The Water Oxidation Reaction Catalyzed by Homogeneous Iridium Carbene Complexes

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Abstract

The efficient conversion of solar energy into a chemical fuel represents a technological milestone that would engender society with a clean and renewable source of energy orders of magnitude more powerful than our current consumption. By dividing the process into two complementary half reactions each step of the conversion can be assessed and modified independently. Of the potential oxidants, few are better than the currently employed dioxygen gas but the formation of oxygen from reduced species is plagued by high thermodynamic barriers and requires multiple concerted proton and electron transfers. Homogeneous catalysis is an excellent platform from which to study these reactions and iridium complexes in particular have been shown to be highly active and long-lived in contrast to several other water oxidation catalysts.

Building on the wealth of knowledge already contained in the literature, this thesis describes the *in situ* speciation and provides evidence for the homogeneity of a class of iridium complexes capable of water oxidation over an extended period of time. In contrast to initial evidence that a single site was sufficient, spectroscopic and computational investigations support the formation of a dimeric species at the expense of a sacrificial place-holder ligand, Cp*. The dimeric complex then undergoes several sequential proton coupled electron transfer steps to generate at least one iridium(V) species followed by nucleophilic attack of a solvent water to form the difficult O-O bond. An additional consequence of dividing the overall reaction into two complementary half reactions is the choice of oxidant. Investigations also support the non-innocence of the oxidants employed underpinning the importance of reaction conditions. Despite these complications, these catalysts are robust and highly active.

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Last but not least my parents, Tony and Susan Woods, thank you for a lifetime of support through all of my good and bad decisions.

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Chapter 1: Introduction

A Growing Population Needs More Energy

As the world population continues to grow it is intuitive that global energy consumption will also increase. Today and in the future, however, the places shaping that demand are no longer developed nations. Beginning in 2008 energy consumption in countries historically labeled as "developed" exceeded that of "developing" nations. Indeed, current projections suggest energy consumption by non-OECD countries will double those of OECD countries by the year 2040 as the less developed rise to the same standard of living.¹ This is not a small amount of energy either: if global energy consumption in 2008 was used to heat Lake Erie, approximately half of the lake would be vaporized as saturated steam. Every year, global energy consumption is projected to increase sufficiently to vaporize an additional cubic mile of water.

Region/Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Total OECD										
Liquids	100	100	99	96	92	93	92	91	90	90
Natural Gas	53	54	55	56	55	57	59	60	60	59
Coal	47	47	48	47	43	45	44	42	42	42
Nuclear	23	23	23	22	22	23	21	20	20	21
Other	21	21	22	23	23	25	26	27	28	29
Total	245	246	247	245	235	242	242	239	240	241
Total Non-OECD										
Liquids	70	71	73	77	79	83	87	89	92	93
Natural Gas	50	52	54	57	54	59	60	60	61	63
Coal	75	81	86	91	97	103	109	112	113	118
Nuclear	4	4	5	5	5	5	5	6	7	7
Other	25	26	27	28	29	32	33	34	35	36
Total	224	235	245	258	264	282	295	301	307	317

Table 1: Energy consumption in quadrillion BTU by OECD and non-OECD countries.

Convention would suggest the means for producing this energy would rely on increasing the production of coal, oil, and natural gas as these fuels currently account for more than 85% of energy production. Indeed, while there have been several significant advances in mining and drilling techniques enabling the economical reclamation of previously unviable deposits of petroleum and natural gas, the novelty of these techniques leaves ample room for environmental liability and personal harm. For example, in 2010 a series of oversights and cost cutting measures at a deep-water oil platform operated by Transocean Ltd. and BP plc lead to the unintentional release of approximately 4.9 million barrels of crude oil into the Gulf of Mexico. To date the resulting criminal and civil penalties for Transocean and BP have exceeded \$42 billion USD,² while estimates for the lingering environmental and industry-spanning economic impacts of the disaster likely exceed those penalties by at least an order of magnitude.³⁻⁵

While disasters of this magnitude are thankfully relatively uncommon, an additional problem systemic to the consumption of fossil fuels is the resulting emissions. While climate change occurring prior to the industrial revolution is well explained by natural causes, recent climate changes are very likely due to anthropogenic emissions.⁶ While the effects of climate change are extraordinarily broad, they include the potential to reduce global GDP by 5% or more,⁷ significantly increased sea levels, and drastic changes to ecosystems.⁸ Despite these long-term consequences, inroads to replacing fossil fuels have been limited. Emissions are also not a small problem: carbon dioxide production due to energy production exceeded 31 billion metric tons in 2010 and projected to increase to 46 billion metric tons by 2040.¹ Without commercially viable alternatives, fossil fuels appear to be an industry- and consumer-accepted risk even if they are likely to impose long-term consequences to the environment and global health.

In the vein of commercial viability, the term "alternative" in alternative energy implicitly denotes impracticability - otherwise it would be convention. With that in mind, it is unfathomable that significantly more research is not devoted toward directly capturing solar energy. While the solar energy a particular point on the earth's surface receives will vary due to cloud cover, the time of day, and other transient factors, global average insolation is approximately 57 petawatts; or, on a daily basis, more than eight times our total *annual* energy consumption.

Even with such abundance, efforts to remove the "alternative" label from solar energy are stymied by a myriad of factors. A key feature of fossil fuels is their portability through high gravimetric and volumetric energy density. Additionally, the point that fossil fuels are a constituent in a large degree of consumer goods is difficult to address with solar energy. While there are numerous research ventures studying thermal solar energy capture or photovoltaic capture, these methods do not address the issue of portability or raw-material aspect of fossil fuels.

Instead of reinventing the wheel, a capture and conversion system for solar energy exists that has already been extensively tested and optimized – photosynthesis.^{9,10} Photosynthesis can be divided into three carefully orchestrated steps of photon-induced charge separation, oxidative water splitting, and the reduction of plastoquinone to plastoquinol with the eventual generation of NADPH and ATP.^{11–13} This process of photosynthesis conveniently produces fuel that powers the majority of life on earth, including humans. Emulating but adapting this scheme, the goal should not be to generate NADPH and ATP, but instead generate some contemporary-compatible feedstock capable of replacing fossil fuels both as an energy source and as a raw material.

There are several potential reduction products that could meet the challenges of portability, energy density, and divergent synthesis – a photon-driven catalytic cycle could conceivably be tailored to function with any number of well-studied reductive pathways including metal salt to metal,¹⁴ water to hydrogen,¹⁵ and carbon dioxide to methanol.^{16–18} Despite the various potential fuel-producing reductive pathways, complementary oxidative half-reactions producing molecular oxygen are necessary. This simplifies reactant delivery by employing the atmosphere as an oxidant reservoir and conveyance. Water, due to its abundance and benignity, would be an ideal feedstock if not for the complex mechanism and high thermodynamic barrier for the oxidation reaction necessary to produce molecular oxygen.

The lynchpin of this scheme is the reversal of an exergonic reaction. Developing a process that reverts water, omnipresent as a product in combustion reactions, to its initial state as dioxygen represents a significant step towards the successful implementation of a fuel producing electrolysis or photocatalysis process. Several decades of research have been invested in the development of materials and techniques designed to improve the overall net efficiency of electrolysis. Two main goals of these efforts have been the development of materials with low oxidation overpotentials and high faradaic efficiency. Several materials with these criteria have been identified. Nickel, either in its elemental state or as mixed oxides (NiCo₂O₄); RuO₂; and IrO₂ have been demonstrated to possess very small oxidation overpotentials with excellent faradaic efficiencies.

While most commercially available electrolyzers employ nickel species due to cost and availability, it is important to remember the less abundant transition metals have equally favorable electro-catalytic properties and the potential for extremely interesting chemistry. Early reviews of anodic oxygen evolution by RuO_2 or IrO_2 rationalized this behavior with correlations

to O_2 exchange energies and heat of formation changes upon increasing the metal redox state in oxides.^{19,20} Second and third row transition metals, due to the breadth of their acceptable oxidation states, would then be natural candidates over first row metals for the oxidation of water. There are two primary reasons effecting their consideration: the increased number of redox states accessible to platinum group metals allows a diversity of reaction intermediates and the relative stability of high oxidation states facilitate oxidative transformations.

Since only a thin slice of atoms are active participants in chemical transformations at an electrode surface, ruthenium and iridium are not cost efficient as a bulk electrode material. However, reframing the metals as reactive coordination complexes in solution²¹ drastically improves atom economy and allows a nascent field to build on the well-founded successes of molecular orbital and ligand field theories. After the pioneering work on dinuclear ruthenium catalysts by Meyer^{22,23} and Grätzel^{24,25}, hundreds of innovative articles focused on the structure-activity relationships in these oxidation catalysts. Elucidating reaction mechanisms in these works has proved quite difficult due to the diverse intermediates exhibiting unusual metal redox states. To develop a greater understanding of these redox states as they are occurring during a water oxidation reaction, we turn to catalysis by molecular iridium(III) complexes since it isoelectronic with the more well-studied ruthenium(II) complexes. Though the field of iridium-catalyzed water oxidation is quite new in comparison to its more studied cousin, there have been several significant contributions that provide context.

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Chapter 2: Previous Iridium-based Water Oxidation Catalysts

Bernhard 2008

The first instance of mononuclear iridium complexes capable of oxidizing water to 2008^{1} bv the familv dioxygen in of complexes $[Ir(5-R_1,4'-R_2,2$ was seen phenylpyridine)₂(OH₂)₂]OTf. The catalytic cycle was driven with Ce(IV) as a chemical oxidant and the work explored the role of ligand modification on the catalysts' activity and lifetime (Figure 1). Initial TOF's varied from less than 4 h^{-1} to 16 h^{-1} by modifying ligand substituents while catalyst lifetimes were as high as 2760 TON. Electrochemical analysis uncovered a distinct structure-activity relationship demonstrating the strong involvement of the supporting ligand in the overall water oxidation mechanism. The highly tunable ligand field splitting observed in these 5d metal complexes proved to be an advantage over their Ru(II) cousins. This redox tuning was greatly aided by the diverse ligand environments possible with the Ir(III/IV/V) center. Consequently, the structural and electronic diversity of these catalysts influenced the catalytic activity greatly. Additionally, free-sites on the metal complex were critical as demonstrated by the absence of water oxidation from bipyridine substituted analogues and mixed-solvent systems where the added solvent is strongly ligating as in acetonitrile or dimethyl sulfoxide.

Figure 1:Top: Ligand substitution on $[Ir(ppy)_2(OH_2)_2]OTf$ framework produces a distinct structure-activity relationship with the rate of oxygen production. **Bottom:** Experiments and calculations show that substitution affecting the ligand-centered HOMO plays an important and predictable role in tuning the electrochemical behavior.



Crabtree 2009

Inferring that strongly donating ligands are required to stabilize the putative Ir(V) oxo species, Crabtree² was able to accelerate the rate of water oxidation an order of magnitude over the initial $[Ir(ppy)_2(OH_2)_2]OTf$ complexes by substituting a Cp* ligand for a phenylpyridine to give (Cp*)Ir(ppy)Cl (**Figure 2**). A continued proof of concept was afforded by a decreased rate of oxygen formation on exchanging phenylpyridine for the less-donating phenylpyrimidine, (Cp*)Ir(ppm)Cl. Chloride and triflate analogues of (Cp*)Ir(ppy)X were found to have identical rates of reaction³ suggesting fast counter ion exchange for solvent water with no effect on the rate limiting step. On the basis of a first-order reaction rate and DFT calculations the authors posit $[(Cp)Ir(O)(ppy)]^+$ as an intermediate leading to O-O bond formation from a solvent H₂O. The ppy-containing catalyst was fully recoverable, displayed reaction rates significantly in excess of the heterogeneous IrO₂, did not have an induction period, and did not form visible deposits or particulates. The authors excluded the formation of IrO₂ or other heterogeneous catalysts on the basis of the combined evidence. Cyclic voltammetry of the complexes in acetonitrile showed three and two irreversible oxidation waves respectively suggesting oxidation to OCl⁻ or Cl₂.



Figure 2: Initial rates for catalysts $(Cp^*)Ir(ppy)Cl$, $(Cp^*)Ir(pym)Cl$, and $[Ir(ppy)_2(OH_2)_2]OTf$ as measured by a Clark electrode using 38 nmol (5.43 μ M) of catalyst and 0.55 mmol (78 mM) of CAN in H₂O (7 mL) at 25°C.

Crabtree 2010

Crabtree further expanded the field of viable WOC's by incorporating $(Cp^*)Ir(N-C)X$, $[(Cp^*)Ir(N-N)X]X$, and [(Cp)Ir(N-N)X]X as catalyst precursors for homogeneous water oxidation (**Figure 3**).³ The N-N chelate ligands, in particular, offer an improvement as the cationic complexes are fully soluble in contrast to the previously studied (Cp*)Ir(ppy)X which was only soluble after oxidant addition. Clear first-order kinetics were observed for $(Cp^*)Ir(ppy)Cl$, $[(Cp^*)Ir(bpy)Cl]Cl$, and $[(Cp)Ir(bpy)I]NO_3$ with initial TOF of 10 min⁻¹, 14 min⁻¹

¹, and 9 min⁻¹, respectively. Rapid solvolysis is believed to occur due to limited long-lasting effects from the counter ion. Rational for the Cp moeity, as opposed to the Cp*-containing complexs, stems from the presence of potentially oxidizable methyl groups on the Cp* ligand. Overall, the Cp complexes showed decreased initial TOF compared to Cp* complexes at 5 μ M; however, the oxygen evolution traces of (Cp*)Ir(ppy)Cl show a decrease in the rate over the span of 1 minute while [(Cp)Ir(bpy)I]NO₃ shows no such decrease over the span of 10 minutes. At low catalyst loadings all three classes of iridium complexes exhibit an indistinguishable linear relationship between concentration and initial TOF. At higher catalyst loadings of 7-30 μ M [(Cp)Ir(bpy)I]NO₃ tends towards zero-order behavior suggesting a catalyst self-passivation deactivation pathway.



Figure 3: $(Cp^*)Ir(ppy)Cl$, $[(Cp^*)Ir(bpy)Cl]Cl$, and $[(Cp)Ir(bpy)I]PF_6$ precatalysts for homogenous water oxidation investigated by Crabtree and coworkers.

Electrochemical analysis of $[(Cp^*)Ir(bpy)Cl]Cl$ revealed the expected 63 mV/pH unit shift in oxidation potential when conducting pH dependent cyclic voltammograms. Further, repeated scans do not show a decrease on intensity expected of a stoichiometric oxidation of chloride. The rate dependence on Ce(IV) is reported without specifying the concentration of catalyst, but the results suggest a change in the rate determining step based on Ce(IV) concentration. A study of the H/D kinetic isotope effect revealed low concentrations of cerium, 8 mM, led to an inverse KIE of 0.65 while at higher concentrations, 243 mM, a KIE of 1.2 was observed. The authors draw contrast to the behavior of IrO₂ nanoparticles which has a KIE of 1.6 at 8 mM cerium and,

at 243 mM, does not catalytically produce oxygen beyond a brief burst. A plausible series of intermediates leading to O-O bond formation was explored via DFT calculations involving hydrogen bonding between a substrate and solvent water molecule. In addition to the aforementioned (Cp*)Ir(N-C)X, [(Cp*)Ir(N-N)X]X, and [(Cp)Ir(N-N)X]X complexes, Crabtree examined several other catalyst precursors. [(Cp*)Ir(tmeda)Cl]Cl (tmeda, tetramethylethylenediamine), [(Cp*)Ir(OH₂)₃]SO₄ and the dimer [{(Cp*)Ir}₂(μ -OH)₃]OH exhibit non-first order reaction rates with similarities in kinetic studies suggesting the tmeda is quickly lost to form the [(Cp*)Ir(OH₂)₃]ⁿ⁺ complex which goes on to form a monomer-dimer equilibrium affecting the rate of catalysis.

