpotential” as “the difference between the equilibrium potential for a given reaction (also called the thermodynamic potential) and the potential at which the catalyst operates at a specific current under specific conditions”\textsuperscript{30}. From a molecular perspective, the anodic water oxidation half reaction is kinetically the more difficult
step likely because not only does it require the efficient transfer of four electron and proton equivalents, but also the difficult formation of a weak O-O single bond must occur in the intermediate steps of the reaction.

**Figure 1.1.** Prevalent mechanistic scenarios for metal catalyzed oxidation of water.

Metals, particularly transition metals, can mediate electron movement during water oxidation and in turn mitigate the energetic cost associated with O-O bond formation. Two prevalent mechanistic scenarios discussed in the literature are: (1) water nucleophilic attack (WNA) and (2) bimoleclar radical oxo-coupling (I2M) (Figure 1). Requisite to both scenarios is the generation of a high valent metal oxo intermediate formed from an aquo ligand through successive proton-coupled electron transfers. The reactivity of the oxo group is then dictated by the d-electron count and the ligand field of the metal. In the WNA pathway, a second water molecule serves as a nucleophile to attack a highly electrophilic oxo ligand. The electrophilicity of the oxo is governed largely by the oxidation state of the metal and the molecular environment effected by the ligand geometry. From an orbital perspective, a σ bonding orbital of water overlaps
with the anti-bonding $\pi^*$ orbital of the metal-oxo group leading to breakage of the double bond, formal reduction of the metal center by $2\ e^-$, and O-O $\sigma$ bond formation. In the 12M pathway, two metal-oxo fragments bearing radical character combine for O-O bond formation. The combination of singly-occupied anti-bonding $\pi^*$ orbitals of the metal-oxo fragments leads to a O-O bonding interaction and reduction of bond order in the metal-oxo double bond.\textsuperscript{31}

1.4. Biological Photosynthesis and Water Oxidation

![Figure 1.2. Z-Scheme – energy diagram for electron transfer in photosynthesis (adapted from refs. 32 and 33)](image)

As it turns out, the oxidation of water is a crucial element of biological photosynthesis and is in fact mediated by a cluster of four manganese and one calcium atom. The seamless choreography between sunlight and water for energy production and storage in plants is directed by two enzymatic reaction centers located in chloroplasts - photosystem II (PS II) and photosystem I (PS I) (Figure 1.2). Light harvesting molecules in PS II capture a photon from sunlight and excite an electron from the excitonic dimer P680 into an electron transport chain consisting of
coenzymes and cofactors that ultimately leads to the reduction of NADP$^+$ in PS I. The resulting P680$^+$ serves as a very powerful oxidant of an adjacent tyrosine residue (TyrZ). The oxidized TyrZ$^+$ radical can then mediate proton-coupled electron transfer (PCET) in a catalytic oxygen-evolving complex (OEC) that has been determined to have the formula Mn$_4$CaO$_5$(H$_2$O)$_4$ where three Mn atoms and a Ca$^{2+}$ atom are arranged in a cubane-like framework connected to another “dangling” Mn atom that is in close proximity to the Ca$^{2+}$ atom.\textsuperscript{34} The mechanism of water oxidation by the OEC has been and continues to be a subject of significant debate.\textsuperscript{35-39} Recently Barber proposed a hydroxyl/water nucleophilic attack mechanism for O-O bond formation based on comparative data from an almost structurally identical Fe-Ni cluster of anaerobic carbon monoxide dehydrogenase.\textsuperscript{39} Based on this model, two individual substrate water molecules are coordinated to Ca$^{2+}$ and the dangling Mn$^{III}$ respectively; a series of PCETs would lead to generation of a highly electrophilic Mn$^V$-oxo moiety and a Ca$^{2+}$-hydroxo fragment that would allow rapid O-O bond formation (Figure 1.3). The Mn$_4$CaO$_5$ cluster is surrounded by a series of precisely positioned amino acid residues that most certainly play a role in O-O bond formation mechanism. Some of these amino acid residues are in the primary coordination sphere coordinated to the Mn atoms while other residues lie in the secondary coordination sphere likely engaging in hydrogen bonding, proton-relaying, and charge compensation.\textsuperscript{34} The high level of synergy afforded by the exquisite cooperation of parts within the OEC sphere allow for rapid evolution of O$_2$ at turnover frequencies greater than 100 s$^{-1}$ at low overpotentials (~70 mV).\textsuperscript{40}
Figure 1.3. Mechanism of water oxidation by OEC proposed by Barber (figure from ref\textsuperscript{39})

1.5. Artificial photosynthesis:

The highly complex yet elegant mechanism of biological photosynthesis has been finely tuned after billions of years of evolutionary iterations. Mimicking such a system\textit{ exactly} for our energy needs would undoubtedly be an impossible feat, however we can certainly borrow certain ideas from Mother Nature. The machinery of biological photosynthesis has three key components:

1) A photosynthetic reaction center that can efficiently harvest photonic energy from the sun and use that energy to excite electrons into an acceptor system.

2) An acceptor system that converts photonic energy into chemical energy by using the excited electrons from the reaction center as reducing equivalents for production of NADPH – the “energy currency” of cells.
3) A donor system that refills the electronic holes in the reaction center with electrons derived from water

The schematic shown in Figure 4 shows a theoretical model for an artificial photosynthetic system that contains conceptual analogs of the three components listed above.\textsuperscript{41,42} In this model, a synthetic molecular photosensitizer serves as the light-harvesting component where an electron is promoted to an excited state from exposure to sunlight and subsequent charge separation occurs as the electron is transferred to the conduction band of an adjacent semi-conducting metal-oxide surface. The resulting “hole” is replenished by electrons extracted from oxidation of water by an efficient water oxidation catalyst (WOC) that may either be covalently attached to the photosensitizer or the metal-oxide surface, or a homogeneous catalyst in the aqueous cell solution. Meanwhile the photo-excited electrons travel to the cathode and are utilized by a second catalyst that efficiently reduces the protons generated in the water oxidation reaction to form hydrogen gas. Alternatively, the electrons may be utilized by a carbon dioxide reduction catalyst (not shown).
Figure 1.4. Schematic for an artificial photosynthetic system (adapted from fig. 1 in ref. 41 and fig. 4.12b in ref. 42)

On the anodic half of Figure 1.4, integration of efficient light absorption, stable charge separation, and a fast water oxidation catalyst presents several challenges and vigorous research is underway to study each of these individual components and the challenges of their integration.\textsuperscript{43–45}

1.6. A Brief History and Mini-review of Ru-based Homogeneous Water Oxidation Catalysis:

A growing number of transition metals, such as manganese,\textsuperscript{46} iridium,\textsuperscript{47} iron,\textsuperscript{48–50} copper,\textsuperscript{51} and cobalt,\textsuperscript{52–56} are known to make WOC but ruthenium, in particular, has received tremendous attention in the last 40 years. Interest in ruthenium began to develop after landmark studies by Thomas J. Meyer’s group between 1978 and 1981 showing that stable Ru-oxo complexes could be formed by proton-coupled electron transfer (PCET);\textsuperscript{57–59} these studies were followed by a
seminal paper describing catalytic water oxidation by a dinuclear ruthenium complex, [(bpy)\textsubscript{2}H\textsubscript{2}O]Ru(\mu-O)Ru(H\textsubscript{2}O)(bpy)\textsubscript{2}\textsuperscript{4+} (I) (bpy = bipyridine) - also known as the “blue dimer”.\textsuperscript{60}

The blue dimer is considered to be the first characterized ruthenium-based homogeneous water oxidation catalyst; its discovery was a culmination of fundamental work done on polypyridyl ruthenium complexes spearheaded in the 1940s to 1960s by an Australian chemist named Francis P. Dwyer along with several collaborators, and then continued by Meyer in the 1970s and 1980s. To this day, the vast majority of ruthenium-based water oxidation catalysts are composed of some type of a polypyridyl framework and much of the focus on their reactivities relies on the foundational work done by Dwyer and Meyer. The following sections will present and briefly discuss the most significant discoveries in the field of homogeneous ruthenium WOC in chronological order leading up to the state of the art today.

1.6.1. The origin of Ru-polypyridyl chemistry

Dwyer’s early work was focused on exploring phenomena related to the optical activities of polypyridyl complexes. For example, in 1949 Dwyer and coworkers synthesized Ru\textsuperscript{II}(phen)\textsubscript{3}\textsuperscript{2+} (phen = phenanthroline) and demonstrated that it maintained its optical activity upon oxidation to Ru\textsuperscript{III} and that a simple electrochemical change was achievable because of its substitutional “inertness”.\textsuperscript{61} Furthermore, in 1950, Dwyer reported the synthesis and isolation of both optical isomers of Os(bpy)\textsubscript{3}\textsuperscript{2+} (in collaboration with Burstall), and demonstrated that mixing equimolar amounts of \textit{d}-Os\textsuperscript{II}(bpy)\textsubscript{3}\textsuperscript{2+} and \textit{l}-Os\textsuperscript{III}(bpy)\textsubscript{3}\textsuperscript{3+} lead to a dynamic electronic equilibrium to form an optically inactive mixture consisting of equal ratios of the \textit{l}- and \textit{d}-forms of both Os\textsuperscript{II}(bpy)\textsubscript{3}\textsuperscript{2+} and Os\textsuperscript{III}(bpy)\textsubscript{3}\textsuperscript{3+}.\textsuperscript{62} Motivated by a publication in 1955 by Brandt that identified mono- and bis-2,2’-bipyridine Ru\textsuperscript{III} complexes as intermediates in the formation for Ru\textsuperscript{II}(bpy)\textsubscript{3}\textsuperscript{2+},\textsuperscript{63} Dwyer reported
procedures to intentionally make both mono- and bis-2,2'-bipyridine complexes. After his death in 1962, numerous collaborators continued work on the ligand substitution properties of polypyridyl Ru and Os complexes until the late 1960s.

In the 1970s, Meyer picked up where Dwyer and his collaborators left off, investigating the novel synthetic chemistry of Ru/Os polypyridyl complexes; however, he was particularly interested in their electron transfer properties and how redox reactions could potentially influence the chemical properties of coordinated ligands. For example, in one study Meyer and coworkers found that primary amines coordinated to ruthenium as in $[\text{Ru}^{II}(\text{bpy})_2(\text{NH}_2\text{R})_2]^{2+}$ were oxidized to nitriles upon oxidation of Ru$^{II}$ to Ru$^{III}$. Presumably based on analogous logic, Bruce Moyer, a graduate student of Meyer’s, prepared a Ru-aquo complex - $\text{Ru}^{II}(\text{bpy})_2(\text{py})(\text{H}_2\text{O})^{2+}$ - with hopes that redox properties of a complex bearing a metal-coordinated water molecule could provide a pathway for the oxidation of water to O$_2$. Results of the redox and chemical properties of $\text{Ru}^{II}(\text{bpy})_2(\text{py})(\text{H}_2\text{O})^{2+}$ were described in a series of landmark studies from 1978 to 1981 (to be discussed in the following section) which have not only inspired modern Ru water oxidation chemistry but also became the basis of the theory of proton-coupled electron transfer (PCET).

1.6.2. A stable Ru-oxo species derived from a Ru-aquo complex: $\text{Ru}^{II}(\text{bpy})_2(\text{py})(\text{H}_2\text{O})^{2+}$

A simple electrochemical comparison of the Ru$^{III/IV}$ and Ru$^{III/IV}$ couples of $\text{Ru(bpy)}_2\text{Cl}_2$ and $\text{Ru(bpy)}_2(\text{py})(\text{H}_2\text{O})^{2+}$ (py = pyridine) in pH 7 buffer reveals interesting differences (Figure 1.5). In the case of $\text{Ru(bpy)}_2\text{Cl}_2$, the Ru$^{III/IV}$ and Ru$^{III/IV}$ couples are observed at 0.0 V and 1.7 V, respectively. In contrast, the Ru$^{III/IV}$ and Ru$^{III/IV}$ couples for $\text{Ru(bpy)}_2(\text{py})(\text{H}_2\text{O})^{2+}$ are observed at 0.67 V and 0.78 V, respectively. The dramatic difference between $\Delta E$ values ($\Delta E = 1.7$ V for $\text{Ru(bpy)}_2\text{Cl}_2$ and $\Delta E = 0.11$ V for $\text{Ru(bpy)}_2(\text{py})(\text{H}_2\text{O})^{2+}$) indicates that the simple replacement of
anionic Cl⁻ ligands with a neutral pyridine and an aquo ligand has a profound influence on redox activity. A Pourbaix diagram of Ru(bpy)₂(py)(H₂O)²⁺ shows that between pH ~0.85 to 10.25, the Ru²⁺/³⁺ couple is pH dependent (ΔE = 59 mV per pH unit) and therefore associated with concomitant transfer of a single proton. Similarly, between pH ~0.85 to 12, the Ru³⁺/⁴⁺ couple is also associated with a single proton transfer.⁵⁸ Considering that the only reasonable choice of dissociable protons would be those of the aquo ligand, it can be deduced that a stepwise 2 e⁻ / 2 H⁺ transition occurs reversibly from [Ru²⁺-OH₂]²⁺ to [Ru⁴⁺=O]²⁺. The important implications of this discovery are the following: (1) PCET prevents excessive charge build-up that would normally disfavor the formation of Ru⁴⁺ species (as exemplified by the high Ru³⁺/⁴⁺ oxidation potential of 1.78 V for Ru(bpy)₂Cl₂), and (2) PCET allows for the facile formation of stable Ru-oxo species that can be exploited for further oxidative chemistry such as oxidation of water or organic substrates.
Figure 1.5. Work done by Meyer showing facile formation of a Ru-oxo intermediate through proton-coupled electron transfer (PCET).

1.6.3 The Blue Dimer – the first homogeneous ruthenium water oxidation catalyst (1982)

Attempts by Meyer and coworkers to oxidize water with Ru(bpy)$_2$(py)(H$_2$O)$_2^{2+}$ and other similar single-site Ru complexes lead to little or no success.$^{66}$ This observation lead to the
presumption that more than one metal center was required to oxidize water – a logical conclusion at the time considering that the oxygen-evolution complex in the photosystem II was determined to contain several manganese atoms (although later both Thummel and Meyer showed that single-site water oxidation was indeed possible – see section 1.6.6.). The “blue dimer,” 1.1, first synthesized in 1975, was a logical choice to test for catalytic activity because it contained two metal centers with aquo ligands in close proximity that could be transformed to oxo fragments by chemistry similar to that observed for Ru(bpy)$_2$(py)(H$_2$O)$_2^+$. Rapid O$_2$ production was observed upon addition of 50-100 fold excesses of CAN to a solution of 1.1 in 0.1 M HClO$_4$. In addition, a large oxidative wave was observed at 1.20 V (vs. Ag/AgCl) by cyclic voltammetry of 1.1 in 0.1 M H$_2$SO$_4$ – this wave was attributed to the catalytic oxidation of water.$^{60}$

1.6.4. An anthracene-bridged dinuclear system – electronically isolated metal centers.

Nearly 18 years after Meyer’s discovery of the blue dimer, Tanaka’s group reported 1.2, a dinuclear complex which consists of two (3,6-tBu$_2$qui)Ru$^{II}$-OH (3,6-tBu$_2$qui = 3,6-di(tert-butyl)-1,2-benzoquinone) moieties connected by btpyan (1,8-bis{(2,2’;6’,2”)-terpyridyl}anthracene), a bridging anthracene ligand.$^{67}$ Tanaka’s discovery was unique because it was a departure from the extensively explored µ-oxo motif following the report of the blue dimer.$^{68–88}$ In contrast to the blue dimer in which the Ru centers are electronically connected via the µ-oxo bridge, the two Ru
centers in 1.2 are significantly more electronically isolated from each other due to the extended terpy-anthracene-terpy bridge of the ligand, yet the two metal centers are positioned closely enough to allow a Ru-O-O-Ru interaction to occur. The redox-active quinone ligands were shown to be reduced to semiquinones upon deprotonation of the Ru\textsuperscript{II}-OH groups. Cyclic voltammetry of 1.2 deposited on an ITO electrode showed a ligand-centered redox wave at 0.40 V, an irreversible wave at 1.20 V corresponding to the Ru\textsuperscript{II/III} oxidation, and a significant catalytic wave with an onset potential of \textasciitilde1.5 V. Controlled-potential electrolysis of 1.2 modified on ITO was conducted at +1.70 V in a pH 4 aqueous solution and oxygen evolution was observed for 40 h with a TON of 33500 (quantified by GC). By contrast, under the same conditions, controlled-potential electrolysis of similar complex - [Ru(OH)(bpy)]\textsubscript{2}(bpy)\textsubscript{2}\textsuperscript{2+} (1.3) - lead to evolution of undetectable amounts of oxygen, suggesting that the redox-active quinone ligands of 1.2 are noninnocent in catalysis.\textsuperscript{89}

1.6.5. Dinuclear catalysts with a more rigid backbone

Llobet’s group discovered the dinuclear Ru-Hbpp catalyst (1.4) bearing a rigid 2,2’-(1H-pyrazole-3,5-diyl)dipyridine) backbone.\textsuperscript{90} Free rotation of the Ru-O moieties in 1.4 is restricted due to the rigidity of the Hbpp ligand and thus, unlike in complexes 1.1-1.3, the Ru-O groups are

![Diagram of 1.4 and 1.5]
intrinsically preorganized for *intramolecular* O-O bond formation via an I2M oxo-radical coupling pathway. An $^{18}$O-labelling study strongly indicated that O$_2$ is indeed generated via an intramolecular radical coupling pathway.$^{91}$ Under acidic conditions (pH = 1) and excess Ce$^{IV}$, turnover numbers close to 500 were obtained. Shortly after, Thummel and coworkers synthesized related dinuclear $\mu$-Cl complexes (1.5a-c) with a rigid polypyridyl backbone positioning two Ru centers in close proximity.$^{92}$ Turnovers achieved by complexes 1.5a-c were nearly twice that using complex 1.4. Interestingly, the $\mu$-Cl bridge appears to be very stable - to the extent that no ionization was observed even in a refluxing solution of Ag$^+$ in acetone - although H$_2$O / Cl$^-$ substitution may be more likely upon oxidation in acidic aqueous conditions. The possibility of the Cl$^-$ bridge remaining intact during the catalytic cycle cannot be ruled out until more thorough mechanistic studies are done.

1.6.6. One metal site is enough!

As described above, the early years of the field of transition-metal WOC were dominated by the paradigm that a single metal site was insufficient to catalyze the oxidation of H$_2$O to O$_2$ because the multi-electron nature of the reaction could not be efficiently mediated by a single metal atom. This belief was largely motivated by structural elucidation of the oxygen-evolving complex
in photosystem II that revealed a multi-metallic Mn cluster as the active catalyst. The success achieved by the blue dimer contrasted with the low or non-existent catalytic activity of mono-nuclear Ru complexes further propagated the perception that at least two metal sites were necessary to support the multiple oxidizing equivalents required for water oxidation. However, in 2005, Zong and Thummel reported competent water oxidation by a series of mono-nuclear Ru complexes bearing a 2,6-di(1,8-naphthyridin-2-yl)pyridine backbone, a bound water molecule, and varying pyridyl axial groups (1.6a-c). The catalytic activities of 1.6a-c were evaluated by measuring O₂ evolution after injecting a solution of each catalyst dissolved in acetonitrile into an aqueous solution containing excess CAN (pH 1). Turnover numbers, particularly for 1.6b, were comparable to previously reported di-nuclear Ru complexes, thus giving credibility for the first time to the idea that mono-nuclear Ru complexes are indeed capable of providing the oxidizing equivalents necessary for water oxidation.
In 2008, Thummel’s group followed up with a systematic study of the catalytic activities of numerous mononuclear Ru complexes with various configurations of polypyridyl ligands. The first group of mononuclear complexes were based on [Ru(terpy)(bpy)Cl]⁺ using bpy
derivatives (1.7a-e) and other related polypyridyl bidentate ligands (1.8-1.14). Complexes 1.7a-e and 1.8 were modestly active showing turnover numbers ranging from 110-570 under the authors’ conditions. Interestingly, with the exception of 1.14, no oxygen evolution was detected (within the sensitivity of the authors’ method) from the remaining complexes (1.9-1.13). The second group of complexes (1.15-1.21) has pyridyl ligands in all six coordination sites, however the denticities of the ligands were systematically varied (pyridine, bipyridine, terpyridine, quaterpyridine). Complexes 1.15-1.17 and 1.20 showed no water oxidation activity while moderate turnover numbers were achieved by 1.18 and 1.19 (95 and 135 TON respectively). One complex that clearly stands out is 1.21 which contains 2,9-di(pyrid-2'-yl)-1,10-phenanthroline as a tetradeutate ligand with 4-picoline ligands in the axial positions; 416 turnovers were achieved with a rate of 0.330 μmol of O₂ min⁻¹ (TOF = 27.5 × 10⁻⁶ s⁻¹). Details on 21 and related derivatives will be discussed in section 1.6.6.

Meanwhile, complementary work on complex 1.7a by Sakai’s group revealed a significant induction period prior to the onset of water oxidation in the presence of excess Ce⁴⁺. In contrast, a maximum initial rate of O₂ evolution and no induction period was observed from complex 1.22, the aquated analog of 1.7a, suggesting that the Ru-Cl complexes are not active water oxidation catalysts but rather they serve as pre-catalysts that undergo Cl⁻ / H₂O substitution to generate the
catalytically active Ru-OH$_2$ analogs.$^{103}$ Nearly coincident to Thummel’s and Sakai’s work on single site Ru-polypyridyl catalysts in 2008, Meyer’s group reported the first *mechanistic* study of two single-site Ru catalysts, [Ru(tpy)(bpm)(OH$_2$)]$^{2+}$ (23) and [Ru(tpy)(bpz)(OH$_2$)]$^{2+}$ (1.24), that are aquated versions of 1.12 and 1.13, respectively.$^{104}$ A general mechanism for these complexes was proposed based on electrochemical data and UV-visible spectroscopy (Figure 1.6., left). Potential vs. pH dependence studies of 1.23 show a 2 e$^{-}$/2 H$^+$ change from pH 0 to pH 9.7 corresponding to the transition from [Ru$^{II}$-OH$_2$]$^{2+}$ to [Ru$^{IV}$=O]$^{2+}$, and a 2 e$^{-}$/1 H$^+$ change from pH 9.7 to pH 14 corresponding to the transition from [Ru$^{II}$-OH]$^{2+}$ to [Ru$^{IV}$=O]$^{2+}$. The [Ru$^{IV}$=O]$^{2+}$ to [Ru$^{V}$=O]$^{2+}$ transition is pH independent at least from pH 0 to pH 3 (no data were shown past pH 3) and the ensuing large increase in current suggests that water oxidation is triggered upon reaching the Ru$^V$ state. Reinforcing the notion that Ru$^V$ plays a role, changes in UV-visible spectral patterns monitored upon addition of three equivalents of Ce$^{IV}$ to a solution of [Ru$^{II}$tpy(bpm)(OH$_2$)]$^{2+}$ suggested formation of a transient [Ru$^{V}$=O]$^{3+}$ species followed by a peroxido [Ru$^{III}$OOH]$^{2+}$ species which decomposed in a matter of minutes back to [Ru$^{II}$-OH]$^{2+}$. Under catalytic conditions (an excess of 30 equiv of Ce$^{IV}$), the resting state appeared to be a [Ru$^{IV}$-OO]$^{2+}$ species where peroxido coordination may be bidentate.
In 2014, Pushkar et al. asserted that the available evidence (from electrochemistry and UV-visible spectroscopy) for formation of a $[\text{Ru}^{\text{V}}=\text{O}]^{3+}$ species in Ru(tpy)(bpy)-type complexes was insufficient. These authors presented spectroscopic data (EPR, x-ray absorption) supported by computations to suggest that $[\text{Ru}^{\text{V}}=\text{O}]^{3+}$ may in fact be absent in the mechanistic cycle of 1.22. Addition of 20 equiv of Ce$^{IV}$ to 1.22 and freezing within 30 sec after mixing resulted in a largely EPR silent species (~95%) ruling out paramagnetic Ru$^{\text{III}}$ or Ru$^{\text{V}}$ as the major species. In addition, XANES spectra showed a significant shift to higher energy consistent with Ru$^{IV}$, and the Ru-O distance calculated from EXAFS measurements (1.82 Å) is consistent with a Ru$^{IV}$=O species. The residual EPR signal (~5%) did not have the characteristic g-tensor of a Ru$^{V}$=O species; based on DFT predictions it was assigned as a Ru$^{\text{III}}$-OOH peroxide alternative. The results of Pushkar et al. complement electrospray ionization mass spectrometric (ESI-MS) analyses by the Berlinguette group in which no signals for a $[\text{Ru}^{\text{V}}=\text{O}]^{3+}$ species were observed after addition of 3-4 equiv of
CeIV or even under catalytic conditions (16 equiv of CeIV).\textsuperscript{106} Furthermore, only minor spectroscopic changes were observed upon addition of 1 equiv of CeIV to the [RuIV=O]\textsuperscript{2+} species, implying that the dominant species is likely [RuIV=O]\textsuperscript{2+}.

The kinetics of O\textsubscript{2} evolution by 1.22 have been studied in the presence of CeIV. Meyer’s and Berlinguette’s groups separately reported O\textsubscript{2} evolution to be first order with respect to [Ru] and zeroth order with respect to [CeIV] when 30-200 equiv of CeIV were used, suggesting that electron transfer is not rate-limiting while chemical steps such as O-O bond formation or O\textsubscript{2} release may be rate-limiting.\textsuperscript{104,106} However, Masaoka and Sakai reported O\textsubscript{2} evolution to be first order with respect to both [Ru] and [CeIV] when 10 equiv of CeIV were used.\textsuperscript{103} As Yagi et al. pointed out, O\textsubscript{2} evolution with respect to CeIV likely operates under Michaelis-Menten-like kinetics where the rate law is dictated by the concentration of oxidant.\textsuperscript{107} It has yet to be conclusively determined whether the rate-limiting step is O-O bond formation of O\textsubscript{2} release in the presence of excess CeIV.

