### Iridium and rhodium analogues of the Shilov cycle catalyst; and the investigation and applications of the Reduction-Coupled Oxo Activation (ROA) mechanistic motif towards alkane upgrading

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## Abstract

This dissertation will cover several disparate topics, with the overarching theme centering on the investigation of organometallic C–H activation and hydrocarbon transformation and upgrading. Chapters 2 and 3 discuss iridium and rhodium analogues of the Shilov cycle catalyst for methane to methanol oxidation, and Chapter 4 on the recently discovered ROA mechanistic motif in catalysts for various alkane partial oxidation reactions. In addition, Chapter 5 discusses the mechanism of nickel pyridine bisoxazoline Negishi catalysts for asymmetric and stereoconvergent C–C coupling, and the appendices discuss smaller projects on rhodium H/D exchange catalysts and DFT method benchmarking.

- Chapter 2: The iridium complex (ONO)Ir(PPh<sub>3</sub>)<sub>2</sub>Me, where (ONO) is a bis(phenolate)pyridine pincer ligand, undergoes C-H activation of benzene, related arenes, and acetonitrile. Labeling and kinetic studies indicate a unique and heretofore undescribed mechanism involve intramolecular C-H activation followed by intermolecular C-H activation.
- **Chapter 3:** The Shilov catalytic cycle for methane to methanol oxidation *via* a homogeneous Pt catalyst has long been a target of investigation, with work focusing on improving catalyst stability, yield, and robustness. A Rh analogue to the Shilov cycle was explored due to its increased stability at high oxidation states. A density functional theory-driven virtual screening of ligand frameworks revealed that the fluorine-substituted amidinate (NN<sup>F</sup>) ligand provides the lowest transition state energies for methane C–H activation and methyl group functionalization, and stands most promising as a target for experimental investigation.
- Chapter 4: The vanadium phosphorus oxide (VPO) catalyst has been used in industry for the remarkably selective conversion of butane to maleic anhydride. Investigation of the reaction mechanism revealed the surprising conclusion that, although redox action occurs in the vanadium centers as expected, initial C-H activation takes place in the phosphorus oxide moieties. Further work has revealed that the same phenomenon can be extended to other transition metal/nonmetal oxo pairs. This phenomenon, which has been named the Reduction-Coupled Oxo Activation (ROA) mechanistic motif, is attributed to the concomitant formation of a strong oxo-hydrogen bond on the nonmetal and a one-electron reduction on the transition

metal. Finally, a homogeneous vanadium phosphorus oxo complex is proposed to incorporate the novel ROA mechanistic pathway as a potential propane oxidation catalyst. Several oxidation pathways are proposed, leading to end products such as propylene, isopropanol, and propylene oxide. These assertions are supported with density functional theory calculations on the potential reaction pathways.

**Chapter 5:** The *in situ* generated Ni(*i*Pr-pybox) complex catalyzes enantioselectively the crosscoupling of secondary  $sp^3$ -C substrates. This system is very notable for its property of stereoconvergence: *both* enantiomers of a racemic substrate may be converted into a single enantiomer of a product. This chapter will computationally explore the mechanism responsible for both the remarkable activity and selectivity of the Ni((S, S)-*i*Pr-pybox system; such a mechanism is believed to deviate substantially from the canonical "textbook" mechanism of Negishi coupling. Furthermore, a generalized calculation scheme is presented that allows for the rapid enantioselectivity prediction of many related pybox ligands as well, in order to help predict the next generation of asymmetric Negishi coupling catalysts.

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### Chapter 1

## Introduction

### 1.1 Iridium and Rhodium analogues of the Shilov cycle catalyst

The facile, selective, and direct conversion of methane into methanol has long been a goal of industrial chemists [1]. Methane, the chief component of natural gas, is typically found in abundant quantities wherever petroleum deposits are found. However, due to its difficulty in liquefaction (its boiling point being only 110 K) and its relative paucity of demand as compared to other hydrocarbons, it is often not economical to harvest this gas, which is essentially a byproduct or co-product of petroleum recovery, and to transport it to market. Since methane is also a potent greenhouse gas, with a global warming potential 72 times more powerful than that of carbon dioxide [2], it cannot simply be released either. Hence it is often flared, a process that is both intrinsically wasteful and which results in a large amount of heat pollution.