Macchioni 2010

Macchioni reports the synthesis of a complex using 2-benzoyl pyridine, $(Cp^*)Ir(bzpy)NO_3$, in an effort to improve water solubility.⁴ The authors continue with a comparison of activity between $(Cp^*)Ir(ppy)Cl$ and $[(Cp^*)Ir(OH_2)_3](NO_3)_2$, exploring the potential for loss of the chelating ligand in both complexes may be a primary degradation pathway (**Figure 4**). Using cerium consumption as a basis, turnover frequencies of 8.5 min⁻¹, 4.7 min⁻¹, and 15.7 min⁻¹ were observed by spectrophotometric means and first order rate constants were calculated of $0.14s^{-1}$, $0.08 s^{-1}$, and $0.26 s^{-1}$ respectively.



Figure 4: $(Cp^*)Ir(ppy)Cl$, $(Cp^*)Ir(bzpy)NO_3$, $[(Cp^*)Ir(OH_2)_3](NO_3)_2$ and investigated by Macchioni yielding evidence of Cp^* degradation.

Albrecht and Bernhard 2010

The next development came when Albrecht et al.⁵ explored the potential for abnormal Nheterocyclic carbene chelating ligands to stabilize the large changes in metal oxidation state required for mononuclear water oxidation. Two new Cp* iridium carbene-containing complexes were synthesized (**Figure 5**) differing by attachment of the chelating methyl pyridine. Initial TOF were similar to $[Ir(ppy)_2(OH_2)_2]OTf$ but greatly accelerated following an induction period. TOF at 1000 seconds was 5.2 min⁻¹ and 2.5 min⁻¹ while maximum TON was 10,000 and 8,350 for the ring-chelated and N-methyl-chelated complexes respectively. Several oxidation waves were observed between +0.7V and +1.0V ascribed to non-innocent ligand behavior and serve as one potential reason for the extreme catalyst lifetimes. The TON reported in this paper correspond to 1.2L of O₂ per mg of iridium, a significant step forward for the goal of producing a water oxidation catalyst capable of positively impacting the global demand for energy.



Figure 5: (Cp*)Ir triazole carbene complexes investigated by Bernhard and coworkers.

Hetterscheid and Reek 2011

Borrowing inspiration from the binuclear ruthenium complexes pioneered by Meyer in the 80's Hetterscheid and Reek⁶ developed an asymmetric binuclear iridium complex bridged by a bispyridyl imine (**Figure 6, Left**). The bispyridyl imine moiety adds an interesting resonance contribution where the imine π -coordination leads to a 2 e⁻ oxidation state ambiguity in the

associated iridium. The reaction was found to be first-order in precatalyst and in cerium with a combined second-order rate constant of 4.7 M^{-1} s⁻¹ and a TOF of 57 min⁻¹. The authors do not speculate into the mechanism or the potential involvement of the second iridium beyond comparison to a similar, mononuclear catalyst using 2-pyridinal-1-ethylimine as a ligand with an order of magnitude less activity.



Figure 6: Hetterscheid & Reek's dimer and monomer.

In a separate publication⁷ they also report the synthesis and characterization of $(Cp^*)Ir(NHC-Me_2)Cl_2$ and $(Cp^*)Ir(NHC-Me_2)(OH)_2$ (NHC = 1,3-dimethylimidazolium-2ylidene) as capable water oxidation catalysts when driven by Ce(IV) (**Figure 6, Right**). Interestingly, the dihydroxy complex has a TOF of 90 min⁻¹; approximately three times faster than the dichloro complex with an order of magnitude greater lifetime at >2000 TON. The dihydroxy complex was also found to rapidly disproportionate hydrogen peroxide suggesting potential mechanisms incorporating a peroxo intermediate. Importantly, preactivation was not required suggesting the dihydroxy or di-aqua complex is the active catalytic species. Increasingly reversible cyclic voltammograms with faster scan rates suggest a quick chemical reaction occurs just after oxidation with voltammograms broadening significantly in the presence of small amounts of water. No electrode deposition occurred in contrast to $[(Cp^*)Ir(OH_2)_3]SO_4$ and $[{(Cp^*)Ir}_2(\mu-OH)_3]OH$ as observed by Crabtree and others. Electrospray mass spectrometry of catalytically active solutions indicates the presence of several species distinctly different from the parent molecule potentially corresponding to various stages of a proposed catalytic cycle involving Ir-OOH or Ir-OOCe moieties.

Crabtree 2011

Continued work by Crabtree⁸ saw the synthesis and characterization as a competent precatalyst of (Cp*)Ir(NHC)Cl (NHC = $\kappa^2 C^2$, $C^{2'}$ -1,3-diphenylimidazol-2-ylidene). Both cerium(IV) ammonium nitrate and sodium periodate were evaluated as chemical oxidants. When driven by cerium, Clark electrode measurements indicated a slight consumption of oxygen followed by the expected oxygen production. The authors attribute this to the oxidation of Cl⁻ to OCl⁻ or other oxyanions under the harsh conditions of aqueous Ce(IV). In contrast, oxidation by periodate at pH 5 shows no consumption prior to activity. Rate experiments give TOF of 8 min⁻¹ and 12-16 min⁻¹ with reaction orders of 1.85 and 0.67 when driven by cerium and periodate exposure to the harsh conditions imposed by cerium may lead to loss of the NHC moiety. Despite the milder conditions afforded by periodate, higher oxidant loadings led to deactivation albeit with well-behaved oxygen traces and shorter lag phases than with cerium. The reaction order of 0.67 suggests the presence of complicated kinetics in part due to periodate's potential to serve as a one- or two-electron oxidant.



Figure 7: Solid line: EPR spectra of $(Cp^*)Ir(\kappa^2C^2, C^{2'}-1, 3-$ diphenylimidazol-2-ylidene)Cl oxidized by 0.75 equiv of $[Ru^{III}(bpy)_3]^{3+}$; Dashed line: $[Ru^{III}(bpy)_3]^{3+}$ as a control.

A comparison of cyclic voltammograms of (Cp*)Ir(NHC)Cl with (Cp*)Ir(ppy)Cl in acetonitrile reveals the carbene's stabilizing effect; the CV of the NHC-containing complex shows both a lower Ir(III/IV) couple and a reversible inner-sphere chloride oxidation wave not present in the ppy-containing complex. Changing the solvent to a 50/50 water/acetonitrile mix clearly indicates water quickly replaces the inner-sphere chloride. Neither the NHC-containing catalyst nor the ppy-containing catalyst degraded after repeated cycling nor did the electrode activity differ from baseline activity when placed in a blank solution in contrast to Crabtree's work involving the anodic deposition of $[(Cp*)Ir(OH_2)_3]SO_4$. The stabilizing effect of the NHC was used to good effect enabling observation of an Ir(IV) species via EPR spectroscopy. $[Ru(bpy)_3]^{3+}$ was used as an oxidant in a 1:1 acetonitrile/toluene glass to give the first-observed rhombic spectra from a (Cp*)Ir species with $g_x = 2.53$, $g_y = 2.17$, and $g_z = 1.85$ (**Figure 7**). The Ir(IV) NHC species was found to be stable on a minute time scale under an inert atmosphere but became EPR silent after 30 minutes. Similar attempts using room temperature ¹H NMR and paramagnetic ¹H obtained at -35°C were unsuccessful at observing resolved spectra.

Crabtree⁹ later compared the behavior of the previously studied $[(Cp^*)Ir(H_2O)_3]^{2+}$ with a new water soluble (Cp*)Ir catalyst chelated with 2-(2'-pyridyl)-2-propanol, (Cp*)Ir(pyr-CMe₂O)X (X = CI', OTf) when studied using an electrochemical quartz nano-balance, rotating ring-disk electrode electrochemistry, and Clark-type oxygen electrode experiments to probe the electrodeposition of metal oxides from molecular precursors. The work was able to observe the deposition of the $[(Cp^*)Ir(H_2O)_3]SO_4$ species in real time on the electrode surface in contrast to (Cp*)Ir(pyr-CMe₂O)X, which produced no change in mass for linear potential sweeps between 0.2 and 1.5 V at 2.5-3 mM in complex (**Figure 8**). A single voltage-dependent ring current was observed in RRDE experiments using this electrochemically stable complex. The ring current was ascribed to dioxygen reduction and not peroxide reduction on the basis of pH independence and further confirmed by measurements with a Clark-type electrode.



Figure 8: Comparison of current and mass responses of solutions containing complexes $[(Cp^*)Ir(OH_2)_3]SO_4$ (left panels) or $(Cp^*)Ir(pyr-CMe_2O)OTf$ (right panels) as a function of time. **Upper panels:** gray solid lines represent applied potential; black solid lines represent current response of $[(Cp^*)Ir(OH_2)_3]SO_4$ (left) and $(Cp^*)Ir(pyr-CMe_2O)OTf$ (right) recorded by the potentiostat. Dashed lines are background current. **Lower panels:** solid lines represent mass response in each experiment, while dashed lines are the corresponding catalyst-free backgrounds. Conditions: 0.1 M KNO3 in air-saturated deionized water; 3 mM $[(Cp^*)Ir(OH_2)_3]SO_4$; ca. 2.5 mM (Cp*)Ir-(pyr-CMe_2O)OTf. Scan rate: 50 mV/s.

Lin 2011

An interesting adaptation was explored by Lin and coworkers¹⁰ where three bis-carboxy phenylpyridine (bcppy) analogues of previously studied homogeneous catalysts, $(Cp^*)Ir(bcppy)Cl$, $[(Cp^*)Ir(bcpy)Cl]Cl$, and $[Ir(bcppy)_2(H_2O)_2]Cl$, were doped inside highly stable, porous metal-organic frameworks (**Figure 9**). Using Ce(IV) as a chemical oxidant, TOFs of 4.8 h⁻¹, 1.9 h⁻¹, and 0.4 h⁻¹ were observed in the MOF-supported catalysts as compared to 37 h⁻¹
¹, 15.7 h⁻¹ and 5.6 h⁻¹ in the unsupported catalysts. The decrease in activity was explained by sizeexclusion; the cerium nitrate anions are ~11.3 Å while the MOF channels are ~6.7 Å as determined by nitrogen isotherms. Surface poisoning with triphenylphosphine was found to completely inactivate the catalyst-doped MOFs as well as the unsupported WOCs. In long term experiments, the catalyst-containing MOFs were added to 4000 equivalents of Ce(IV) yielding complete consumption of Ce(IV) over the course of weeks. The MOFs were then recaptured via centrifugation and reused with no loss of catalytic activity. In contrast, MOFs synthesized with IrO₂ were not reuseable and did not support catalytic activity beyond 30 minutes.



Figure 9 Left: Structural model of UiO-67 framework doped with (Cp*)Ir(ppy)Cl analogues. **Right:** SEM micrograph showing intergrown nanocrystals of the doped MOF.

Macchioni 2011

In 2011 Macchioni performed a more in depth analysis of catalyst activity and degradation pathways for $(Cp^*)Ir(bzpy)NO_3$, $[(Cp^*)Ir(bpy)Cl]Cl$, and the heterogeneous precursor $[(Cp^*)Ir(OH_2)_3](NO_3)_2$ (**Figure 10**).¹¹ This was accomplished by comparing UV-Vis measurements of Ce(IV) decay, oxygen measurements by Clark electrodes, and volumetric observations of all three complexes across 0.5-10 µM in precatalyst and 1-28 mM in Ce(IV). By monitoring the ¹H NMR spectra following addition of 0-300 equivalents Ce(IV) to 100-130 µM solutions of these three complexes, Macchioni and coworkers were able to observe the formation

of acetic and formic acid along with the concurrent decay of the initial catalyst signal in all three complexes. A series of 1D- and 2D-NMR experiments following addition of 6, 10 and 12 molar equivalents of Ce(IV) to 30 mM solutions of (Cp*)Ir(bzpy)NO₃ and [(Cp*)Ir(OH₂)₃](NO₃)₂ at pH 1 by HNO₃ in 1:3 CD₃CN/D₂O and neat D₂O respectively identified two different intermediates to decomposition products of the two catalysts.



Figure 10: Schematic depiction of two (Cp*)Ir(bzpy)NO₃ intermediates proposed by Macchioni and coworkers in their investigation of Cp* degradation.

Ce(IV) consumption was found to be first order for $[(Cp^*)Ir(bpy)CI]Cl$ and zeroth order for $(Cp^*)Ir(bzpy)NO_3$ and $[(Cp^*)Ir(OH_2)_3](NO_3)_2$ for 1 mM Ce(IV) across 0.5-10 μ M catalyst, while catalyst reaction orders were 1, 1, and 1.5 respectively. Sequential addition of cerium aliquots to catalyst solutions found both $(Cp^*)Ir(bzpy)NO_3$ and $[(Cp^*)Ir(bpy)CI]Cl$ decreased in activity by 20% between additions regardless of delay between additions while $[(Cp^*)Ir(OH_2)_3](NO_3)_2$ decayed only when there was a delay between additions. A second body of work by Macchioni and coworkers describes the oxidative degradation of $[(Cp^*)Ir(OH_2)_3](NO_3)_2$ and $(Cp^*)Ir(bzpy)NO_3$ by hydrogen peroxide in acidic media and characterized several degradation products similar to the previously identified species. NMR analysis required much higher catalyst concentrations of 20-30 mM which was oxidized with successive aliquots of 9.8M H₂O₂. ¹H NMR spectra were recorded over 20 minute intervals and

clearly indicate the susceptibility of quarternary carbon atoms of the Cp* moiety to oxidative attack at these conditions.

Grotjahn 2011

Later in 2011, Grotjahn and coworkers illustrate a few issues incipient to the use of iridium and cerium in the study of catalyzed water oxidation.¹² They report the presence of iridium-cerium nanoparticles as observed by STEM and EDX after evaporating a 1.35 mM acetonitrile/water solution of (Cp*)Ir(ppy)Cl treated with 78 mM Ce(IV). Attempts to separate the cerium and iridium materials via dialysis and ultracentrifugation were not described beyond being unsuccessful. They next turned to powder x-ray diffraction studies of lyophilized aliquots withdrawn at regular intervals from a 0.46 mM solution of (Cp*)Ir(ppy)Cl in 85:15 v/v acetonitrile/water following treatment with Ce(IV) at 8 mM active concentration (18:1 Ce(IV) to catalyst). These studies did not clearly indicate the presence of iridium oxide with low treatments of Ce(IV) however treatment with 78 mM Ce(IV) (176:1 Ce(IV) to catalyst) more noticeable, though still quite small, bands associated with iridium oxide are apparent. A large portion of this work attempts to relate the UV-visible spectra of the investigated compounds and the development of absorbance peaks centered between 550-650 nm with similar bands observed in IrO₂ and IrO_x nanoparticles; however, they conducted no *in situ* analysis that positively or negatively indicates the presence of nanoparticles. As with Macchioni, they report the presence of formic acid and acetic acid following the addition of 15 equivalents of Ce(IV) which may indicate the loss of the Cp* moiety, but does not conclusively indicate nanoparticle formation. Unfortunately, the role of co-solvent acetonitrile on the reaction mechanism were not explored or assessed in the presented manuscript.