1.6.7. Emergence of tetradentate motif

\begin{center}
\textbf{Figure 1.7.} a) depiction of a common scenario of \textit{cis-trans} isomerism in Ru(bpy)\textsubscript{2}(L)\textsubscript{2} complexes where the \textit{cis} configuration is favored, b) utilization of a tetradentate ligand as a strategy to prevent isomerization.
\end{center}

Work done in the 1980s and 1990s demonstrated that \textit{trans}-[Ru(bpy)\textsubscript{2}L\textsubscript{2}]\textsuperscript{2+} complexes are often prone to isomerization to their \textit{cis} counterparts, thus making it difficult to study or exploit the chemical/photochemical properties of \textit{trans} complexes (Figure 1.7.a).\textsuperscript{108–111} One strategy to
minimize the likelihood of a *trans*-to-*cis* conversion is to covalently link the two bipyridine ligands via a linker short enough to highly disfavor the *cis* configuration. The simplest and a promising homolog for such a strategy is the ligand quaterpyridine which links two bipyridine units through a single C(*sp*²)-C(*sp*²) covalent bond (Figure 1.7.b). Ruthenium quaterpyridine complexes were first reported by Che and coworkers in 1994, including *trans*-\([\text{Ru}^{II}(L)(\text{OH}_2)_2]^{2+}\) (\(L = 2,2':6',2''\)-quaterpyridine) and a crystal structure for *trans*-\([\text{Ru}^{II}(L)(\text{PPh}_3)_2[\text{ClO}_4]^2\) (\(L = 3'',5',5''\)-tetramethyl-2,2':6',2''-quaterpyridine).\(^{112}\) The crystal structure shows that despite significant angle strain, the quaterpyridine ligand coordinates through all four binding sites, adopting a highly distorted square planar configuration where the N₁-Ru-N₂ angle involving the terminal pyridine groups is as wide as \(\sim123^\circ\). One problem that is often encountered with quaterpyridine is rotation around the central C(*sp*²)-C(*sp*²) bond which leads to formation of a dinuclear species (not shown) where each half of the ligand separately participates in bidentate coordination to a single ruthenium atom.\(^{113}\) To overcome this problem, Thummel’s group synthesized 2,9-di-(2'-pyridyl)-1,10-phenanthroline (dpp), in which the rigid phenanthroline moiety precludes any rotation around the central C(*sp*²)-C(*sp*²), and tetradentate coordination to ruthenium occurs readily.\(^{113}\) As mentioned in section 1.6.5., complex 1.21 performed better than most of the other polypyridyl Ru complexes tested with a TON of 416 and at the rate of 0.330 \(\mu\text{mol of O}_2 \text{min}^{-1}\) (TOF = \(27.5 \times 10^6 \text{s}^{-1}\)) in the presence of excess Ce\(^{IV}\).\(^{102}\) Unlike \([\text{tpy}(\text{bpy})\text{Ru}^{II- \text{OH}_2}]^{2+}\)-type complexes where an aquo ligand is pre-coordinated in the first coordination sphere and available to participate in the ensuing catalytic cycle, complex 1.21 is coordinatively *saturated* with polypyridyl ligands. Thummel hypothesized that a Ru\(^{IV}\) 16 e⁻ complex, after loss of 2 e⁻, would be sufficiently electrophilic to accommodate metal-coordination of a water molecule as a *seventh* ligand to form an 18 e⁻ Ru\(^{IV}\)(OH₂) pentagonal bipyramidal intermediate and the wide N-
Ru-N angle of 1.21 may be conducive to such a pathway (Figure 1.8.). This hypothesis was supported by geometry optimization calculations where dissociation of water was observed in Ru^{II}-OH\_2 and Ru^{III}-OH\_2 complexes but not Ru^{IV}-OH\_2.\(^{102}\)

![Figure 1.8. Thummel’s hypothesis on the mechanism of water oxidation by 1.21.](image)

1.6.8. Anionic ligands stabilize higher oxidation states.

Thummel previously demonstrated that electron-donating groups on pyridyl ligands could lower oxidation potentials,\(^{92,102,113–115}\) but Akermark and Sun made a pivotal discovery: anionic
ligands, in contrast to neutral ligands, can effectively stabilize higher metal oxidation states and drastically lower redox potentials. This phenomenon was first demonstrated in 2002 by comparison of two dinuclear Mn complexes, 1.25 and 1.26, bearing similar ligands. Complex 1.25 consists of two octahedral Mn$^{2+}$ centers, where each Mn is bound by an amino functionality with two tethered pyridyl groups also bound to the metal, two bridging acetato ligands, and a bridging phenolate oxygen. Complex 1.26 is similar, however one of the tethered pyridyl groups on each amino functionality is substituted with an anionic phenolate group and the two Mn centers are each in the 3+ oxidation state. A combination of electrochemistry and EPR in CH$_3$CN (0.1 M NBu$_4$PF$_6$) revealed the redox potentials for 1.25 and 1.26 and these data demonstrate dramatic stabilization of the higher oxidation states of Mn via substitution of neutral ligands with anionic ligands. For example, the Mn$^{II}$/Mn$^{II}$ to Mn$^{II}$/Mn$^{III}$ transition is lowered by nearly 820 mV (0.50 V for 1.25 and -0.32 V for 1.26). Similarly, the Mn$^{II}$/Mn$^{III}$ to Mn$^{III}$/Mn$^{III}$ transition occurs at 1.06 V for 1.25 and 0.04 V for 1.26. Furthermore, the Mn$^{III}$/Mn$^{III}$ to Mn$^{III}$/Mn$^{IV}$ oxidation occurs at 0.96 V for 1.26 while completely unobserved for 1.25, presumably because its potential is too anodic for detection.
Akermark and Sun applied this strategy to Thummel’s dinuclear Ru complex 1.5 by designing a ligand with terminal carboxylates rather than pyridyl functionalities. Attempts to metalate the ligand resulted in complex 1.27 that has an anti configuration where the Ru centers are connected at opposing sides of the pyridazine ring, one with a C-Ru bond, the other with a N-Ru bond. Significantly, the oxidation potentials for 1.27 were dramatically lowered compared to 1.5 presumably due to the presence of anionic ligands, the two carboxylates and the unintended carbon ligand. In a subsequent report in 2010, Akermark and Sun reported Ru complex 1.28 with a similar ligand where the pyridazine ring was replaced by a phthalazine moiety to promote syn coordination, where the two ruthenium centers are adjacent to each other, and thus allow for a more appropriate comparison with 1.5. Interestingly, under the same conditions ([CeIV]=20 mM, [catalyst] = 0.1-0.5 µM), the rate for 1.28 was nearly four times greater than that observed by 1.27.

1.6.9. Catalysts bearing 2,2’-bipyridine-6,6’-dicarboxylate as tetradentate ligands

With the success achieved from incorporating anionic ligands into dinuclear Ru systems, Sun’s group applied the same tactic to complexes with tetradentate ligands such as 1.21. A pivotal
moment in the field was the discovery of complex (1.29) with 2,2’-bipyridine-6,6’-dicarboxylate (bda) as a tetradeinate ligand which bears similarity to 1.21, however the phenanthroline subunit is substituted with bipyridine and anionic carboxylates are incorporated in place of the terminal pyridyl groups.¹²¹ X-ray crystallography of 1.29 confirmed tetradeinate chelation of bda, and a wide O-Ru-O angle of 122.9° similar to the N-Ru-N angle of 1.21. A side-by-side comparison of electrochemical data of 1.21 and 1.29, shows that redox potentials of 1.29 are considerably more negative over a wide pH range.¹²² For example, at pH 1, the Ru\textsuperscript{II}/\textsuperscript{III} transition is nearly ~0.5 V more negative for 1.29 (E\textsubscript{1/2} = ~0.6 V) compared to 1.21 (E\textsubscript{1/2} = ~1.1 V). Similarly at pH 7, the Ru\textsuperscript{II}/\textsuperscript{III} and Ru\textsuperscript{III}/\textsuperscript{IV} transitions occur at 0.55 V and 0.80 V respectively for 1.29 and the 2 e\textsuperscript{−} Ru\textsuperscript{II}/\textsuperscript{IV} transition for 1.21 occurs at 0.85 V. Furthermore, the onset potential for the catalytic oxidation wave occurs at ~1.55 V for 1.21 and at ~1.05 V for 1.29, nearly ~0.5 V more negative and representing the lowest observed overpotential in the field thus far! Sun and coworkers also acquired a fascinating crystal structure of a seven-coordinate Ru\textsuperscript{IV}-hydroxo intermediate from crystals grown after addition of 2 eq. of CAN to 1.29 and precipitation in the presence of excess NH\textsubscript{4}PF\textsubscript{6} (Figure 9).¹²¹ The crystal structure gives credence to the theory of a seven-coordinate Ru\textsuperscript{IV} intermediate initially proposed by Thummel with respect to complex 1.21. The wide O-Ru-O angle may encourage coordination of a water molecule as a seventh ligand.
**Figure 1.9.** X-ray crystal structure derived from crystals grown after addition of 2 equiv of CAN to 1.29 in the presence of NH$_4$PF$_6$.\textsuperscript{121}

**Figure 1.10.** Calculated “encounter complex” of two Ru$^\text{V}$=O molecules with $\pi$-stacking interactions between the four isoquinoline units (figure from ref.\textsuperscript{123})
In another astounding discovery, Sun showed that replacement of the axial 4-picoline ligands with isoquinoline ligands (1.30) lead to an improvement in catalytic rate by nearly an order of magnitude. The second order kinetics of O₂ evolution with respect to catalyst concentration point to an I2M pathway and DFT calculations suggest that greater π-stacking between isoquinoline units of two approaching molecules facilitates O-O bond formation (Figure 1.10). Richmond et al. showed that implementation of isoquinoline units with a methoxy group (MeO-isoq) on the C-6 carbon led to even greater turnover frequencies (about 1.5 to 3 times greater than for 1.30 under identical Ce⁴⁺ conditions). Structural analysis of calculated dimeric [Ru-O⋯O-Ru]²⁺ transition states exhibited shorter distances for 1.31 compared to 1.30 due to increased π-stacking from a stacking geometry that favors an electrostatic interaction between a positively charged C-6 atom on one MeO-isoquinoline half and a negatively charged C atom on the other half. Furthermore, catalyst 1.32 with two axial phthalazine ligands was found to have very high turnover number (>50,000) consistent with calculations that show a directly proportional correlation between the longevity of catalysis and the HOMO energy of the axial ligand.

Figure 1.11. a) Pourbaix diagram of 1.29 constructed by Sun’s group; b) Pourbaix diagram of 1.30 constructed by Meyer’s group.
Sun’s group performed E vs. pH studies and constructed a Pourbaix diagram of 1.29 (Figure 1.11.a). From pH 1 to ~5.5, $E_{1/2}$ of Ru$^{II/III}$ remains unchanged signifying a simple 1 e\textsuperscript{-} transfer, however PCET is observed for Ru$^{III/IV}$ and Ru$^{IV/V}$. At pH > ~5.5, PCET is observed for Ru$^{II/III}$ and Ru$^{III/IV}$ however the potential remains unchanged for Ru$^{IV/V}$. They proposed that between pH 1 to ~5.5, formation of the Ru-OH\textsubscript{2} complex occurs as early as the Ru$^{II}$ oxidation state however the two aquo protons are lost with the Ru$^{III/IV}$ and Ru$^{IV/V}$ transitions and the Ru$^{II/III}$ transition only involves electron transfer. At pH > ~5.5, they proposed two PCET steps from Ru$^{II}$-OH\textsubscript{2} to Ru$^{IV}$=O followed by a simple electron transfer to Ru$^{V}$=O. The E vs. pH dependence of 1.30, independently investigated by Meyer’s group, closely resembles that of 1.29 by Sun’s group suggesting that both catalysts operate fundamentally by a similar mechanism (Figure 1.11.b).\textsuperscript{126} In contrast to Sun’s interpretation however, Meyer proposed that between pH 1 to ~5.5, water coordination does not occur until oxidation to Ru$^{III}$ allowing two sequential PCETs to occur from Ru$^{III}$-OH\textsubscript{2} to Ru$^{V}$=O. At pH > ~5.5, the basicity of the cell solution is great enough to promote immediate proton transfer upon formation of Ru$^{III}$-OH\textsubscript{2}. A recent study provided EPR evidence of a Ru$^{III}$ seven-coordinate species.\textsuperscript{127}
1.6.10. External bases accelerate catalysis

Figure 1.12. Complexes used by Meyer to show enhanced catalytic activity upon adding external bases.

In 2010, Meyer’s group made an important discovery in the field showing that electrocatalytic water oxidation, specifically the O-O bond formation step in WNA, is significantly enhanced by the addition of external bases.\textsuperscript{128} Studies to explore this phenomenon were performed on [Ru(Mebimpy)(bpy)(OH\textsubscript{2})\textsuperscript{2+} (1.33) in solution and its related phosphonate derivative \{Ru(Mebimpy)[4,4′-((OH)\textsubscript{2}OPCH\textsubscript{2}bpy]OH\textsubscript{2})\}\textsuperscript{2+} (1.34) covalently functionalized on an indium-tin oxide (ITO) electrode. Cyclic voltammetry was conducted on 1.33 and 1.34 in the presence of various external bases such as H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−}, OAc\textsuperscript{−}, and HPO\textsubscript{4}\textsuperscript{2−}, where the ionic strength was kept constant at 0.1 M with appropriate addition of KNO\textsubscript{3}, and in all cases the data show an increase in catalytic current density ($i_{\text{cat}}$) when compared to cyclic voltammetry performed with no added bases. Moreover, $i_{\text{cat}}$ appeared to increase as a function of base concentration and base
strength, consistent with a base-associated rate dependence. The experimental observations were corroborated with quantum mechanical calculations on 1.33. The lowest energy pathway calculated for O-O bond formation involves another water molecule in the secondary coordination sphere (Fig. 1.13, Scenario #2) that works to solvate the proton released upon water-nucleophilic attack. Computations done without the proton-solvating water molecule lead to a highly charged and energetically unfavorable hydrogen peroxide intermediate \([\text{Ru}^{III}(\text{Mebimpy})(\text{bpy})(\text{OOH}_2)]^{3+}\) (Fig. 1.13, Scenario #1), demonstrating the necessity of the secondary water molecule. Analogous calculations with an acetate anion instead of a water molecule as the external base (Fig. 1.13, Scenario #3) resulted in an even lower activation barrier (7.6 kcal/mol vs. 10.4 kcal/mol), consistent with experimental results.

Meyer’s group published another study in 2015 exploring the effect of external bases on water oxidation by complex 1.30. The observed trend was similar to the 2010 study, where the rate of water oxidation increased as a function of base strength and base concentration. Two

![Figure 1.13. Relative energetics of O-O bond formation by WNA.](image)
separate mechanistic scenarios were presented: 1) a concerted atom-proton transfer mechanism similar to complex 1.30 where base-assisted water nucleophilic attack on a [Ru\(^{\text{V}}\text{=O}\)]\(^{+}\) is the rate-limiting step, or 2) a mechanism where PCET from [Ru\(^{\text{IV}}\text{-OH}\)]\(^{+}\) to [Ru\(^{\text{V}}\text{=O}\)]\(^{+}\) is rate-limiting while the O-O bond formation step via bimolecular radical coupling is rapid. In each scenario, the proton transfer plays a critical role.

1.6.10. Bifunctional catalysis – internal bases to accelerate catalysis

![Bifunctional mechanism of 30 constructed from experimental and computational evidence](image)

Figure 1.14. Bifunctional alkyne hydration catalyst and proposed mechanism
Proton transfer is critical to accelerating the rate of water oxidation. One strategy to optimize proton transfer in a catalytic cycle is to incorporate basic sites *internally* within the ligand architecture. Such a strategy has been implemented in the context of organic transformations and yielded impressive results. For example, *anti*-Markovnikov hydration of terminal alkynes was accomplished with enzyme-like rates and selectivity using catalyst 1.35.\textsuperscript{129} A series of mechanistic studies point to heavy involvement of the nitrogen atoms of the pendent heterocycles as basic sites (Figure 1.14).\textsuperscript{130,131} Complexes 1.37 and 1.36, containing two PPh\textsubscript{3} ligands, where a locally basic environment near the active-site is absent, show limited to no detectable catalytic activity, respectively, where 1.37 is more than 1000 times slower than 1.35. In the first step, the alkyne coordinates to the metal to form an alkyne π-complex 1.35a which isomerizes into a vinylidene intermediate. The alkyne-to-vinylidene transformation in 1.36 required heating the mixture at 50 °C; in contrast, the same transformation in 1.35 was accomplished at temperatures 50-90 °C lower. Spectroscopic characterization of alkyne coordination in 1.35 using \textsuperscript{13}C-labelled acetylene and \textsuperscript{15}N-labelled ligands indicated the presence of C-H------N hydrogen bonding between the alkyne protons and the pyridyl nitrogens. As proton transfer is implicated in the alkyne-to-vinylidene isomerization, it is conceivable that the rate may be enhanced by an imidazole N atom hosting the migrating proton. This scenario is supported by calculations in which the acetylene-to-vinylidene conversion by CpRu(PMe\textsubscript{3})\textsubscript{2}\textsuperscript{+} has a barrier that is \textasciitilde 6 kcal mol\textsuperscript{-1} higher than CpRu(PMe\textsubscript{2}Im)\textsubscript{2}\textsuperscript{+} (where Im = 1,4-dimethylimidazole-2-yl).\textsuperscript{131} Addition of water to the vinylidene intermediate 1.35b leads to formation of an unsymmetrical species at -100 °C which was confirmed by \textsuperscript{15}N NMR data to be 1.35d where the proton resides on a pyridine nitrogen and maintains a hydrogen bonding interaction to the metal acyl fragment. Stabilization of the transition state 1.35c by hydrogen donation to the imidazole N atom as water approaches the vinylidene
**Figure 1.15.** Bifunctional alkene isomerisation catalyst (1.38) and proposed mechanism.
intermediate is supported by calculations.\textsuperscript{131} From these data it is clear that hydrogen bonding and proton transfer play a pivotal role in the remarkable catalytic ability of \textbf{1.35}.

In another example, the presence of an internal basic site in \textbf{1.38} significantly facilitates the isomerization of alkenes.\textsuperscript{132} Compared to analog \textbf{1.39} which contains no internal basic sites, \textbf{1.38} yields turnover frequencies that are as much as 10,000 times higher (Fig. 1.15). Moreover, alkenes were observed to move up to nearly 30 positions in a carbon chain when isomerized by \textbf{1.39} earning it the moniker – “alkene zipper”. In an initial mechanistic hypothesis Grotjahn and coworkers proposed that the pendent nitrogen atom may directly deprotonate the allylic position to generate an allyl intermediate; the imidazolium moiety can then transfer the proton to the other end of the allyl intermediate to form the isomerized alkene. In a computational study, Tao et al. proposed an alternative mechanism in which $\eta^3$-allyl hydride species are intermediate to the deprotonation and protonation steps between each isomer.\textsuperscript{133} While further studies are being conducted to pinpoint the mechanism, the pendent nitrogen atoms undoubtedly play an indispensable role as proton transfer agents.
Llobet and coworkers reported [Ru\textsuperscript{II}(tda-κ-N\textsubscript{3}O)(py)] (1.40, tda = [2,2’:6’,2”-terpyridine]-6,6”-dicarboxylate), an astounding example of the power of bifunctional catalysis.\textsuperscript{134} The ligand tda is reminiscent of bda but with an added pyridine to allow five potential binding sites. NMR spectroscopy of the Ru\textsuperscript{II} state of 1.40 shows symmetry in the peaks corresponding to tda, suggesting rapid fluxionality in metal-coordination of the two carboxylate groups on the NMR time scale. As shown by x-ray crystallography, upon oxidation to the Ru\textsuperscript{IV} state, the metal becomes electrophilic enough to form a [Ru\textsuperscript{IV}(tda-κ-N\textsubscript{3}O\textsubscript{2})(py)\textsubscript{2}]\textsuperscript{2+} seven-coordinate species where both carboxylates are bound to Ru\textsuperscript{IV}. Electrochemical data show that in neutral or basic aqueous solutions, a seven-coordinate [Ru\textsuperscript{IV}(OH)(tda-κ-N\textsubscript{3}O)(py)\textsubscript{2}]\textsuperscript{+} species is generated where decoordination of a carboxylate group allows metal-coordination of a hydroxide. The [Ru\textsuperscript{IV}(OH)(tda-κ-N\textsubscript{3}O)(py)\textsubscript{2}]\textsuperscript{+} species undergoes PCET to form a Ru\textsuperscript{V}=O species that is active for water oxidation via the WNA pathway. At pH 7, a large electro-catalytic wave is observed at an
onset potential of ~1.2 V (vs. Ag/AgCl) for which the TOF$_{\text{max}}$ was calculated to be ~8000 s$^{-1}$, the highest reported thus far at neutral pH; for 1.29 the measured value was ca. 11 s$^{-1}$. The free energy of activation (ΔG$^\ddagger$) calculated for O-O bond formation by WNA on the Ru$^\text{V}=\text{O}$ species concomitant with proton-transfer to the dangling carboxylate was significantly lower compared to other examples. The incorporation of Lewis bases and hydrogen bonding functionalities on the ligand near the active site is a highly promising strategy for increasing rates of water oxidation and will be a recurring theme in the following chapters.

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Chapter 2

Synthesis, characterization, and reactivity of ruthenium complexes bearing 2,2’-bipyridine-6,6’-dipyrazolato ligands towards water oxidation

2.1. Introduction

As discussed in Chapter 1, Sun and coworkers discovered that the incorporation of anionic carboxylate groups into the tetradentate motif significantly lowers the overpotential required to activate catalysis. Furthermore, a computational study revealed that a simple structural modification of the ligand from 1,10-phenanthroline-2,9-dicarboxylate to the more flexible 2,2’-bipyridine-6,6’-dicarboxylate (bda) alters the mechanism of CeIV-driven catalysis from a water nucleophilic attack (WNA) pathway to a bimolecular radical coupling (I2M) pathway. In the transition state characterized for the WNA pathway, one of the carboxylates accepts a proton in a hydrogen-bonding network leading to the water molecule performing nucleophilic attack on the [RuV=O] oxo moiety. In such a scenario, one can expect that replacing the carboxylate groups with more basic functionalities may have a beneficial effect on the rate of O-O bond formation by increasing the nucleophilicity of H2O attack on [RuV=O].

Searching for potential substitutes for carboxylate ligands we turned our attention to pyrazolate ligands, arranged so that one nitrogen is coordinated to the metal and the other is available for proton acceptance. Pyrazolate anions are significantly more basic than carboxylate anions (pyrazole pKₐ = 14.0, acetic acid pKₐ = 4.2) and although data on the acid-base properties
of coordinated pyrazoles are scarce,\textsuperscript{3–8} we can expect that on the same metal fragment, pyrazolato ligands certainly will be significantly more basic than carboxylato ligands. Catalysis with complexes bearing pyrazole/pyrazolate ligands in the context of organic transformations has been explored fairly extensively, particularly in the last decade,\textsuperscript{9–13} and the role of the free nitrogen atom as a proton mediator has been invoked in a number of examples.\textsuperscript{14–18} Especially relevant to water oxidation, there are a handful of examples of hydrogen bonding from pyrazole N-H moieties to terminal or bridging oxo, peroxo, and hydroperoxo ligands coordinated to a metal center (Figure 2.1).\textsuperscript{19–23} Motivated by examples 2.2, 2.4, and 2.5, one can imagine a scenario where a transition state for O-O bond formation via WNA is stabilized by intramolecular hydrogen bonding and ultimately proton acceptance by the free pyrazolate nitrogen (figure 2.1, bottom left).

\begin{align*}
\text{Figure 2.1.} & \quad \text{Top: literature examples hydrogen bonding from pyrazole N-H moieties to oxo, peroxo, and hydroperoxo ligands; bottom: depiction of water oxidation by WNA assisted by a pendent pyrazolate.}
\end{align*}
In literature, there is one report by Roeser et al. of Ru WOCs incorporating monocoordinated pyrazole fragments adjacent to the active site. In that report, the ligands \(2-(5\text{-phenyl}-1H\text{-pyrazol-3-yl})\text{pyridine}\) and \(2,2'-(1H\text{-pyrazole-3,5-diyl)dipyridine}\) were used to prepare two sets of isomers, one set where the pyrazolyl group is located \(cis\) to Ru-OH and another set where it is located \(trans\) to the Ru-OH. \(\text{O}_2\) evolution was induced under acidic conditions by addition of \(\text{Ce}^{IV}\) and also photochemically under neutral conditions with \([\text{Ru(bpy)₃}]^{2+}\) and \([\text{Co}^{III}(\text{Cl})(\text{NH}_3)_5]^{2+}\). The results were remarkably different; under acidic conditions the \(trans\) isomers gave rates 2 to 11 times greater than the \(cis\) isomers, and under neutral conditions the trend was reversed where the \(cis\) isomers gave greater rates. Without explanation, the role of different pH was invoked for the divergent reactivity.

Here we present a series of Ru complexes with tetradeutate ligands composed of a \(2,2'\)-bipyridine backbone with various pyrazolyl-containing groups in the 6,6' positions: Ru(bdpz-
In addition to having pyrazolate internal bases, these complexes maintain the wide N₁-Ru-N₂ angle that appears to be beneficial to water oxidation catalysis through formation of a seven-coordinate Ru-oxo intermediate (Figure 2.1). Presented below are details on the synthesis, characterization, reactivity and other unique properties of complexes 2.6-2.8.