One potential solution is to convert these vast quantities of methane into methanol. As methanol is liquid at room temperature and pressure, it is much more easily transported and stored. Methanol can be used as a fuel in flex fuel vehicles, blended with gasoline, or converted to gasoline or diesel fuel. In addition, it has many applications as an industrial solvent and chemical feedstock. As methanol is both more easily processed and in greater demand than methane, the efficient conversion from the former to the latter has the potential to be both environmentally friendly and economically favorable.

Although the reaction  $CH_4 + \frac{1}{2}O_2 \longrightarrow CH_3OH$  is exoenergetic by 30 kcal/mol, efficient catalysis is hampered by the fact that the C-H bond dissociation energy (BDE) of methane is 104 kcal/mol, whereas the C-H BDE of methanol is only 95 kcal/mol. Hence, overoxidation is a major problem. In fact, potential methods that involve radicals have a theoretical maximum yield of only 5%, even with perfect conversion [3]. Hence, the currently favored industry-scale conversion of methane to methanol involves an indirect pathway *via* syngas [1]:

$$CH_4 + H_2O \xrightarrow{Ni} CO + 3H_2$$
 (1.1)

$$CO + 2H_2 \longrightarrow CH_3OH$$
 (1.2)

However, this pathway suffers from a difficult first step that is highly endergonic, requiring very high temperatures and pressures (700-1100°C, 40 atm). Hence, this state-of-the-art pathway requires large inputs of energy and very expensive production facilities despite the significantly exothermic nature of the overall reaction. An alternative mechanism that does not require such extreme conditions would thus be highly desirable.

Molecular compounds in solution have long been investigated as potential catalysts for this transformation, as they are typically well-defined, easy to characterize and model, and operate under relatively mild conditions. Much of the focus has been on routes involving C–H activation at a transition metal center followed by oxidative cleavage of the resulting C–M bond, which offer greater possibilities for good selectivity by avoiding radical-based pathways. Platinum complexes have received a great deal of attention [4], starting with Shilov's seminal work on the  $PtCl_4^{2-}/PtCl_6^{2-}$  system, which can oxidize methane to methanol with some selectivity [5], and including the platinum bipyrimidine system, which has achieved the most impressive performance to date, converting methane to methyl bisulfate in up to 70% yield [6].

However, none of this platinum-based chemistry has yet been shown to lead to a practical process, owing in part to low reactivity, and a good deal of research activity has turned to other metals. Chapters 2 and 3 will address certain Ir and Rh analogues, respectively. The original Pt Shilov cycle, as well as modifications incorporating Ir and Rh, is given in Scheme 1.1.



Scheme 1.1. Left: The original  $Pt^{II}/Pt^{IV}$  cycle of the Shilov catalyst. Center: A potential analogous  $Ir^{III}/Ir^{V}$  cycle. Right: A potential analogous  $Rh^{I}/Rh^{III}$  cycle.

Chapter 2 focuses on bis(phenolate)pyridineiridium(III) ((ONO)Ir) complexes as an Ir analogue to the Shilov catalyst. Iridium as an alkane oxidation catalyst has been a popular choice; many (primarily low-valent) Ir complexes have been reported to show good activity for C–H activation [7], and examples of oxidative functionalization with Ir systems are known as well [8]. Interconversions between  $Ir^{III}$  and  $Ir^{V}$  might be important in this chemistry, by analogy to the Shilov system, which involves  $Pt^{II}$  and  $Pt^{IV}$ . In Chapter 2, the experimental synthesis and characterization of a multitude of ((ONO)Ir) complexes in the +III and +IV oxidation state are described. In particular, the complex (ONO)Ir(PPh<sub>3</sub>)<sub>2</sub>Me has been found to undergo oxidation with iodine to release MeI, analogous to the Shilov system's production of MeCl. Furthermore, (ONO)Ir(PPh<sub>3</sub>)<sub>2</sub>Me has been found to undergo an unusual C–H activation route with benzene that initially proceeds by intramolecular C–H activation, followed by intermolecular C–H activation.