Fukuzumi 2011

Rounding out 2011, Fukuzumi conducts a structure activity relationship study of substituted $[(Cp^*)Ir(4,4'-R_2-bpy)(OH_2)]SO_4$ complexes (R = OH, OMe, Me and COOH).¹³ After adding Ir-containing complexes at 5 µM active concentration to a 10 mM solution of Ce(IV), the authors observed accelerating rates of catalytic activity for R = OH but not for R = OMe, Me, or COOH. ¹H NMR experiments on a 5 mM solution of the 4,4'-(OH)₂-bpy complex reveal a decrease in signal intensity from the bpy ligand without signal broadening that is proportional to the quantity of cerium added (0-10 mol eq. Ce(IV)). Dynamic light scattering measurements on a 50 µM solution 4,4'-(OH)₂-bpy complex following addition of 10 mM CAN indicate the formation of particles with an average size of 348 nm distributed over 180-1000 nm. Increasing the complex concentration either to 250 or 500 µM causes an increase in the average particle size to 600 nm distributed over 300-1100 nm. Experiments were performed employing simultaneous solution UV-vis and GC headspace analysis which allowed the researchers to observe carbon dioxide production and cerium consumption for three of the catalysts. The catalyst with 4,4'-(COOH)₂-bpy was not evaluated due to poor aqueous solubility. All three catalysts produced CO_2 to varying degrees with 4,4'-(OH)₂-bpy producing significantly more than by 4,4'-(OMe)₂bpy or 4.4'-Me₂-bpy. The onset of CO₂ production was instantaneous for 4.4'-(OH)₂-bpy which rapidly with correlating decrease in Ce(IV) produced CO_2 a concentration. Thermogravimetric/Differential thermal analysis (TG/DTA) and X-ray photoelectron spectroscopy (XPS) of the nanoparticles obtained from oxidation of a 2 mM solution of the 4,4'-(OH)₂-bpy complex indicate a structure comprised of Ir(OH)₃ and carbonaceous residues.

Lin 2012

Following investigations of MOF-supported molecular catalysts, Lin and coworkers investigated the properties of molecular catalysts covalently bound to carbon electrodes as diazonium-grafted analogues of $[(Cp^*)Ir(5-NH_2-bpy)Cl]Cl$, $[(Cp^*)Ir(4-NH_2-bpy)Cl]Cl$, and $(Cp^*)Ir(5-NH_2-ppy)Cl$ (**Figure 11**).¹⁴ The orientation of the grafting site appears to significantly affect surface coverage at 2.18, 0.55, and 0.26 molecules/nm², respectively. This was ascribed to solubility issues and ambiguity in the reduction potential necessary to initiate grafting. Initial TOF's at pH 5 in acetate buffer was found to be 1.67, 0.59, and 3.31 s⁻¹ respectively, as measured by cyclic voltammetry.



Figure 11: Diazonium grafted (Cp*)Ir(ppy)Cl analogue for electrode driven water oxidation.

Electrolysis using a $[(Cp^*)Ir(5-NH_2-bpy)Cl]Cl$ grafted electrode at 1.6 V yielded sustained TOF's of 0.113-0.178 s⁻¹ over one hour and in good agreement with cerium-drive TOF reported in 2010.³ The grafted complex completes exhibited 400-650 TON over 1 hour as compared to 150 total TON after 7.5 h for a 25 μ M solution of $[(Cp^*)Ir(5-NH_2-bpy)Cl]Cl$ with 50 mM CAN at pH 1 in 0.1 N HNO₃. Electrode-derived TOF were difficult to determine beyond 1 h due to surface degradation in both the background and grafted carbon electrodes. Phosphorescent oxygen sensor measurements of the solutions surrounding the background and grafted carbon electrode confirmed the absence and presence of oxygen respectively. Additionally, the binding energy of the Ir $4f_{7/2}$ and $4f_{5/2}$ energy levels in the grafted complex do not change over 900 minutes of continuous electrolysis beyond decreasing in intensity as a result of surface degradation. The limiting factor in carbon-grafted electrolysis appears to be carbon oxidation with subsequent loss of grafted catalyst.

Crabtree 2012

In 2011¹⁵ and 2012^{16,17} Crabtree gathered evidence suggesting sodium periodate serves as a suitable primary oxidant for catalysts with low kinetic barriers by examining its efficacy versus a variety of complexes. Specifically, [(Cp*)Ir(bpy)(OH₂)]SO₄, [(Cp*)Ir(OH₂)₃]SO₄, and (Cp*)Ir(pyr-CMe₂O)Cl were found effective as precatalysts for oxygen production using periodate. The rate of oxygen evolution was found to be first order in periodate from 2.5 to 20 mM at 0.5 mM catalyst, which is consistent with a rate determining step dictated either by oxidation of the catalyst or by reaction of free periodate with a periodate-catalyst oligomer. First order dependence would manifest at low concentrations of periodate with the former mechanism and at high concentrations of periodate with the latter; however, the authors describe how limited reactivity and solubility combined with the ineffectiveness of isotope labeling prevent an unambiguous depiction of the rate determining step. Due to fast oxygen exchange between water and periodate it is not possible to exclude periodate as a source of oxygen. The use of periodate is additionally complicated by its role as either a one- or two-electron oxidant and by the potential for the resulting iodate to serve as a ligand or as a weakly oxidizing species. Despite these complications, the authors show periodate has the potential to provide significant insight into pH-dependent catalyst behavior as well as enables a broader window for UV-vis

measurements of catalytic intermediates. Results from periodate studies should therefore be analyzed in conjunction with experiments employing other oxidizing conditions.

The complex $[(Cp*)Ir(bpy)(OH_2)]SO_4$ was shown to be significantly more resistant to periodate than cerium as carbon dioxide is observed during reactions employing the latter but not the former. Dynamic light scattering measurements and ethanol-reduction tests indicate the absence of iridium dioxide nanoparticles in contrast to reactions performed with IrCl₃ and with $[(Cp*)Ir(OH_2)_3]SO_4$. NMR spectra of recovered $[(Cp*)Ir(bpy)(OH_2)]SO_4$ following addition of 100 equivalents of periodate indicate partial oxidation has occurred with three distinct Cp* methyl peaks and broad, shifted bpy peaks. Further, IR spectra indicate the formation of a carbonyl resonance that the authors ascribe to a carboxylic acid in the absence of an aldehyde signal from NMR. While the reaction of $[(Cp*)Ir(bpy)(OH_2)]SO_4$ exhibits an induction period, reactions with (Cp*)Ir(pyr-CMe₂O)Cl have no measurable induction period and proceed 2 orders of magnitude faster than with $[(Cp*)Ir(bpy)(OH_2)]SO_4$ (TOF of 0.042 and 2.2 s⁻¹ respectively). The authors attribute the rate increase due to the non-innocent involvement of the deprotonated alkoxy group in close proximity.

Conclusively ascribing the predominant reaction responsible for water oxidation to a molecular species is a nearly intractable problem clouded by the fitness of various iridium oxide species for water oxidation. Despite this, further work by Crabtree¹⁷ effectively illustrates the import role reaction conditions play on the formation of nanoparticles relevant to the oxidation of water by iridium precursors. It also conclusively shows that absorbance at 580 nm is more likely the result of various Ir(IV) species rather than nanoparticle formation through the use of *in situ* time-resolved dynamic light scattering. DLS measurements of $[{(Cp*)Ir}_2(\mu-OH)_3]OH$, $[(Cp*)Ir(bpy)(OH)]BF_4$, (Cp*)Ir(ppy)OH, and $(Cp*)Ir(pyr-CMe_2O)OH$ following oxidation with

sodium periodate in water underline these differences. In contrast to the other mentioned catalysts, $[{(Cp^*)Ir}_2(\mu-OH)_3]OH$ readily forms nanoparticles effected by buffers, ions, and large quantities of oxidant. At 2.5 mM, each catalyst was oxidized with 100-200 equivalents of sodium periodate and developed UV-vis absorption peaks centered on 580-610 but only $[{(Cp^*)Ir}_2(\mu-OH)_3]OH$ produced a recoverable precipitate.

The blue-black precipitate recovered from solutions of $[{(Cp^*)Ir}_2(\mu-OH)_3]OH$ was initially amorphous but converted to tetragonal IrO₂ on calcination. Importantly, both the supernatant and the recovered nanoparticles were shown to be competent oxidation catalysts. A key finding in this work was the reappearance of a deep blue color and the absence of scattering upon addition of concentrated HCl to a colorless suspension of the recovered nanoparticles. A rutile dimeric structure was proposed as a catalytically relevant intermediate. These changes are in contrast to anhydrous IrO₂, Crabtree's blue-layer, IrO_x nanoparticles, and bulk IrO₂ catalysts: all of which do not dissolve in concentrated HCl and do not produce a color change. The blue solution so-obtained could be reduced with ethanol or sulfite to particle-free bright yellow solutions. No particles were observed when only 50 equivalents of periodate was added to neat aqueous $[{(Cp^*)Ir}_2(\mu-OH)_3]OH$ solutions. The addition of either NaNO₃ or NaCl was found to increase both the rate and extent of particle formation. Furthermore, catalyst concentration plays a significant role on the kinetics of particle formation. Light scattering intensity was nonexistent over the course of 18 hours following addition of 100 equiv. NaIO₄ to 0.6 mM neat aqueous $[{(Cp^*)Ir}_2(\mu-OH)_3]OH$ solutions. Doubling the catalyst concentration to 1.2 mM caused scattering intensity to increase sigmoidally following a brief induction period. Doubling the catalyst concentration again drastically increased scattering intensity and completely eliminated the induction period.

Beller 2012

Beller and coworkers examined the activity of several Ir-phenylazole complexes as chloro-bridged dimers and Cp* or di-ppy containing monomers and compared that activity with those of $Ir(acac)_3$, $IrCl_3 \cdot xH_2O$, and IrO_2 .¹⁸ Through the use of x-ray absorption spectroscopy techniques, XANES and EXAFS, the authors were able to estimate the fraction of Ir(IV) to Ir(III) both of the precatalysts and of in situ oxidation reactions. On the basis of the initial catalytic activity observed with the various catalysts examined in conjunction with investigations involving nanopore-supported IrO₂, Beller outlines a general kinetic model with interconversion between five species, three of which are active water oxidation catalysts (Figure 12). An initial induction period separates the molecularly defined precatalyst from the active homogeneous catalyst, which then converts either to nanoparticles in the 1-3 nm range or to an inactive iridium species. Increased nanoparticle loadings cause agglomeration to bulky, active heterogeneous species that could also decay to an inactive iridium species. Expanding on this concept, Beller and coworkers conject relative rates of activity could be used to identify the predominant active species as a reaction mixture progresses. More quantitatively however, *in situ* reaction particlesizing coupled with observations of degradation products should be used to identify the speciation of reactive intermediates. The general kinetic scheme described in this work, when linked with the dynamic light scattering results presented by Crabtree, offers a potentially unifying concept that could explain the reports of varied activity and array of statements proscribing homogeneous/heterogeneous mechanisms.



Figure 12: Proposed general kinetic scheme describing the transformation of molecularly-defined Ir(III) precursors to active catalytic species with interconversion between inactive Ir species.

Lin 2012

Late in 2012 Lin and coworkers incorporated analogues of [(Cp*)Ir(bpy)Cl]Cl and (Cp*)Ir(ppy)Cl as structural components in metal organic frameworks and investigated their kinetics in cerium-driven water oxidation reactions (**Figure 13**).¹⁹ This approach offers two benefits over a completely homogeneous approach: intermolecular degradation pathways are minimized due to the rigid linking groups and the heterogeneous MOFs are easily separated from solutions for post-reaction characterization. Time dependent measurements of cerium consumption and detected oxygen were in good agreement for the bpy-containing catalyst and did not vary significantly between runs where the catalyst was recovered and reused. Negligible quantities of iridium were detected in the supernatant with 3 mM Ce(IV), but supernatant leaching significantly increased at 10 mM Ce(IV) and above. In contrast, the ppy-containing catalyst was found to be much more prone to decay with 6% of iridium leaching into the supernatant following treatment by 3 mM Ce(IV). The initial rate of cerium consumption is an order of magnitude greater than measured oxygen production suggesting significant oxidative

transformations occur. These transformations increase TOFs for the second and third run by a factor of five over the first run.

Samples of the bpy-containing MOF were analyzed following prolonged treatment with cerium and indicate loss of the Cp* fragment with replacement by either a formate or acetate ligand. Furthermore, the absence of an induction period seems to suggest similar levels of catalytic activity at both the Cp* containing sites and the oxidatively-degraded sites. These results motivated the synthesis and investigation of K[Ir(bpy)Cl₄], which was found *not* to be active. In contrast, the mixture of species present following chloride abstraction was highly active with initial TOF of 2.5 min⁻¹ at 25 μ M catalyst and 10 mM Ce(IV) at pH 1. Reactions longer than an hour yielded a decrease in activity along with formation of dark-blue solids suggesting intermolecular deactivation pathways serve a limiting role on catalyst lifetimes. Further instances of catalyst deactivation are afforded by cerium concentrations higher than 3 mM which degrades catalyst-containing MOFs, but not an analogous UiO²⁰ MOF lacking catalytic sites. In any event MOF-supported catalysis appears to be a valuable investigative technique for molecular species.



Figure 13: Scheme depicting oxidative modifications of Cp^* moiety in MOF-supported precatalyst with subsequent ceriumdriven water oxidation employing a putative Ir(V) oxo species.

Lloblet and Macchioni 2012

Llobet and Macchioni²¹ synthesized several highly active Cp* Ir complexes based on a pyridinecarboxylate framework. The activity of (Cp*)Ir κ^2 -N,O 2-pyridinecarboxylic acid and analogues functionalized with uncoordinated carboxyl groups at positions 4 or 6 was compared to the previously studied (Cp*)Ir(ppy)Cl and (Cp*)Ir(bzpy)NO₃. Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) experiments revealed several interesting redox properties suggesting the ligand is an active participant in the catalytic scheme. The reaction order of all three new compounds was found to be very close to one with catalyst concentrations ranging from 0.5-5.0 µM at 1 mM Ce(IV). Long-term turnover frequencies derived from these kinetic experiments ranged from 2.6-5 min⁻¹. In contrast, initial TOF values were significantly higher than long-term activity and differed strongly between (Cp*)Ir(κ^2 -N,O 2-carboxypyridine)NO₃, (Cp*)Ir(bzpy)NO₃, and (Cp*)Ir(ppy)Cl at 70 min⁻¹, 31 min⁻¹, and 15 min⁻¹, respectively (Figure 14). Lloblet and Macchioni noted significant effects due to experimental conditions and suggest a means to counter the observed variance. While different experimental conditions produced appreciable differences in catalyst activity, the ratio of catalyst activities was extremely consistent from reaction to reaction.



Figure 14: Evolved oxygen from 20 mM solutions of CAN (pH 1 by HNO₃) containing $(Cp^*)Ir(\kappa 2-N,O 2-carboxypyridine)NO_3$, $(Cp^*)Ir(bzpy)NO_3$, and $(Cp^*)Ir(ppy)Cl$ at 1 μ M.

Ison 2013

Diverging slightly from the theme of water oxidation catalysts is a topical analysis of H/D exchange by Cp*Ir^{III} catalysts conducted by Lehman et al. in 2013 (**Figure 15**).²² The researchers studied the exchange of hydrogen and deuterium in benzene catalyzed by a variety of catalysts that have also have been found active toward water oxidation. They also investigated the effects of differing solvents and additives on the H/D exchange. The salient discoveries from this work with regards to water oxidation are threefold: 1) polar/apolar solvent effects on H/D exchange are drastic, 2) electron-donating ligands promote the formation of iridium hydride complexes, and 3) poorly-donating ligands can support efficient exchange if the deuterium source is strongly acidic. Similar behavior was observed in a variety of studies on water oxidation and, in conjunction, these three points suggest a hydride-iridium species as a possible intermediate in water oxidation catalysis.



Figure 15: Catalysts employed in H/D exchange study.