2.2. Synthesis and characterization of complexes

**Synthesis.** The tert-butylated ligand bdpz-tBu was prepared by a well-established procedure for synthesis of 3,5-substituted pyrazoles (figure 2.3).\textsuperscript{25,26} Slow addition of pinacolone to a refluxing mixture of diester 2.10 and sodium hydride in 1,2-dimethoxyethane afforded a mixture of 2.11 and its enol tautomer which was identified by the distinctive \( ^1 \)H NMR singlet at \(~16\) ppm for the OH proton. Condensation of 2.11 with hydrazine in a Knorr-type synthesis lead to the facile formation the tert-butylated dipyrazole ligand 2.12.\textsuperscript{27} Synthesis of the un-alkylated analog 2.17 (figure 2.4) was achieved in five-steps beginning with a Sonogashira coupling of 6,6’-dibromo-2,2’-bipyridine with trimethylsilylacetylene to yield the bis-(trimethylsilyl)ethynyl compound 2.14, which was directly converted to the diacetyl compound 2.15 by a Hg(OAc)\(_2\) mediated Markovnikov hydration. Following a literature procedure,\textsuperscript{28} a refluxing mixture of 2.15 in N,N-dimethylformamide dimethylacetal lead to precipitation of 2.16, which was condensed with hydrazine in refluxing ethanol to give 2.17 in good yield. For the indazole analog (figure 2.5), stannylation of THP-protected iodoindazole 2.20 to make 2.21 followed by a double Stille-coupling to 6,6’-dibromo-2,2’-bipyridine generated the THP-protected diindazole ligand 2.22. Deprotection was accomplished by refluxing in a concentrated solution of \( p \)-toluenesulfonic acid; NMR data and combustion analysis were consistent with isolation of the mono-tosylate salt 2.23.
Figure 2.3. Synthesis of 2.6.

Figure 2.4. Synthesis of 2.7.
Figure 2.5. Synthesis of 2.8.

Figure 2.6. Synthesis of 2.6(2H)(PF$_6$)$_2$. 
Complexation of bdpz-\textit{tBu} was achieved by reaction with Ru(DMSO)$_4$Cl$_2$ and excess NEt$_3$ in CH$_3$OH and subsequent addition of excess 4-picoline lead to the doubly picolinated complex \textbf{2.6}. The remaining NEt$_3^+$ salts were easily removed by allowing the reaction mixture to stir with strongly basic Amberjet® OH 4400 resin. Characterization data for the compounds in this section are discussed below. Addition of excess aqueous HPF$_6$ to a solution of \textbf{2.6} dissolved in a mixture of 1:2 trifluoroethanol:H$_2$O lead to precipitation of the diprotic (\textbf{2.6})(2H)(PF$_6$)$_2$ salt which was filtered, washed with water, and isolated in 81\% yield (Figure 2.6). (\textbf{2.6})(2H)(PF$_6$)$_2$ was synthesized for use in electrochemical and UV-visible spectroscopic studies. Complexes \textbf{2.7} and \textbf{2.8} were prepared in a similar manner as \textbf{2.6}, however yields thus far have been extremely poor. In both cases, the desired complexes were eluted in the first band during silica gel chromatography using a gradient of CH$_2$Cl$_2$ / CH$_3$OH with 5\% NEt$_3$. Two subsequent bands contained an unsymmetrical species (as determined by $^1$H NMR spectroscopy) that we have not yet identified; the bulk of the crude mixtures consists of this undesired species. Anionic pyrazolates can adopt a variety of coordination modes, including an exobidentate mode where metal coordination occurs through both nitrogen atoms.$^{29}$ Grotjahn and coworkers demonstrated that intermolecular hydrogen bonding interactions could be completely avoided by implementing a very bulky tert-butyl substituent in the C-5 position of a metal-coordinated pyrazole ring.$^3$ The lack of steric hindrance on the pyrazolate C-5 carbons of \textbf{2.7} and \textbf{2.8} may promote formation of multi-metallic species where the ligands exhibit exobidentate coordination.

**X-ray crystallography.** X-ray quality crystals of \textbf{2.6} (Figure 2.7) and \textbf{2.8} (Figure 2.9) were acquired by vapor diffusion. The structure of \textbf{2.6} showed planar coordination of the tetradeinate ligand and interestingly, a single oxygen atom of a water molecule was identified to be located at a position equidistant [2.97 Å] from each un-coordinated pyrazolate nitrogen atom.
The hydrogen atoms of the water molecule could not be located, however known N----H-O hydrogen bonds show N-O distances in the range of 2.84 Å to 3.03 Å;\(^{30}\) thus, one can expect hydrogen bonding interactions between the un-coordinated pyrazolate nitrogen atoms to each respective hydrogen atom. The water molecule maintained its position at the N(3)-Ru-N(4) pocket in a dry CD\(_2\)Cl\(_2\) solution as indicated by the broad singlet at 6.01 ppm in its \(^1\)H NMR spectrum with integration consistent with 2H. These phenomena demonstrate the high propensity for the uncoordinated pyrazolate nitrogen atoms to participate in hydrogen bonding interactions. Similarly, the crystal structure of \(2.8\) also revealed a water molecule hydrogen bonded to the uncoordinated pyrazolate nitrogen atoms N\(_1\) and N\(_2\). Despite the different electronic natures of \(bdpz-tBu\) and \(bdiz\), Ru-N bond lengths in \(2.6\) and \(2.8\) are not appreciably different (see table 2.1).

In the crystal structure of the doubly-protonated dichloride salt of \(2.7\) (Figure 2.8), one of the two chloride counterions was determined to be nearly equidistant from each pyrazole N-H functionality. The only parameters that appear to be significantly affected by protonation of the free nitrogens are the Ru-N(3) and Ru-N(4) bond lengths which are about 0.022 – 0.044 Å longer for \([2.7+2H](Cl^-)\)\(_2\) compared to those of \(2.6\) and \(2.8\). Lengthening of these bonds may occur due to the stronger \(\pi\)-donating character of pyrazolates compared to pyrazoles.\(^{31-33}\) Alternatively, the coulombic attraction between the anionic pyrazolates and the cationic metal center may be greater.
Figure 2.7. ORTEP drawing of x-ray crystal structure of 2.6 (ellipsoids at 50% probability level)
Figure 2.8. ORTEP drawing of x-ray crystal structure of $[2.7+2\text{H}](\text{Cl})_2$ (ellipsoids at 50% probability level)
**Figure 2.9.** ORTEP drawing of x-ray crystal structure of 2.8 (ellipsoids at 50% probability level)

**Table 2.1.** Comparison of key bond distances (Å) and angles (degrees) in x-ray crystal structures of 2.6, [2.7+2H](Cl)₂, and 2.8. *a*Two independent molecules in unit cell. *b*Three independent molecules in unit cell.

<table>
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<th>2.6&lt;sup&gt;a&lt;/sup&gt;</th>
<th>2.8&lt;sup&gt;b&lt;/sup&gt;</th>
<th><a href="Cl">2.7+2H</a>₂</th>
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<td>N(3)-Ru</td>
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<td>2.090(10), 2.094(9), 2.094(10)</td>
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<td>1.964(3)</td>
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<td>2.094(9), 2.08(4), 2.06(3)</td>
<td>2.091(3)</td>
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<td>N(7)-Ru-N(8) angle</td>
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<td>173.26(12)</td>
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2.3. UV-Vis spectroscopy and Acid-Base properties

**UV-vis spectroscopy in nonaqueous solvents.** Complexes **2.6-2.8** exhibited intriguing solvatochromic behavior. Figure 2.10 shows the color profile of complex **2.6** in a series of protic and aprotic solvents. Dissolution of **2.6** in aprotic solvents produced greenish solutions (Fig. 2.10, samples h-k). Methanol and ethanol produced red-maroon solutions, however alcohols bearing R groups with ≥3 carbon atoms afforded dull green colors (Fig. 2.10, samples e-g). Furthermore, the intensity of the red color increases with the acidity of the protic solvent (Fig. 2.10, samples a-b; pKₐ of 1,1,1,3,3,3-hexafluoroisopropanol = 9.3; pKₐ of 2,2,2-trifluoroethanol = 12.4).

**Figure 2.10.** Solvatochromic behavior exhibited by **2.6**. All samples were prepared by dissolving 1.0 mg of **1** in 4 mL of solvent: (a) 1,1,1,3,3,3-hexafluoroisopropanol, (b) 2,2,2-trifluoroethanol, (c) methanol, (d) ethanol, (e) 1-propanol, (f) isopropanol, (g) 1-butanol, (h) dichloromethane, (i) ethyl acetate, (j) acetone, (k) tetrahydrofuran.
Figure 2.11. UV-visible spectroscopy of 2.6 in EtOAc (green), methanol (purple), and trifluoroethanol (red).

UV-visible spectra of 2.6 in EtOAc, methanol, and trifluoroethanol revealed three very distinct observable spectroscopic states (figure 2.11). UV-visible spectroscopy of 2.6 in EtOAc showed two large bands at $\lambda_{\text{max}} = 296$ nm ($\varepsilon = 25000$ L mol$^{-1}$ cm$^{-1}$) and $\lambda_{\text{max}} = 395$ nm ($\varepsilon = 17000$ L mol$^{-1}$ cm$^{-1}$) and two smaller bands at 485 nm ($\varepsilon = 3300$ L mol$^{-1}$ cm$^{-1}$) and $\lambda_{\text{max}} = 605$ nm ($\varepsilon = 2900$ L mol$^{-1}$ cm$^{-1}$). All four $\lambda_{\text{max}}$ absorbances are blue-shifted in methanol with five clearly observable isosbestic points at 585 nm, 524 nm, 379 nm, 334 nm, and 288 nm. Similarly, the absorbances are even further blue-shifted in trifluoroethanol and seven isosbestic points are observed at 555 nm, 492 nm, 468 nm, 425 nm, 346 nm, 309 nm, and 264 nm. The three observed spectroscopic states likely correspond to the three protonation states of 2.6 (Figure 2.13). For
example, in aprotic solvents, 2.6 remains fully deprotonated, while protonation of a single pyrazolate or both pyrazolates occurs in protic solvents depending on the pKₐ value of the solvent used. In addition, looking at ethanol, propanol, and butanol, that all have similar pKₐ values, the role of decreasing dielectric constant in the series and destabilization of the protonated, ionic state may explain the shift from red to green. Shifting of absorbance maxima to lower energies upon deprotonation of Ru-pyrazolyl fragments has been well-documented in literature.6,31–33 The conversion of pyrazole, a weak π-acceptor, into a pyrazolate, a strong π-donor, results in increased charge density on the metal and thus destabilization of the Ru HOMO leading to a smaller HOMO-LUMO dπ→Lπ* gap.

**pKₐ determination.** The dependence of the solvatochromic behavior on protonation states motivated us to determine pKₐ values of 2.6(2H)²⁺ in solvents containing significant amount of water. Due to poor yields we have not yet been able to prepare sufficient amounts of complexes 2.7 and 2.8, thus characterization efforts throughout the present work will focus heavily on 2.6. An added bonus is that complex 2.6 appears to be significantly more soluble than 2.7 and 2.8 in a myriad of solvents. The pKₐ values of a diprotic (2.6)(2H)(PF₆)₂ salt were established by a UV-visible spectroscopic titration. Complex 2.6(2H)(PF₆)₂ was dissolved in a 1:1 mixture of isopropanol:water due to insufficient solubility in pure water and UV-visible spectra were obtained between pH 5.7 and pH 12.8 by titration with sequential aliquots from an NaOH stock solution. Three distinct absorbance profiles observed for each of the predominant protonation states at pH ~5.7, 10, and ~12.8 showed great resemblance to those of 2.6 in trifluoroethanol, methanol, and ethyl acetate, respectively, giving credence to the assigned protonation states in those solvents. Sigmoidal curves derived from absorbance vs. pH plots for selected absorption bands between pH
5.7 to 10 ($\lambda_{\text{max}} = 536$ and 568 nm) and pH 10 to 12.8 ($\lambda_{\text{max}} = 568$ and 595 nm) allowed for determination of $pK_{\text{a1}}$ and $pK_{\text{a2}}$ to be 7.8 and 11.8, respectively (figure 2.12).

**Figure 2.12.** Data derived from UV-visible spectroscopic titration of 2.6. *Left:* absorbance vs. pH plots for selected absorption bands between pH 5.7 to 10.6 ($\lambda_{\text{max}} = 536$ and 568 nm); *right:* absorbance vs. pH plots for selected absorption bands between pH 10.6 to 12.8 ($\lambda_{\text{max}} = 568$ and 595 nm)

**Figure 2.13.** Depiction of colors and $pK_{\text{a}}$ values between protonation states of 2.6.
2.4. Electrochemistry

Non-aqueous electrochemistry. Cyclic voltammetry of 2.6 and 2.6(2H)(PF$_6$)$_2$ was performed in CH$_3$CN (0.1 M (Bu)$_4$NP$_6$). Cyclic voltammetry of 2.6 shows a reversible wave at 0.45 V for the Ru$^{II/III}$ couple while that of 2.6(2H)(PF$_6$)$_2$ revealed major and minor reversible waves at 1.21 V and 0.81 V, respectively (figure 2.14, left). The CH$_3$CN used was not previously dried, thus we suspected that the minor wave present in CV of 2.6(2H)(PF$_6$) could be associated with 2.6(H)(PF$_6$) produced from mono-deprotonation by trace water in the solvent. Addition of a weak base such as DBU to the solution of 2.6(2H)(PF$_6$)$_2$ lead to diminution of the major wave and growth of the minor wave, lending more evidence for the identity of the minor wave to likely be the Ru$^{II/III}$ couple of 2.6(H)(PF$_6$) (figure 2.14, right). A scanning experiment in deoxygenated CH$_3$CN where the potential was scanned repeatedly between -1.0 V and +1.6 V showed no changes in ratios of 2.6(2H)(PF$_6$)$_2$ and 2.6(H)(PF$_6$) (figure 2.15, left). The same scanning experiment in non-deoxygenated CH$_3$CN solutions however showed very different behavior: an initial negative scan, which showed the reduction of O$_2$ to O$_2^-$ ($E_{pc} \approx 0.72$ V), was followed by a significant magnitude increase in the minor wave and decrease in the major wave, suggesting that the superoxide anion, remarkably, is capable of removing the first proton of 2.6(2H)(PF$_6$)$_2$ (figure 2.15, right). There was no appearance of an additional redox wave at 0.45 V suggesting that double deprotonation to 2.6 does not occur. Similar reactivity was observed by Meyer’s group for [Ru(bpy)$_2$(pzH)$_2$]$^{2+}$ (pyH = pyrazole), however in their case, double deprotonation was indeed achieved by the superoxide ion.$^{31}$ The stabilization of the Ru$^{III}$ oxidation state by anionic groups is obvious by the nearly -400 mV shift of the Ru$^{II/III}$ couple with removal of each proton, consistent with similar observations in other pyrazole and imidazole systems.$^{31,32,34–36}$ Cyclic voltammetry of 2.6 compared to that of Ru(bda)(pic)$_2$ in CH$_3$CN shows that The Ru$^{II/III}$ wave of 2.6 is shifted by –
0.07 V and the Ru$^{III/IV}$ wave is shifted by -0.36 V (Figure 2.16). Pyrazolato ligands are expected to stabilize higher oxidation states more effectively compared to carboxylato ligands because pyrazolato ligands are stronger $\pi$-donors. The lack of reversibility, particularly for the Ru$^{III/IV}$ wave, may arise from coordination of CH$_3$CN to Ru$^{IV}$.

**Figure 2.14.** Left: cyclic voltammetry of 2.6 (green) and 2.6 (2H)(PF$_6$)$_2$ (red) in CH$_3$CN. Right: cyclic voltammetry of 2.6 (2H)(PF$_6$)$_2$ before addition of DBU (red) and after addition of 1 µL (dashed) and 2 µL (blue) of DBU. Conditions: CH$_3$CN (wet, electrolyte = 0.1 M (Bu)$_4$NPF$_6$), concentration of 2.6 = 0.5 mM, concentration of 2.6(2H)(PF$_6$)$_2$ = 0.5 mM.

**Figure 2.15.** Cyclic voltammetry of 2.6(2H)(PF$_6$)$_2$ (0.5 mM) dissolved in deoxygenated (left) and non-deoxygenated (right) CH$_3$CN solutions (wet, electrolyte: 0.1 M (Bu)$_4$NPF$_6$). Blue = first scan, dotted = second scan, red = third scan.
Figure 2.16. Comparison of cyclic voltammetry of 2.6 (blue) and Ru(bda)(pic)$_2$ (red) in CH$_3$CN (0.1 M (Bu)$_4$NPF$_6$)

Figure 2.17. Left: cyclic voltammetry of 2.6 (0.1 mM) in 5.0 mL of potassium phosphate buffer (pH 7, 0.1 M) with no cosolvent. Right: cyclic voltammetry after sequential addition of CF$_3$CH$_2$OH. Green = no CF$_3$CH$_2$OH, blue dashed = 50 µL, yellow dashed = 100 µL, red = 200 µL.
Figure 2.18. Cyclic voltammetry (red) and DPV (dashed brown) of 2.6 in HNO₃ (0.05 M). dotted = background scan.
Aqueous electrochemistry. Complexes 2.6-2.8 showed limited or no solubility in purely aqueous solutions. Interestingly, in spite of having the greatest number of sp³ carbons, complex 2.6 was the most water soluble of all three complexes; one can speculate that in the solid, the presence of tert-butyl groups reduces the strength of crystal packing. Complexes 2.7 and 2.8 showed effectively no solubility in purely aqueous acidic or neutral solutions. We were able to achieve full homogeneity of 2.6 at a concentration of 0.1 mM in potassium phosphate buffer (0.1 M, pH 7). Cyclic voltammetry at glassy carbon begins with a nearly reversible wave at 0.59 V for the Ru<sup>II/III</sup> couple, followed by a second oxidative wave at 1.17 V for Ru<sup>III/IV</sup>, and then onset of a large current increase indicative of catalysis (Figure 2.17, left). The catalytic wave is associated
with oxidation of water, evident from the presence of a broad reductive wave on the return scan at \(~-0.66\text{ V}\) consistent with reduction of \(O_2\) generated during catalysis. We sought to test complexes 2.6-2.8 under identical conditions for meaningful comparison of their electrochemical properties; however, the extreme lack of solubility of 2.6 and 2.8 in purely aqueous solutions motivated us to try various ratios of co-solvents. We initially tried using CF\(_3\)CH\(_2\)OH, but significant inhibition of catalytic activity was noticed in CVs of 2.6, evident from decreased catalytic current with respect to \(i_p\) of the Ru\(^{II/III}\) oxidation and disappearance of the \(O_2\) reduction wave (Figure 2.17, right). The Ru\(^{II/III}\) and Ru\(^{III/IV}\) couples shifted to more positive potentials with addition each portion of CF\(_3\)CH\(_2\)OH indicating that there is likely some mode of interaction between the alcohol O-H and the free pyrazolate nitrogens. The use of CH\(_3\)CN as a co-solvent also leads to some loss of catalytic activity - perhaps because of competitive binding to the metal center – however the effect was not as dramatic as with CF\(_3\)CH\(_2\)OH. Thus we performed cyclic voltammetry on complexes 2.6-2.8 using a 0.1 M potassium phosphate buffer solution (pH 7) containing 20\% CH\(_3\)CN (Figure 2.16). Under these conditions, 2.7 showed minimal, if any, catalysis when the electrode was driven to 1.6 V and complex 2.8 showed a slightly greater magnitude of current compared to 2.7 with an onset between \(~1.2 – 1.3\) V. In CV of 2.8, a reduction wave observed near \(~0.42\) V, following the positive scan to 1.6 V, does not match with \(O_2\) reduction from negative scans after deliberate introduction of ambient air to the cell solution. Thus, further studies will be required to determine conclusively whether water is being electrochemically oxidized by 2.8. The Ru\(^{III}\) oxidation waves shift from 0.60 V to 0.65 V to 0.68 V for 2.6, 2.7, and 2.8, respectively; these values seem appropriate given the electronics of each ligand (inductive electron donating effect from tert-butyl groups of 1 and electron withdrawing effect of expanded \(\pi\)-system in indazole of 2.8). Under acidic conditions, the Ru\(^{III}\) and Ru\(^{III/IV}\) couples of 2.6 shift to 0.95 V and \(~1.44\) V, respectively,
and no catalytic wave is observed (Figure 2.18) consistent with results from addition of CF$_3$CH$_2$OH under neutral conditions.

**Figure 2.20.** Oxygen evolution of 2.6 (blue), 2.7 (red) and Ru($bda$)$_2$(pic)$_2$ (purple) measured using a pressure transducer. Conditions: 250 µM catalyst conc., 250 mM ceric ammonium nitrate.

**2.5. Ce$^{IV}$ testing**

Rapid oxygen evolution by 2.6 and 2.7 was observed in the presence of excess Ce$^{IV}$ as a sacrificial oxidant. The amount of oxygen produced was quantified by measuring the associated pressure in the vessel using a pressure transducer. Under conditions with 250 µM catalyst and 250 mM Ce$^{IV}$ (1000 equiv excess), O$_2$ production by 2.6 reached the theoretical limit (250 µmol O$_2$) within ~3 minutes. However, O$_2$ evolution only begins after an initial lag period of ~1.5 min. A
turnover frequency of ~235 min\(^{-1}\) (3.9 s\(^{-1}\)) was calculated from the slope of the O\(_2\) evolution curve after the lag period. Similarly, a shorter lag period of ~1 min was observed during testing of \(\text{2.7}\) under the same conditions, and oxygen evolution occurred at turnover frequency of ~195 min\(^{-1}\) (3.3 s\(^{-1}\)) reaching close to the theoretical limit of O\(_2\) within 2 min of injection. The observed turnover frequencies, while an order of magnitude smaller than Ru(\(bda\))(pic)_2 (41 s\(^{-1}\) under the same conditions, consistent with prior reports\(^{37}\)), are an order of magnitude greater than most homogenous Ru catalytic systems.\(^{38}\) The initial lag period may simply be the result of very slow solubilization given the extreme insolubility of complexes \(\text{2.6 and 2.7}\). To give some perspective, the inherent solubility of \(\text{2.6}\) in a 0.05 M HNO\(_3\) solution is roughly 0.05 mM, however, the graphs shown in Figure 2.20 are derived from reaction solutions nearly five times more concentrated with respect to catalyst (0.250 mM). Upon initial injection of \(\text{2.6}\) dissolved in CF\(_3\)CH\(_2\)OH to the Ce\(^{IV}\) solution, some haziness is observed and within minutes the solution becomes homogeneous. It may be the case that the complex becomes increasingly more soluble upon oxidation to the higher oxidation states.

An alternative explanation for the presence of the lag period would be that the complexes actually serve as precursors to more active catalysts. Catalyst modification pathways in the presence of excess Ce\(^{IV}\) have been a topic of interest, particularly in the last few years.\(^{39-48}\) Ruthenium polypyridyl frameworks are often considered to have highly stable configurations, however under such extreme oxidizing conditions (1000 equiv Ce\(^{IV}\), a particularly harsh oxidant) they are susceptible to several oxidative transformations. For example, there are reports of pyridine N-oxide formation, that can lead to new structures incorporating the N-oxide as a ligand or ligand loss promoting formation of dimeric species.\(^{40,42,43,46,47}\) In one case, the Ce\(^{IV}\)-induced oxygen evolution profile of \([\text{Ru}^{II}(\text{NPM})(\text{pic})_2(\text{H}_2\text{O})]^{2+}\) (NPM = 4-tert-butyl-2,6-di-(1',8'-
naphthyrid-2'-yl)-pyridine) exhibited a similar lag period (albeit only a few seconds); through spectroscopic studies it was found that the in situ generated Ru^{IV}=O species undergoes O-atom transfer to the adjacent uncoordinated nitrogen atoms for N-oxide ligand formation. For the complex [Ru(qtpy)(pic)]^{2+}, N-oxide formation was found to occur on pyridyl groups directly coordinated to the metal to form [Ru(qtpy-NO,NO)(pic)]^{3+} as the real catalyst. Generation of pyrazole N-oxides is less common than of pyridine N-oxides, however it is clear that addition of peroxides to pyrazoles can form N-oxides at room temperature. Another possible site of oxidation is the unprotected pyrazole C-4 position in 2.6 or either C-4 or C-5 position in 2.7. Bozoglian et al. conducted a detailed study of catalysis by dinuclear complex Ru-hbpp bearing a bridging pyrazole group; after exhaustive electrochemical oxidation they were able to isolate crystals of an oxidized species with a ketone on the C-4 carbon of the pyrazole. One of our motivations for synthesizing 2.8 was to block both C-4 and C-5 positions, however we have been unable to test it yet under Ce^{IV} conditions due to insufficient supplies.

The impressive results of 2.6 in a pH 1 solution containing Ce^{IV} are in disagreement with the lack of electro-catalytic activity under acidic conditions even when the electrode is driven to 1.8 V and 2.0 V (not shown) – well past the reduction potential of Ce^{IV} (~1.5 – 1.6V vs. Ag/AgCl). Above, we discussed potential inner-sphere catalyst modifications; given the propensity of Ru-pyrazolate fragments to seek out protons or Lewis acidic entities, we also invoke the possibility of mechanisms involving outer-sphere interactions with Ce^{IV}. Codolá et al. encountered such a phenomenon in iron-diaquo complexes where a [O=Fe^{IV}-O-Ce^{IV}] adduct was evident from spectroscopic and spectrometric characterization. One can imagine formation of a similar [O=Ru^{IV}-N-N-Ce^{IV}] adduct with the pyrazolate complexes described in this chapter.
Figure 2.21. Cerium non-innocence in $O_2$ evolution: (a) proposed O-O bond formation pathway via a $[O=Fe^{IV}$-$O$-$Ce^{IV}]$ adduct formed from an iron-diaquo complex (Codolá et al.); (b) proposed O-O bond formation pathway via 2,2'-bipyridine-6,6'-dipyrazolate framework.