Chapter 3 focuses on rhodium due to its well-documented nature as an effective C–H activating metal [9] and whose lower electronegativity may allow it to avoid poisoning by coordinating media. In this chapter, a computational screening of a variety of ligands was undertaken in order to find a Rh-ligand complex with the predicted optimal combination of low methane activation energy, low methyl group functionalization energy, and overoxidation protection of the MeX product. Our best results were the Rh<sup>III</sup> bis(*N*-pentafluorophenyl)pentafluorobenzylamidinate (Rh<sup>III</sup>(NN<sup>F</sup>)) complex and the Rh<sup>III</sup> bis(quinolinyl)benzene (Rh<sup>III</sup>(bisq)) complex. In addition, we also report a correlation between Rh–Me bond energies and methane activation barriers that would allow us to easily predict the suitability of new complexes for methane activation.

### 1.2 Investigation and applications of the Reduction-Coupled Oxo Activation (ROA) mechanistic motif towards alkane upgrading.

Vanadium phosphorus oxide (VPO) is an inorganic complex that catalyzes the oxidation of *n*-butane to maleic anhydride with a surprisingly high selectivity of 60-70% [10] (Scheme 1.2). Although the overall yield is only *ca.* 50%, its ease of synthesis, use of common elements, and selectivity have allowed this catalyst to be commercialized, producing *ca.* 500 kilotons of maleic anhydride annually [11].



Scheme 1.2. The oxidation of *n*-butane to maleic anhydride using vanadium phosphorus oxide as a catalyst.

Surprisingly, the mechanism has been shown to initiate with C-H activation by a P=O moiety [12]. Whereas the many vanadium oxos and peroxos investigated bound with hydrogen with a maximum energy of only 70.0 kcal/mol, too low for initial C–H activation of *n*-butane to occur, the phosphorus oxo has a much larger bond strength with hydrogen, at 84.3 kcal/mol. This implies a first step that is endothermic by only 5.0 kcal/mol, with an activation energy later calculated to be 13.6 kcal/mol, which is within the experimental range. The stability of the resulting monohydrogenated species was attributed to the fact that spin density appears to be localized on the neighboring vanadium atoms (Figure 1.1).

**Figure 1.1.** C–H activation by a phosphorus oxo leads to a one electron reduction on the neighboring vanadium. Hence the oxidation state of the phosphorus atom does not change.



Chapter 4 focuses on deeper investigations into the ROA mechanistic motif. Specifically, questions such as the generalizability of the mechanism to other metal-main group pairs, as well as the applications of the ROA motif to homogeneous catalysts, are addressed. We have designed the homogeneous complex  $\kappa$ -P bis(2-phenoxyl)phosphinite vanadium ((OPO)V) to be a catalyst that may activate propane using the ROA mechanistic motif. We then continued to follow the reaction forward, tracing pathways for the catalytic oxidation of propane in aqueous solution using O<sub>2</sub> as the terminal oxidant. We found that the ((OPO)V) system has the potential to be a viable catalyst in acidic aqueous solution, converting propane to either propylene or isopropanol.