Brudvig and Crabtree 2013

In 2013 Brudvig and Crabtree²³ attempted to address a lingering question applicable to any single-site water oxidation catalyst: whether the intimate mechanism of the rate-determining oxo-coupling step occurs through a bimolecular radical oxyl-coupling mechanism or through the nucleophilic attack of water on a high-valent iridium-oxo species. In related ruthenium-catalyzed water oxidation reactions both mechanisms are feasible. To investigate the different mechanisms the researchers synthesized monomeric and dimeric Cp*Ir^{III} complexes featuring chelating (bis)pyridine-pyrazolide ligands (**Figure 16**) with the pyrazole moiety ensured facially-selective complexation of the Cp*Ir^{III}. Water oxidation was accomplished with the aid of sodium periodate as a sacrificial oxidant with the important caveat that water may not be the source of oxygen due to periodate dismutation i.e. $2 \operatorname{IO}_4^- \rightarrow 2 \operatorname{IO}_3^- + \operatorname{O}_2$.



Figure 16: Monodentate and bidentate mononuclear and dinuclear iridium complexes investigated by Crabtree and Brudvig probing the intimate mechanism of O-O bond formation.

Differentiating the two mechanisms is important because nucleophilic attacks would require a higher overall oxidation state and consequently react more slowly than a radical oxocoupling mechanism. Dynamic light scattering measurements of non-chelating monomers and flexibly linked monomers and dimers indicated the formation of particles of approximately 200 and 400 nm after two hours in contrast to the more robust rigidly-linked chelating pyridinepyrazole complexes (2.5 mM [Ir] with 250 mM NaIO₄). There were no discernable differences in electrochemistry and first order rate constants of the monomer and dimer were found to be 4.77 \pm 0.12 min⁻¹ and 0.83 \pm 0.06 min⁻¹ respectively on a per metal bases. These experiments in conjunction with the non-formation of a stable peroxo Ir^{III}-Ir^{III} species following the addition of sodium peroxide strongly point to a nucleophilic attack by solvent water as the critical O-O bond forming step in contrast to related ruthenium and cobalt-based systems.

Crabtree 2013, Lin 2013

Building on the previous body of research by Macchioni, Fukuzumi, and Beller in late 2013 Crabtree²⁴ enlisted the expertise of Richard Zare to examine the speciation of Cp*Ir^{III}

complexes milliseconds to seconds after oxidation with sodium periodate using an online flow reactor and desorption electrospray ionization mass spectrometry. The complexes in this work are the same investigated by Crabtree in 2012 with the addition of a 1,4-cyclooctadiene homologue of Cp*Ir(pyr-CMe₂O)OH. A key finding of this work was the rapid oxidation of the Cp* moiety as expressed in the proposed mechanism of **Figure 17**. The Cp* and cod ligands of these complexes were found to be the weak links and the supporting chelate ligand was not found to be oxyfunctionalized. Interestingly, numerous different oxidation pathways were observed to simultaneously occur with differing intermediates but all eventually yielding a single major product which high-resolution and fragmentation mass spectra confirms correspond to the previously proposed rutile dimer¹⁷ suggesting the Cp* and cod ligands serve as sacrificial placeholder ligands for the formation of the active dimeric catalyst.

These sentiments were echoed in later studies by Crabtree into the domain structure of the electrodeposited "blue layer"²⁵ and a study by Lin and coworkers²⁶ where Cp*Ir(bpy) complexes with varied 4,4' and 6,6' substitution patterns were synthesized and analyzed for electrochemical and sacrificial water oxidation. Lin's work performed electrochemical water oxidation at pH 1 on these complexes illiciting the deposition of a blue film at the electrode surface which, when analyzed by XPS, confirms retention of the chelating bpy ligand. Analyzing these two works in conjunction is highly suggestive of a common species differing only by the chelating ligands. Though Lin does not conduct TEM, XPS measurements by Lin provide further evidence against the formation of IrO_x or Ir(OH)_x species as no oxygen was observed by fluorescence sensors or rotating ring-disk electrode voltammetry. While [Ru(bpy)3]³⁺ possessed insufficient driving force to initiate water oxidation, it was able to slowly oxidize the complexes

suggesting a potential investigative tool toward synthesizing the putative dimeric rutile species in later works.



Figure 17: Oxidative scheme of Cp* moiety uncovered by Crabtree and Zane.

Macchioni 2013

A comprehensive study by Macchioni and coworkers further characterizes the common intermediates arising from precatalyst oxidation through the use of NMR and ESI spectroscopies. As in the work by Crabtree, this work accomplished the difficult task of intercepting different intermediates in the process of catalytic activation, this time with sufficient temporal resolution to produce kinetic traces of the iridium-containing intermediates and accompanying aliphatic and oxidized secondary products.

A good portion of the work by Macchioni and coworkers is the structural elucidation of the various intermediates concurrently existing as a complex reaction mixture through the use of HMBC NMR. Additional support for their proposed structures was afforded through crystal structures of the more stable intermediates and ESI spectra with structural hypothesis for the less-stable. This work strongly supports the noninnocence of the Cp* moiety in the oxidative transformation of the explored complexes into active catalysts through an Cp*- η^3 intermediate following epoxide formation at the sp² carbons. The proposed mechanism ring-opens, leading to the formation of acetate which subsequently decays into acetic acid as has been observed in numerous previous works by several authors (**Figure 18**).



Figure 18: Oxidative transformation scheme proposed by Macchioni and coworkers.

Hetterscheid, Reek, and Koper 2013

In 2013 Hetterscheid and Reek built upon their previous analysis by incorporating the expertise of Marc Koper to study Cp*Ir complexes using electrochemistry, spectroelectrochemistry, surface enhanced Raman spectroscopy, and online electrochemical mass spectroscopy. Their motivation was to avoid the complications of chemical oxidants employed by other groups and sound out the potential for electrode-driven oxidation. Using surface-enhanced Raman spectroscopy, they demonstrated the Cp*Ir-N-dimethylimidazolin-2ylidene catalyst readily but reversibly dimerizes under anodic electrode conditions (**Figure 19**). They also demonstrated that the dimeric species is the active catalytic side for the water oxidation reaction and conclusively showed that no IrO_2 was formed in the process, at least under these specific experimental conditions. They further demonstrated the catalytic activity was highly dependent on the supporting electrolyte anions and ionic strength with an optimal pH for their system close to 4. Beyond the textual discoveries in this paper the underlying theme appears to be the importance of clearly-defined reaction conditions.



Figure 19: Reversible dimerization observed by Hetterscheid, Reek, and Koper.

Conclusions

After examining the evidence that has been confidently obtained thus far, there are several key points to be made in regards to the field of homogeneous iridium-based water oxidation. Firstly, conditions matter. Certain experimental conditions directly effect the formation of nanoparticles in an otherwise homogeneous system.^{13,17,18} Catalyst and oxidant concentrations in particular have well documented effects on reaction homogeneity. Reaction mechanisms are more likely than not affected by the choice of oxidant and likely differ still from electrode-driven reactions.¹⁴ Furthermore, ionic strength and species, pH, and presence of co-solvents all have the potential to affect equilibrium concentrations of these primary species or their collective intermediates. The solution conditions necessitated by different oxidants may anorthogonally affect reaction conditions.

There appears to be a moderately-variable upper threshold for catalyst and oxidant concentrations before homogeneous activity breaks down.²⁷ Resistance to concentration-induced agglomeration appears to largely be related to the specific catalyst and oxidant species.¹⁷ As evidenced by Fukuzumi's work¹³ with 4,4' hydroxyl substituted bipyridines, easily oxidizable catalyst substructures exacerbate catalyst agglomeration at catalyst loadings of 50 μ M with 10

mM CAN. With the related $[{(Cp)*Ir}_2(\mu-OH)_3]OH$ Crabtree was able to selectively initiate particle formation by varying catalyst concentrations between 0.6 and 2.5 mM with 100 equivalents of NaIO₄.¹⁷ In contrast, Crabtree observed no particle formation for 2.5 mM solutions $[(Cp*)Ir(bpy)(OH)]BF_4$, (Cp*)Ir(ppy)(OH), and $(Cp*)Ir(pyr-CMe_2O)(OH)$ with 250 mM NaIO₄. Concentration-dependent particle formation is not a novel concept and is exploited with great effect in the field of nanocluster synthesis.²⁸



Figure 20: A solution of a (Cp^*) Ir triazole carbene complexe after the addition of 160 equivalents of Ce(IV). The homogeneous character of the oxygen-evolving catalyst solution was established by dynamic light scattering.

One interpretation of the current body of evidence suggests the several recently identified Cp*-containing precatalysts lose the capping Cp* to form [(L)Ir(OH₂)₃]ⁿ⁺ or similar hydroxyl analogues. A significant amount of work has been performed identifying the products of Cp* oxidation beginning with aquo attack at either sp² or sp³ carbons on the Cp*. However, work by Crabtree has shown several water oxidation catalysts also capable of stereoselectively oxidizing C-H bonds under conditions similar to water oxidation indicating retention of the Cp*-moiety.²⁹ Subsequent mechanistic and computational studies support the notion of a homogeneous active catalyst derived from the initial precatalyst with retention of chelating ligands.³⁰ Llobet and Macchioni's recent water oxidation work with various supporting ligands that yield different levels of kinetic activity suggest a molecular active species though DLS measurements would confirm these results.²¹ Additionally, their suggestion to evaluate *ratios* of TOF values of new

compounds with a known standard under identical conditions is a significant step forward provided the known standard possesses similar active site speciation or is at least homotopic³¹ under the chosen conditions. Despite recent activity in the field of homogeneous iridium-catalyzed water oxidation, conclusively identifying catalytically active species has remained problematic. This challenge may become less problematic once conditions where homogeneous activity dominates have clearly been established.

The discussion seems to have reached a similar point as palladium-catalyzed crosscoupling some ten years ago. It is not prudent to categorically affirm a homogeneous or heterogeneous mode of action for iridium-catalyzed water oxidation. If the general kinetic scheme outlined by Beller proves to be an effective model, there could be as many as five primary iridium-containing species present in a reaction mixture with numerous intermediates and several intersecting catalytic cycles. In operando, rather than post-reaction, analysis is necessary to confidently obtain the necessary data. The challenges ahead involve accurately identifying active molecular species capable of water oxidation, understanding the chemical transformations occurring in the catalytic cycle, and applying that understanding to intelligently design ligands capable of supporting the homogeneous active catalyst. Additionally, the chemical potential currently provided by cerium or other chemical oxidants must be replaced with photochemical analogues that are compatible with a fuel-producing half-reaction.

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Chapter 3: Abnormal Carbene Iridium Complexes for Water Oxidation

Iridium complexes of Cp* and mesoionic carbene ligands

The Albrecht group's discovery of bidentate cyclometalated N-heterocyclic carbene complexes **2** and **3**¹ and their subsequent catalytic activity for water oxidation was subsequently expanded by the synthesis of complexes **1-10**. Motivated by the success of other Cp*Ir complexes¹⁻⁶ and their earlier discovery of triazolylidene iridium complexes as potent water oxidation catalysts, the Albrecht group synthesized a family of complexes to study the effects of ligand modification. Ligand synthesis was generally accomplished via click chemistry between 2-ethynylpyridine and the appropriate *insitu*-formed azide. Complexation with $[Cp*IrCl_2]_2$ was afforded via the silver-mediated triflate salt of the ligand through non-selective C-H bond activation. Fortunately, the multiple complexes were readily separated by column chromatography or by exploiting solubility differences.



Figure 21: Catalysts investigated in this chapter incorporating diverse ligand environments.

These complexes represent a significant expansion of the original *C*,*C*- or *C*,*N*-bidentate complexes explored previously¹ and can be divided into three main subsets. The first series of complexes exhibit a *C*,*N*-bidentate ligand with a neutral *N*-bound triazole unit and either a formally neutral abnormal pyridylidene⁷ fragment e.g. C_{pyr} , N_{trz} -bidentate complexes **1** and **3** or an anionic phenyl chelate e.g. the C_{aryl} , N_{trz} -bidentate complex **2**. The second set varies the substitution around the triazolylidene core^{8,9} but maintains the *N*-bound pyridine as the chelating group e.g. N_{pyr} , C_{trz} -bidentate complexes **4-6**. The third class of complexes employed anionic phenyl ligands to form *C*,*C*-bidentate chelates as in the C_{aryl} , C_{trz} -bidentate complexe **8** and **9**. Complex **10**, a minor product in the synthesis of **9**, was found to contain a C_{ylide} , C_{trz} -bidentate arrangement unlike any of the other studied complexes.



Figure 22: ORTEP representations of complexes 1 (a), 4a (b), 5 (c), 6a (d), 7 (e), and 8 (f).

The variable connectivity afforded by complexes 1-10 suggests a strong difference in the donor properties of the ligand and the resulting reactivity at the iridium center. Complexes 2 and 7, for example were not capable of chelation through a pyridyl-nitrogen and cyclometalation occurred entirely *via* C_{aryl} -H bond cleavage. Similar reactivity patterns have been observed in

triazolylidene palladium complexes^{10,11} and suggest a pattern of electrophilic bond activation¹². Comparing complexes **1** and **2**, which form as a mixture from the same precursors, this C_{aryl} -H bond activation appears to compete with $C_{pyridinium}$ -H bond activation dependent on whether N2 or N3 of the triazole is coordinated to the iridium center.¹³ Electrophilic activation at the N2 position is suppressed entirely in favor of N3 coordination when the N1 substituent is exchanged for a methyl group e.g. the N_{trz} , $C_{pyridium}$ -bidentate complex **3**.

Complexes with a nitrogen donor ligand were prepared as monocationic species with iridium-bound chloride ligands that could be readily abstracted with AgOTf yielding a dicationic, iridium-solvent complex. *C*,*C*-bidentate complexes, on the other hand were synthesized and isolated as the dicationic species due to the stronger donor properties of *C*,*C*-bidentate complexes compared to their *C*,*N*-bidentate homologues. The greater electron density at the iridium center^{14,15} would weaken any assumed Ir-Cl bond and can be rationalized further by the mesoionic character^{16–18} of these formally neutral abnormal carbene complexes. Since the distal iminium fragment enforces a formally anionic carbon bound to the iridium center, this mesoionic character may lead to greater intermolecular stabilization and longer catalyst lifetimes. Exceeding equimolar ratios of ligand to iridium precursor resulted in the formation of a minor product, the bis(carbene) complex as seen in **11**, e.g. a *C*,*N*-bidentate triazolylidene ligand with an additional monodentate ligand.

The complexes rapidly exchange counter ions for aqua ligands as observed by two sets of pyridyl signals when D_2O solutions of the complexes are observed via NMR spectroscopy. The two species exist in a pH and concentration-dependent equilibrium and addition of KCl completely suppresses the formation of the aqua species. These complexes maintain the extreme inertness of aqueous Ir^{3+} under acidic conditions as no additional signals due to free pyridinium

or triazolium were observed when spectroscopically monitoring a solution of **4a** or **8** in 1M HCl $(D_2O, pH = 0)$. These observations are not surprising given the half-life of aqua exhange for $[Ir(OH_2)_6]^{3+}$ of approximately 15 years under acidic conditions at 40 °C.¹⁹ All complexes except **2** and **4b** were analyzed by single crystal X-ray diffraction yielding the expected connectivity patterns (**Figure 22**). The observed bond lengths for Ir-C_{trz} are within an expected range²⁰ and substantially shorter than the dative Ir-N_{pyr} and, in the case of complex **8**, shorter than the Ir-C_{aryl} bond. As expected there is little difference in ligand bite angles across all complexes.

Initial screenings for complexes were conducted with a sacrificial oxidant and monitored via digital manometry with reaction end points being verified by gas chromatography and mass spectrometry. Each reaction was performed inside 20 mL, 40 mL, or 60 mL screw-neck EPA vials originally purposed for volatile organic component analysis of water or soil samples. Vials were affixed to custom-manufactured manifolds using a Vitron o-ring to ensure an air-tight seal. The manifolds were outfitted with a septum seal and temperature-corrected linear response differential pressure transducers. After transferring a degassed solution of oxidant, either cerium(IV) ammonium nitrate or sodium periodate, into the vial along with a 5 mm stir bar, the vial was attached to the manifold and the headspace atmosphere was evacuated and refilled with argon at least seven times to ensure a homogenous, inert and non-oxygenic atmosphere.