2.6. Conclusions and Future Work.

We have prepared three novel ruthenium complexes (2.6-2.8) bearing 2,2'-bipyridine ligands with various pyrazolate derivatives in the 6,6'-positions. These complexes were characterized by NMR spectroscopy and x-ray crystallography. The solvatochromic and acid-base properties of complex 2.6 were investigated by non-aqueous and aqueous UV-visible spectroscopy and electrochemistry. Reactions to make complexes 2.7 and 2.8 lead to low yields and thus the products have not been fully characterized yet. Under neutral conditions, a preliminary assessment of electrocatalytic reactivity by cyclic voltammetry points to complex 2.6 being the most catalytically active, evident by a catalytic wave between 1.2 – 1.3 V followed by $O_2$ reduction wave on the negative scan. Rates of $O_2$ production under acid conditions in the presence of $Ce^{IV}$ were measured to be 3.9 s$^{-1}$ and 3.3 s$^{-1}$ for 2.6 and 2.7, respectively. These apparent rates are in the upper range of rates observed by ruthenium-based molecular catalysts, however the lag periods observed for 1 – 1.5 min prior to $O_2$ production are of concern because they may indicate either slow dissolution of catalyst or catalyst modification.

To evaluate the possibility of $Ce^{IV}$ non-innocence during catalysis as observed by Codola et al., we propose synthesizing and testing complexes 2,2'-bipyridine ligands with imidazolate
ligands in the 6,6’-positions. Imidazolate ligands are electronically similar to pyrazole ligands, but the free N would face away from the active site, which would prevent formation of a putative CeIV-adduct. We have already synthesized 2.24, shown in figure 2.21 (see section 2.7.1 for synthetic procedure and section 2.7.2 for full NMR characterization data), and preliminary results have shown that it is a slow catalyst in the presence of CeIV where only 25% of the theoretical O2 yield is achieved even after 10 h (data not shown). Complex 2.25 will allow for a more direct comparison with 2.6 due to its steric similarity. In addition to synthesizing new complexes, a Pourbaix diagram of 2.6 will be instructive towards elucidating its mechanism under electrochemical conditions.

![Chemical structures](image)

**Figure 2.22.** Proposed ruthenium complexes with 2,2’-bipyridine-6,6’-imidazolate ligands.
Chapter 2 contains material that is currently being prepared for publication. Kamdar, J. M.; Aspacio, D. S.; Boisaubert, P.; Spire, M. T.; Marelius, D.M.; Golen, J.; Moore, C. E.; Rheingold, A. L.; Smith, D. K.; Grotjahn, D.B. “Synthesis, characterization, and reactivity of ruthenium complexes bearing 2,2’-bipyridine-6,6’-dipyrazolato/imidazolato ligands towards water oxidation”. Manuscript in preparation. The dissertation author was the primary researcher for the data presented. I would like to thank Derek Aspacio and Pierre Boisaubert for their tenacity in getting through difficult ligand syntheses. I would like to thank Dave Marelius and Matthew Spire for performing CeIV experiments that in part guided the synthesis of the complexes presented. I thank Dr. James Golen, Dr. Curtis Moore, and Dr. Arnold Rheingold for their support in x-ray crystallography. I also thank Dr. Diane Smith for assistance with electrochemical techniques.

2.7. Experimental

2.7.1. Preparation of compounds

![N-chelate](image.png)

Synthesis of dimethyl 2,2’-bipyridine-6,6’-dicarboxylate (2.10): In a round bottom flask, a suspension of 2,2’-bipyridine-6,6’-dicarboxylic acid (10.2253g, 41.9 mmol) in CH3OH (150 mL) was cooled to ~0 °C in an ice-water bath and SOCl2 (9.3 mL, 125.7 mmol) was added dropwise over 1 h via an addition funnel. The reaction flask was equipped with a condenser and after stirring the reaction mixture at 50 °C for nearly 24 h, it was concentrated to a brown mixture by rotary evaporation. The crude residue was re-dissolved in CHCl3 (50 mL) and the resulting solution washed three times with saturated Na2CO3 (100 mL each wash) and once with saturated NaCl (50
mL). The organic layer was dried with anhydrous sodium sulfate, filtered, and the filtrate concentrated via rotary evaporation to obtain a yellow solid. A hot recrystallization in CHCl₃ was performed to obtain white micro-crystals of 2 (7.4855 g, 66%). ^1H NMR (δ, 499.944 MHz, CDCl₃): 8.75 (d, 2H, ^3J_HH = 7.8 Hz), 8.16 (d, 2H, ^3J_HH = 7.8 Hz), 8.00 (t, 2H, ^3J_HH = 7.8 Hz), 4.04 (s, 6H). ^13C NMR (δ, 125.724 MHz, CDCl₃): 165.79, 155.59, 147.66, 138.20, 125.60, 124.96, 53.00. NMR signals match with those previously reported in literature.⁵³

Synthesis of 1,1'-([2,2'-bipyridine]-6,6'-diyl)bis(4,4-dimethylpentane-1,3-dione) (2.11) :
Under an inert atmosphere, 2 (2.7853 g, 10.230 mmol) and NaH (60% in oil, 1.9873 g, 49.683 mmol) were weighed out in a three-neck round bottom flask and suspended in 1,2-dimethoxyethane (70 mL, dry and de-oxygenated). The reaction mixture was refluxed in a 110 °C oil bath under inert conditions (note: dissolution was observed upon heating). After 25 min, pinacolone (96 %, 3.00 mL, 23.0 mmol) was added dropwise into the refluxing reaction mixture over 15 min. After refluxing for nearly 17 h, the reaction was allowed to cool to room temperature and subsequently quenched with saturated NaHCO₃ (250 mL) during which precipitation of a yellow-orange solid was observed. The aqueous suspension was transferred to a separatory funnel and extracted three times with EtOAc (200 mL for first extraction, 150 mL each for second and third extractions). The combined organic layers were washed twice with saturated NaCl (50 mL each wash) and then dried with anhydrous sodium sulfate, filtered, and the filtrate concentrated by
rotary evaporation to a beige solid. The crude product was further purified by silica gel column chromatography (9:1 CH$_2$Cl$_2$ : EtOAc) to afford a beige solid product (3.6619 g, 88%). Elemental analysis data were not consistent with calculated C, H, N values (Calcd. for C$_{24}$H$_{28}$N$_2$O$_4$ (408.50): C, 70.57; H, 6.91; N, 6.86. Found: C, 75.18; H, 7.81; N, 4.83), however the product was used without further purification in the next step. See section 2.7.2 for full NMR characterization data.

![Chemical Structure]

**Synthesis of the 6,6'-bis(5-(tBu)-1H-pyrazol-3-yl)-2,2'-bipyridine (2.12):** In a round bottom flask, 3 (4.4086 g, 10.8 mmol) was partially dissolved in a mixture of 1:1 MeOH/Et$_2$O (210 mL). Hydrazine monohydrate (1.31 mL) was added to the flask and the reaction mixture was allowed to stir at room temperature. Reaction progress was monitored by TLC; upon completion (after nearly 1 h) the reaction mixture was concentrated by rotary evaporation and purified by silica gel column chromatography (gradient elution: 9:1 EtOAc : CH$_3$OH with 15% NEt$_3$ to 4:1 EtOAc : CH$_3$OH with 15% NEt$_3$) to afford the desired product as a white solid (2.3978 g, 55%). Calcd. for C$_{24}$H$_{28}$N$_6$ (400.53): C, 71.97; H, 7.05; N, 20.98. Found: C, 65.45; H, 7.55; N, 9.21. Anal. Calcd. for C$_{24}$H$_{28}$N$_6$ + 2.2 H$_2$O (440.16): C, 65.49; H, 7.42; N, 9.09. See section 2.7.2 full NMR characterization data.
Synthesis of Ru(bdpz-tBu)(pic)₂ (2.6): In a glovebox, 2.12 (0.0999 g, 0.249 mmol) and Ru(DMSO)₄Cl₂ (0.1206 g, 0.2489 mmol) were weighed out in a 20 mL vial containing a stir bar and CH₃OH (15 mL, deoxygenated) was added to make a dirty-yellow solution and suspension. Excess NEt₃ (350 µL, dry, deoxygenated) was added and immediately the solution began changing to a dark-maroon color. After allowing the reaction to stir at room temperature overnight, excess 4-picoline (200 µL) and the reaction was heated in a 100 °C oil bath overnight. Strongly basic Amberjet OH 4400 resin (2.0168 g) was charged into the reaction mixture, the suspension was allowed to stir at room temperature for 1 h and then filtered through a fritted funnel (class C). The filtrate was concentrated to a dark green solid by rotary evaporation and placed under an oil-pump vacuum overnight. The dried solid was transferred to a fritted funnel (class M) with sufficient Et₂O (20 mL) and thoroughly rinsed with five portions of Et₂O (25 mL each wash). After 24 h under an oil pump-vacuum the weight was 0.1401 g (78 %). Anal. Calcd. for C₃₆H₄₀N₈Ru (685.84): C, 63.05; H, 5.88; N, 16.34. Found: C, 60.06; H, 6.16; N, 15.02. Anal. Calcd. for C₃₆H₄₀N₈Ru + 2 H₂O (721.87): C, 59.90; H, 6.14; N, 15.52. See section 2.7.2 for full NMR characterization.
Synthesis of 6,6’-bis[2-(trimethylsilyl)ethynyl]-2,2’-bipyridine (2.14): In a glovebox, 6,6’-dibromo-2,2’-bipyridine (2.0000 g, 6.37 mmol), CuI (0.1442 g, 0.757 mmol), and Pd(PPh₃)₂Cl₂ (0.4471 g, 0.637 mmol) were weighed out in a 150 mL pressure vessel (previously dried via heat gun under vacuum) and suspended in dry, de-oxygenated NEt₃ (80 mL). Trimethylsilylacetylene (3.6 mL) was added to the suspension, the vessel was sealed, and the reaction was heated in a 100 °C oil bath for 15 h. Reaction progress was ascertained by ¹H NMR spectroscopy of a ~0.2 mL aliquot of the reaction mixture diluted with ~0.4 mL CDCl₃ (deoxygenated) in a glovebox. Upon completion, the reaction mixture was transferred to a round-bottom flask using two portions of Et₂O (50 mL each) and concentrated to a dark solid by rotary evaporation. The solid was re-suspended in Et₂O and the mixture was filtered through a class M filter funnel. The collected solid was thoroughly washed two more times with Et₂O (100 mL each wash) and the filtrate was concentrated by rotary evaporation to yield a tan solid. The crude product was purified by silica gel column chromatography (gradient elution from 100 % hexanes to 1:10 EtOAc : hexanes). The product containing fractions were combined and concentrated by rotary evaporation. The resulting solid was suspended in a 1:20 EtOAc : hexanes mixture (50 mL) and filtered to through a class F filter funnel to remove residual triphenylphosphine oxide. The white solid collected on the funnel was thoroughly rinsed two more times with 1:20 EtOAc : hexanes (50 mL each wash) and then once more with pentane (25 mL). After drying under an oil-pump vacuum overnight, the product weighed 1.1933 g (54 %). ¹H NMR (δ, CDCl₃): 8.44 (dd, 2H, 4J₃H = 0.8 Hz, 3J₃H = 8.0 Hz), 7.77
(tt, 2H, \(^3J_{HH} = 7.6\) Hz), 7.49 (dd, 2H, \(^4J_{HH} = 0.8\) Hz, \(^3J_{HH} = 7.6\) Hz), 0.31 (s, 18H). Anal. Calcd. for C\(_{20}\)H\(_{24}\)N\(_2\)Si\(_2\) (348.60): C, 68.91; H, 6.94; N, 8.04. Found: C, 67.96; H, 7.70; N, 8.10. Anal. Calcd. for C\(_{20}\)H\(_{24}\)N\(_2\)Si\(_2\) + 0.4 H\(_2\)O (355.80): C, 67.52; H, 7.03; N, 7.87. NMR signals match with those previously reported in literature.\(^{54}\)

![Diagram of molecule]

**Synthesis of 6,6'-diacetyl-2,2'-bipyridine (2.15):** This compound was made using a procedure similar to one employed by Bianchiani et al. to make 1-(5-bromo-2-pyridinyl)ethanone from 5-bromo-2-[((trimethylsilyl)ethynyl]pyridine.\(^{55}\) 6,6'-bis[(trimethylsilyl)ethynyl]-2,2'-bipyridine (0.6015 g, 1.726 mmol) and Hg(OAc)\(_2\) (1.1556 g, 3.626 mmol) were weighed into a round bottom flask, and an 8:1 mixture of acetone : H\(_2\)O (20 mL) was added to form a suspension. The reaction mixture was allowed to stir at room temperature for 30 min. Aqueous H\(_2\)SO\(_4\) (2.0 M, 5.2 mL) was added and the mixture was refluxed in a 95 °C oil bath over 6 h. To determine if the reaction was complete, a ~0.3 mL aliquot was removed, worked up, and analyzed by \(^1\)H NMR spectroscopy. The aliquot was worked up by concentrating and basifying the mixture to pH 6-7 with 5% NaHCO\(_3\) (~5 mL), extracting the product with EtOAc (3 mL), and concentrating to a solid. \(^1\)H NMR spectroscopy in CDCl\(_3\) confirmed the presence of the acetyl groups as a singlet at ~2.86 ppm with an integration of 6H relative to 2H of any of the three bipyridine signals. Upon confirming that the reaction was complete, the bulk of the acetone in the reaction mixture was removed by rotary evaporation and 5% NaHCO\(_3\) (150 mL) was added over 10 min to neutralize the mixture. The mixture was transferred to a separatory funnel and extracted three times with EtOAc (3 x 150 mL). The combined organic extracts were dried with anhydrous Na\(_2\)SO\(_4\), filtered,
and the filtrate concentrated to dryness on a rotary evaporator to yield a yellow-beige solid. The crude product was passed through a silica plug (eluted with 100 % EtOAc). The product containing fractions were concentrated to dryness on a rotary evaporator and further dried under an oil-pump vacuum, affording a white powdery solid (0.2360 g, 57 %). $^1$H NMR (δ, 499.944, CDCl$_3$): 8.74 (d, $^3$J$_{HH}$ = 7.5 Hz), 8.11 ($^3$J$_{HH}$ = 8.0 Hz), 8.02 (t, 2H, $^3$J$_{HH}$ = 8.0 Hz), 2.86 (s, 6H). $^{13}$C NMR (δ, 125.724 MHz, CDCl$_3$): 200.16, 154.77, 153.16, 138.09, 124.46, 122.02, 25.89. Anal. Calcd. for C$_{14}$H$_{12}$N$_2$O$_2$ (240.26): C, 69.99; H, 5.03; N, 11.66. Found: C, 63.73; H, 5.79; N, 9.88. Anal. Calcd. for C$_{14}$H$_{12}$N$_2$O$_2$ + 1.4 H$_2$O (265.48): C, 63.34; H, 5.62; N, 10.55. NMR signals match those previous reported in literature.$^{56}$

![Synthesis of 1,1'-[2,2'-bipyridine]-6,6'-diylbis[3-(dimethylamino)-2-propen-1-one (2.16):]

This compound was made using a procedure similar to one employed by Couchman et al.$^{28}$ In a round bottom flask, 2.15 (0.2264 g, 0.9423 mmol) was suspended in N,N-dimethylformamide dimethyl acetal (20 mL). The suspension was refluxed in a 135 °C oil bath for nearly 24 h under N$_2$ during which orange solid precipitated out. The precipitate was filtered through a class F filter funnel and washed with hexanes (3 x 15 mL) and pentane (15 mL). The solid was dried in a dessicator under an oil-pump vacuum for 3.5 h. (0.2376 g, 72 %). $^1$H NMR (δ, 499.944 MHz, CDCl$_3$): 8.63 (d, 2H, $^3$J$_{HH}$ = 7.5 Hz), 8.21 (d, $^3$J$_{HH}$ = 7.5 Hz, 2H), 7.97 (d, 1H, $^3$J$_{HH}$ = 12.5 Hz), 7.96 (t, 2H, $^3$J$_{HH}$ = 7.5 Hz), 6.69 (d, 2H, broad, $^3$J$_{HH}$ =12.0 Hz), 3.22 (s, 6H, broad), 3.07 (s, 6H,
broad). Anal. Calcd. for C\textsubscript{20}H\textsubscript{22}N\textsubscript{4}O\textsubscript{2} (350.42): C, 68.55; H, 6.33; N, 15.99. Found: C, 68.29; H, 6.80; N, 16.01. Instability of the compound prevented full NMR characterization; the product was used in the next step.

**Synthesis of 6,6'-bis(3-pyrazolyl)-2,2'-bipyridine (2.17):** This compound was made using a procedure similar to one employed by Couchman et al.\textsuperscript{28} In a round bottom flask, excess hydrazine monohydrate (1.2 mL) was added to a suspension of 2.16 (0.2157 g, 0.6156 mmol) in ethanol (10 mL). The mixture was refluxed 13 h in a 115 °C oil bath during which white solid product precipitated out of solution. The solid was filtered through a class F filter funnel and rinsed thoroughly with ethanol (3 × 10 mL) and Et\textsubscript{2}O (3 × 10 mL). The off-white solid was dried in a dessicator under an oil-pump vacuum overnight (0.1495 g, 84 \%). Anal. Calcd. for C\textsubscript{20}H\textsubscript{22}N\textsubscript{4}O\textsubscript{2} (288.31): C, 66.66; H, 4.20; N, 29.15. Found: C, 66.26; H, 4.60; N, 29.02. The extreme insolubility of the compound (even in d\textsubscript{6}-DMSO) precluded full NMR characterization.
Synthesis of Ru(6,6’-bis(3-pyrazolyl)-2,2’-bipyridine)(pic)$_2$ (2.7): Under an inert atmosphere, 2.17 (0.0451 g, 0.156 mmol) and Ru(DMSO)$_4$Cl$_2$ (0.0758 g, 0.156 mmol) were weighed out in a 20 mL vial containing a stir-bar and suspended in CH$_3$OH (5 mL, de-oxygenated). Excess triethylamine (325 µL, dry and de-oxygenated) was added to the mixture and the mixture was heated at 70 °C for 30 h. Excess 4-picoline (150 µL) was added to the dark-brown heterogeneous solution and the mixture was heated at 100 °C for 36 h. The reaction solution was concentrated by rotary evaporation and purified by silica gel column chromatography (5 % NEt$_3$ : CH$_2$Cl$_2$) to afford a dark brown solid. The solid was dissolved in a 1:1 mixture of CH$_2$Cl$_2$ : CH$_3$OH (10 mL), Amberjet OH 4400 resin (0.5001 g) was added, and the suspension was stirred for 5 h. The mixture was filtered through a cotton plug in a pipette and the filtrate was concentrated to a solid. The solid was redissolved in 1:1 CH$_2$Cl$_2$ : CH$_3$OH (3 mL) and triturated with Et$_2$O until a dark microcrystalline solid precipitated out of solution. The solid was filtered through a filter funnel (class F) and rinsed with acetone (3 × 5 mL) and Et$_2$O (3 × 10 mL). After drying under an oil-pump vacuum in a dessicator, the weight was 12.1 mg (13 %). See section 2.7.2 for full NMR characterization data.
Synthesis of crude 1-(tetrahydro-2H-pyran-2-yl)-3-iodo-1H-indazole (2.20): Under an inert atmosphere, 3-iodo-1H-indazole (3.1340 g, 12.842 mmol) and p-TsOH·H₂O (0.3421 g, 1.799 mmol) were weighed out in an oven-dried round bottom flask and dissolved in dry CH₂Cl₂ (60 mL, distilled from CaH₂). Addition of dihydropyran (4.5 mL) produced a dark brown mixture which was stirred at room temperature for nearly 21 h. After reaction completion was confirmed by TLC, the reaction mixture was transferred to a separatory funnel with enough CH₂Cl₂ (40 mL) to rinse the reaction flask and washed with saturated NaHCO₃ (100 mL). The aqueous layer was back extracted once with CH₂Cl₂ (50 mL) and the combined organic layers were dried with anhydrous Na₂SO₄, filtered, and the filtrate concentrated to a dark brown oil by rotary evaporation. The crude oil was purified via silica gel column chromatography (eluent: 100 % CH₂Cl₂; product was dry-loaded onto column) to yield an off-white solid (4.1607 g, 99%). ¹H NMR ( δ, 499.944 MHz, CDCl₃): 7.57 (d, 1H, ³JₕH = 8.5 Hz), 7.49 (d, 1H, ³JₕH = 8.5 Hz), 7.46 (td, 1H, ³JₕH = 8.0 Hz, ¼JₕH = 0.5 Hz), 7.24 (t, 1H, ³JₕH = 7.5 Hz), 5.71 (dd, 1H, ³JₕH = 9.0 Hz, ³JₕH = 3.0 Hz), 4.04 (m, 1H), 3.74 (m, 1H), 2.58 (m, 1H), 2.16 (m, 1H), 2.08 (m, 1H), 1.72-1.81 (m, 2H), 1.66 (m, 1H). ¹³C NMR ( δ, 125.724 MHz, CDCl₃): 140.09, 129.09, 127.76, 122.07, 121.76, 110.40, 93.47, 85.79, 67.63, 29.56, 25.16, 22.62. Elemental analysis data were not consistent with calculated C, H, N values (Anal. Calcd. for C₁₂H₁₃IN₂O (328.15): C, 43.92; H, 3.99; N, 8.54. Found: C, 48.38; H, 4.23; N, 9.38), however the product was used without further purification in the next step. NMR signals match with signals previously reported in literature.⁵⁷
Synthesis of crude 1-(tetrahydro-2H-pyran-2-yl)-3-(trimethylstannyl)-1H-indazole (2.21):

Under an inert atmosphere, Pd(PPh₃)₂Cl₂ (0.7979 g, 1.14 mmol) was added to a dissolved solution of 7 (3.64 g, 11.1 mmol), and hexamethylditin (2.9 ml, 14.0 mmol) in dry, de-oxygenated 1,4-dioxane (72.5 mL) in a pressure vessel (dried via heat gun under vacuum prior to use). The reaction mixture was stirred in a 100 °C oil bath for 24 hours, transferred to a round bottom flask with sufficient ethyl acetate (20 mL) to rinse the pressure vessel, and concentrated by rotary evaporation to remove the 1,4-dioxane. The crude solid was re-dissolved in ethyl acetate (70 mL), transferred to a separatory funnel, and washed once with H₂O (80 mL). The aqueous layer was back-extracted with three portions of ethyl acetate (3 x 30 ml) and the combined organic layers were washed once with saturated NaCl (50 mL). The organics were dried with anhydrous Na₂SO₄, filtered, and concentrated by rotary evaporation and then further dried under an oil pump vacuum for 24 hours to give a crude yellow oil (4.361 g). In a J. Young tube, internal standard tetrakis(trimethylsilyl)silane (5.0 mg) and a sample of crude product (70.8 mg) were dissolved in CDCl₃. Based on ¹H NMR integration values of the desired product with respect to internal standard, the mass of product in the crude mixture was determined to be 3.654 g (90 % yield). The crude mixture was used in the next step without further purification.
Synthesis of 6,6’-bis(1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-3-yl)-2-2’-bipyridine (2.22)

A solution of crude 8 (3.6545 g, 10.00 mmol) in toluene (dry, de-oxygenated, 151 mL) was prepared under an inert atmosphere and a portion of the solution (75.1 mL) was transferred to an oven-dried pressure vessel with a stir bar. Reactant 6,6’-dibromo-2,2’-bipyridine (0.7793 g, 2.48 mmol) and tetrakis(triphenylphosphine)palladium(0) (1.1839 g, 1.02 mmol) were added to the solution and the resulting mixture was heated in a 130 °C oil bath for 24 h. Reaction progress was ascertained by conducting NMR spectroscopy and mass spectrometry on aliquots of the mixture. Upon completion, the reaction mixture was filtered through a fine glass frit and the filtrate was transferred to a round bottom flask with a stir bar. A 1 M sodium hydroxide solution (49.3 mL) was added to the flask and the mixture was stirred vigorously for 24 hours. The organic and aqueous layers were separated in a separatory funnel and the aqueous layer was extracted with toluene (3 × 50 mL). The combined organic layers were dried with anhydrous Na₂SO₄, filtered, and concentrated by rotary evaporation to give a crude orange oil. The orange oil analyzed by NMR (in CDCl₃) and mass spectrometry showed no evidence of any trimethyltin-containing species. The crude product was passed through a silica gel column (gradient elution: CH₂Cl₂ to 10: 1 CH₂Cl₂ : methanol), however the eluted product (1.8126 g) still contained triphenylphosphine and triphenylphosphine oxide impurities. Silica gel column chromatography was performed once more with EtOAc (~ 5% NEt₃) however significant amounts of
triphenylphosphine/triphenylphosphine oxide impurities still remained. In a J. Young tube, internal standard tetrakis(trimethylsilyl)silane (0.0069 g) and a small portion of crude product (0.0427 g) were dissolved in CDCl$_3$ and the yield of desired product in the crude mixture (1.6746 g) with respect to the internal standard was determined to be 0.4745 g (36.5 %). The crude mixture was used in the next step without further purification.

Synthesis of 2.23: Crude 2.22 (1.6746 g, 28.34% product by weight) and p-toluenesulfonic acid monohydrate (19.8 mg, 0.104 mmol) were added to a flask with a stir bar and MeOH (50 mL) was added. The reaction mixture was stirred for 24 hours at room temperature, then refluxed for 24 hours at 100°C. The mixture was not completely soluble. Additional p-toluenesulfonic acid monohydrate (208.3 mg, 1.095 mmol) was added to the flask then the reaction mixture stirred for 11 hours at room temperature. The mixture was refluxed for 3 hours at 100°C and then even more p-toluenesulfonic acid monohydrate (209.1 mg, 1.099 mmol) was added to the reaction mixture. The mixture was refluxed for 48 hours during which a yellow solid precipitated out. The solid was filtered through a fritted funnel (class F) and washed with MeOH (4 × 30 mL) until the washings were colorless. To confirm the identity of the solid as the deprotected product, a small sample of the solid was dissolved in DMSO-d$_6$ and $^1$H NMR spectroscopy presence of product and peaks corresponding to excess tosylate anion. The mustard yellow solid in the frit was washed with water (3 × 30 mL), MeOH (2 × 30 mL), CH$_2$Cl$_2$ (3 × 30 mL), and diethyl ether (2 × 30 mL), and
then placed under oil pump vacuum in a desiccator for 24 h (99.4 mg, 20 %). Anal. Calcd. for C\textsubscript{31}H\textsubscript{24}N\textsubscript{6}O\textsubscript{3} (560.63): C, 66.41; H, 4.32; N, 14.99. Found: C, 64.04; H, 4.93; N, 14.73. Anal. Calcd. for C\textsubscript{31}H\textsubscript{24}N\textsubscript{6}O\textsubscript{3} + 0.8 H\textsubscript{2}O (578.65): C, 64.75; H, 4.49; N, 14.61. See section 2.7.2 for full NMR characterization.