#### **1.3** Other projects

Chapter 5 is a computational mechanistic study of the 2,6-bis(4-isopropyl-2-oxazolin-2-yl)pyridine nickel (Ni((iPr)-pybox)) system, a Negishi C-C coupling catalyst. In our computational work, we investigated the coupling of 1-bromoindane with methylzinc iodide catalyzed by the Ni((S, S-iPr)pybox) system to form 1-methylindane. The chiral diastereomers of this catalyst are most notable for their stereoconvergence: Using Ni((S, S-iPr)-pybox) as a catalyst, both enantiomers of racemic 1bromoindane will couple with methylzinc iodide to form (S)-1-methylindane with 90% enantiomeric excess [?]. We confirm that the mechanism proceeds through a Ni<sup>I</sup>-Ni<sup>III</sup> couple, in contrast to the classic Ni<sup>0</sup>-Ni<sup>II</sup> cycle that Negishi catalysts are typically assumed to undergo [?] (Scheme 1.3).

Appendix A is an experimental and computational study of the (L)Rh<sup>I</sup>(COE)(TFA) complexes in which L is DAB<sup>F</sup> or BOZO (DAB<sup>F</sup> = N, N-bis(pentafluorophenyl)-2,3-dimethyl-1,4-diaza-1,3butadiene, COE = cyclooctene, TFA = trifluoroacetate, BOZO = bis(2-oxazolin-2-yl)). These com-



Scheme 1.3. The generalized mechanism of the Ni((iPr)-pybox) Negishi coupling catalyst as it proceeds through a Ni<sup>I</sup>-Ni<sup>III</sup> cycle. The overall equation is ind-Br + MeZnI  $\longrightarrow$  ind-Me + ZnBrI.

plexes have been shown to catalyze the H/D exchange of benzene in trifluoroacetic acid. Computationally, the mechanism was found to occur by the reversible oxidative addition and reductive elimination of benzene to and from the (L)Rh<sup>I</sup>(TFAH)(TFA) species.

Appendix B is a comparison of various DFT and electron-correlation methods for calculating the group 10 transition metals Ni, Pd, and Pt. These elements are notable in that, despite being in the same periodic group, they each have a different electronic configuration  $(d^8s^2, d^{10}, \text{ and } d^9s^1,$ respectively). The accuracy of DFT and electron-correlation methods in reproducing the transition energies between the three configurations for the three elements is an important consideration that has deeper implications in the reactivity of more complex systems including these elements.

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### Chapter 2

## Intra- and intermolecular C–H bond activation by bis(phenolate)pyridineiridium(III) complexes

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#### 2.1 Abstract

A bis(phenolate)pyridine pincer ligand (henceforth abbreviated as ONO) has been employed to support a variety of iridium complexes in oxidation states I, III, and IV. Complexes (ONO)IrL<sub>2</sub>Me (L = PPh<sub>3</sub>, PEt<sub>3</sub>) react with I<sub>2</sub> to cleave the Ir-C bond and liberate MeI, apparently *via* a mechanism beginning with electron transfer to generate an intermediate Ir<sup>IV</sup> complex, which can be isolated and characterized for the case  $L = PEt_3$ . The PPh<sub>3</sub> complex is transformed in benzene at 65°C to the corresponding phenyl complex, with loss of methane, and subsequently to a species resulting from metalation of a PPh<sub>3</sub> ligand. Labeling and kinetics studies indicate that PPh<sub>3</sub> is the initial site of C-H activation, even though the first observed product is that resulting from intermolecular benzene activation. C-H activation of acetonitrile has also been observed.



#### 2.2 Introduction

Functionalization of alkanes, such as the selective oxidation of methane to methanol, has long been a desired goal of both academic and industrial research [1]. Much of the focus has been on routes involving C–H activation at a transition metal center followed by oxidative cleavage of the resulting C–M bond, which offer greater possibilities for good selectivity by avoiding radical-based pathways. (Yields of methanol from the direct reaction of methane with dioxygen, where radical pathways predominate, appear to be limited to about 5%, because methanol is more rapidly oxidized than methane, a consequence of its weaker C-H bond [1]d.) Platinum complexes have received a great deal of attention [2], starting with Shilov's seminal work on the  $PtCl_4^{2-}/PtCl_6^{2-}$  system, which can oxidize methane to methanol with some selectivity [3], and including the platinum bipyrimidine system, which has achieved the most impressive performance to date, converting methane to methyl bisulfate in up to 70% yield [4].