Originally transducers were sourced from Omega Engineering Incorporated (PX138-030A5V) and operated at 8 VDC while later experiments employed the more cost efficient and readily available Honeywell SSCSNBN030PAAA5 operated at 5 VDC with negligible differences in sensitivity. The transducers were powered in parallel at the indicated voltage with a variable-output laboratory power supply (Temna 72-6152). The pressure transducers employed two ports – one sealed and one connected to the manifold headspace rendering voltage readings

proportional to the absolute pressure of gas in the headspace. This configuration requires all reactions to have an additional vial prepared that will not produce gas serving as a temperature-correcting reference. The time-dependent voltage signal from this reference is subtracted from the time-dependent voltage signal for each individual reaction vessel thereby offsetting any pressure changes due to aggregate changes in temperature. Despite this, the reaction vessels require moderate shielding from air currents as cyclical "on-off" of the building air handling system caused a significant differential pressure response in the more productive vials.

The transducer voltage signal was averaged over five seconds and recorded to a computer in along with a time value associated with each measurement in ASCII format through the use of a National Instruments' LabVIEW program. The voltage readings from the pressure transducers were correlated with the vial's headspace pressure from an experiment where several vials with varying headspace volume from 5 mL to 40 mL were repeatedly injected with a known quantity of argon at 1 atmosphere. After subtracting the temperature correction from the reference vial, the response of the voltage increase for each addition at a particular headspace volume, $\left(\frac{\partial Volts}{\partial moles}\right)_{vol}$, was found via the method of least squares. The slope of $\left(\frac{\partial Volts}{\partial moles}\right)_{vol}$ with respect to inverse headspace volume was found yielding a voltage calibration directly proportional to the molar quantity of gas and inversely proportional to the volume of headspace with a combined coefficient of determination (R²) in excess of 0.999.

To verify the transducer-derived gas production, the headspace composition at reaction completion was analyzed using a Gow-Mac 400 gas chromatograph using a Thermal Conductivity Detector. At reaction completion a quantity of gas was transferred using a Hamilton SampleLock syringe from the vial headspace into a eudiometer fashioned from a plastic syringe body and a rubber septum with the open end immersed in a 50 mL beaker filled with water. A linear calibration generated using various oxygen-argon and oxygen-nitrogen mixtures then yielded the headspace oxygen content which was corrected for the slow ingress of air by subtracting a quantity of oxygen extrapolated from the quantity of nitrogen observed in the reaction vial headspace. As the GC is unable to quantify the carbon dioxide content of the headspace gases a similar approach was employed using various carbon dioxide-argon mixtures calibrated on a Stanford Research Systems QMS 200 gas-phase mass spectrometer.

Catalytic Activity

The initial parallel screening-reactions of complexes **3-10** with cerium(IV) ammonium nitrate was monitored with digital manometry with endpoint-composition analyses as described above. As described in **Figure 23**, catalyst concentrations of 0.5 ± 0.05 mM and 0.45 M cerium(IV) with 1 mL total volume produced oxygen quantities consistent with the stoichiometric limit (100 ± 4%) of added CAN. In contrast to previously explored catalysts of the [Ir(ppy)₂(OH₂)₂]OTf family, no carbon dioxide was observed via headspace mass spectrometry during the reaction. This is notable because it suggests retention of the carbonaceous ligand components. Even doubling the catalyst concentrations failed to yield any carbon dioxide.



Figure 23: Catalytic activity of complexes **3–10** and $[Ir(ppy)_2(OH_2)_2]OTf$ at 0.5±0.05 mM catalyst and 0.45 M cerium(IV) (1 mL total volume). All solutions produced oxygen consistent with the stoichiometric limit of added cerium(IV).

Notably complexes **3-10** are significantly faster than the previously studied [Ir(ppy)₂(OH₂)₂]OTf family of complexes. Close inspection of **Figure 23** reveals distinct differences in the catalytic performance of these new complexes. These differences, in conjunction with persistent NMR spectra at catalytically-relevant pH and ionic strength (**Figure 37, Bottom**) albeit in the absence of cerium, suggest the retention of the carbene-containing ligands. Further evidence of at least partial ligand retention is afforded by predictable steric and electronic effects; however, due to the presence of a short induction period, the turnover frequency at 50% conversion was used to compare the different catalysts (**Table 2**).

Complex	3	4a	5	6a	7	8	9	10
$TOF_{50}(h^{-1})$	190	365	197	301	327	451	279	191

Table 2: Turnover frequencies at 50% conversion, TOF₅₀

Analogous to similar ruthenium-catalyzed water oxidation reactions,²¹ steric bulk on the triazole N1 position leads to a decrease in catalytic activity (cf. activity of 4a vs. 6b and 8 vs. 9). Changing the ylide-carbene motif in complex 10 to a dicarbene system improved catalytic activity from 191 h⁻¹ to 451 h⁻¹, suggesting the role of electronic effects in tuning catalytic performance. Indeed, examining the pressure trace for complex 10, the ylide-carbene motif expresses significantly different levels of activity and may possess an entirely different reaction mechanism than the other complexes investigated. The stronger donor properties of C,Cbidentate ligands appeared to effect greater activity as compared to their C,N-homologues (cf. the activity of complexes 4a and 8) putatively through a higher electron density at the iridium center afforded through stronger ligand donation^{14,15} or electron negativity differences.² And, as illustrated by the poor performance of complex 3, increasing the ligand donor properties from triazole N-coordination to triazolylidene C-bonding (cf. $\mathbf{8}$) is beneficial and leads to greater activity. All of these predictable differences in activity support the retention of the carbenecontaining ligand and, in contrast to reports suggesting the formation of a heterogeneous species implicated as an active intermediate in the water oxidation reaction,^{6,22,23} exploratory reactions yielded no particles visible to the naked eye prompting more in depth analysis.

Mechanistic Details

Definitively interpreting reaction progress into discrete mechanistic steps is complicated by numerous factors: the initial pre-equilibrium due to solvolysis, disproportionation between catalytic intermediates and various cerium(III)/cerium(IV) species,^{24–26} the effects of ionic strength, and the potential interactions of any supporting or non-innocent ions with reaction intermediates. To date, there has also been limited analysis comparing the effects of different oxidants.²⁷ There is a high likelihood that reactions driven by the ostensibly single-electron oxidant cerium would have significantly different electron transfer mechanisms than periodate driven reactions would be different still from electrode-driven reactions rendering direct comparisons between methods inconclusive at best. Moreover, any investigations involving *ex situ* analysis, for example electron microscopy following solvent evaporation, may lead to potentially misleading conclusions as the sample preparation will inherently affect the constitution of the observed species. We therefore set out to analyze reactions via non-invasive "*in operando*" techniques.²⁸

Despite the reaction complexity important information can be garnered from in-depth kinetic investigations. Three different types of experiments conducted on the most active species, **4a**, provided a significant quantity of relevant information: varying the catalyst concentration (**Figure 24**), varying the cerium concentration (**Figure 27**), and stepwise addition of cerium to catalyst solutions (**Figure 28**). While an impressive number of total turnovers (mole O_2 per mole precursor) in excess of 30,000 was observed in extended oxidation experiments,^{29,30} the combined results of these three experiments reveals nuanced patterns that describe the underlying catalyst behavior.

Varying the concentration of **4a** from 1 μ M to 10 μ M with a large excess of cerium(IV) suggests a major reaction path varies based on the concentration of **4a**, in agreement with papers describing the activity of dinuclear iridium complexes.^{30,31} At low catalyst concentrations ($\leq 2 \mu$ M), oxygen evolution was found to be linear with respect to time while at higher concentrations of 4a (>2 μ M) the reaction appears to be limited by higher order steps (**Figure 24, Top**). In particular, note the sigmoidal response of the 4 μ M trace which conclusively eliminates the possibility of a single elementary reaction mechanism completely explaining the kinetics.



Figure 24 Top: O_2 formation for complex **4a** at concentrations ranging up to 10 μ M following addition to 20 mL aqueous cerium ammonium nitrate solutions (0.835 M). The dotted trace describes a least squares fit employing the integrated rate law described in **Scheme 1**. **Bottom:** plot of maximum rate of O_2 formation from above illustrating concentration-dependent mechanism.

At higher pre-catalyst **4a** concentrations, support for a series of sequential first-order reactions leading to oxygen evolution is first suggested by the accelerated rate of oxygen production at 4 μ M. While the catalysis step leading to the formation of dioxygen is assumed to

be irreversible, the oxidation state and speciation of the catalyst in solution is believed to be a complex mixture with several equilibria. The typically employed method of initial rates is not effective due to these equilibria. Support is instead afforded by applying the integral method to the oxygen evolution traces.³² For a first-order reaction $A \rightarrow P$, carried out in a constant-volume batch reactor, the mole balance and rate law, respectively are:

$$\left(\frac{dC_A}{dt}\right) = r_A = -r_P = -\left(\frac{dC_P}{dt}\right)$$
$$\frac{dC_P}{dt} = kC_A$$

With the limit $C_P(t) = C_P^{max}$ as $t \to \infty$ this gives a relationship between the current amount of product and the final amount of product with respect time for a first order reaction

$$ln \frac{C_P(t)}{C_P^{max} - C_P(t)} = kt$$

Consequently, plotting the reaction progress given as the l.h.s. of the equation above vs. time will produce a straight line with slope of k when the overall product-forming reaction is first order. Substituting the rate equation for a second order reaction produces a similar equation which, when plotted as before, will yield a straight line with slope of k when the overall productforming reaction is second order

$$\frac{C_P(t)}{C_P^{max} - C_P(t)} = kt$$

Accordingly, a semi-log plot of reaction progress vs. time will be linear when the dominant reaction order is one while reaction progress vs. time on a linear scale will produce a straight line when the dominant reaction order is two as illustrated in **Figure 25**. Application of

this technique to the sigmoidal oxygen evolution traces indicates the reaction is initially overall second-order before transitioning into an overall first-order reaction. This behavior is characteristic of two, sequential first-order reactions where the first reaction is significantly faster than the second as in $A \xrightarrow{k_1} B \xrightarrow{k_2} C$ with $k_1 \gg k_2$. During the initial stages of the reaction, the two first-order reactions combine, emulating an overall second order reaction. However as time progresses, the concentration of A eventually decreases to the point that the overall reaction is defined by $B \xrightarrow{k_2} C$.



Figure 25: First and second-order linearization of oxygen evolution traces as described in **Scheme 1** illustrating the change in mechanism as the reaction progresses.

In this concentration range and under these conditions, the catalytic species evolving into dioxygen and a dioxygen-deficient species requires a preceding (pseudo)first-order reaction. Neglecting the contributions of cerium dependence, the two (pseudo)first-order reactions resulting in oxygen formation can be modeled as in **Scheme 1**. Accordingly, the value C_{0_2} represents the integrated quantity of oxygen as a function of time while the value C_A° represents the total quantity of oxygen-evolving precursor. Interestingly, the value of C_{0_2} was determined to be one half of the number of equivalents of cerium(IV). Since the quantity of oxygen is
stoichiometrically determined by the quantity of cerium added, this suggests the initial species – or resting state – is a two electron intermediate analogous to the putative cerium coordinated species described in similar works employing ruthenium and iron. $^{33-35}$

$$A \xrightarrow{k_1} B \xrightarrow{k_2} C + O_2$$

$$C_{O_2} = C_A^{\circ} \left(1 - \frac{k_2 \exp(-k_1 t) - k_1 \exp(-k_2 t)}{k_2 - k_1} \right)$$

Scheme 1

As seen in the dotted traces on **Figure 24**, there is excellent agreement between least squares fitting of the integrated rate law from **Scheme 1** and the experimentally-observed oxygen evolution data across all three regions of catalytic activity (overall second order at high catalyst concentration, pseudo-sigmoidal behavior due to consecutive reactions and overall first-order at low catalyst concentrations). In this "high" concentration range, the maximum rate of oxygen evolution for **4a** was found to be linearly correlated to catalyst concentration with deviation from linearity at concentrations below 2 μ M suggesting a fundamental change in mechanism or rate-limiting step outside of this range (**Figure 24, Bottom**). Due to the complicated kinetics, a log-log plot of oxygen evolution rate *vs*. catalyst concentration is not particularly useful but does further indicate the presence of a mixed-order reaction (slope of 1.5, **Figure 26**).



Figure 26: Log-Log plot of 4a Rate vs. concentration.

The effect of varying the cerium concentration from 3 mM to 0.865 M, while holding the concentration of **4a** at 8.6 μ M is shown in **Figure 27**. Cerium solutions were buffered in 1 N HNO₃ for four primary reasons: (i) to prevent the thermodynamic decay of cerium(IV) at high pH values; (ii) to avoid reaction complexity by limiting the speciation of ions present; (iii) to take advantage of faster reaction kinetics;³⁶ and (iv) to preclude the precipitation of cerium(III) species. These conditions may also increase the solubility or decrease the propensity for aggregation of iridium species and an important caveat comes from the wide variation in ionic strength across this concentration range.



Figure 27: Variation of maximum O_2 rate due to changing cerium(IV) concentration at 8.6 μ M **4a** in 1N HNO₃. Inset: Expanded scale of 0 mM to 15 mM illustrating linear trend in maximum rate at low cerium(IV) concentrations.

Under these conditions, the maximum rate of oxygen production occurs at 50 mM cerium(IV) with 0.18 mmol O_2 h⁻¹ (TOF 20.9 h⁻¹). Prior to this maximum, between 0-20 mM cerium(IV) or roughly 300-2400 cerium(IV) equivalents, the rate of maximum oxygen evolution increases linearly, suggesting a first-order dependence on cerium(IV) a gradual decrease in the maximum rate of oxygen evolution is observed at concentrations greater than 100 mM cerium(IV), likely the result of the significantly increase ionic strength or the aggregation of cerium(IV) into dimeric species.²⁶ This initial first-order behavior and concentration-dependent inhibition is consistent with mechanisms involving either inner-sphere electron transfer or the fast decay of a M-O-O-Ce species as described in similar ruthenium and iron water oxidation studies.^{34,35}

As observed previously with related $Ir(Cp^*)$ complexes, addition of cerium(IV) induces a color change in the initial yellow **4a** solution to green then blue within seconds. While the formation of a blue mixture or a blue layer has periodically been attributed to IrOx formation due to the oxide's general tendancy to absorb broading around 580 nm, similar color changes have previously been noted in high-valent iridium aqua complexes and for an iridium μ -oxo dimer. The observed color changes are consistent with those observed of related chloro and aqua complexes of iridium (green, $[IrCl_6]^{3-}$;yellow, $[Ir^{3+}(OH)_3(OH_2)_3]$; blue and purple, Ir^{4+} .

UV-Vis studies

As UV-visible spectroscopy may provide insight into the catalyst speciation, early stages of the reaction of **4a** were investigated by additions of 20 equivalents of cerium(IV) with concurrent manometric and UV/vis measurements (**Figure 28** and **Figure 30**). When a single addition of 20 equivalents of cerium(IV) was added to a 0.5 mM solution of **4a**, no measurable oxygen production was observed (**Figure 28**) though a rapid color change from yellow to blue and back occurs over the course of 15 minutes (**Figure 30, Top left**). After 8 hours, a second aliquot of 20 equivalents of cerium(IV) was added and 8 hours later, another addition of 20 equivalents. This process was repeated for a total of 8 steps or 160 total equivalents of cerium(IV over the course of 64 hours. A sub-stoichiometric quantity of oxygen was produced during the second through fourth additions with the deviation from stoichiometric predictions decreasing on each subsequent addition. Approximately 30 equivalents of cerium(IV) in total are unaccounted for by manometry.