**Synthesis of Ru(bdz)(pic)

2.8**): Under an inert atmosphere, tosylate salt 2.23 (39.4 mg, 70.28 umol) and Ru(DMSO)\textsubscript{4}Cl\textsubscript{2} (34.0 mg, 70.17 umol) were weighed in a 20 mL vial containing a stir bar. MeOH (5 mL) was added to the vial to make a partially dissolved solution. Triethylamine (150 uL) was added to the reaction mixture and the vial was heated in a 70 °C oil bath for 22 h. 4-picoline (32 µL) was added and the reaction mixture was heated for 19 h in a 100 °C oil bath. The reaction mixture was concentrated to a dark crude solid which was purified by silica gel column chromatography (gradient elution: CH\textsubscript{2}Cl\textsubscript{2} : MeOH : NEt3, 20:0:1 to 20:2:1). A second column was run on the crude product collected (eluent: 5:1 CH\textsubscript{2}Cl\textsubscript{2} : NEt3). The crude product was then dissolved in CH\textsubscript{2}Cl\textsubscript{2} and filtered through a syringe filter (0.2 µm pore diameter). The crude product was then concentrated and rinsed with Et\textsubscript{2}O (2 × 15mL) to yield pure 2.8 (3.4 mg, 7.2 %).
Synthesis of Ru(2,2'-bipyridine-6,6'-dibenzimidazolate)(pic)$_2$ (2.24): Under an inert atmosphere, 2,2'-bipyridine-6,6'-dibenzimidazole (0.0181 g, 46.6 µmol) and Ru(DMSO)$_4$Cl$_2$ were weighed in a J. Young tube and CD$_3$OD (1.2 mL) was added to make a suspension. Excess triethylamine (100 µL) was added to the tube which was then sealed and placed in a 70 °C oil bath. After 14 h of heating, the mixture was transferred to a 20 mL vial with a stir bar with sufficient CH$_3$OH to rinse the tube (4 × 0.6 mL). The mixture was heated for another 20 h in a 70 °C oil bath after which excess 4-picoline (25 µL) was added. The mixture was heated for 14 h in a 100 °C oil bath and then concentrated to a dark brown solid under rotary evaporation. The crude solid was purified by silica gel column chromatography (~5 g silica, gradient elution: from 100% CH$_2$Cl$_2$ to CH$_2$Cl$_2$ with 2.5 % NEt$_3$ to 1:40 CH$_2$Cl$_2$ : CH$_3$OH with 2.5 % NEt$_3$) and the product containing fractions were concentrated under rotary evaporation. The product was redissolved in CH$_2$Cl$_2$ (5 mL), Amberjet 4400 OH (0.5316 g) was added, and the suspension was allowed to stir overnight. The mixture was then filtered through a cotton plug and the filtrate was concentrated under rotary evaporation. The product was passed through another column (~5 g; gradient elution: 100% CH$_2$Cl$_2$ to 1:6:10 CH$_3$OH : NEt$_3$ : CH$_2$Cl$_2$) and then further purified by vapor diffusion in CH$_2$Cl$_2$ with Et$_2$O as the anti-solvent. The crystalline solid was scraped out of the vial to yield 7.8 mg (45 %) of product. Anal. Calcd. for C$_{36}$H$_{28}$N$_8$Ru (673.75): C, 64.18; H, 4.19; N, 16.63. Found:
C, 59.36; H, 4.52; N, 15.15. Anal. Calcd. for C_{36}H_{28}N_{8}Ru + 3 H_{2}O (578.65): C, 59.41; H, 4.71; N, 15.40. See section 2.7.2 for full NMR characterization data.

Section 2.7.2. NMR characterization of compounds

Table 2.2. 2D NMR spectroscopy data for 2.11

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<td>8.16 &lt;-&gt; 8.03</td>
<td>16.14</td>
<td>151.91</td>
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Insufficient sensitivity of the HBMC experiment thus far has precluded definitive assignments of the indicated resonances. Tentative assignments have been made based on trends in NMR shifts of other 6,6'-substituted 2,2'-bipyridine compounds in this section.

Table 2.3. 2D NMR spectroscopy data for 2.12.

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<td>7.63</td>
<td>2* 156.01</td>
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<td>6.76 148.03</td>
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<td>3 158.11</td>
<td>1.30 30.53</td>
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Table 2.4. 2D NMR spectroscopy data for 2.6.

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<td>2.02</td>
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Solvent: CD$_2$Cl$_2$
$^1$H NMR (499.945 MHz) - red
$^{13}$C NMR (125.724 MHz) - black
Solvent: CD$_2$Cl$_2$ with ~17% CH$_3$OH
$^1$H NMR (499.945 MHz) - red
$^{13}$C NMR (125.724 MHz) - black

Table 2.4. 2D NMR spectroscopy data for 2.7.

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$^1$H-$^{13}$C gHSQC

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Solvent: $d_2$-DMSO
$^1$H NMR (499.945 MHz) - red
$^{13}$C NMR (125.724 MHz) - black

Note: only one set of $^1$H and $^{13}$C signals is seen likely because of rapid fluxionality of the pyridinium proton on the NMR time scale.

*For the indicated shifts, the resolution of the NMR did not allow us to identify the individual coupling constants.

**Table 2.5.** 2D NMR spectroscopy data for 2.23.

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a,b,c The shifts of the indicated aromatic signals on the benzimidazole group could not be differentiated. Tentative assignments have been given based on chemical logic.

**Table 2.6.** 2D NMR spectroscopy data for 2.24.

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<td>6.45</td>
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2.8. References


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(54) Li, P.; Ahrens, B.; Bond, A. D.; Davies, J. E.; Koentjoro, O. F.; Raithby, P. R.; Teat, S. J. *Dalton Trans.* **2008**, *1635*.


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Chapter 3

Ruthenium Complexes of 2,2’-Bipyridine-6,6’-diphosphonates

Ligands for Water Oxidation

3.1. Introduction

Phosphonates are versatile ligands, particularly for the design of porous materials.\(^1\) In the context of WOC, the affinity of phosphonate groups for metal oxide surfaces has been exploited for electrode functionalization;\(^2\) however, using phosphonates as ligands for the catalytic metal(s) in molecular WOC appears to be completely unexplored.\(^3,4\) We considered that phosphonates are promising for WOC because of unique characteristics that may prove to be advantageous. Phosphonate groups contain three O atoms in tetrahedral geometry. If only one O is coordinated to a metal, there remain one OH and one O, and this HO-P=O unit can be protonated or deprotonated depending on the pH; therefore, unlike metal-bound carboxylates, phosphonate ligands have the advantage of being pH responsive. Scattered examples in literature show that redox potentials of metal-phosphonate complexes are indeed pH responsive,\(^5\) where deprotonation of non-coordinated P-OH groups reduces oxidation potentials. To reduce catalytic overpotential, our group became interested in designing catalysts bearing pH responsive ligands. Here we report the synthesis of two novel complexes, 3.2 and 3.3, both mimicking the general framework of 3.1 but with the carboxylates replaced by phosphonate groups. Comparing 3.2 and 3.3 is important because P-OH groups can switch charge states under varying pH conditions whereas P-OR groups
will block pH-responsivity. The present chapter describes the synthesis, characterization, electrochemistry, and catalytic activity of 3.2 and 3.3 towards water oxidation.

![Chemical Structures](image)

**Figure 3.1.** Catalysts discussed in this work.

### 3.2. Synthesis and Characterization

Starting material 3.4 was synthesized using modifications of literature procedures\(^6a\) and then converted to 3.5 by a Hirao-type cross-coupling, where the use of \(^i\)-Pr rather than Et groups gave significantly cleaner reactions, presumably because of reduced side-reactions involving attack of nucleophilic amine on the alkyl group.\(^6b\) Reaction of bromotrimethylsilane with 5 and subsequent methanolysis produced 3.6 in near-quantitative yield. Complex 2 was prepared by the reaction of 3.6 with NEt$_3$ (excess) and [Ru(benzene)Cl$_2$]$_2$ followed by a large excess of 4-picoline. The insolubility of 3.2 in organic solvents proved to be advantageous for purification as the undesired by-products of the reaction and excess picoline were easily washed away with dichloromethane.
Extensive efforts were made to determine the protonation state of 3.2 by NMR spectroscopy. The solubility of 3.2 was only moderate even in highly polar aprotic d₆-DMSO, and no P-OH proton peak(s) were detected presumably due to broadening. Polar protic solvents dissolved 3.2 well, but the P-OH protons were not visible even in mixtures of OD/OH solvents, a tactic we used successfully in another study.⁷ Elemental analysis of isolated solid 3.2 suggests a doubly-protonated species, inasmuch as C, H, N percentages are consistent with those calculated for 3.2 + 2H₂O. Furthermore, X-ray crystallography of 3.2 (Figure 3.3, to be discussed below in detail) confirmed the neutral doubly-protonated species.

To make the P-OR species 3.3, disodium salt 3.7 was prepared by hydrolysis of 3.5 with a slight excess of NaOH and then reacted with Ru(DMSO)₄Cl₂ and 4-picoline to afford 3.3. Combustion analysis of the isolated solid of 3.3 matches the calculated values (3.3 + 1.5H₂O); interestingly, the ³¹P NMR spectrum of 3.3 dissolved in CD₂Cl₂ shows two peaks of equal intensity suggesting the presence of two diastereomers in a 1:1 ratio. ¹H NMR spectra in CD₂Cl₂ show three singlets in the range of 2.2-2.3 ppm (methyl peaks of bound 4-picoline) that integrate in a 2:1:1 ratio, a pattern that is consistent with two diastereomers in which the PO-iPr groups are trans or cis to each other.
Figure 3.2. Synthesis of 3.2 and 3.3.

X-ray data for 3.2 show (Figure 3.3, left) distorted octahedral geometry, notably a large O-Ru-O angle (110.2°), less distorted than 3.1 (123.1°) because C(sp²)-P and P-O bonds are longer than C(sp²)-C and C(sp²)-O bonds. The greater bond lengths associated with the tetrahedral phosphonate groups allow puckering of the two five-membered chelate rings, and a slight twist (~4°) is observed between the two rings of the bipy backbone. Intermolecular hydrogen bonding between the P=O and P-OH groups of neighboring molecules in the unit cell likely contributes to the orientation of the phosphonate groups. A crystal structure of 3.3 was also obtained, although with an R factor (11%) that precludes detailed structural discussion, but clearly the grown crystals...
consisted of two co-crystallized diastereomers. The connectivity of one of the diastereomers was resolved unambiguously, while that of the second diastereomer was not; the clearly resolved diastereomer was that with PO-iPr groups *trans* to each other (Figure 3.3, right), consistent with assignments of one set of peaks in NMR spectra. The O-Ru-O angle of this *trans* diastereomer was 109.0°, similar to that of 3.2. Interestingly, the five-membered chelate rings involving the phosphonates do not appear to be as puckered as observed in 2, which may be a consequence of the lack of intermolecular hydrogen bonding in the crystal packing.

*Figure 3.3. X-ray crystal structure of 3.2 and 3.3 (note: R-factor for 3.3 is 11%).*
3.3. pK\textsubscript{a} determination

A UV-visible spectrophotometric titration (Figure 3.4) was conducted to determine the pK\textsubscript{a} values of 3.2. Above pH 5.5, two absorption bands were observed at \(\lambda_{\text{max}} = 300\) and 390 nm. As the pH was lowered to <2.5, two new absorption bands were observed at \(\lambda_{\text{max}} = 296\) and 370.5 nm. Plots of absorbance at the above-mentioned wavelengths vs. pH (ranging from pH 1 to pH 8) show only one inflection between pH 2.5 and 5 (Fig. 3.5).

![Figure 3.4. Spectrophotometric titration of Ru(2,2'-bipyridine-6,6'-diphosphonate)(pic)\textsubscript{2} (3.2).](image-url)
Figure 3.5. Absorbance vs. pH at 299.5 nm and 296.5 nm (left) and 390.5 nm and 370.5 nm (right) (Note: yellow line corresponds to the half-equivalence point, where pH = pKₐ).

The pKₐ was determined from these inflections to be ~4.1. From the data alone, it is unclear whether this pKₐ value corresponds to a one-proton change [(3.2-2H)²⁻ to (3.2-H)¹⁻] or a two-proton change [(3.2-2H)²⁻ to 3.2]. Attempts were made to find a second protonation event below pH 4, but no changes in absorbance maxima were observed and pH measurements below 1 were unreliable. There are literature precedents for multi-proton changes from loss of one proton each from separate protic functional groups at a single pH, including complexes bearing one diprotic dihydroxy-2,2’-bipyridine ligand,⁸ and Ru complexes containing either one or two tetraprotic bipyridydiphosphonic acid ligands,⁹ where the phosphonates were away from the metal and not involved coordination, in contrast to 3.2. Data for coordinated phosphonato acidity are rare; in a tris(phosphonato)Fe(III) species, loss of all three protons (one from each functional group) occurs in a narrow range (pH ~0.7 to 4.1) with approximate pKₐ values differing only by one unit (~1.3, 2.7, and 3.7).⁵a Given our data and the literature, we conclude that the observed pKₐ value for 3.2
Figure 3.6. Top: Titration of 3.2 – pH vs. volume of NaOH. Bottom: first derivative of top graph to determine precise value of equivalence point. The pKₐ was assigned by determining the pH at the half-equivalence point (pH = pKₐ at half-equivalence point). Volume of NaOH at half-equivalence point = ½(0.15 mL) = 0.075 mL; pH at half-equivalence point = ~4.1 = pKₐ.

Standard titration procedure: To analyte 3.2 (10.19 mg) in deionized H₂O (5 mL) were added 5 µL aliquots of an NaOH solution (0.136 M) and pH of the solution was measured.
likely corresponds to a two-proton change between 3.2 and (3.2-2H)\(^2\). A simple titration performed on 3.2 also gave a similar pK\(_a\) value of ~4.1 (Fig. 3.6).\(^4\)  

3.4. Electrochemistry and Catalytic Testing

![Cyclic voltammetry of 3.2 and 3.3 in a 0.1 M pH 7 potassium phosphate buffer (blue = 3.2, red = 3.3, dotted = background). Inset: close-up of Ru\(^{II/III}\) couples (dashed lines represent differential pulse voltammetry data). Catalyst conc. = 0.5 mM, working: glassy carbon, reference: Ag/AgCl, counter: Pt wire. Scan rate = 0.1 V/s.](image)

**Figure 3.7.** Cyclic voltammetry of 3.2 and 3.3 in a 0.1 M pH 7 potassium phosphate buffer (blue = 3.2, red = 3.3, dotted = background). Inset: close-up of Ru\(^{II/III}\) couples (dashed lines represent differential pulse voltammetry data). Catalyst conc. = 0.5 mM, working: glassy carbon, reference: Ag/AgCl, counter: Pt wire. Scan rate = 0.1 V/s.

Cyclic voltammetry of 3.2 and 3.3 was initially conducted in aqueous potassium phosphate (0.1 M, \(\mu = 0.1\), pH 7) on a glassy carbon working electrode with an Ag/AgCl reference electrode and a Pt wire counter electrode (Figure 3.7). A striking feature for 3.2 is the appearance of the Ru\(^{II/III}\) redox wave at 0.17 V, a potential substantially more negative than the Ru\(^{II/III}\) redox waves observed for 3.1 (0.39 V) and 3.3 (0.62 V).\(^4\) As observed for other complexes bearing phosphonates,\(^4\) the redox potential of 3.2 is more negative because both P-OH groups are deprotonated at pH 7 (as determined by pK\(_a\) studies above) and species (3.2-2H)\(^2\) dominates in
solution. The \(^i\)Pr groups of 3.3 preclude proton loss and as a result, like 3.1, 3.3 must exist as a neutral species at pH 7. Fascinatingly, at pH 7, when the electrode is driven to 1.4 V (vs. Ag/AgCl), 3.3 clearly outperforms 3.2, evidenced by a large catalytic oxidative wave beginning at \(~1.25\) V and a significant reductive wave at \(~0.6\) V for \(O_2\) reduction.\(^d\) Catalytic activity at pH 7 is observed for 3.2 only at an onset

**Figure 3.8.** Comparison of cyclic voltammetry of 3.2 (blue) and 3.3 (red) when working electrode is driven to 1.6 V at pH 7 (0.1 M potassium phosphate buffer). Scan rate: 100 mV s\(^{-1}\). Catalyst concentration: 0.5 mM.

potential of \(~1.5\) V\(^d\) (Fig. 3.8). For 3.2, the DPV data in Fig. 3.12 clarify the rise at \(~1.28\) V in Fig. 3 as a likely Ru\(^{\text{III/IV}}\) wave, that apparently lies at 1.4 V at pH 1. Thus, the deprotonated P-OH groups obviously stabilize the Ru\(^{\text{III}}\) state of 3.2, and likely at the higher oxidation states (e.g. Ru\(^{\text{IV}}\), Ru\(^{\text{V}}\)) typically involved in catalysis.
A closer look at the Ru$^{II/III}$ couples of 3.2 and 3.3 gives insight into catalyst mass transport properties and rates of electron transfer. At a scan rate of 100 mV s$^{-1}$, the $\Delta E_p$ of the Ru$^{II/III}$ couple of 3.3 is 0.065 V, close to that for a reversible electron transfer (0.059 V), whereas the $\Delta E_p$ of 3.2 is 0.10 V, indicating a lack of electrochemical reversibility. Thus, the rate of electron transfer is slower at the electrode for 3.2 than for 3.3, corroborated by smaller oxidation peak current ($i_{pa}$) of 3.2 compared to that of 3.3 (Fig. 3.9 and 3.10, CV and differential pulse voltammetry, respectively). Scan rate dependence experiments were conducted on both 3.2 and 3.3 and the data were plotted according to the Randles-Sevcik equation ($i_{pa}$ vs. $v^{1/2}$). Data for 3.3 exhibited a good linear fit, whereas data for 3.2 strayed significantly from linearity, suggestive of slower electron transfer. Simulation of the scan rate dependence of 3.2 using DigiSim® and a simple 1 e$^-$ transfer

![Graph](image)

**Figure 3.9.** Close-up of Ru$^{II/III}$ couples of 3.2 (blue) and 3.3 (red) at pH 7 (0.1 M potassium phosphate buffer). Scan rate = 100 mV s$^{-1}$. Catalyst concentration: 0.5 mM. Dashed lines represent background scans.
mechanism was not possible, but was fully consistent with a CEC mechanism where the reversible 1 e⁻ transfer is preceded and succeeded by chemical equilibria (Fig. 3.11). We do not know if the chemical equilibria are (for example) solvation changes or electrode interactions, however the localized charges of the deprotonated P-OH groups are likely implicated. It can be expected that 3.2 will have a smaller diffusion coefficient relative to 3.3 because it is a doubly-charged species and likely to experience greater coulombic interactions with buffer ions in the liquid. The diffusion coefficients calculated from the scan-rate dependence experiments and simulations of 3.2 and 3.3 were $3.0 \times 10^{-6}$ cm s⁻¹ and $3.3 \times 10^{-6}$ cm s⁻¹ respectively, where the smaller value for 3.2 will also contribute to the smaller $i_{pa}$ of 3.2 compared to that of 3.3.
Figure 3.10. Differential pulse voltammetry comparing 3.2 (blue) and 3.3 (red). Top: pH 7 (0.1 M potassium phosphate buffer). Bottom: pH 1 (0.1 M CF$_3$SO$_3$H). Dashed lines highlight relative peak heights. Catalyst concentration: 0.5 mM
Figure 3.11. Scan rate dependence of the Ru$^{II/III}$ couple for 3.2 was fitted by Digisim® according to the following electrochemical mechanism with the specified chemical parameters:

POH ↔ POHX

\[ k_s \ (\text{cm} \ s^{-1}) \quad k_f \ (\text{M} \ s^{-1}) \quad k_b \ (\text{M} \ s^{-1}) \quad K_{eq} \]

POH ↔ POHX + e

0.017

In the equations, POH is 3.2, POHX is a species in chemical equilibrium with 3.2 and is the true electrochemically active species, and POHY is a species in chemical equilibrium with the oxidized form of POHX.
Figure 3.12. Scan rate dependence of 3.3 was fitted by Digisim® according a simple 1 e⁻ transfer mechanism:

\[ k_1 \text{ (cm s}^{-1}) = 0.038 \]
Cyclic voltammetry of 3.2 and 3.3 was also conducted at pH 1 (Fig. 3.13). As expected, the Ru$^{II/III}$ potentials of 3.3 at pH 1 and pH 7 are almost identical (0.61 and 0.62 V) because the ligand cannot change its protonation state. In contrast, the Ru$^{II/III}$ potential of 3.2 is 0.48 V at pH 1, 0.31 V more positive than at pH 7, consistent with pK$_a$ data above implying that the fully protonated species 3.2 should predominate in solution at pH 1 and the zero charge of the complex would match that of consistently neutral 3.3. Both 3.2 and 3.3$^{4c}$ show minimal, if any, catalytic activity under electrochemical conditions at pH 1 (Fig. 3.14 and discussion in caption), but using ceric ammonium nitrate (CAN) as sacrificial oxidant (Fig. 3.14), both complexes produced O$_2$ (measured with a pressure transducer), and interestingly their performances were nearly identical (TOF $\approx$ 1450 h$^{-1}$) with initial rates first order in catalyst concentration (Fig. 3.17 and 3.18), suggesting a single-site water nucleophilic attack (WNA) mechanism.$^{4b}$ Rapid O$_2$ production in the presence of Ce$^{IV}$ (approximate reduction potential: $\approx$1.6-1.7 V vs Ag/AgCl)$^{10}$ is surprising considering that unappreciable catalytic activity was observed electrochemically when the potential was driven even as far 1.8 V. Catalysis may be promoted by the large excess of CAN used, or individual Ce$^{IV}$ ions may play an active role as observed by Codolá et al.$^{11}$
Figure 3.13. Comparison of cyclic voltammetry of 3.2 (blue) and 3.3 (red) when working electrode is driven to 1.8 V at pH 1. Catalyst concentration: 0.5 mM. Scan rate: 100 mV s\(^{-1}\).

Insets: Air was bubbled into the solutions of 3.2 and 3.3 in their respective electrochemical cells; the resulting O\(_2\) reduction waves (dashed yellow) did not appear to match the reduction waves seen for 3.2 or 3.3 at ~ -0.5 V. It is possible that the O\(_2\) generated from electrocatalysis may reduce at a more positive potential compared to O\(_2\) from air due to the increased concentration of H\(^+\) near the electrode surface after catalysis. If indeed O\(_2\) is being generated, it is noteworthy that the onset potential for 3.2 (1.48 V) appears to be slightly lower than that of 3.3 (~1.49-1.52 V). In any case, O\(_2\) production is not significant at pH 1 and there is not an appreciable difference between 3.2 and 3.3.
Figure 3.14. Comparison of 3.2 (blue) and 3.3 (red) by CAN testing. Catalyst concentration = 250 µM, CAN concentration = 250 mM, volume of reaction mixture = 4.0 mL.
Figure 3.15. Top: O₂ yield vs. time (h) for varying concentrations of 3.2. Bottom: initial rates. Inset: plot of initial rates vs. concentration depicting a first-order relationship.
Figure 3.16. Top: $O_2$ yield vs. time (h) for varying concentrations of 3.3. Bottom: initial rates. Inset: plot of initial rates vs. concentration depicting a first-order relationship.
A preliminary mechanistic understanding of the catalysis can be deduced from the electrochemical data. One chemical event that must occur before the catalyst can oxidize water is metal coordination of a water molecule. It is clear from analysis of the Ru$^{II/III}$ couple of 3.3 at pH 7 that a simple 1 e$^-$ redox event is taking place (Fig. 3.12) and that on the time scale of the electrochemical experiment no immediate chemical event, such as water coordination, is associated with the generation of the Ru$^{III}$ species. The higher Ru states (e.g. Ru$^{IV}$, Ru$^{V}$) are indiscernible because they are overshadowed by the catalytic current that follows the Ru$^{II/III}$ oxidation, consistent with a combination of opening of a seventh-coordination site because of oxidation to a 16-e$^-$ species, H$_2$O coordination, and immediate onset of catalytic current because succeeding steps in the catalytic cycle are rapid. In the case of 3.2, oxidation (presumably Ru$^{III/IV}$) occurs at $\sim$1.36 V following the Ru$^{II/III}$ oxidation and onset of catalysis begins at $\sim$1.5 V. It is not immediately clear from the data at what point water binds to the metal center of 3.2. One possibility is that water binds to Ru$^{IV}$ and catalysis begins once the Ru$^{IV}$-aquo or (Ru$^{IV}$-hydroxo) complex is oxidized to a Ru$^{V}$ species. Alternatively, water may only bind to a Ru$^{V}$ species.

An important fundamental difference between 3.2 and 3.3 is the net charges they hold as their metal centers are oxidized. For example, when 3.3 is oxidized by 2 e$^-$ to the Ru$^{IV}$ species (3.3-2e)$^{2+}$, the overall net charge on the complex becomes +2; when 3.2 is oxidized to the Ru$^{IV}$ species (3.2-2H-2e), the net charge is zero. In a broader sense, one can expect that 3.3 maintains a more positive net charge throughout its catalytic cycle compared to 3.2. Given the data collected thus far, an explanation for the enhanced catalytic activity of 3.3 at pH 7 can only be speculative, however we suspect that net charges may be implicated in the catalysis. For example, one possible scenario is that (3.3-2e)$^{2+}$ would be more electrostatically likely to bond to water than (3.2-2H-2e). Complexes 3.3 and 3.1 have the same overall charge therefore we can expect that catalytic
intermediates will have the same charge, yet 3.1 has a significantly lower overpotential (Fig. 3.17). We hypothesize that the wider O-Ru-O angle (by nearly 13°) of 3.1 compared to that of 3.3 plays an important role.