However, none of this platinum-based chemistry has yet been shown to lead to a practical process, owing in part to low reactivity, and a good deal of research activity has turned to other metals. Iridium in particular has been a popular choice; many (primarily low-valent) Ir complexes have been reported to show good activity for C–H activation [5], and examples of oxidative functionalization with Ir systems are known as well [6]. Interconversions between  $Ir^{III}$  and  $Ir^{V}$  might be important in this chemistry, by analogy to the Shilov system, which involves  $Pt^{II}$  and  $Pt^{IV}$ . A separate program in our group has examined dianionic tricoordinate ("LX<sub>2</sub>") pincer ligands for reactions involving highvalent early transition metal centers [7], and it occurred to us that such strongly electron donating, hard, and robust ligands might also be useful here, to provide more facile access to the relatively high  $Ir^{V}$  oxidation state.

We previously reported some chemistry of a bis(phenolate)-*N*-heterocyclic carbene ligand (OCO) that supports complexes in the oxidation states  $Ir^{I}$ ,  $Ir^{III}$ , and  $Ir^{IV}$ , but no C–H activation chemistry was demonstrated [8]. Here we report on two related bis(phenolate)pyridine ligands (ONO = pyridine-2,6-bis[2-(4,6-di-*tert*-butylphenolate)]; ONO<sup>tBu</sup> = 4-*tert*-butylpyridine-2,6-bis[2-(4,6-di-*tert*-butylphenolate)]; ONO<sup>tBu</sup> = 4-*tert*-butylpyridine-2,6-bis[2-(4,6-di-*tert*-butylphenolate)] 2.1), which also enable synthesis of a wide variety of  $Ir^{I}$ ,  $Ir^{III}$ , and  $Ir^{IV}$  complexes. In addition, the  $Ir^{III}$  complex (ONO<sup>tBu</sup>) $Ir(PPh_3)_2$ Me readily activates C–H bonds of benzene and acetonitrile, as well as of coordinated triphenylphosphine.

#### 2.3 Results and Discussion

### 2.3.1 Synthesis and Characterization of Ir<sup>I</sup> complexes

Because  $Ir^{III}$  is usually highly substitutionally inert, we decided to enter the Ir(ONO) system via  $Ir^{I}$ . H<sub>2</sub>(ONO) [9] was doubly deprotonated with NaH, followed by metalation with  $[Ir(cod)Cl]_2$ , giving



Na[Ir(cod)(ONO)], **1**, which was characterized by NMR and mass spectrometry. The symmetry of the <sup>1</sup>H NMR (only two *tert*-butyl peaks, for example) is consistent with either a five-coordinate structure or a fluxional four-coordinate structure, with the phenolates coordinated to Na<sup>+</sup> and Ir rapidly interchanging (**1a** and **1b**, respectively, in Scheme 2.1). The latter appears more likely on two grounds: First, the related OCO complex of Ir<sup>I</sup> was crystallized (as the [K(18-crown-6)]<sup>+</sup> salt **2**) and shown to have a structure analogous to that of **1b** [8]. Second, attempted crystallization of **1** in the presence of 15-crown-5 (attempts to crystallize **1** without 15-crown-5 were unsuccessful) instead yielded **3**, the result of C–H activation at the 3-position of the central pyridine ring (Figure 2.2).



Scheme 2.1. Synthesis of Na[Ir(cod)(ONO)], 1.