Figure 28: Stepped oxygen production following addition of 20 equivalents cerium(IV) to 0.5 mM **4a** in 1N HNO_3 with an 8 hour interval between additions overlaid with the same experiment with **4c**. No oxygen production occurs for the first thirty equivalents of cerium(IV) with stoichiometric oxygen production occurring after the third addition.

No carbon dioxide was observed via headspace mass spectrometry even when the experiment was repeated with double the concentration of catalyst (1 mM vs. 0.5 mM, 1 mM absorbed too strongly for meaningful UV-vis measurement). The gas analyzer employed is ostensibly sensitive into the part-per-million range; but, more conservatively if even one mole of carbon dioxide was produced per mole of catalyst it would occupy 1-2% mol of the overall headspace *i.e.* well within the limits of detection. One feasible contribution to the cerium discrepancy investigated was the oxidation of the initial chloride ligand to perchlorate either by

cerium or oxidized catalyst via $ClO_4^- + 4H_2O + 8e^- \rightarrow Cl^- + 8OH^-$ at 0.56 V. As a control, the experiment was repeated with an aqua complex, **4c**, yielding no significant differences from the chloride analogue **4a** (**Figure 28**, blue overlay).

Progressively examining each oxygen evolution trace through the method of first- and second-order linearizations yields the same sequential first-order behavior observed in **Figure 25**. Least squares fitting of the integrated rate equation described in **Scheme 1** to the final four oxygen evolution steps yields first-order rate constants, k_1 and k_2 , of *ca.* 40 h⁻¹ and 13 h⁻¹ respectively (**Figure 29**).

While the initial rates of all oxygen-producing steps were identical, the first four steps were poorly fit by the sequential first-order model and not assessed using **Scheme 1**. The active species of oxidant, a Ce(IV)OH species, exists in an equilibrium with a relatively less active μ -oxo cerium dimer.²⁶ Explaining the initial discrepancy between expected and observed oxygen production is complicated by a combination of the concentration-dependent equilibria between the iridium complexes and active oxidant species as well as putative oxidative transformations required of the initial iridium complexes.^{37,38} Indeed, a paramagnetic cerium-iridium complex, as proposed in the literature would further explain the decrease in intensity and broadening observed in NMR signals following addition of CAN to catalyst observed in **Figure 37** and **Figure 38**. Several EPR experiments were attempted at varying concentrations of CAN and complex **4a** however this method proved inadequate for resolving any signal beyond the broad absorption of cerium(III).



Figure 29: Agreement of fitted with measured data points.fits employing sequential first order reactions (**Scheme 1**) of additions 5, 6, 7, and 8 (abscissa: hours, ordinate: moles of dioxygen) with residual plots included under the appropriate graph.

Long-term catalyst deactivation was assessed via reaction progress kinetic analysis³⁹ by plotting the rate of oxygen evolution vs. the quantity of oxygen evolved for the final four, well behaved, steps. These plots yielded overlapping traces demonstrating the absence of catalyst deactivation following the initial induction period; the active catalyst species observed in these stepped experiments with a gross excess of cerium are therefore likely the same species present after the fourth addition of cerium in the stepwise experiments.



Figure 30: UV-vis absorption spectra of an aqueous solution of 4a after regular sequential additions of cerium(IV) as described above

The UV-Vis spectra are quite complicated as seen in **Figure 30**. To extract more information from the stepwise addition experiments described above the UV-vis spectra vs. time data from the final four stepwise additions was subjected to factor analysis techniques as provided in detail in **Chapter 5** along with relevant MATLAB code supplied in **Appendix B**. As a brief synopsis to stay focused on chemistry, the spectral data was assembled into matrices of [time, wavelength] (Y) which was then subjected to singular value decomposition. Both the subjective method of a semi-log plot of the singular values and the minima in the factor indicator function⁴⁰ were used to assess the rank of these matrices suggesting the presence of five-iridium containing species.

The reduced matrix (\overline{Y}), reconstructed with the significant singular values, was plotted with the residual signal to confirm the absence of additional species within limits of detection (**Figure 32**). Normalized concentration profiles (C) and molar absorptivities (A) of the individual species were obtained from this reconstructed matrix using resolving factor analysis. Briefly, evolving factor analysis^{41,42} was used to provide an initial guess for a Levenberg-Marquard minimization of the residuals of the equation $R = \overline{Y} - CA = \overline{Y} - (\overline{U}T) \times (T^{-1}\overline{S} \overline{V})$ subject to the constraints that the matrices C and A are both non-negative and the concentration profiles are unimodal above a threshold of 0.2 normalized concentration. An example of the reduced data matrix and residuals extracted from the data corresponding to the eighth addition of cerium to the reaction are included in **Figure 31** while the complete set of individual components is included in **Figure 33**.



Figure 31: Reconstructed wavelength-time matrix of injection 8 using the singular values identified as significant (left) and insignificant (right).



Figure 32 Left: Semilog plot of singular values. **Right:** Histogram of residuals illustrating general Gaussian distribution of remaining signal (white noise).



Figure 33 Top: Individual component spectra of species A through E from the eighth addition. **Bottom:** Normalized concentration of species A through E and corresponding oxygen evolution trace (black line) from the eighth addition of cerium(IV).

DFT Calculated Spectra - Mononuclear Species

DFT Calculated Spectra - Dinuclear species

Factor Analysis - Observed Individual Component Spectra

Figure 34: Comparison of calculated spectra of (Cp*)-containing mononuclear and dinuclear species resulting from various oxidation states and protonation with the spectra obtained by factor analysis.

The application of factor analysis to the experimental data obtained in the stepwise additions of cerium to catalyst solutions as described above produced distinct molar absorptivity patterns as apparent in the top panel of **Figure 33**. To determine the catalyst speciation associated with these molar absorptivity patterns a large number of potential species were modeled using time-dependent density functional theory (TD-DFT). Geometry optimizations were performed using the unrestricted B3LYP function with the 6-31G(2d,2p) basis set for carbon, nitrogen, oxygen, and hydrogen atoms and LANL2DZ for iridium atoms. Optimizations were conducted with solvent water using the continuous polarizable continuum model as implemented in Gaussian 09 Rev. D.⁴³ Time-dependent calculations were performed at the optimized ground-state geometry using the LANL2DZ basis set since that basis set has previously resulted in superior agreement of TD-DFT spectra with experimental data.⁴⁴ The energy and oscillator strengths were computed for each of the 150 lowest excitations and electronic transitions were expanded as Gaussian curves with a FWHM (full width at half-maximum) for each peak set at 0.372 eV (3000 cm⁻¹).⁴⁵

The individual iridium-containing component spectra (**Figure 34**) did not correspond with solvent-corrected DFT calculations of UV-vis spectra belonging to proposed mononuclear species of **4a** lending further credence to the notion of a rutile dinuclear iridium species.^{19,37} Modeling the numerous potential dinuclear species is complicated by long geometry optimizations and produces only modest agreement between the observed individual component spectra. A plausible discussion of kinetics conjectures similar steps to the related ruthenium or iron water oxidation catalysts *via* a dinuclear Ir(III,III) to Ir(V,V) or Ir(IV,V) with peroxocoupled cerium species but currently lacks inarguable evidence besides the suggestion of an aquo Ir(III,III) and peroxo-containing species (**4w**). Calculations do suggest the participation of the mononuclear iridium(V) species in the role of pre-catalyst activation as the hapticity of the Cp* moiety is predicted to change *via* solvolysis and oxidation of **4c**.

The normalized concentration profiles resulting from factor analysis (**Figure 33, Bottom**) are highly supportive of the sequential first-order behavior suggested from the first- and second-order linearizations and the least-squares fitting presented above. Species A and B from the figure correspond to the proposed pathway in **Scheme 1** while species C corresponds to the oxygen-deficient intermediate. The maximum rate of oxygen production occurs, within reasonable agreement, at the maximum concentration of species B, the putative oxygen-releasing intermediate. Species D and E would then represent a solvation and preparatory intermediate that would then be triggered by further addition of cerium(IV).

DLS Studies

In contrast to Grotjahn et al. no precipitate was observed at any point. Dynamic light scattering measurements of a 5 mM solution of **4a** in 1 N HNO₃ following addition of 20 equivalents of CAN produced variable scattering intensities over time. Dynamic light scattering indicating particle sizes as large as 1000 nm were observed by the fourth addition of 20 equivalents (**Figure 35**); however, application of a slight vacuum to the solution and remeasuring the scattering intensity yields a decrease in the observed size (**Figure 36**). During the degassing procedure, bubbles were visible to the naked eye. Additionally, after 40 hours at atmospheric pressure, particle sizes returned to baseline measurements. A plausible explanation exists that by decreasing the pressure on the solution, larger nucleated oxygen bubbles increased in size and buoyancy sufficient to dislodge from the walls of the cuvette. Smaller nucleated bubbles did not increase in size sufficiently for the increased buoyancy force to overcome interfacial adhesion and, on remeasuring the sample at atmospheric pressure, only the smaller bubbles were visible.

Size Distribution by Number

Figure 35 Top: DLS response of a solution of complex **4a** at pH 0 (5 mM, 1 M HNO₃). Addition of a first batch of CAN (20 equiv.), measured immediately after addition (First from Top), 15 min after addition (Second from Top) and 2 h after addition (**Bottom**).

Size Distribution by Number

Figure 36: Addition of a excess CAN (600 equiv. total) to a fresh solution of **4a** in 1 M HNO_3 measured 22 h after addition of CAN (top), after applying a vacuum (600 mbar for 30 s; middle), and after standing under atmospheric pressure for 10 min (bottom).

NMR Studies

In attempt to further elucidate the reaction mechanism, NMR measurements under identical conditions indicated **4a** undergoes rapid solvolysis when dissolved in water to produce a mixture of **4a** and **4c** with a chloride counter ion in a 4:1 ratio. Following addition of 10 equivalents cerium(IV) to the 1 mM NMR sample, integrals of both **4a** and **4c** decrease and the ratio of **4a:4c** decreases from 4:1 to 2:1. Repeating the experiment with the addition of 2 equivalents cerium(IV) establishes a 3:1 ratio of **4a:4c**. The integrals and ratios remained constant over several days, yet all signals disappeared upon addition of a second 10 equivalents of cerium (IV), indicating the formation of a paramagnetic species. Addition of 20 equivalents cerium(IV) to a fresh solution of **4a** buffered in 1 N HNO₃ yielded identical results. NMR signals at 8.25 ppm lend support to the formation of formaldehyde which is in agreement with proposed oxidation mechanisms of carbene wingtip methyl groups.^{46,47} The Cp* methyl sinal is noticeable downfield shifted from the original spectra of **4a** following addition of can and broad signals of the chelating carbene are clearly present (**Figure 37 and Figure 38**).

Figure 37: Addition of 20 equiv. of ceric ammonium nitrate to **4a** in 1N HNO₃ buffered D_2O with subsequent monitoring over 12 hours. The spectrum of **4a** before addition of CAN (bottom trace in red) shows two species as a consequence of the equilibrium with the corresponding aquo complex akin to **4c**.

Figure 38: Expansion illustrating broad NMR signals indicating the presence of a paramagnetic Ir species.

Future Directions

The reproducible and well-behaved reaction kinetics, negative results from dynamic light scattering experiments, a lack of carbon dioxide from headspace gasses, and significantly faster rate of reaction compared to IrO_2 nanoparticles all reinforce the molecular nature of active species derived from 4a. Additionally, modifications to the ligand scaffold have noticeable and predictable effects on the reaction kinetics. While it is difficult, with complete certainty, to eliminate the presence of a heterogeneous species active towards water oxidation, especially under catalytically relevant conditions with very low catalyst loading, this work shows that the most competent catalytically active species under the conditions applied here is most likely a molecular species which catalyzes water oxidation in two sequential first-order molecular reaction steps.

Mesoionic triazolylidenes may be particular suitable as ligands for the ensuing redox processes. Their strongly mesoionic character is capable of stabilizing varius redox states and may give rise to proton-couped electron transfer from a putative iridium hydroxide intermediate to the triazolylidene ligand (Scheme 2). Previous results with related abnormal carbene ligands demonstrated that the mesoionic carbene ligand is involved in hydrogen exchange reactions and in metal-catalyzed E-H bond breaking processes.^{48–50}

Scheme 2

Conclusions

A variety of novel iridium complexes containing mesoionic carbene ligands were synthesized and found to serve as competent precatalysts for the oxidation of water. Turnovers in excess of 30,000 were recorded with turnover frequencies exceeding 450 h⁻¹ for the most active catalytic system. No significant efforts were devoted toward optimizing conditions suggesting a path for future research. Turnover numbers were limited by the availability of sacrificial oxidant and not by the robustness of the catalyst, suggesting the mesoionic carbene motif may be suitable for a continuous water oxidation process. Mechanistic investigations, especially under stoichiometric or near stoichiometric conditions, strongly support a tunable molecular species as the catalytic entity. Additionally, dynamic light scattering measurements support the absence of light-scattering particles not incipiently present in cerium solutions. While it is not possible to definitively exclude multiple active catalytic species of differing composition, this work, together with mechanistic studies of similar dinuclear iridium complexes strongly supports the presence of a homogeneous, tunable, and log-lived iridium water oxidation catalyst.

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Chapter 4: Ancillary Iridium Complexes

Photolytic water oxidation catalyzed by a molecular carbene iridium complex

In 2012 Albrecht¹ synthesized the complex $IrCl_2(Cp^*)(\kappa C^5-1,3-dimethyl-4-phenyl-1,2,3-triazolylidene)$ which was found to reversibly cyclometalate as the $\kappa C^{2^{\prime}}$ complex under basic conditions. While this C_{aryl} -Ir bond was highly sensitive to pH, the C_{trz} -Ir bond was stable across a broad range of pH values. (Cp*)Ir complex to oxidize water both by a hematite-driven photoelectrochemical cell and by a long-lived Ce(IV)-driven dark reaction. A 5 μ M aqueous solution of (Cp*)Ir(trz)Cl₂ (trz = 1,3-dimethyl-4-phenyl-1,2,3-triazolium) and 0.83 M Ce (IV) was found to produce 1.2 mmol oxygen over 250 hours corresponding to ca. 22,800 TON based on the original catalyst loading. Under these conditions the rate of oxygen evolution was constant at 0.14 h⁻¹ for roughly 100 hours, producing close to 0.7 mmol O₂. Aqueous catalyst solutions change from a straw-color to light blue following oxidation with 10-100 equivalents of CAN. This blue color decays back to the solution's original straw color with a second order rate dependence.

Figure 39 ORTEP plot of $IrCl_2(Cp^*)(\kappa C^{5}-1,3-dimethyl-4-phenyl-1,2,3-triazolylidene) with co$ crystallized CH2Cl2 molecule omitted for clarity. $Selected Bond lengths (Å) and angles (°): <math>Ir-C^{11}$ 2.0521(14), C^{11} -Ir-Cl¹ 92.97(4) C^{11} -Ir-Cl² 93.86(4), Cl¹-Ir-Cl² 84.471(12).

Adaptation of this cerium-driven reaction to a photocatalytic reaction was afforded by coating fluorine-doped tin oxide with a thin layer of hematite serving as a working electrode and photoabsorber. Activity was measured by illuminating the electrode with an AM 1.5 spectra while immersed in a solution of catalyst using 3.5 wt% NaCl as an electrolyte and comparing the photocurrents of photoelectrode-catalyst systems with photoelectrode-only systems. These experiments yielded pH and catalyst-concentration dependent responses which suggest that at high pH values the catalyst is susceptible to degradation while catalyst concentrations above 100 μ M were found to suppress photocurrents in a manner consistent with electrodeposition. The highest light-induced activity was found to be between 5-30 μ M catalyst and pH values below 7. Extended photoelectrochemical measurements, beginning at pH 0, show an increase up to pH 5 with a corresponding decrease in photocurrent that is regained on reacidification with HCl.