![Graph showing cyclic voltammetry results for 3.1 (purple), 3.2 (blue), and 3.3 (red) under the same conditions - 0.1 M potassium phosphate buffer (pH 7). Catalyst concentration = 0.25 mM. There was difficulty in dissolving 3.1 in purely aqueous solutions at concentrations greater than 0.25 mM, so all three catalysts were tested at 0.25 mM for accurate comparison – free of any organic co-solvents. CVs are background subtracted.]

**Figure 3.17.** A comparison of 3.1 (purple), 3.2 (blue), and 3.3 (red) tested by cyclic voltammetry under the same conditions - 0.1 M potassium phosphate buffer (pH 7). Catalyst concentration = 0.25 mM. We had difficulty dissolving 3.1 in purely aqueous solutions at concentrations greater than 0.25 mM, therefore we tested all three catalysts at 0.25 mM for accurate comparison – free of any organic co-solvents. CVs are background subtracted.

### 3.5. Studies of catalyst stability

Careful examination of the CV data reveals preliminary evidence that the P-OR groups of some fraction of 3.3 at the electrode may be undergoing hydrolysis during catalysis (Fig. 3.18). Some degree of hydrolysis could be favored once the metal achieves higher oxidation states (e.g.
Ru$^{\text{III}}$, Ru$^{\text{IV}}$) and becomes a better Lewis acid. When the electrode is driven to 1.4 V in a solution of 3.3, two reduction peaks appear in the return scan. The first reduction peak (at ~0.6 V) corresponds to the reduction of 3.3$^{1+}$, and the second reduction peak (at ~0.37 V) may correspond to reduction of (3.3-\text{iPr})$^0$, a species in which one of the P-OiPr groups is hydrolyzed to P-O$^-$. When the electrode is driven to 1.6 V, an additional reduction peak appears (at ~0.11 V) which overlaps very closely with the reduction of (3.2-\text{2H})$^{1-}$, suggesting that at high potentials such as 1.6 V, to some extent both P-OiPr groups of 3.3 are hydrolyzed. Note that the ~0.37 V reduction peak is approximately halfway between reduction peaks for 3.3$^{1+}$ and of (3.2-\text{2H})$^{1-}$, consistent with the assigned charges of the various species being reduced.
Figure 3.18. Cyclic voltammetry of 3.2 (blue) and 3.3 (red = electrode driven to 1.4V, green = electrode driven to 1.6 V) at pH 7.

The non-steady-state behavior of the catalytic current for both 3.2 and 3.3 suggests the possibility of some electrode surface chemistry occurring even near 1.4 V under neutral conditions (Fig. 3.19-3.23). Nearly 50 cycles between -1.0 V and +1.4 V in a solution of 3.2 in potassium phosphate buffer (0.1 M, pH 7) resulted in evolution of a large catalytic wave with an onset potential of ~1.1 V, nearly 400 mV more negative than its onset potential in the first scan, and an
increase in magnitude of the O₂ reduction wave (fig. 3.21). Interestingly, along with these changes, there was only a negligible change in the \( i_p \) of the Ru^{II/III} wave. Cyclic voltammetry of 3.2 before and after 1 min of controlled-potential electrolysis (CPE) with the potential held at 1.4 V, shows the same dramatic increase in current (fig. 3.19). When the solution was allowed to sit for 5 to 40 min, the current began to decrease significantly and then vigorous bubbling of argon into the solution lead to a CV that looked very similar to the initial scan prior to CPE. A large catalytic current was also observed when a freshly polished electrode was exposed to 1 min of CPE at 1.4 V in a solution of 3.2 and then lightly rinsed with water and transferred to a cell containing pure potassium phosphate buffer (fig. 3.20). Additional redox features between 0.0 V and 0.9 V could only be seen after magnification; these features and the catalytic wave disappeared almost completely after allowing the electrode to sit in the cell solution for 30 min and then bubbling argon through the solution for 5 min (fig. 3.20, inset). The observed behavior suggests the possibility of a transient interaction between the catalyst and electrode where the apparent interaction is beneficial to catalysis. Under aqueous conditions at highly anodic potentials (>1.4 V), glassy carbon is prone to oxidation to form various C-O containing functionalities on its surface.¹³ Phosphonate derivatization is a common strategy to covalently anchor molecular catalysts to metal-oxide surfaces;¹⁴ thus it is conceivable that the phosphonate functionalities of 3.2 could interact by hydrogen bonding or reversible hydrolysis with C-O functionalities on an oxidized carbon surface. Alternatively, we cannot rule out a scenario where the catalyst may be decomposing to deposit a highly active Ru species on the surface, similar to a phenomenon observed by Matheu et al. where oxidative scans on a glass carbon electrode covalently functionalized with a catalyst bearing the Ru(bda) framework lead to deposition of a RuO₂ catalyst.¹⁵ These phenomena will be studied in due course.
Figure 3.19. Cyclic voltammetry of 3.2 after 1 min of controlled potential electrolysis (CPE) at pH 7 (0.1 M potassium phosphate buffer) at 1.4 V. Catalyst concentration: 1 mM. dotted black = background. Inset: close up of O\textsubscript{2} reduction waves. CVs were performed before and after as follows:

\begin{itemize}
  \item[i)] CV of 3.2 prior to CPE
  \item[ii)] immediately after CPE
  \item[iii)] after allowing cell solution to sit for 5 min
  \item[iv)] after allowing cell solution to sit for another 5 min
  \item[v)] after allowing cell solution to sit for a further 30 min
  \item[vi)] after vigorously bubbling argon through the cell solution for 5 min
  \item[vii)] after vigorously bubbling argon through cell solution and directly on the electrode for 20 min
\end{itemize}
Figure 3.20. Test for accumulation of active species on electrode after 1 min of controlled potential electrolysis (CPE) in a solution of 3.2. First, 1 min of CPE was performed on a solution of 3.2 (1 mM) at 1.4 V, as for Fig. 3.19. Then, the electrode was rinsed very lightly with water after CPE to remove any residual 3.2 and then transferred to pure phosphate buffer for ii-vi. Cyclic voltammetry was performed on electrode in pure 0.1 M phosphate buffer alone, without 3.2. The data suggest that the accumulation of the active species at the electrode becomes smaller over time or from mechanical agitation of the electrode surface. Inset: close up of redox features between 0.0 V and 1.1 V. CVs were performed before and after as follows:

i) background CV prior to CPE  
ii) immediately after CPE – note: electrode was rinsed very lightly with water after CPE to remove any residual 3.2 and then transferred to pure phosphate buffer  
iii) after allowing electrode to sit in cell solution for 10 min  
iv) after allowing electrode to sit in cell solution for another 10 min  
v) after allowing electrode to sit in cell solution for another 10 min  
vi) after vigorously bubbling argon through the cell solution for 5 min
Figure 3.21. Cyclic voltammetry of 3.2 conducted at pH 7 (in 0.1 M potassium phosphate buffer) with 51 cycles between -1.0 V to +1.4 V (top) and +1.6 V (bottom). Dashed blue line represents the first cycle and dotted green line represents the last cycle. Catalyst concentration: 0.5 mM. Scan rate: 100 mV s$^{-1}$.
Figure 3.22. Test for electrode accumulation of active species after one or three scans up to 1.4 V in a 1 mM catalyst solution of \( \text{3.2} \) in 0.1 M potassium phosphate buffer (pH 7). The results suggest that there may be some minor accumulation of active species after each successive scan to 1.4 V. The CVs were performed according to the following conditions:

\( i) \) CV of polished electrode in fresh phosphate buffer

\( ii) \) CV of electrode in fresh phosphate buffer after scanning to 1.4 V in a 1 mM solution of \( \text{3.2} \). Electrode was lightly rinsed with water prior to transferring into the phosphate buffer solution to remove any residual catalyst.

\( iii) \) CV of electrode in fresh phosphate buffer after three scans to 1.4 V in a 1 mM solution of \( \text{3.2} \). Electrode was again lightly rinsed with water prior to transferring into the phosphate buffer solution to remove any residual catalyst.
Figure 3.23. Test for accumulation of active species on electrode surface after only one scan up to 1.6 V in a 1 mM catalyst solution of 3.2 in 0.1 M potassium phosphate buffer (pH 7). The results suggest that there is significant accumulation of active species on the electrode even after one scan to 1.6 V, however over time or through mechanical agitation of electrode the degree of accumulation becomes less (iii vs ii, as in Fig. S22-23). The CVs were performed according to the following conditions:

i) CV of polished electrode in fresh phosphate buffer

ii) CV of electrode in fresh phosphate buffer after driving to 1.6 V in a 1 mM solution of 3.2. Electrode was lightly rinsed with water prior to transferring into the phosphate buffer solution to remove any residual catalyst.

iii) CV of electrode in fresh phosphate buffer after vigorous bubbling of argon through the solution for 5 min.

3.6. Conclusion

In summary, we report the synthesis and catalysis-relevant chemical properties of the first water oxidation complexes, 3.2 and 3.3, deliberately bearing phosphonate groups positioned to serve as metal-bound ligands. Charge states of P-OH / P-OR groups have great influence on redox and
catalytic properties, features that are absent in much more commonly studied carboxylate analogs. Preliminary evidence is consistent with a single-site mechanism near pH 1 using Ce(IV), and catalytic activities at neutral pH may be largely affected by electrostatic interactions governed by the net charges of the complexes upon oxidation.

The contents of Chapter 3 are similar to the material published in the following manuscript: Kamdar, J. M.; Marelius, D. C.; Moore, C. E.; Rheingold, A. L.; Smith, D. K.; Grotjahn, D. B. "Ruthenium complexes of 2,2'-bipyridine-6,6'-diphosphonate ligands for water oxidation". ChemCatChem, 2016, 8, 3045. The dissertation author was the primary researcher for the data presented. I would like to thank Dave Marelius for his support in CeIV experiments. Dr. Curtis Moore and Dr. Arnold Rheingold are thanked for their support in x-ray crystallography. I owe a debt of gratitude to Dr. Diane Smith and Patrick Staley for invaluable help with cyclic voltammetry and teaching me how to use Digisim®. In addition, partial support of this work by San Diego State University and San Diego Cleantech initiative is acknowledged.

3.7. Experimental

3.7.1. Preparation of compounds

![Chemical Structure](image)

**Synthesis of tetraisopropyl 2,2'-bipyridine-6,6'-diphosphonate (3.5):** In a Teflon-capped pressure tube with stir-bar, 6,6'-dibromo-2,2'-bipyridine (2.989 g, 9.550 mmol), 1,1'-bis(diphenylphosphino)ferrocene (0.0662 g, 0.119 mmol), Pd(OAc)2 (0.0240 g, 0.107 mmol), diisopropylphosphite (4.1288 g, 24.91 mmol), and diisopropylethylamine (3.1414 g, 24.31 mmol)
were weighed out and dissolved in CH₃CN (36 mL). The mixture was heated in a 95 °C oil bath for 28 h. More 1,1’-bis(diphenylphosphino)ferrocene (0.0646 g, 0.1165 mmol) and Pd(OAc)₂ (0.0233 g, 0.1038 mmol) were added to the reaction mixture and the mixture was again placed in a 95 °C oil for another 22 h to complete the reaction. The reaction mixture was concentrated to dryness on a rotary evaporator. The resulting solid was transferred to a separatory funnel with water (50 mL) and EtOAc (50 mL). The aqueous phase was basified with saturated Na₂CO₃ until pH = 9. After vigorous shaking the layers were separated, and the aqueous layer was washed two more times with EtOAc (2 × 50 mL). The combined organics were washed with water (50 mL). The aqueous layer was back-extracted with EtOAc (50 mL). The combined EtOAc layers were dried with anhydrous sodium sulfate, filtered, and the filtrate was concentrated to dryness on a rotary evaporator. The crude product was purified by column chromatography (gradient elution: CH₂Cl₂ to CH₂Cl₂:EtOAc with 1% NEt₃) and re-crystallized by vapor diffusion (solvent: acetone, anti-solvent: petroleum ether) to obtain pure product as a white, crystalline solid (1.6128 g, 35%). Anal. Calcd. for C₂₂H₃₄N₂O₆P₂ (484.46): C, 54.54; H, 7.07; N, 5.78. Found: C, 54.70; H, 7.46; N, 5.91.

Synthesis of 2,2’-bipyridine-6,6’-diphosphonic acid (3.6): In a glovebox, 3.5 (0.2024 g, 0.4178 mmol) was weighed out in a stir bar-equipped 20 mL vial (dried in an oven overnight prior to use) and then dissolved in CH₂Cl₂ (1.0 mL) to produce a light yellow mixture. Bromotrimethylsilane (97%, 0.5485 g, 3.583 mmol) was added to the solution of 3.5 and the mixture was allowed to stir for 4 h in a 70 °C oil bath. To assess the completion of the reaction, an aliquot of the reaction
mixture (~0.1 mL) was diluted with CDCl$_3$ (0.5 mL, dry, deoxygenated) in a J. Young tube in a glovebox, and analyzed by NMR spectroscopy (1H, 31P). The NMR mixture was transferred back to the crude reaction mixture and the reaction mixture was concentrated to a solid under an oil-pump vacuum through a Schlenk manifold in order to maintain anhydrous conditions. In the glovebox, methanol (4 mL) was added to the resulting light beige-colored solid and the suspension was allowed to stir overnight. The suspension was filtered through a sintered glass funnel and the collected solid was rinsed with cold methanol (5 mL) and twice with diethyl ether (10 mL each wash). The solid was placed in a dessicator under an oil-pump vacuum for 25 h to give 3.6 as a white solid (0.1242 g, 94%). Calcd. for C$_{10}$H$_{10}$N$_2$O$_6$P$_2$ (316.15): C, 37.99; H, 3.19; N, 8.86. Found: C, 37.62; H, 2.95; N, 8.97.

Synthesis of Ru(2,2'-bipyridine-6,6'-diphosphonate)(pic)$_2$ (3.2): Diphosphonic acid 3.6 (0.0400 g, 127 µmol) and [Ru(benzene)Cl]$_2$Cl$_2$ (0.0316 g, 63.2 µmol) were weighed out in a 20 mL vial with stir bar in the glovebox. Methanol (7 mL, deoxygenated) was added to the vial to produce a suspension. Dry, deoxygenated NEt$_3$ (0.0771 g, 0.762 mmol) was added to the mixture to form a dark olive-green solution which was then heated in an oil bath at 70°C for 5.5 hours. 4-picoline (170 µL, 1.75 mmol) was added to the reaction and the mixture was heated in an oil bath at 100°C for 4 hrs to produce an opaque, dark-maroon mixture. The reaction mixture was
concentrated to leave a maroon solid that was dried overnight under an oil-pump vacuum. Dichloromethane (3 mL) was added to produce a suspension which was filtered through a class M filter funnel and the desired solid 3.2 was collected as a dark maroon solid. The product was washed three times with CH2Cl2 (3 mL each wash) and twice with Et2O (5 mL each wash). A small amount of the washed product (3.0 mg) was transferred to a J. Young tube, partially dissolved in CD3OD (0.5 mL), and fully solubilized by adding a few drops of H2O. Once the purity of the product was confirmed by NMR spectroscopy (1H, 31P), the NMR solution was transferred to a vial. The remainder of the collected solid was also transferred to the vial using 15 mL of a ~4:1 mixture of CH3OH : H2O and concentrated under an oil pump vacuum to leave product as a dark maroon solid (0.0681 g, 89%). Calcd. for C22H22N4O6P2Ru (601.45): C, 43.93; H, 3.69; N, 9.32. Found: C, 42.11; H, 4.55; N, 9.08. Calcd. for C22H22N4O6P2Ru + 1.75 H2O (632.98): C, 41.75; H, 4.06; N, 8.85.

**Synthesis of Ru(diisopropyl-6,6’-diphosphonate-2,2’-bipyridine)4(pic)2 (3.3):** In a glovebox, tetraisopropyl phosphonate ester 3.5 (0.0253 g, 52.2 µmol) and NaOH (0.0048 g, 120.0 µmol) were weighed out in a 20 mL vial and dissolved in 0.50 mL of a ~1:1 mixture of deoxygenated H2O and deoxygenated isopropanol. The mixture was heated in a 100°C oil bath overnight for 15 h to produce 7. Ru(DMSO)4Cl2 (0.0254g, 52.2 µmol) was added to the reaction mixture and the
mixture was heated in a 70°C oil bath for 20 h. Excess 4-picoline (51 μL, 0.524 mmol) was added to the reaction mixture and the mixture was heated at 100 °C overnight. The reaction mixture was concentrated to an oily solid on a rotary evaporator and placed on high vacuum overnight to remove any excess 4-picoline. The crude mixture was purified via column chromatography (gradient elution from CH₂Cl₂ to 2:5 MeOH:CH₂Cl₂), followed by recrystallization by vapor diffusion (solvent: MeOH; anti-solvent: Et₂O) to afford dark reddish-brown crystals. The crystals were rinsed with two 5 mL portions of Et₂O and separated from residual non-crystalline solid by scraping into a separate vial. The crystals were placed in a dessicator under oil-pump vacuum (0.0180 g, 50%). Calcd. for C₂₈H₃₄N₄O₆P₂Ru (685.62): C, 49.05; H, 5.00; N, 8.17. Found: C, 46.95; H, 4.88; N, 8.19. Calcd. for C₂₈H₃₄N₄O₆P₂Ru + 1.5 H₂O (712.64): C, 47.19; H, 5.23; N, 7.86.
3.7.2. NMR Characterization Data

*For $^1$H NMR shifts at 8.08 ppm and 7.87 ppm, td and dd splitting patterns expected, respectively, however the limited digital resolution of the NMR did not allow us to see the individual coupling constants - instead an average of the coupling constants was observed.

Table 3.1. 2D NMR spectroscopy data and $^{13}$C-$^{31}$P coupling constants for 3.6.

<table>
<thead>
<tr>
<th>gCOSY</th>
<th>$^1$H-$^{13}$C gHMBC</th>
<th>$^{13}$C-$^{31}$P coupling constants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$^{13}$C</td>
<td>$^1$H bonds $^{13}$C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.87 3 121.94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.87 2 137.23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.87 4 154.88</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.87 2 156.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.08 2 121.94</td>
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<td></td>
<td></td>
<td>8.08 2 126.38</td>
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<td></td>
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<td>8.08 3 154.88</td>
</tr>
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<td></td>
<td></td>
<td>8.08 3 156.05</td>
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<tr>
<td></td>
<td></td>
<td>8.53 3 126.38</td>
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<tr>
<td></td>
<td></td>
<td>8.53 2 137.23</td>
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<td></td>
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<td>8.53 2 154.88</td>
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<td>7.87</td>
<td>8.08</td>
<td></td>
</tr>
<tr>
<td>8.53</td>
<td>8.08</td>
<td></td>
</tr>
<tr>
<td>$^{13}$C (150.724 MHz)</td>
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</tr>
<tr>
<td>np = 131072</td>
<td>xJ&lt;sub&gt;CP&lt;/sub&gt;</td>
<td></td>
</tr>
<tr>
<td>156.05 (d)</td>
<td>217.2 Hz (1)</td>
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</tr>
<tr>
<td>154.88 (d)</td>
<td>21.3 Hz (3)</td>
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</tr>
<tr>
<td>137.23 (d)</td>
<td>11.0 Hz (3)</td>
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</tr>
<tr>
<td>126.38 (d)</td>
<td>24.4 Hz (2)</td>
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</tr>
<tr>
<td>121.94 (d)</td>
<td>3.2 Hz (4)</td>
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</table>
*For ¹H NMR shifts at 7.92 ppm and 7.98 ppm, td and dd splitting patterns expected, respectively, however the limited digital resolution of the NMR did not allow us to see the individual coupling constants - instead an average of the coupling constants was observed.

**Table 3.2.** 2D NMR spectroscopy data and ¹³C-³¹P coupling constants for 3.5.

<table>
<thead>
<tr>
<th>gCOSY</th>
<th>¹H-¹³C gHMBC</th>
<th>¹³C-³¹P coupling constants</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.64 vs 7.92</td>
<td>¹H</td>
<td>bonds</td>
</tr>
<tr>
<td>7.98 vs 7.92</td>
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<td>3</td>
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<tr>
<td>1.42 vs 4.90</td>
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<td>2</td>
</tr>
<tr>
<td>1.34 vs 4.90</td>
<td>7.98</td>
<td>3</td>
</tr>
<tr>
<td>1.42 vs 4.90</td>
<td>7.98</td>
<td>2</td>
</tr>
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<td>1.34 vs 4.90</td>
<td>7.92</td>
<td>3</td>
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<tr>
<td>1.42 vs 4.90</td>
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<td>1.34 vs 4.90</td>
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<td>1</td>
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<tr>
<td>1.34 vs 4.90</td>
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<td>2</td>
</tr>
<tr>
<td>1.34 vs 4.90</td>
<td>1.34</td>
<td>1</td>
</tr>
</tbody>
</table>

Solvent: CDCl₃

¹H NMR (599.359 MHz) - red
¹³C NMR (150.723 MHz) - black
³¹P NMR (161.826 MHz) - blue

¹H-¹³C gHSQC

<table>
<thead>
<tr>
<th>¹H</th>
<th>¹³C</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.64</td>
<td>123.26</td>
</tr>
<tr>
<td>7.98</td>
<td>128.11</td>
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<td>7.92</td>
<td>136.94</td>
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<tr>
<td>4.90</td>
<td>71.78</td>
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<tr>
<td>1.42</td>
<td>24.15</td>
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<td>1.34</td>
<td>23.93</td>
</tr>
</tbody>
</table>
*For 1H NMR shifts at 7.92 ppm and 7.98 ppm, td and dd splitting patterns expected, respectively, however the limited digital resolution of the NMR did not allow us to see the individual coupling constants - instead an average of the coupling constants was observed.

**Table 3.3.** 2D NMR spectroscopy data and $^{13}$C-$^{31}$P coupling constants for 3.2.

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<tr>
<th>COSY</th>
<th>$^3$H-$^{13}$C gHMBC</th>
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</thead>
<tbody>
<tr>
<td>$^{1}$H</td>
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<td>$^{1}$H bonds</td>
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<td>7.70</td>
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<td>163.18</td>
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<tr>
<td>7.70</td>
<td>3</td>
<td>161.87</td>
</tr>
</tbody>
</table>

P-OH protons could not be located by NMR.

solvent: D$_2$O

$^1$H NMR (599.361 MHz) - red

$^{13}$C NMR (150.724 MHz) - black

$^{31}$P NMR (161.826 MHz) - blue
For the indicated shifts, the limited digital resolution of the NMR did not allow us to see the individual coupling constants - instead an average of the coupling constants was observed.

The assignment of the indicated 4-picoline shifts of the cis diastereomer is arbitrary because it cannot be determined from the available data which 4-picoline they are associated with.

31P NMR shifts were arbitrarily assigned; it cannot be determined which diastereomer they are associated with.

Overlap with other signals precludes definitive assignment of the indicated chemical shifts.

See below for 2D NMR spectroscopy data and 13C, 31P coupling constants.
Table 3.4. 2D NMR spectroscopy data and $^{13}$C-$^{31}$P coupling constants for 3.3.

<table>
<thead>
<tr>
<th>gCOSY (cis + trans)</th>
<th>$^{1}$H-$^{13}$C gHSQC (cis + trans)</th>
<th>$^{13}$C-$^{31}$P coupling constants (cis + trans)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.65 ←→ 7.94</td>
<td>8.65</td>
<td>160.54</td>
</tr>
<tr>
<td>7.75 ←→ 7.94</td>
<td>8.65</td>
<td>128.33</td>
</tr>
<tr>
<td>7.11 ←→ 7.67</td>
<td>7.94</td>
<td>160.54</td>
</tr>
<tr>
<td>7.07 ←→ 7.61</td>
<td>7.94</td>
<td>157.86</td>
</tr>
<tr>
<td>7.15 ←→ 7.73</td>
<td>7.94</td>
<td>128.33</td>
</tr>
<tr>
<td>3.46 ←→ 0.91</td>
<td>7.75</td>
<td>157.86</td>
</tr>
<tr>
<td>3.46 ←→ 0.73</td>
<td>7.75</td>
<td>132.54</td>
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<tr>
<td>3.35 ←→ 0.91</td>
<td>7.75</td>
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<td>3.35 ←→ 0.73</td>
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</tr>
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<td></td>
<td>0.73</td>
<td>23.13</td>
</tr>
<tr>
<td></td>
<td>0.73</td>
<td>70.85</td>
</tr>
</tbody>
</table>

$d$ Resolution of the HSQC experiment was insufficient to show $^1$H-$^{13}$C correlations of the 4-picoline methyl groups of the cis diastereomer

$e$ The sensitivity of the HMBC experiment was insufficient to show the $^1$H-$^{13}$C correlations of the cis diastereomer.

$f$ Overlap with three other signals precludes definitive assignment of the $^{3}J_{CP}$ value.

All peaks of both cis and trans diastereomers were clearly resolved when 3.3 was dissolved in C$_6$D$_6$ making it a promising choice for full NMR characterization. However, we found that the initial solubility of 3.3 in C$_6$D$_6$ did not persist. For example, a $^{13}$C NMR experiment set up to acquire data overnight resulted in an inadequate spectrum, and inspection of the NMR sample showed that 3.3 had crystallized in the NMR tube. Precipitation of 3.3 in C$_6$D$_6$ was a persistent
problem (even when the NMR probe was heated to 60-70 °C) and therefore precluded acquisition of $^{13}$C and hetero-nuclear 2D NMR data.