Figure 40: Pressure trace over 10 days for 90 nmol $IrCl_2(Cp^*)(\kappa C^{5}-1,3-dimethyl-4-phenyl-1,2,3-triazolylidene)$ added to 10 mL CAN (1N HNO₃, 0.835M CAN)

Bimetallic Iridium-Carbene Complexes with Mesoionic Triazolylidene Ligands

Mechanistic investigations were conducted on complexes related those described in the previous section. A key step in water oxidation catalysis is generally accepted to be the ratelimiting O-O bond formation from the cruicial oxidized M=O species. Mechanistically, two distinct pathways have been proposed for this step including either the interaction of two highvalent metal-oxo species (M=O···O=M interaction),^{2–7} or the nucleophilic attachment of a water molecule to a metal-oxo site (M=O···OH₂ interaction).⁸ These different mechanisms have crucial consequences on the ligand and catalyst design, and also on potential catalyst immobilization strategies. A bimetallic mechanism will clearly benefit from a close proximity of the two metal centers (e.g., through intramolecular linkage), whereas the nucleophilic attack will require only one metal site and might become deactivated by the close proximity of the other metal center.^{9–11} Since directly probing the mechanism is extremely challenging due to the multielectron, multiproton transfer in water oxidation,^{12–16} the Albrecht group synthesized two diiridiumtriazolylidene complexes capable of testing this theory.¹⁷

Scheme 3: Synthesis and structure of bimetallic complexes.

The electrochemical properties of the bimolecular complexes did not differ strongly from their mononuclear counterparts and do not show any distinct redox features below +1V (aqueous solution 1 M HNO₃, pH 0) and reveals solvent discharge above this potential. Both complexes were evaluated as catalysts for the oxidation of water using cerium(IV) as the terminal oxidant. An initial set of experiments was carried out at approximately 0.6 mM complex with a 0.67 M aqueous solution of cerium(IV). Under these conditions, essentially all CAN was consumed within 90 minutes and oxygen production was close to the stoichiometric limit. Close inspection of the early stages of the reaction indicates only minor differences occurred between the monometallic and bimetallic species. This similarity is remarkable because the bimetallic complexes possess two active metal centers and hence a higher activity would be expected. This may support a mechanistic model that involves multiple active species with differing levels of catalytic activity as postulated by Beller and co-workers.¹⁶

min of the reaction.

A second set of experiments was subsequently performed under more dilute conditions. Lower concentrations were expected to increase the relevance of mononuclear processes (i.e. water nucleophilic attack) in monometallic systems; however, in bimetallic complexes O-O bond formation might still occur through a M=O····O=M interaction due to the locally high concentration of metal centers. Water oxidation with the four iridium complexes #, #, #, and # was thus carried out using approximately 35 μ M catalyst concentration with a cerium(IV)/complex ratio of approximately 20000:1. Oxygen evolution was complete around 24 h after addition at which point turnover numbers were slightly higher than 5000, thus indicating essentially complete consumption of CAN.

In contrast to the experiments performed at higher catalyst loading, inspection of early stage conversions with low iridium concentrations revealed a significantly higher productivity of the bimetallic complexes than the monometallic analogue. The different initial reaction rates are illustrated in **Figure 42** and clearly demonstrate the maximum turnover frequency of complex # is twice as high as that of $\# (0.47 \text{ s}^{-1} \text{ vs}. 0.22 \text{ s}^{-1})$ suggesting an increasing relevance of water nucleophilic attack relative to the interaction of two iridium-oxo species. The experiments performed suggest the rate limiting step in water oxidation by these complexes varies by catalyst concentration. At high concentrations, the reaction is zeroth order in catalyst while lower concentration reactions afford support for a bi-metallic O-O bond-forming mechanism dependent on the number of active iridium sites.

Figure 42: Oxygen evolution from a reaction with a cerium(IV)/complex ratio of approximately 20,000:1 (0.03 mM complex) for mono- and bimetallic complexes. **Inset:** Oxygen evolution at initial 1.5 h of reaction.

Imidazolylidene and Triazolylidene-containing catalysts

Two complexes differing most significantly by the heterocyclic nature of the chelating ligand were found to have significantly different behavior under water oxidation conditions using cerium as a sacrificial oxidant. All catalyst solutions completely consumed the cerium(IV) solutions yielding 2 mM dioxygen or approximately 2000, 4000, and 8000 TON. Both catalysts follow predictable concentration-dependent trends. For A474 (blue traces) there is an initiation period where catalyst activity is significantly lower followed by more robust turnover frequencies. This initiation period persists longer at lower concentrations of A474. For A226 (green traces) this initiation period is either too short to be measured or is completely absent. There are two possible explanations for this behavior: either the imidazole/triazole exchange enforces completely different mechanisms or the triazole inhibits the formation of the putative dimeric species believed to be the active species in other water oxidation chemistry.

Figure 43: Structure and water oxidation kinetics of water oxidation of imidazolylidene and triazolylidene-containing catalysts

Electronically-Bridged Dinuclear Iridium Complexes

In an effort to gain insight into the mechanism of water oxidation by the Cp*Ir(ppy) family of complexes investigated by Crabtree, the mononuclear and dinuclear analogs were synthesized and subjected to water oxidation employing cerium(IV) as a sacrificial oxidant. It was believed that the two metal centers, electronically connected, would enable faster oxidation through a lower combined redox potential. The two complexes were originally synthesized as chloride complexes but the dinuclear analogue proved to be significantly less soluble in water than its mononuclear counterpart. This was addressed by employing silver metastasis to replace the chloride ligand with a nitrate. The initial screenings of this complex were quite promising with activities of the dinuclear species significantly exceeding the mononuclear analogue however further scrutiny by time-resolved dynamic light scattering indicated the formation of persistant nanoparticles. Experiments under a variety of conditions produced significant quantities of precipitate even in the presence of strong buffers.

Figure 44: Structures, pressure traces, and turnover counts for 90 μ M and 9 μ M reactions of Cp*Ir(ppy)Cl and (Cp*Ir)₂ μ -pdpyCl₂ with 10 mL saturated CAN

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Chapter 5: Factor Analysis

Introduction

Often the framework we develop to explain repeated observations can be quite simple. Observations frequently follow a monotonic trend when modifying one variable and this trend is readily discernable among all other muddling signals. Unfortunately, more complicated problems a where multiple variables interact to create a combined, confounded measurement are very common. Positively ascribing one aspect of a measurement to an individual observable can be difficult by conventional least squares fitting due to this confounding. An alternative technique, factor analysis, attempts to resolve the individual signals of a measurement and potentially allows the signal of interest to be separated from less desirable signals.

A very relatable example of factor analysis is given in Malinowski's comprehensive book on factor analysis,¹ where several students' laboratory reports are each graded by several instructors. For a single essay, each instructor is likely to arrive at a different overall grade due to differences in the importance each instructor assigns to categories, or *factors* such as grammar, organization, and focus. Firstly, the relative merit of each category varies between instructors according to personal preference. Secondly, the different grades the essays receive depend on the differences between instructors' personal preference. For *i* different reports, *j* different factors, and *k* different instructors, the grade, d_{ik} , that one particular report receives can then be expressed as in **Equation 1** where s_{ij} is the true *score* of the report while l_{jk} is the importance, or *loading* each instructor ascribes to factor *j*.

$$d_{ik} = s_{i1}l_{1k} + s_{i2}l_{2k} + \dots + s_{in}l_{nk} = \sum_{j=1}^{n} s_{ij}l_{jk}$$

In this way, factor analysis attempts to express measurements as a series of weighted, linear sums of variables. These measurements are typically arranged in matrix format where, in this example, each row of the matrix references an individual report while each column references an individual instructor.. We can then compare the effects of different factors or different instructors on the resulting grade or we have effectively isolated the thing being measured, reports in this case, from the thing doing the measuring and reduce or remove prejudices from the act of measuring. In a chemical problem, instead of grades we would have physical observations such as molar absorptivity, fluorescence lifetimes, calorific heat flux, or chromatographic retention values. In this way the information contained in the rows of the data matrix would correspond to a particular molecule while the columns correspond to a particular measurement.

$$\begin{bmatrix} d_{11} & d_{12} & d_{13} \\ d_{21} & d_{22} & d_{23} \\ d_{31} & d_{32} & d_{33} \\ d_{41} & d_{42} & d_{43} \end{bmatrix} = \begin{bmatrix} s_{11}l_{11} + s_{12}l_{21} & s_{11}l_{12} + s_{12}l_{22} & s_{11}l_{13} + s_{12}l_{23} \\ s_{21}l_{11} + s_{22}l_{21} & s_{21}l_{12} + s_{22}l_{22} & s_{21}l_{13} + s_{22}l_{23} \\ s_{31}l_{11} + s_{32}l_{21} & s_{31}l_{12} + s_{32}l_{22} & s_{31}l_{13} + s_{32}l_{23} \\ s_{41}l_{11} + s_{42}l_{21} & s_{41}l_{12} + s_{42}l_{22} & s_{41}l_{13} + s_{42}l_{23} \end{bmatrix}$$

$$= \bigotimes_{\substack{\text{SS} \\ \text{SS} \\ \text{SS}$$

Equation 1

Singular Value Decomposition

The first issue in the use of factor analysis lies in the chosen method to decompose the data matrix into two of scores and loadings. Historically, applications of factor analysis have been plagued by ad hoc methods yielding irreconcilable differences in comparing results obtained by different methods. Decompositions such as LU^2 or Cholesky³ rely on the data matrix being invertible or self-adjoint, severely limiting their uses beyond manufactured data sets.
Advances in algorithms⁴ and computational abilities enable the use of the robust, effective, and more importantly, reproducible method of singular value decompositions (SVD).^{5,6}

The SVD is an application of the fundamental theorem of linear algebra⁷ in that it decomposes a matrix into fundamental subspaces: column space, right null space, row space, and left null space. This method of decomposing a data matrix is accomplished without imposing a choice of basis and is defined for all matrices – it develops an orthonormal basis from the data itself. In simple terms starting from a data matrix, **Y**, the SVD separates the information in the rows, **U**, from the information in the columns, **V**^T, and shows how strongly the two sets of information are related with Σ . The SVD is accomplished by solving for the eigenvectors and eigenvalues of **Y**^T**Y** and **YY**^T. The eigenvectors arising from **Y**^T**Y** form an orthonormal basis in the row space, **V**, while those arising from **YY**^T form an orthonormal basis in the column space, **U**. The eigenvalues are the same from each ordering and are typically arranged in a descending-order diagonal matrix, Σ

 $\mathbf{Y} = \mathbf{U} \mathbf{\Sigma} \mathbf{V}^{\mathrm{T}}$



Figure 45: Complete dataset **Y** expressed in terms of its SVD.

In more complicated terms, the SVD of an $m \times n$ matrix can be thought as finding the best k-dimensional subspace that approximates the span of the original $m \times n$ matrix. In a noise-free example, the number of non-zero eigenvalues in the Σ matrix would indicate the rank or the number of linearly independent rows and columns in the data matrix. In a chemical example these might represent the number of independent chemical species in a reaction mixture. Since actual experimental data will always contain some quantity of noise, some thought is required to separate the signal and the noise. A qualitative method to determine the number of chemical species from the Σ matrix is to plot the diagonal elements on a semi-logarithmic scale.⁸ Those values which appear significantly greater in magnitude than the others are data (See **Figure 46**).



Figure 46: Representative example of singular values for a three component chromatogram plotted on a semilog scale. The complete matrix Σ would use all 21 values while the reduced matrix, $\overline{\Sigma}$, would use only the first three.⁸

Data Reproduction

Since all other eigenvalues are significantly smaller, we can qualitatively conclude the presence of three chemical species in the data matrix i.e. approximate it as a rank 3 matrix with the other eigenvalues being attributable to a combination of machine rounding and instrument-

derived noise. While there are several quantitative methods for deriving the rank of a data matrix, the best-known probably being the "little-jiffy" rule of thumb^{9,10} or Malinowski's indicator function^{1,11}, they generally suffer from arbitrarily determined cutoff values or require large computational times. Qualitative results are generally useful as long as sufficient signal to noise is present as in most analytical instruments employed in a chemical laboratory.

Several caveats must be established in using the rank of the data matrix to identify the number of species in a mixture. Consider an example where factor analysis is applied to UV-vis spectroscopy data collected while monitoring a chemical reaction as in Chapter 3. First, only species absorbing in the depicted range will contribute to the rank. Solvents and electrolytes, for example, are typically chosen because they do *not* appear and hence will not affect the rank of a matrix. Secondly, the species being investigated must have distinguishable or linearly independent spectra e.g. factor analysis is unable to differentiate two species that are chemically different yet produce the same signal. Thirdly, concentration profiles must also be linearly independent e.g. when factor analysis is applied to chromatographic separations, co-eluting species cannot be distinguished. Finally, spectator species will not independently increase the rank of a matrix – any number of spectator species will only result in the rank of a matrix increasing by one as the spectator species do not change concentration.

While the full data matrix, summed over *n* singular values, would be expressed as $\mathbf{Y} = \sum_{i=1}^{n} \mathbf{u}_{:,i} \sigma_{i,i} \mathbf{v}_{i,:}$ we can consider a reduced data matrix that incorporates only the *ne* significant singular values. This reduced data matrix, $\overline{\mathbf{Y}} = \sum_{i=1}^{ne} \mathbf{u}_{:,i} \sigma_{i,i} \mathbf{v}_{i,:} = \overline{\mathbf{U}} \overline{\mathbf{\Sigma}} \overline{\mathbf{V}} \approx \mathbf{Y}$, differs from the original matrix only by the error captured in the insignificant singular values. By comparison to the pictorial representation of **Y** above it is apparent that including only the significant singular values dramatically reduces the complexity of the decomposed matrices (**Figure 47**). One method of verifying the correct number of significant singular values is to evaluate the residuals by subtracting the reconstituted matrix from the original matrix. The distribution of residuals summed across a dimension should conform to the expected instrument-derived distribution via a χ^2 -squared test and tolerances e.g. in a UV/Visible spectrophotometer, a normal distribution and levels of error consistent with the manufacturer's specifications.



Figure 47: Reduced dataset containing only factors identified as significant.

Preparation

Multiple types of spectroscopic data can be analyzed at once. Consider a reaction vessel whose contents are concurrently monitored by UV-vis, NMR, Raman, and MS over time. A single row of the data matrix could consist of the entire UV-vis spectra appended to the right with the NMR spectra and the Mass spectra, all obtained at a particular time. Sequential rows would be measurements of the same variables (e.g. wavelength, ppm, or m/z) at subsequent time points. For the data to be factor-analyzable it must be complete i.e. if the time interval of mass spectra and NMR does not match the time interval of the UV-vis measurements an interpolation function must be used to generate a regular field of measurements. This is usually accomplished

by application of a Savitzky-Golay filter¹² which models successive sub-sets of adjacent data points in the incomplete-dimension with low-degree polynomials using linear least squares.

The data from each instrument must then be normalized to a meaningful scale – in this spectral example significant precision errors can be introduced in comparing very disparate measurements i.e. hundreds of thousands of counts in a Raman measurement with absorption from a UV-vis measurement. In other experiments other transformations may be required of the raw data i.e. the logarithm of equilibrium constants or rate constants because of the additive nature of thermodynamic free energy.