3.8. References


(3) As far as we know, prior to the start of our work the only reported metal phosphonates in the context of water oxidation are Co-P$_i$ and Co-MeP$_i$ films generated by electrolysis of aqueous Co$^{2+}$ solutions. (a) Surendranath, Y.; Dinca, M.; Nocera, D. G. J. Am. Chem. Soc., 2009, 131, 2615. (b) Surendranath, Y.; Lutterman, D. A.; Liu, Y.; Nocera, D. G. J. Am. Chem. Soc., 2012, 134, 6326.

(4) (a) During the revision phase of the manuscript containing the work presented in this chapter, a paper (Xie, Y.; Shaffer, D. W.; Lewandowska-Andralojc, A.; Szalda, D. J.; Concepcion, J. J. Angew. Chem., Int. Ed. 2016, 55, 8067) appeared featuring 3.2 and the ethyl analog of 3.3. As detailed below, many facts here and in the other paper match well, but there are some significant differences. (b) Facts and conclusions that match well include the following: pK$_a$ values for 3.2, including the two-proton change; redox potentials of the II/III couples for 3.2 at varying pH; using Ce(IV), O$_2$ formation kinetics that are first order in [3.2]. Finally, using [3.2]$_0$ = 50 M, using data in Fig. S18 for O$_2$ formation, we found TOF $= 0.31$ s$^{-1}$, and Xie et al. found 0.30 s$^{-1}$. (c) Xie et al. reported no catalysis performance data for the ethyl analog of 3.3 near pH 7. (d) Our catalysis performance data for 3.2 using electrochemistry at pH 7 differ from the pH 6.5 data in Fig. 3 of Xie et al., who show onset of a catalytic wave at 1.2 V vs. NHE, corresponding to 1.0 V vs Ag/AgCl. We were unable to see onset below 1.5 V vs Ag/AgCl. For 3.2, DPV in Fig. S12 clarifies the rise at ~1.28 V in Fig. 3 as a likely Ru$^{III/IV}$ wave. (e) Xie et al. also conclude that water coordinates to the Ru$^{IV}$ state.


Chapter 4

Water Oxidation by cis-Diaquo Ru Complexes with Pendent Phosphonate Groups in the Secondary Coordination Sphere.

4.1 Introduction

As discussed in Chapter 1, more than three decades ago, Meyer’s group laid the foundation for modern molecular Ru water oxidation chemistry by demonstrating that Ru^{IV}=O complexes are thermodynamically accessible through sequential transfers of 2 e^- / 2 H^+ from mono-aquo species of the form Ru^{II}-OH.\(^1,2\) Preparation of complexes with two aquo ligands has garnered some interest because the transition from Ru^{II}(OH)\(_2\) to Ru^{VI}(O)\(_2\) could conceivably provide the 4 e^- / 4 H^+ equivalents necessary for the water oxidation half-reaction.\(^3-9\) Amongst the many Ru catalysts reported, as far as we know, there are only two examples of mononuclear ruthenium WOC systems consisting of two cis-aquo ligands bound to a single Ru^{II} metal center.\(^7,8\) One such system is cis-[Ru(bpy)\(_2\)(H\(_2\)O)\(_2\)]\(^{2+}\) (4.1), often considered to be the mononuclear counterpart to the “blue dimer”.\(^3-5\) Dioxygen evolution was initially attributed to in situ formation of RuO\(_2\) because of the appearance of a black solid in the reaction vessel,\(^4,5\) however Sala et al. demonstrated that 4.1 is indeed the dominant catalyst.\(^7\) Under their conditions, less than ~5 turnovers were achieved by 4.1 after which the catalyst is thought to deactivate via photoisomerization to inactive trans-[Ru(bpy)\(_2\)(H\(_2\)O)\(_2\)]\(^{2+}\). Radaram et al. reported another system, cis-(H\(_2\)O)\(_2\)Ru(κ\(^4\)-TPA)\(^2 [\text{4.2}, \text{TPA = tris(2-pyridylmethyl)amine}], however only one equivalent of dioxygen was observed in the
presence of excess Ce\textsuperscript{IV}.\textsuperscript{8} Despite the interesting chemistry to come out of these studies, it is clear that these approaches have not led to development of an effective catalyst.

Here we establish a new family of Ru di-aquo complexes 4.5-4.7 (see figure 4.1) composed of Ru(biimPO-\textit{R})(H\textsubscript{2}O)\textsubscript{2}(pic)\textsubscript{2} (4.5), Ru(biimPO-\textit{R})(H\textsubscript{2}O)\textsubscript{2}(isoq)\textsubscript{2} (4.6) (where biimPO-\textit{R} = 2,2’-biimidazole-4,4’-diisopropylphosphonate, pic = 4-picoline, and isoq = isoquinoline) and Ru(biimPO-\textit{H})(H\textsubscript{2}O)\textsubscript{2}(pic)\textsubscript{2} (4.7) (where biimiPO-\textit{H} = 2,2’-biimidazole-4,4’-diphosphonate).

**Previous work:**

![Previous work structures](image)

**This work:**

![This work structures](image)

**Figure 4.1.** Catalysts discussed in this chapter.

Examples of 4,4’-substituted 2,2’-biimidazole ligands are generally scarce in literature and completely unexplored in the context of water oxidation;\textsuperscript{10,11} thus biimiPO-\textit{R} and biimiPO-\textit{H} are
highly unusual ligands. The two aquo ligands in complexes 4.5-4.7 are involved in hydrogen bonding interactions with two phosphonate moieties in the secondary coordination sphere.

The inspiration for the biimPO-type ligands came largely from bda in the Ru(bda)(L₂) (bda = 2,2’-bipyridine-6,6’-dicarboxylic acid; L = 4-picoline (4.3a) or isoquinoline (4.3b)) framework which has demonstrated the lowest overpotentials in a ruthenium-based homogeneous system thus far.¹²-¹⁴ Although the intimate details of the catalytic cycle of Ru(bda)-type catalysts are not yet fully understood, a preliminary picture of at least the initial steps can be constructed from available studies. To initiate the mechanistic discussion, two interesting features come to mind: (1) the remarkably wide O-Ru-O angle (~123°) imposed by tetradentate-bound bda, and (2) the absence of a pre-coordinated water molecule.¹² Most molecular Ru catalysts in their active state have a water molecule that is pre-coordinated to Ru⁰ and ready to participate in the ensuing catalytic cycle, however Ru(bda)-type catalysts are coordinatively saturated in the Ru⁰ state, implying that water binds at a later stage in the cycle. One possibility is that one of the carboxylates de-coordinates to open up a coordination site for a water molecule.¹⁵ At least under acidic conditions however, there are several pieces of evidence in the literature to suggest that despite its highly distorted geometry, Ru(bda) remains tetradentate throughout the catalytic cycle. For example, in recent work, EPR spectral patterns of an electrochemically generated Ru³⁺ species suggest that H₂O coordinates to form a seven-coordinate Ru³⁺-H₂O species.¹⁶ Furthermore, a crystal structure of the Ru⁴⁺ state acquired from crystals grown after addition of two equivalents of Ce⁴⁺ to 4.3a reveals expansion of the O₁-Ru-O₂ angle to ~144° to accommodate hydroxo-coordination with pentagonal bipyramidal geometry.¹² The Ru⁴⁺-OH species generated from addition of 2 equivalents of Ce⁴⁺ likely undergoes a 1 H⁺/ 1 e⁻ PCET event to form the Ru⁵⁺=O species which is primed for O-O bond formation via either water nucleophilic attack (WNA) or the radical oxo-
coupling pathway (I2M). There has been some speculation on the rate-limiting step. Sun and coworkers observed second order kinetics with respect to the catalyst in the presence of excess CeIV and thus proposed that the rate limiting step is O-O radical coupling between two RuV=O moieties. Meyer and coworkers studied 4.3b under electrochemical conditions and proposed two scenarios: 1) a concerted atom-proton transfer mechanism where base-assisted water nucleophilic attack on a [RuV=O]+ is the rate-limiting step, or 2) a mechanism where PCET from [RuIV-OH]+ to [RuV=O]+ is rate-limiting while the O-O bond formation step via bimolecular radical coupling is rapid.

We became particularly fascinated by the role of the wide O-Ru-O angle of 4.3 after testing the catalytic activity of phosphonate analog 4.4 which is significantly less active under both chemical and electrochemical conditions. In the presence of excess CeIV, the turnover frequency of 4.4 (~0.4 s⁻¹) is about two orders of magnitude smaller than that of 4.3 (reported values range from 19 s⁻¹ to 41 s⁻¹). Similarly under electrochemical conditions (pH 7), the onset potential of 4.3 is nearly ~400 mV lower than that of 4.4. These results were somewhat surprising considering that both 4.3 and 4.4 are composed of similar frameworks (i.e. dianionic tetradentate ligands and two axial picoline ligands) and they are isoelectronic, which implies that their catalytic intermediates should maintain the same charges. A closer look at their individual crystal structures (Figure 4.2) reveals that the O-Ru-O angle of 4.4 is significantly less distorted (110°) than that of 4.3 (123°). If indeed catalysis by 4.4 proceeds via a seven-coordinate catalytic intermediate, one can imagine a scenario in which ligand sphere rearrangement to accommodate pentagonal bipyramidal geometry would require greater reorganization energy. By that same logic, a catalyst bearing an O-Ru-O angle even wider than that of 4.3 (>123°) may require even less reorganization energy to reach the seven-coordinate intermediate.
Figure 4.2. O-Ru-O angle variations between Ru complexes with 2,2'-bipyridine-6,6'-dicarboxylate and 2,2'-bipyridine-6,6'-phosphonate ligands and possible implications for formation of the pentagonal bipyramidal intermediate involved in catalysis.

Thus, the initial impetus for the present work was to design a tetradentate ligand that would force an O$_1$-Ru-O$_2$ angle that is wider than that imparted by bda and consequently decrease the activation energy required to access the pentagonal bipyramidal intermediate. We envisioned that replacing the six-membered rings of the 2,2'-bipyridine backbone of bda with five-membered rings of a 2,2'-biimidazole backbone would intrinsically force the ancillary groups (connected at the 4,4'-positions) to extend further away from the metal center and thus would lead to a wider O$_1$-Ru-O$_2$ angle upon tetradentate coordination. Phosphonates were chosen as the ancillary ligands rather than carboxylates because C(sp$^2$)-P and P-O bonds are longer compared to the C(sp$^2$)-C(sp$^2$) and C(sp$^2$)-O bonds, therefore the angle strain for tetradentate coordination would be less.

Although tetradentate coordination was not favored, to our pleasant surprise the unique bidentate configuration in 4.5-4.7 was observed. The present work will discuss the synthesis,
characterization, electrochemistry, and catalytic activities of 4.5-4.7 and potential mechanisms by which the phosphonates in the secondary coordination sphere could play a non-innocent role in catalysis.

**Figure 4.3.** Proposed strategy to widen the O-Ru-O angle. Note: 4-picoline ligands are not shown in computed structure (c).

### 4.2 Synthesis and Characterization

2,2-biimidazole (4.8) was synthesized following a procedure similar to one described in literature,\(^\text{18}\) and subsequently methylated to 4.9 by treating its conjugate base with methyl iodide.\(^\text{19}\) Attempts to directly brominate the 4, 4’ positions of 4.9 to synthesize 4.11 were unsuccessful and instead bromination of the 5, 5’ positions was observed (as is known for other 1-alkylated imidazoles) likely because the methyl groups are not sterically hindered enough to favor electrophilic aromatic substitution in the 4, 4’ positions.\(^\text{20}\) To overcome this problem, a two-step approach was employed: first, 4.9 was tetrabrominated to give 4.10 by a Lewis-base catalyzed
halogenation method described by Gustafson’s group;\textsuperscript{21} subsequently, selective debromination of the 5, 5’ positions by n-BuLi-mediated lithium-halogen exchange yielded 4.11 in moderate yield. The latter step was inspired by previous work done by Sanchez-Garcia et al.;\textsuperscript{20} lithiation of the C-4 carbon is disfavored presumably because of a destabilizing interaction between the C-4 carbon lone pair and N-3 lone pair [adjacent lone pair (ALP) effect].\textsuperscript{22} Regioselectivity was confirmed by NOESY, where saturation of the peak at 6.92 ppm ascribed to the biimidazole aromatic protons lead to enhancement of the peak at 4.01 ppm associated with the N-methyl protons. The bromo groups of 4.11 were then easily converted to PO(O-iPr)\textsubscript{2} groups by a Hirao-type cross-coupling to yield 4.12.\textsuperscript{23} Heating 4.12 at 120 °C in the presence of 2.5 eq. of NaOH resulted in selective hydrolysis to symmetrical disodium salt 4.14 which was used \textit{in situ} to make complexes 4.5 and 4.6. Complete deprotection of 4.12 was achieved by silylation with bromotrimethylsilane followed by methanolysis to produce 4.13 in near-quantitative yield.
Figure 4.4. Ligand synthesis.
Figure 4.5. Metalation of ligands.

Initial attempts to metalate ligands 4.13 and 4.14 with a number of Ru precursors (e.g. Ru(DMSO)$_4$Cl$_2$, [Ru(cymene)Cl$_2$], [Ru(C$_6$H$_6$)Cl$_2$]) were not straightforward and generally unsuccessful. For example, reaction of either 4.13 (with excess NEt$_3$ present) or 4.14 with Ru(DMSO)$_4$Cl$_2$ after heating at 70 °C - 100 °C (prompted by lack of a reaction at room temperature) lead to samples that displayed an extremely complex mixture of $^1$H and $^{31}$P peaks. Room temperature reaction of 4.13 with [Ru(cymene)Cl$_2$]$_2$ in the presence of excess NEt$_3$ lead to observance of two $^{31}$P signals at 22.86 ppm and 3.26 ppm roughly equal in magnitude and the expected $^1$H NMR splitting pattern for the aromatic protons of coordinated cymene (four doublets of an ABCD spin system between ~ 4.4-5.2 ppm). We note that in this system, a 22-25 ppm chemical shift seems diagnostic for phosphonate O-coordination, whereas free phosphonates give
signals more upfield, between 0 and 5 ppm. The widely-spaced $^{31}$P signals are reminiscent of N,O-coordination to a Ru(cymene)Cl species by one half of the ligand while the other half remains freely rotating.\textsuperscript{17,24} The reaction was further heated with a hope that the unbound half of the ligand would ultimately coordinate, however only minimal changes were observed even after nearly 47 h of heating at 70-100 °C. By contrast, reaction of 2,2'-bipyridine-6,6'-diphosphonic acid (the bipyridine analog of 4.13) with [Ru(C$_6$H$_6$)Cl]$_2$ in the presence of excess NEt$_3$ yielded a symmetrical species with a single $^{31}$P signal at ~24.2 ppm consistent with relatively effortless tetradeinate coordination of the ligand. Thus, as was somewhat expected, tetradeinate coordination by biimPO-type ligands is not always easily achievable. In addition to the angle strain predicted to be associated with tetradeinate coordination, cis-coordination of biimidazole is likely associated with the energetic cost of overcoming steric hindrance between the N-methyl groups. Calculations done by Zhang et al. on 1,1'-dimethyl-2,2'-biimidazole showed that the trans configuration is favored by as much as 19.2 kcal/mol.\textsuperscript{25} One can imagine that if the first half of the ligand participates in N,O-coordination, the conditions for coordination of the second half must be highly favorable to prevent it from undergoing alternate reactivity. Bearing these challenges in mind, we considered that it may be critical to use a Ru precursor with highly labile ligands that impose little steric hindrance. A precursor that was previously synthesized in the Grotjahn lab following literature procedures – Ru(H$_2$O)$_6$(OTs)$_2$ – piqued our interest because aquo ligands are small and labile.\textsuperscript{26} To our delight, reactions of 4.13 (with excess NEt$_3$) or 4.14 with Ru(H$_2$O)$_6$(OTs)$_2$ were considerably cleaner than our attempts with the above-mentioned precursors. The initial reaction in CH$_3$OH likely forms a L$_2$Ru(CH$_3$OH)$_4$ intermediate in solution – evidenced by an x-ray crystal structure (Fig. 4.7) acquired from the reaction of 4.14. Subsequent
addition of ~2 equivalents of the heterocycle (i.e. 4-picoline or isoquinoline) led solely to axial coordination to yield the Ru(CH$_3$OH)$_2$ analogs of 4.5-4.7.

Figure 4.6. CH$_3$OD/H$_2$O ligand exchange in 4.5 monitored by $^1$H NMR changes in N-methyl resonances.

Facile exchange of coordinated methanol and water was observed by NMR spectroscopy upon addition of a series of aliquots of H$_2$O (50 µL each) to a solution of 4.5 in CD$_3$OD. Relative ratios of the asymmetric mono-aquated and symmetric di-aquated species were easily identified by monitoring the $^1$H signals of the biimidazole N-methyl groups. Addition of the first 50 µL aliquot of H$_2$O (17.0 mol % H$_2$O) lead to the appearance of two adjacent singlets for
Ru(CD$_3$OD)(H$_2$O) and one singlet for Ru(H$_2$O)$_2$ and $^1$H NMR signals for the Ru(CD$_3$OD)$_2$ species were almost completely gone after addition of 150 µL of H$_2$O (38.2 mol % H$_2$O) (Figure 4.6).

Interestingly, vapor diffusion of Et$_2$O into a methanolic solution of 4.5 afforded orange crystals which were revealed by NMR and x-ray crystallography to be the Ru(H$_2$O)$_2$ species rather than Ru(CH$_3$OH)$_2$ species (Figure 4.8). The methanol used for crystallization was not previously dried (e.g. with 3 Å molecular sieves), nor was the glassware. In the crystal structure, measured interatomic distances between the phosphonate oxygen atoms and hydrogen atoms of the aquo ligands (O=P-O--H-O-Ru) are near ~1.7 Å, indicative of moderate strength hydrogen-bonding interactions.$^{27,28}$ Ligand coordination forces the two biimidazole halves to bend away from the central vertical plane of symmetry leading to perturbation of the sp$^2$ geometry around the central biimidazole C-C bond (e.g. $\angle$N$_1$C$_2$C$_2'$ = ~134°, see fig. 4.8 for atom labels). As a result, steric interactions between the two N-methyl groups are minimized, allowing the biimidazole backbone to adopt an effectively planar configuration (e.g. N$_1$C$_2$C$_2'$N$_1'$ dihedral angle = 0.59°). A survey of crystal structures of cis-diaquo ruthenium complexes in the Cambridge Structural Database (CSD)$^{29}$ resulted in 20 hits which show O-Ru-O angles ranging from 79° to 94°; the O-Ru-O angle of 4.5 measures at the lower end of this range at ~81.2° possibly due to the steric influence of the phosphonate groups. Lastly, there is no significant distortion of the N-Ru-N angle (~178°) between the axial picoline ligands as is often seen in complexes bearing tetradentate ligands. Vapor diffusion of Et$_2$O into a solution of 6 in dry methanol (dried by storing in activated 3 Å molecular sieves) yielded orange crystals of the corresponding Ru(CH$_3$OH)$_2$ complex (Figure 4.9). Structural characteristics of 6 do not deviate significantly from those of 4.5.
Figure 4.7. ORTEP drawing of the x-ray crystal structure of a Ru(CH$_3$OH)$_4$ intermediate formed after reaction of ligand 4.14 with Ru(H$_2$O)$_6$(OTs)$_2$ in CH$_3$OH (ellipsoids shown at the 50% probability level)
Figure 4.8. ORTEP drawings of the x-ray crystal structure of 4.5 (ellipsoids shown at the 50% probability level); Top: front view; bottom: overhead view (bottom)
Figure 4.9. ORTEP drawing of the x-ray crystal structure of 4.6 (ellipsoids shown at the 50% probability level)

Hydrogen bonding is also observed in solution, as demonstrated by pronounced isotopic perturbation of the $^{31}$P shift by OH/OD substitution (Figure 4.10), an analytical technique used for studying hydrogen bonding in proteins that Grotjahn and coworkers have used in non-WOC work on bifunctional catalysis.$^{30}$ The $^1$H NMR shifts likely experienced no observable perturbation
because of $\geq 5$ bond separation between the ligand protons and the OH/OD substitution.

![Chemical structure](image)

**Figure 4.10.** Stepwise addition of CH$_3$OH to solution of 4.5 in CD$_3$OD. $^1$H NMR intensites were scaled to adjust for dilution.
Figure 4.11. Cyclic voltammetry of 4.5 in potassium phosphate buffer (0.1 M, pH 7)
Figure 4.12. Comparison of Ru$^{\text{IV/III}}$ waves of 4.5 in 0.1 M pH 7 potassium phosphate buffer (purple), 0.1 M KNO$_3$ (green), 0.1 M CF$_3$SO$_3$H (red).

4.3. Electrochemistry

Initial cyclic voltammetry experiments of 4.5 performed in neutral media (0.1 M potassium phosphate buffer, pH 7) revealed a nearly reversible wave at $\sim$0.25 V (vs. Ag/AgCl), assigned as the Ru$^{\text{IV/III}}$ couple, a small oxidative shoulder at $\sim$1.0 V which we assign to the Ru$^{\text{III/IV}}$ couple, followed by a remarkably pronounced catalytic wave observed at an onset potential of $\sim$1.10 V (Figure 4.11). With the unique hydrogen-bonding arrangement in the ligand sphere, the phosphonates appear to be optimally poised to participate in an intramolecular PCET mechanism. In the case of the Ru$^{\text{IV/III}}$ couple, one can imagine a scenario where proton transfer from an aquo ligand to P-O$^-$ can occur in concert with oxidation of the metal to Ru$^{\text{III}}$ (Figure 4.13A). If an intramolecular PCET pathway is predominant, one can expect that in the absence of external bases,
the Ru$^{II/III}$ couple should not experience a significant shift in potential as the phosphonate arms would remain poised for proton transfer. However, under acidic conditions (0.1 M CF$_3$SO$_3$H), the Ru$^{II/III}$ couple shifts by +140 mV to 0.39 V suggesting that there is indeed involvement of an external base in PCET. Furthermore, in a non-basic, near-neutral ionic medium (0.1 M KNO$_3$, pH ~6.4), the Ru$^{II/III}$ couple shifts only negligibly ($\Delta E_{1/2} \approx$ -0.01 V) compared to acidic conditions indicating that OH$^-$ concentrations in the regime of pH 1-7 are not appreciable to play a role in PCET and the influence of the buffer base is significant. Figure 4.13 outlines two scenarios (B and C) by which the buffer base may be involved in the Ru$^{II/III}$ oxidation. In scenario B, an aquo ligand proton is transferred directly to the base. In scenario C, the proton is initially transferred to the phosphonate group and subsequently relayed to an external base. Experimental pK$_a$ values of alkyl alkylphosphonic acids range from ~2.0 - 2.5 and pK$_a$ values of alkyl arylphosphonic acids are expected to be even lower due to the electron-withdrawing influence of the aryl group.$^{31}$ Potential vs. pH dependence studies (to be discussed in more detail below) revealed that the Ru$^{III}$-OH$_2$ species has a pK$_a$ of about ~5. Based on these values, scenario C does not seem reasonable, because the pendent phosphonate base is expected to be too weak a base.
Figure 4.13. Potential PCET mechanisms for Ru$^{II/III}$ couple.

The Ru$^{III/IV}$ redox event of 4.5 does appear to be pH dependent; for example, in 0.1 M KNO$_3$ it occurs at ~1.1 V, and in 0.1 M CF$_3$SO$_2$H it shifts about +200 mV to ~1.3 V. Presumably, the pK$_a$ of Ru$^{IV}$(OH)$_2$ should be low enough (likely < 0) to experience a pH effect with the concentration of OH$^-$ ions available between pH 1-7. The reduced magnitude of current in the Ru$^{III/IV}$ redox event under all conditions suggests a slow electron transfer process. The Ru$^{III/IV}$ oxidation is often associated with formation of Ru$^{IV}$-OH or Ru$^{IV}$=O intermediates for which Ru$^{IV}$-O bond lengths are considerably shorter (~1.7-1.9 Å)$^{12,32-37}$ than those observed in Ru$^{II}$-O and Ru$^{III}$-O species (~2.1-2.2 Å)$^{38-43}$. Accordingly, the inner-sphere reorganization energy associated with oxidation to the Ru$^{IV}$ state may be a source of sluggish electron transfer.$^{44,45}$ Kinetically inhibitted Ru$^{III/IV}$
waves are observed in cyclic voltammograms of existing Ru diaquo catalysts 4.1 and 4.2. Hirai et al. utilized resonance Raman spectroscopy and XPS to show that two equiv CeIV to 4.2 led to evidence of a RuIV=O bond in a RuIV(O)(H2O) species. In contrast, DFT calculations and XAS and EXAFS data of 4.1 preclude the presence of a RuIV=O bond after addition of CeIV and are consistent with a RuIV(OH)2 species. DFT calculations performed on 4.5 favor the RuIV(OH)2 configuration by 13.8 kcal/mol, however we are not yet ruling out the possibility of a RuIV(O)(OH2) species until further experimental evidence is acquired.