The last few paragraphs have described two steps which are common to all forms of factor analysis: "Preparation" and "Reproduction" using the summary of steps from Malinowski (Scheme 4). These two steps are common to all factor analyses but the next step, the transformation of abstract representations into interpretable data, is dependent on the type of factor analysis being applied. There are a broad number of types of factor analysis but they can generally be lumped into three methods of Target Testing, Abstract Rotation, and everything else (Special Methods). The type of factor analysis performed here takes advantage of two special methods unfortunately titled fixed-size window evolving factor analysis^{13,14} and resolving factor analysis.¹⁵





Evolving Factor Analysis

EFA was initially employed to analyze chromatograms, an example that illustrates its application and its flaws. At the initial time a detector for a chromatogram is turned on, only solvent is observed i.e. blind to the detector. A slice of the data matrix is then subjected to SVD. As the slice of the data-matrix is traversed across the time-dimension, eventually one eigenvalue in the Σ matrix will increase above a threshold and can be considered significant. In a chromatogram where the components are sufficiently resolved, this eigenvalue will rise to a maximum and decrease back to the same level as instrument-derived noise before the second component elutes. However, in a chromatogram without sufficient resolution, as long as the components are not co-eluting at some point a second eigenvalue will emerge.

Figure 48 graphically represents this behavior. The top panel represents the input chromatogram i.e. the true data while the second and third panels represent the singular values obtained with a slice-height of three and nine, respectively. By counting the number of significant singular values at any particular time, information about the elution can be obtained. Initially, there is only one significant singular value. At approximately two minutes, another singular value has reached a maximum, indicating the elution of another chemical species. The slice-size for this panel is only three rows tall. Consequently, only three separate components can be identified at once. The overlapping elutions between 6-8 minutes are hardly discernable from a noisy spectrum. In comparison, the nine row slice is able to capture the overlapping tailings and onset occurring at 4 minutes as well as the more complicated overlapping elutions occurring from 6-8 minutes. The drawback of using a larger slice-height as a broadening of the singular values - cf, the second singular value at time zero in the nine row slice with the three row slice.

Smaller window sizes are better at identifying the onset of a concentration window while larger window sizes are better at capturing detailed concentration information.



Figure 48: Fixed-window evolving factor analysis with two different windows. **Top:** Actual concentration profile. **Middle:** FW-EFA using a three-row slice. **Bottom:** FW-EFA using a nine-row slice.⁸

Resolving Factor Analysis

The concentration profiles obtained by FW-EFA are a step in the right direction but they are clearly not suitable as a final result due to noise and can be improved on significantly by incorporating the EFA results into resolving factor analysis. RFA is a hybrid method that relies on the physical constraints of the data to reduce rotational ambiguity.¹⁶ The data matrix **Y** consists of absorptivity measurements and can be considered solely a function of the concentration profiles, **C**, and molar absorptivities, **A**. Unfortunately, the matrices \overline{U} and \overline{V}^{T} contain eigenvectors, or abstract representations, which in the example are not directly relatable to the absorption and concentration information contained in the matrix \overline{Y} . To interpret these eigenvectors into concentration and absorptivities, we insert a square transformation matrix **T** applied as in **Equation 2**.

 $Y = \overline{U}\overline{\Sigma}\overline{V}^{T} = \overline{U}TT^{-1}\overline{\Sigma}\overline{V}^{T} = CA$ $C = \overline{U}T$ $A = T^{-1}\overline{\Sigma}\overline{V}^{T}$ $R(T) = Y - C(T) \times A(T)$ $ssq = \sum \sum R_{i,j}^{2}$

Equation 2

While there is no closed-form expression for the transformation matrix, **T**, a solution can be determined analytically via the Levenberg–Marquardt algorithm¹⁷ (Scheme 5) – an

interpolation of gradient descent and the Gauss-Newton algorithm. This method requires an initial guess for \mathbf{T} and can be quite sensitive to this initial guess in the event of multiple local minima. A sensible initial guess is afforded by the technique of Fixed-Sized-Window Evolving Factor Analysis.



Scheme 5

With an initial guess for the transformation matrix, **T**, provided by EFA the algorithm proceeds by calculating residuals. Since in the initial pass the residuals likely do not satisfy the convergence criteria, the Jacobian matrix, **J**, is calculated. The Jacobian matrix is the first-order

partial derivative of the residuals with respect to the various parameters e.g. the entries are $\partial \mathbf{R}_i / \partial \mathbf{T}_j$. In our example, the dimensionality of our Jacobian is proportional to the number of

species – it is effectively a species-dimensional Taylor expansion and represents the slope at a particular point on the surface describing the shape of the residual. To figure out where to go on this surface, a shift vector is calculated via $\delta \mathbf{p} = -\mathbf{J}^+ \mathbf{r}(\mathbf{p})$. Combined, the Jacobian and the shift vector describe where and how far, respectively to travel on the residual function to find the smallest gap between $\mathbf{C}(\mathbf{T}) \times \mathbf{A}(\mathbf{T})$ and \mathbf{Y} . If the residuals are not minimizing quickly enough, appending the matrix with a Marquardt parameter allows the algorithm to shorten the shift vector $\partial \mathbf{p}$ and behave more like the quick-converging Gauss-Newton algorithm or lengthen the shift vector and behave more like the steepest descent algorithm.

Using time-step analysis on the MATLAB code in Appendix B, the step involving the calculation of the Jacobian matrix, J, requires approximately 90% of the overall computation time. For perspective, a single 9-component experiment requires 150-200 iterations of the Levenberg-Marquardt algorithm or approximately 3-5 minutes on an Intel Quad-Core i7. This is effectively trivial for such small systems but can be quickly become computationally prohibitive in larger systems. A modest improvement to computational complexity is afforded from the fact that any one element of each column vector in the transformation matrix can be freely chosen. To avoid machine rounding issues, if the largest element in each column vector is held constant the problem is reduced from solving nc^2 parameters to solving nc(nc - 1) parameters.

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Appendix A: Computational Studies of Mononuclear and Dinuclear Iridium Complexes

Computational Studies of Carbene-containing Iridium Complexes

Computational modeling of plausible iridium complexes are contained in this appendix. Potential species were modeled using time-dependent density functional theory (TD-DFT). Geometry optimizations were performed using the unrestricted B3LYP function with the 6-31G(2d,2p) basis set for carbon, nitrogen, oxygen, and hydrogen atoms and LANL2DZ for iridium atoms. Optimizations were conducted with solvent water using the continuous polarizable continuum model as implemented in Gaussian 09 Rev. D.¹ Time-dependent calculations were performed at the optimized ground-state geometry using the LANL2DZ basis set since that basis set has previously resulted in superior agreement of TD-DFT spectra with experimental data.² The energy and oscillator strengths were computed for each of the 150 lowest excitations and electronic transitions were expanded as Gaussian curves with a FWHM (full width at half-maximum) for each peak set at 0.372 eV (3000 cm⁻¹).³

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Figure 50: Compound 4d Ir(III)=O (singlet)



Figure 51: Compound 4e Ir(III)-OH (singlet)



Figure 52: Compound 4f Ir(III)-OH₂ (singlet)



Figure 53: Compound 4g Ir(IV)=O (doublet)







Figure 55: Compound 4i Ir(IV)-OH₂ (doublet)



Figure 56: Compound 4j Ir(V)=O (singlet)



Figure 57: Compound 4k Ir(V)=O (triplet)



Figure 58: Compound 4l Ir(V)-OH (singlet)



Figure 59: Compound 4m Ir(V)-OH (triplet)



Figure 60: Compound 4n Ir(V)-OH₂ (singlet)



Figure 61: Compound 40 Ir(V)-OH₂ (triplet)



Figure 62: Compound 4p (sans Cp*) Ir(III) (OH₂)₄ (singlet)



Figure 63: Compound 4q (sans Cp*) Ir(III) (OH₂)₄ (triplet)



Figure 64: 4r Dimer: Ir(3,3) A 2 OH B 2 OH (triplet)



Figure 65: 4s Dimer: Ir(3,3) A 2 OH B 2 OH (singlet)





Figure 66: 4t Dimer: Ir (3,4) A ax OH eq O B 2 O (doublet)



Figure 67: 4u Dimer: Ir(5, 5) A 2 O B 2 O (singlet)



Figure 68: 4v Dimer: Ir(5,5) A ax OH eq O B 2 O (singlet)



Figure 69: 4w Dimer: Ir(5,5) A ax OOH eq O B 2 O (singlet)



DFT Calculated Spectra - Dinuclear species





Figure 70: Comparison of calculated spectra of (Cp*)-containing mononuclear and dinuclear species resulting from various oxidation states and protonation with the spectra obtained by factor analysis.

Appendix B: MATLAB Code
```
% This is largely an adaptation of Main RFA.m from
% Practical Data Analysis in Chemistry
% Marcel Maeder & Yorck-Michael Neuhold
% University of Newcastle, Australia, 2006
function [Y,S,R,C guess,C,A,sig R]=RFA Data(data,nc,cut,step,it max,pressure)
%Data is the data source arranged with wavelength along the horizontal,
%time in the vertical
%nc is the number of components to test
%cut is the number of entries from the front to truncate
%step is just a way to mark graphs with the step from the sequential addition
%it max is the maximum number of iterations
%pressure is a pressure trace vector to overlay on the concentration
%profiles
    function [time,lambda,Y,m,n]=parse data(data)
        [m,n]=size(data);
        time=data(cut:m,1);
        lambda=data(1,2:n);
        Y=data(cut:m,2:n);
    end
[time,lambda,Y,m,n]=parse data(data);
% First bit figures out how many significant values to use from the S
% matrix.
\$ spectrum sig = 0.99;
temp time=time-min(time);[U,S,Vt]=svd(Y,0);
sig R=NaN(length(time),length(lambda));
for i=0:nc
    R=Y-U(:,1:i) *S(1:i,1:i) *Vt(:,1:i)';
    sig R(i+1) = std(R(:));
    g=i;
end
 figure(1);
 subplot(1,2,1)
    mesh(lambda,temp_time,U(:,1:i)*S(1:i,1:i)*Vt(:,1:i)');
     axis tight
     xlabel({'Wavelength', '(nm)'});ylabel({'Time', '(h)'});
     zlabel(['Y(' num2str(g) ')']);
 subplot(1,2,2)
     mesh(lambda,temp time,R)
     axis tight
     xlabel({'Wavelength', '(nm)'});ylabel({'Time', '(h)'});
     zlabel(['R(' num2str(g) ')']);
figure(2);
     subplot(1,2,1)
     plot(log10(diag(S)), 'ok');
 subplot(1,2,2)
     hist (R, -3*10^{-3}:10^{-4}:3*10^{-3});
% Now we do EFA Analysis to figure out a first guess for our matrix T
\% We'll use this quess to minimize the residuals of Y-C(T)×A(T)
% and extract concentration/absorption profiles of the resulting species
% This section is adapted from and uses EFA.m, norm max.m, and nglm3.m
```

```
[EFA f, EFA b] = EFA(Y,nc);
EFA \overline{f}(isnan(EFA f) == 1) = 0;
EFA b(isnan(EFA b)==1)=0;
C guess=min(EFA f(:,1:nc),fliplr(EFA b(:,1:nc)));
sig level=0.01;
C window=C guess>sig level;
C guess=norm max(C guess);
%plot(time,C guess);
U bar=U(:,1:nc);
S bar=S(1:nc,1:nc);
V bar=Vt(:,1:nc)';
T=U bar'*C guess;
% from nglm3.m & Rcalc eqAH2.m
% BTW: the way nglm3's setup to use structs and feval's and repetitive code
% is a pain in the cravat... (good example of how not to be intuitive)
    function [r]=Rcalc(U bar,S bar,V bar,T,C window)
        C=U bar*T;
                                % Calc. Conc.
        C=C.*C window;
                                % Apply window from EFA
        C(C < 0) = 0;
                                % C>0
        C=norm max(C);
        A=T\S bar*V bar; % Calc. A
                             % A>0
        A(A<0)=0;
        R=Y-C*A;
                                % Calc. Resid.
        r=R(:);
        ssq=sum(r.^2);
    end
% Quote from:
% Practical Data Analysis in Chemistry
% Marcel Maeder & Yorck-Michael Neuhold
% University of Newcastle, Australia, 2006
% "Any one element of each column vector of T can be freely chosen while
% the other elements in that column define the shape of the concentration
% profile. In order to avoid numerical problems with very small or very
% large numbers in each column of T, we choose the largest absolute element
% of each column of the matrix of initial guesses Tguess and keep it fixed
% during the iterative refinement of the others. This reduced the number of
% parameters that need fitting to nc(nc-1).
    function par str=build par str(T)
        [\sim, index] = max(abs(T));
        %par str=NaN(1,nc*(nc-1));
        k=0;
        for j=1:nc
            for i=1:nc
                if i ~= index(j)
```

k=k+1;

```
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```

```
par str{k}=['T(' int2str(i) ',' int2str(j) ')'];
                 end
            end
        end
    end
    function par=get par(par str)
        par=NaN(length(par str),1);
        for i=1:length(par str)
            par(i,1)=eval(par str{i});
        end
    end
    function s=put par(s)
        for i=1:length(par str)
            eval([par str{i}] '= par(i);']);
        end
    end
ssq old=1e50;
mp = 7000;
mu=1e-6;
delta=1e-15;
it=0;
par str=build par str(T);
par=get par(par str);
stoprunning = 0;
while it<it max;</pre>
    r0=Rcalc(U bar, S bar, V bar, T, C window);
    ssq=sum(r0.^2);
    conv_crit=(ssq_old-ssq)/ssq_old;
    fprintf(1,'it=%i, ssq=%g, mp=%g, conv crit=%g\n', it,ssq,mp,conv crit);
    if abs(conv crit) <= mu</pre>
        if mp==0
            break
        else
            mp=0;
            r0_old=r0;
        end
    elseif conv crit > mu
        mp = mp/3;
        ssq old = ssq;
        r0 old = r0;
        %J=NaN((m-30)*(n-1),length(par));
        for i=1:length(par)
            eval([par str{i} '=' par str{i} '*(1+delta);']);
            r=Rcalc(U bar,S bar,V bar,T,C window);
            eval([par str{i} '=' par str{i} '/(1+delta);']);
             J(:,i) = (r-r0) / (delta*par(i));
        end
    elseif conv crit < -mu</pre>
```

```
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```

```
if mp ==0
            mp = 0.1*ssq old;
        else
            mp=mp*5;
        end
        par=par-delta par;
    end
    J mp = [J;mp*eye(length(par))];
    r0 mp=[r0 old;zeros(size(par))];
    delta par=-J mp\r0 mp;
    par=par+delta par;
    put par(par str);
    it=it+1;
   % stoprunning = input('Close enough?');
end
    figure(3) % plot of lambda values
    axes('FontSize',18);
    lamplot = plot(lambda,A);
    xlim([400, 1000])
    xlabel({'Wavelength', '(nm)'}, 'FontSize', 18);
    ylabel({'\epsilon'}, 'FontSize', 18); %dec 949 is ?
    for i=1:length(lamplot)
        set(lamplot(i), 'DisplayName', strcat(char(64+i), num2str(step)));
    end
    legend('show');
    figure(4) % plot of normalized concentration
    axes('FontSize',18);
    concplot =
plot(temp time,C,pressure(:,1),pressure(:,2)/max(pressure(:,2)));
    xlim([0, 8])
    xlabel({'Time','(h)'},'FontSize',18);
    ylabel({'Norm. Conc.',''},'FontSize',18)
    for i=1:length(concplot)
        set(concplot(i), 'DisplayName', strcat(char(64+i), num2str(step)));
        if i==length(concplot)
            set(concplot(i), 'DisplayName',
'02', 'Marker','.', 'LineStyle', 'none', 'DisplayName', '02', 'Color', [0 0 0]);
        end
    end
    legend('show');
end.
```