To gain further insight on the potential vs. pH dependence of 4.5, a Pourbaix diagram was constructed using a Britton-Robinson universal buffer system with enough NaClO4 added to maintain an effectively constant ionic strength (µ = 0.5 M). The first redox event is pH-independent below pH 5, but maintains a slope of 59 mV / pH unit above pH 5 indicating that pKa = ~5 for the loss of 1 H+ from RuIII(H2O)2 to form RuIII(H2O)(OH). The second oxidation event is pH dependent for the full range of pH values; the slope of 59 mV / pH unit is likely associated with a 1H+/1e− PCET event and formation of a RuIV(OH)2 or RuIV(H2O)(O) species as discussed above. Onset of the catalytic wave occurs less than 100 mV above the RuIII/IV couple between pH 2 to pH 8 after which it becomes pH independent. We are tentatively assigning the ~59 mV / pH slope from pH 2 to 8 to a 1H+/1e− PCET associated with RuIV(H2O)(OH) to RuV(OH)2.
Figure 4.14. Pourbaix diagram of 4.5 in a Britton-Robinson buffer (ionic strength adjusted to 0.5 M using NaClO₄)

Cyclic voltammetry (CV) was performed on complexes 4.6 and 4.7 as well. In potassium phosphate buffer (0.1 M, pH 7), the initial wave for Ru^{II/III} oxidation of 4.6 occurs at about 0.33 V, and then a large catalytic wave is seen with an onset near ~0.95 V, about 100 mV more negative compared to that of 4.5 (Figure 4.15). On the return scan, a sharp reductive feature – one that was not observed in CVs of 4.5 – is seen at ~0.22 V, highly reminiscent of CVs shown by Matheu et al. where attempts to covalently anchor a catalyst with the Ru(bda) framework on glassy carbon led to electro-deposition of a thin RuO₂ film.⁴⁷ Further evidence of surface modification was acquired by running CVs using an electrode rinsed with water after 30 sec of controlled potential electrolysis at 1.1 V in a cell solution containing 4.6; the voltammogram showed a large catalytic
wave that persisted even after rinsing the electrode further with water. Further X-ray absorption spectroscopic analysis will be required to further characterize the deposited material. We were unable to fully purify 4.7, however we conducted some preliminary testing using a crude sample, acknowledging that the results cannot be conclusive. Under neutral conditions, a broad, non-reversible wave was observed at ~0.17 V likely corresponding to the Ru$^{II/III}$ couple. The lack of reversibility may be a consequence of the localized charges of P-O$^-$ groups produced from deprotonation at pH 7; a similar phenomenon was seen for 4.4a. A notable catalytic wave was observed for 4.7 as well, however the onset potential was ~100 mV more positive compared to 4.5. The observed difference in onset potential may be a charge-related phenomenon that was similarly observed in our previously reported work on 4.4a and 4.4b. Interestingly, under electrochemical conditions complexes 4.5 and 4.7 have significantly reduced overpotentials compared to 4.4a and 4.4b (see Figure 4.16).
Figure 4.15. Cyclic voltammetry of 4.6 in potassium phosphate buffer (0.1 M, pH 7)
For comparative purposes, complexes 4.1 and 4.2 were synthesized by literature procedures,\textsuperscript{48,49} and examined by cyclic voltammetry under neutral conditions (Figure 4.17). For both complexes, presence of four sequential, redox waves consistent with the transition from Ru\textsuperscript{II}(H\textsubscript{2}O) to Ru\textsuperscript{VI}(O)\textsubscript{2}, matches well with literature results.\textsuperscript{5,6} No catalysis was observed by 4.2, however complex 4.1 showed onset of a catalytic wave near ~1.25 V. In contrast, 4.5 begins rapid oxidation of water at ~1.10 V, nearly 150 mV below the value for 4.1.

**Figure 4.16.** Comparison of cyclic voltammetry of 4.5 (purple) and 4.7 (green) with 4.4a (blue) and 4.4b (red)
Figure 4.17. Comparison of cyclic voltammetry of 4.1 (orange), 4.2 (blue), and 4.5 (purple) in potassium phosphate buffer (0.1 M, pH 7).

4.4. Oxygen evolution experiments with CeIV

Oxygen evolution was quantified under acidic conditions in the presence of excess CeIV (ceric ammonium nitrate) using a pressure transducer to measure O2. Rapid oxygen evolution was observed by 4.5 with the kinetics being first order with respect to catalyst concentration (Figure 4.18). The turnover frequency at an initial catalyst concentration of 250 µM was ~800 h⁻¹, slightly less than half that of catalysts 4.4a and 4.4b (~1450 h⁻¹). The turnover frequency of 4.1 under the same conditions (250 µM catalyst, 250 mM CAN) was ~46 h⁻¹, nearly 20 times smaller than TOF
Figure 4.18. Top: \( \text{O}_2 \) evolution from 4.5 monitored upon adding CAN. Total reaction volume was 4 mL. Bottom: initial rates. Inset: plot of initial rates vs. catalyst concentration depicting a first-order relationship.
of 4.5 (Figure 4.19), similar to the much lower catalytic current seen in CV under neutral conditions.

![Graph showing oxygen production over time](image)

**Figure 4.19.** Comparison of 4.5 (green) and 4.1 (pink) in the presence of excess CAN. Conditions: 250µM catalyst in the presence of 250 mM CAN, total reaction volume = 4 mL.

4.5. Possible Mechanisms

To facilitate hypotheses on potential mechanistic pathways, it is useful to review mechanisms of other well-studied Ru diaquo complexes. Electrochemistry of 4.1 has shown that the metal center can undergo a stepwise 4 H⁺ / 4 e⁻ PCET process over a narrow potential window (0.8 – 1.5 V) to access a RuVI bis-oxo intermediate. The cis orientation of the oxo groups prompts the interesting question of whether an *intramolecular* O-O bond formation mechanism is possible. Sala et al. obtained mechanistic insight on catalyst 4.1 through ^18_O-labeling experiments and DFT
calculations. In $^{18}$O-labeling studies, the catalyst and solvent were labeled to varying degrees, and the resulting isotopic ratios of O$_2$ generated from one Ce$^{IV}$-induced turnover match well with ratios expected for a water nucleophilic attack scenario. To complement the experimental data, the calculated activation free energies for water nucleophilic attack and intramolecular radical coupling scenarios strongly favor the former by nearly ~32 kcal/mol. The intramolecular radical coupling scenario is likely disfavored due to significant coulombic repulsion between the oxo σ lone pairs; computations predicted the O-Ru-O angle to increase from 83° in the Ru$^{II}$ state to 124° in the Ru$^{VI}$ state.

In contrast to 4.1 and 4.2, where redox waves corresponding to a sequential loss of 4 H$^+$ / 4 e$^-$ from Ru$^{II}$(H$_2$O)$_2$ to Ru$^{VI}$(O)$_2$ are clearly visible, only the Ru$^{II}$/III and Ru$^{III}$/IV couples of 4.5 and ensuing catalytic wave are observed. We tentatively propose a Ru$^V$ species with either a Ru(OH)$_2$ or Ru(O)(OH$_2$) configuration as the active catalytic intermediate to mediate O-O bond formation. The remarkable improvement in catalysis by 4.5-4.7 compared to other Ru diaquo complexes suggests that phosphonates in the secondary coordination sphere may be involved as pendent basic sites. Figure 4.20 outlines a number of intra- and inter-molecular mechanistic scenarios for O-O bond formation involving the phosphonate moieties.
4.6. Conclusions and Future Work

We have synthesized a unique family of Ru-diaquo complexes bearing novel 2,2’-biimidazole-4,4’-diphosphonate ligands that undergo bidentate coordination via the biimidazole nitrogen atoms. The phosphonates do not bind to the metal but they are located in the secondary coordination sphere and participate in hydrogen bonding interactions with the aquo ligands. The prepared complexes 4.5-4.7 appear to oxidize water more efficiently than previously reported Ru-diaquo complexes (4.1 and 4.2), showing significantly lower overpotentials and large catalytic currents by electrochemistry and 20-fold increases in rate when driven by Ce$^{IV}$. Furthermore, the chemical properties of 4.5 were characterized by NMR spectroscopy and cyclic voltammetry. Hydrogen bonding between the phosphonates and the aquo ligands is observed in the solid-state by x-ray crystallography and in solution as demonstrated by H/D isotopic perturbation of the $^{31}$P NMR signal. Kinetic studies with Ce$^{IV}$ point to a WNA mechanism and the Pourbaix diagram.

Figure 4.20. Proposed mechanisms of O-O bond formation.
suggests that the active intermediate prior to O-O bond formation may be either Ru$^\text{V}$(O)(H$_2$O) or Ru$^\text{V}$(OH)$_2$. Based on our knowledge of previous work (Hirai et al. and Planas et al.)$^{6,46}$ we anticipate that a combination of resonance Raman spectroscopy and x-ray techniques (XPS, EXAFS, XAS) should allow us to determine whether a Ru$^\text{IV}$=O group is present. Furthermore, Ce$^\text{IV}$-induced water oxidation in $^{18}$O-labelled water and quantification of resulting $^{32}$O$_2$, $^{34}$O$_2$, and $^{36}$O$_2$ ratios by mass spectrometry should reveal whether O-O bond formation is intra- or inter-molecular.$^7$ We suspect that the phosphonates in the secondary coordination sphere are involved in catalysis. We hope to elucidate such phenomena in ongoing studies.

Chapter 4 contains material that is currently being prepared for publication. Kamdar, J. M.; Spire, M. T.; Moore, C. E.; Rheingold, A. L.; Smith, D. K.; Grotjahn, D. B.; “Water oxidation by cis-diaquo ruthenium complexes with pendent phosphonate groups in the secondary coordination sphere”. Manuscript in preparation. The dissertation author was the primary researcher for the data presented. I thank my advisor Doug Grotjahn for giving me the freedom to actually pursue the crazy idea of trying to “widen the O-Ru-O angle”. I am grateful to be able to have a collaboration with small molecule x-ray crystallography experts Dr. Curtis Moore and Dr. Rheingold; the elusive structures of Ru-diaquo complexes presented in this chapter may have still been a mystery without their help. Matt Spire is acknowledged for very useful data from Ce$^\text{IV}$ testing. Lastly, I would like to thank Dr. Smith for her patience and very useful discussions on electrochemical phenomena observed by the presented complexes.
4.7. Experimental

4.7.1. Preparation of Compounds

![Chemical structure of 4, 4’, 5, 5’-tetrabromo-2, 2’-biimidazole (4.10)]

**Synthesis of 4, 4’, 5, 5’-tetrabromo-2, 2’-biimidazole (4.10):** 1, 1’-dimethyl-2, 2’-biimidazole (0.5046 g, 3.111 mmol) and triphenylphosphinesulfide (0.0923 g, 0.3136 mmol) were weighed out in a 20 mL vial equipped with a stir bar and CH$_2$Cl$_2$ (7.5 mL, dried with CaH$_2$/distillation) was added. N-bromosuccinimide (2.2460 g, 12.62 mmol) was added to the reaction mixture and the mixture was allowed to stir overnight at room temperature. The reaction solution was concentrated using a rotary evaporator and the resulting crude solid was transferred to a class F fritted funnel. The solid was rinsed thoroughly on the frit itself with water (3 x 20 mL) and then thoroughly with Et$_2$O (3 x 30 mL) to yield a fine beige powder (1.2192 g, 82 %). (Calcd. for C$_8$H$_6$Br$_4$N$_4$ (477.78): C, 20.11; H, 1.27; N, 11.73. Found: C, 20.50; H, 1.67; N, 11.73. See section 4.7.2 for full NMR characterization data.

![Chemical structure of 1,1’-dimethyl-4,4’-dibromo-2,2’-biimidazole (4.11)]

**Synthesis of 1,1’-dimethyl-4,4’-dibromo-2,2’-biimidazole (4.11):** 4, 4’, 5, 5’-tetrabromobiimidazole (1.0078 g, 2.1093 mmol) was weighed out in a Schlenk flask with a stir bar. The flask was evacuated and refilled three times with nitrogen gas after which dry THF (48 mL, dried using a sodium/benzophenone still) was added to the flask to create a suspension. The suspension was cooled in an acetone/dry-ice bath. Over 10 min, n-butyllithium (2.5 M in hexanes, 1.90 mL, 4.75 mmol) was added to the cold suspension. After 40 min of stirring at -78 °C, a ~0.2
mL aliquot was transferred to a vial containing isopropanol (1 mL) and the sample was further quenched with saturated NH₄Cl (3 mL). The product was extracted from the sample with EtOAc (2 mL), the organic layer was concentrated to dryness on a rotary evaporator, the residue redissolved in CDCl₃, and reaction progress was assessed by ¹H NMR spectroscopy. Another 1.50 mL of n-butyllithium (2.5 M in hexanes, 3.75 mmol) was added to complete the reaction. After an additional 1 h reaction time, isopropanol (8 mL) was added to the reaction over 10 min, while keeping the reaction on an acetone/ice-bath. The mixture was subsequently allowed to warm up to room temperature and saturated NH₄Cl (50 mL) was added over 10 min. The quenched mixture was transferred to separatory funnel and extracted three times with EtOAc (50 mL each). The combined organic layers were dried with anhydrous Na₂SO₄, filtered, and the filtrate was concentrated to dryness on a rotary evaporator. The crude product was further purified by silica gel column chromatography (100 % EtOAc) and the product was isolated as a light pink solid (0.4125 g, 61%). Calcd. for C₈H₈Br₂N₄ (319.99): C, 30.03; H, 2.52; N, 17.51. Found: C, 30.35; H, 2.87; N, 17.42. See section 4.7.2 for full NMR characterization data.

**Synthesis of 1,1’-dimethyl-4,4’-tetraisopropyldiphosphonate-2,2’-biimidazole (4.12):** In a glovebox, 4,4’-dibromo-2,2’-biimidazole (1.0000 g, 3.1251 mmol), Pd(OAc)$_2$ (0.0160 g, 71.27 µmol), and 1,1’-bis(diphenylphosphino)ferrocene (0.0483 g, 87.12 µmol) were weighed out in a 20 mL vial containing a stir bar. The contents of the vial were suspended in CH$_3$CN (9 mL, dried by CaH₂/distillation and deoxygenated) and diisopropyl phosphite (1.4 mL, 8.4003 mmol) and
N,N-diisopropylethylamine (1.4 mL, 8.0371 mmol, dried by CaH$_2$/distillation) were added to the vial, which was then sealed. The mixture was heated in a 100 °C oil bath for nearly 24 h and subsequently concentrated to an orange solid on a rotary evaporator. The crude solid was dissolved in CH$_2$Cl$_2$ (100 mL), transferred to a separatory funnel, and washed once with saturated NaHCO$_3$ (100 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (50 mL) and the combined organic layers were washed once with H$_2$O (100 mL). The aqueous layer was back extracted with CH$_2$Cl$_2$ (50 mL), and the combined organic layers were combined, dried with anhydrous Na$_2$SO$_4$, filtered, and the filtrate was concentrated to dryness on a rotary evaporator. The crude product was further purified by silica gel column chromatography (gradient elution: CH$_2$Cl$_2$ to 1:10 MeOH : CH$_2$Cl$_2$) and the product-containing fractions were combined and concentrated to dryness on a rotary evaporator. The product was re-dissolved in minimal CH$_2$Cl$_2$ and precipitated out as a micro-crystalline solid by slow addition of pentane. The solid was collected by vacuum filtration, washed twice with pentane (30 mL each wash), and placed in a dessicator under an oil-pump vacuum overnight. Yield of fine, light-yellow solid: 1.2499 g, 82%. Calcd. for C$_{20}$H$_{36}$N$_4$O$_6$P$_2$ (490.48): C, 48.98; H, 7.40; N, 11.42. Found: C, 49.20; H, 7.75; N: 11.37. See section 4.7.2 for full NMR characterization data.

![Chemical structure](image)

**Synthesis of 1,1’-dimethyl-2,2’-biimidazole-4,4’-diphosphonic acid (4.13):** In a glovebox, 1,1’-dimethyl-4,4-tetraisopropylidiphosphonate-2,2’-biimidazole (0.5007 g, 1.021 mmol) was weighed out in a 20 mL vial containing a stir bar. To the vial was added CH$_2$Cl$_2$ (2.4 mL, dried by distillation over CaH$_2$) to produce a light brown mixture. Bromotrimethylsilane (1.20 mL, 8.75 mmol) was
added to the mixture which was allowed to stir for 6 h at room temperature. To assess the completion of the reaction, an aliquot of the reaction mixture (~0.1 mL) was diluted with CDCl₃ (0.6 mL, dried with molecular sieves) in an NMR tube in a glovebox, and analyzed by NMR spectroscopy (¹H, ³¹P). The NMR mixture was transferred back to the crude reaction mixture and the mixture was concentrated to a light-pink solid under an oil-pump vacuum through a Schlenk manifold in order to maintain anhydrous conditions. In the glovebox, methanol (7 mL) was added to the solid and the milky suspension was allowed to stir for 2.5 h. The suspension was filtered through a sintered glass funnel and the collected solid was rinsed twice with cold methanol (5 mL each wash) and three times with diethyl ether (10 mL each wash). The solid was placed in a dessicator under an oil-pump vacuum for 18 h to give 4.13 as a fine white solid (0.3223 g, 98%). Calcd. for C₈H₁₂N₄O₆P₂ (322.15): C, 29.83; H, 3.75; N, 17.39. Found: C, 28.22; H, 3.70; N, 16.11. Calcd. for C₈H₁₂N₄O₆P₂ + 1 H₂O: C, 28.25; H, 4.15; N, 16.47. See section 4.7.2 for full NMR characterization data.

![Chemical Structure](image)

**Synthesis of disodium disopropyl (1,1'-dimethyl-2,2'-biimidazole-4,4'-diphosphonate (4.14) (stock solution):** In a glovebox, 1,1'-dimethyl-4,4-tetraisopropyldiphosphonate-2,2'-biimidazole (0.3001 g, 611.85 µmol) and powdered NaOH (0.0616 g, 1.5396 mmol) were weighed out in a 20 mL vial containing a stir bar. The contents of the vial were dissolved in a 4 : 1 mixture of H₂O : iPrOH (10 mL) and the vial was heated at 120 °C for 5 days to produce the disodium salt. The reaction solution was concentrated to a solid and the solid was placed in a dessicator under an oil-pump vacuum overnight and the resulting solid was dissolved in CH₃OH (9.0 mL, deoxygenated).
to make a stock solution (0.068 M). $^1$H NMR (δ, 499.946, CD$_3$OD): 7.49 (s, 2H), 4.46 (m, 2H), 3.89 (s, 6H), 1.18 (d, $^3$J$_{HH}$ = 6.2 Hz). $^{31}$P NMR (δ, 202.381 MHz, CD$_3$OD): 4.99.

![Chemical Structure](image)

**Synthesis of Ru(biimPO-R)(H$_2$O)$_2$(pic)$_2$ (4.5)**: Under an inert atmosphere, a portion (3.0 mL) of the stock solution of disodium salt 4.14 (0.06798 M) was transferred to a 20 mL vial equipped with a stir bar. In a separate 20 mL vial, Ru(H$_2$O)$_6$(OTs)$_2$ (0.1124 g, 203.8 µmol) was dissolved in CH$_3$OH (2 mL, deoxygenated) and the solution was slowly transferred to the ligand solution to produce a dark yellow-brown mixture. The mixture was heated at 70 °C for 37 h after which 4-picoline (42 µL) was added and then the mixture was heated at 70 °C again for ~23 h. The reaction mixture was concentrated on a rotary evaporator to a dark-brown solid and purified by silica-gel column chromatography (gradient elution from CH$_2$Cl$_2$ to 1:1 CH$_2$Cl$_2$: CH$_3$OH). The product containing fractions were combined and concentrated to an orange solid and further purified by recrystallization by vapor diffusion (solvent: CH$_3$OH; anti-solvent: Et$_2$O) to afford orange crystals. The mother liquor was pipetted out and the crystals were rinsed with three 3 mL portions of Et$_2$O. The crystals were separated from residual non-crystalline solid by scraping into a separate vial and then they were placed in a dessicator under oil-pump vacuum to dry overnight (0.0757 g, 50 %).
Calcd. for C$_{26}$H$_{40}$N$_6$O$_8$P$_2$Ru (727.66): C, 42.92; H, 5.54; N, 11.55. Found: C, 41.94; H, 5.49; N, 11.29. Calcd. for C$_{26}$H$_{40}$N$_6$O$_8$P$_2$Ru + 1 H$_2$O (745.67): C, 41.88; H, 5.68; N, 11.27. See section 4.7.2 for full NMR characterization data.

**Synthesis of Ru(biimPO-R)(H$_2$O)$_2$(isoq)$_2$ (4.6):** Under an inert atmosphere, a portion (0.9 mL) of the stock solution of disodium salt 4.14 (0.068 M) was transferred to a 20 mL vial equipped with a stirbar. In a separate 20 mL vial, Ru(H$_2$O)$_6$(OTs)$_2$ (0.0338 g, 61.3 µmol) was dissolved in CH$_3$OH (0.5 mL, deoxygenated) and the solution was slowly transferred to the solution of 4.14 to produce a dark yellow-brown mixture. The mixture was heated at 70 °C for ~12.5 h after which isoquinoline (15.0 µL, 128 µmol, 2.09 equiv) was added and then the mixture was heated at 70 °C again for ~23.5 h. The reaction mixture was concentrated on a rotary evaporator to a reddish-brown solid and purified by silica-gel column chromatography (gradient elution from CH$_2$Cl$_2$ to 1:2 CH$_3$OH : CH$_2$Cl$_2$). The product containing fractions were combined and concentrated to an orange solid. The product was redissolved in a minimal amount of CH$_3$OH and passed through a Sephadex G-15 plug to remove residual tosylate salts. The product containing fractions were concentrated using rotary evaporation and the resulting solid was transferred into a glovebox. The
solid was dissolved in dry CH$_3$OH (2 mL, deoxygenated and dried with activated 3 Å molecular sieves) and concentrated under reduced pressure; this process was repeated twice more, with the objective of homogenizing the product to consist of primarily the Ru(CH$_3$OH)$_2$ species. The homogenized product was redissolved in dry CH$_3$OH (1 mL) and precipitated out of solution by addition of excess Et$_2$O (dry, deoxygenated). The solid was filtered through a filter funnel (class M), rinsed three times with more Et$_2$O, and then crystallized via vapor diffusion. (0.0078 g, 15%). See section 4.7.2 for full NMR characterization data.
4.7.2. NMR Characterization

**Table 4.1.** 2D NMR spectroscopy data for 4.10.

<table>
<thead>
<tr>
<th>$^1$H-$^{13}$C gHSQC</th>
<th>$^1$H-$^{13}$C gHMBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^1$H</td>
<td>$^{13}$C</td>
</tr>
<tr>
<td>4.01</td>
<td>35.44</td>
</tr>
<tr>
<td>4.01</td>
<td>35.44</td>
</tr>
</tbody>
</table>

solvent: CDCl$_3$

$^1$H NMR (499.943 MHz) - red
$^{13}$C NMR (125.710 MHz) - black

**Table 4.2.** 2D NMR spectroscopy data for 4.11.

<table>
<thead>
<tr>
<th>$^1$H-$^{13}$C gHSQC</th>
<th>$^1$H-$^{13}$C gHMBC</th>
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</thead>
<tbody>
<tr>
<td>$^1$H</td>
<td>$^{13}$C</td>
</tr>
<tr>
<td>6.92</td>
<td>122.00</td>
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<tr>
<td>4.01</td>
<td>35.79</td>
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<tr>
<td>6.92</td>
<td>3</td>
</tr>
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<td>6.92</td>
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</table>
Table 4.3. 2D NMR spectroscopy data for 4.12.

<table>
<thead>
<tr>
<th>gCOSY</th>
<th>1H-13C gHSQC</th>
<th>1H-13C gHMBC</th>
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</thead>
<tbody>
<tr>
<td>4.75</td>
<td>4.75</td>
<td>1.30</td>
</tr>
<tr>
<td>1.30</td>
<td>23.89</td>
<td>1.30</td>
</tr>
<tr>
<td>1.37</td>
<td>24.08</td>
<td>1.37</td>
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<tr>
<td>4.08</td>
<td>36.10</td>
<td>4.08</td>
</tr>
<tr>
<td>4.75</td>
<td>71.02</td>
<td>4.75</td>
</tr>
<tr>
<td>7.53</td>
<td>131.88</td>
<td>7.53</td>
</tr>
</tbody>
</table>

1H NMR (399.750 MHz) - red
13C NMR (100.527 MHz) - black
31P NMR (161.826 MHz) - blue

solvent: CDCl$_3$
*Note: A cross peak for the aromatic C-H ($^1$H 7.64 to $^{13}$C 130.20) was not observed in the HSQC experiment.

Table 4.4. 2D NMR spectroscopy data for 4.13.

<table>
<thead>
<tr>
<th>$^1$H-$^{13}$C gHSQC</th>
<th>$^1$H-$^{13}$C gHMBC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>$^1$H</strong></td>
<td><strong>$^{13}$C</strong></td>
</tr>
<tr>
<td>3.96</td>
<td>35.47</td>
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<tr>
<td>7.64</td>
<td>3</td>
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<tr>
<td>7.64</td>
<td>2</td>
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</tbody>
</table>

solvent: DMSO-d$_6$

$^1$H NMR (499.946 MHz) - red

$^{13}$C NMR (125.724 MHz) - black

$^{31}$P NMR (202.381 MHz) - blue
Table 4.5. 2D NMR spectroscopy data for 4.5.

<table>
<thead>
<tr>
<th>gCOSY</th>
<th>1H-13C gHMBC</th>
<th>1H-13C gHSQC</th>
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</thead>
<tbody>
<tr>
<td>1.24</td>
<td>1.24-1,3</td>
<td>1.24-1,3</td>
</tr>
<tr>
<td>2.33</td>
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<td>8.84</td>
<td>1.24-2</td>
<td>8.84-2</td>
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</table>

solvent: CD$_2$OD  
$^1$H NMR (499.946 MHz) - red  
$^{13}$C NMR (125.724 MHz) - black  
$^{31}$P NMR (202.381 MHz) - blue
Table 4.6. 2D NMR spectroscopy data for 4.6.

<table>
<thead>
<tr>
<th>gCOSY</th>
<th>1H-13C gHMBC</th>
<th>1H-13C gHMBC cont’d</th>
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<tbody>
<tr>
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<td>9.88, 4 122.08</td>
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<td>9.88, 3 128.68</td>
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<td>7.90</td>
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<td>9.88, 3 130.36</td>
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<td>7.75</td>
<td>8.89, 2 149.16</td>
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<td></td>
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<td>4.65, 70.72</td>
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<td></td>
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<td>4.08, 39.21</td>
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<td></td>
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<td>1.17, 24.82</td>
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<tr>
<td></td>
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<td>7.75, 3 136.41</td>
</tr>
</tbody>
</table>

Solvent: dry CD$_2$OD
1H NMR (499.946 MHz) - red
13C NMR (125.725 MHz) - black
31P NMR (161.822 MHz) - blue
4.8. References