C-H activation probably results from complexation of the sodium ion by 15-crown-5, making it too sterically bulky to coordinate to the pendant phenolate in structure **1b**, and thus labilizing the pyridine, which can flip over to allow the oxidative addition of the 3-C-H bond; the resulting Figure 2.2. Crystal structure of 3. The nearest Na(15-crown-5) is located above the plane of the ligand and has been omitted for clarity. Because of crystal sensitivity, the structure obtained was only of sufficient quality to establish connectivity.



iridium (III) hydride is deprotonated by the pendant phenolate to regenerate square-planar  $Ir^{I}$ . This reactivity appears to require a solution of **1** to contain the isomer **1b**, either as the sole species present or, at least, in equilibrium with **1a**. C–H activation in preference to N-coordination of a pyridine ring has been observed previously for an NHC-pyridine ligand [10]; in that case (and probably here as well) N-coordination is disfavored sterically.

In order to prevent this unwanted ligand C–H activation, we prepared  $H_2(ONO^{tBu})$ , with an additional *tert*-butyl group to inhibit C–H activation of the pyridine linker. The synthesis of the ligand, which was straightforward and analogous to that of  $H_2(ONO)$ , is shown in Scheme 2.2. Deprotonation of  $H_2(ONO^{tBu})$  with NaH, followed by metalation with half an equivalent (i.e. one Ir per ligand) of  $[Ir(cod)Cl]_2$ , gave deep red  $[NaIr(cod)(ONO^{tBu})]_2$  (4, Scheme 2.3), shown crystallographically to have a dimeric structure (Figure 2.3). Unlike ONO complex 1, 4 is readily soluble in pentane, presumably because the hydrophilic  $Na_2O_2$  core is surrounded by a lipophilic shell of *tert*-butyl-substituted phenyl rings. As with 1, the <sup>1</sup>H NMR spectrum indicates either a more symmetric structure in solution or a fluxional process; on cooling to  $-100^{\circ}C$ , the spectrum exhibited some line broadening, but no decoalescence of peaks. 4 reacts with CO to give  $Ir_4(CO)_{12}$  and is reduced by  $H_2$  to metallic Ir.

If instead a full equivalent of  $[Ir(cod)Cl]_2$  is added to one equivalent of  $Na_2(ONO^{tBu})$ , the orange diiridium complex  $[Ir(cod)]_2(ONO^{tBu})$  (5) is obtained. 5 may also be prepared from 4 plus half an equivalent of  $[Ir(cod)Cl]_2$ , but 4 is not formed from 5 and additional  $Na_2(ONO^{tBu})$  (Scheme 2.3). The two iridium atoms in 5 are inequivalent: Ir1 is five-coordinate, bound to both oxygens and the



Scheme 2.2. Synthesis of the ligand  $H_2(ONO^{tBu})$ .



Scheme 2.3. Synthesis and reactivity of  $[NaIr(cod)(ONO^{tBu})]_2$ , 4.

Figure 2.3. Crystal structure of 4. The *tert*-butyl groups and a disordered pentane solvent molecule have been removed for clarity. Selected bond lengths (Å) and angles (°): Ir-O1, 2.0990(1); Ir-N1, 2.1274(1); O1-Na1, 2.2145(1); O2-Na1, 2.1926(1); O2'-Na1, 2.2841(1); O1-Ir-N1, 81.268(3); O1-Na1-O2, 104.799(3); O1-Na1-O2', 106.989(3); O2-Na1-O2', 100.484(2).



nitrogen of the ligand, while Ir2 is square planar and coordinated only to the two phenolate oxygens (Figure 2.4). (The Ir1-N and Ir2-N distances are 2.07 and 3.00 Å, respectively.)

### 2.3.2 Synthesis and Characterization of Ir<sup>III</sup> Complexes

Complex 4 is oxidized by  $AgPF_6$  or  $[FeCp_2][PF_6]$  in a mixture of THF and acetonitrile to  $[(ONO^{tBu})$ - $Ir(cod)(MeCN)][PF_6]$  (6, Scheme 2.4), which was isolated as a crystalline product, although it decomposes over time in the presence of excess acetonitrile. Oxidation of 4 with AgOTf in benzene gave the neutral triflate complex  $(ONO^{tBu})Ir(cod)OTf$  (7). Both complexes exhibit approximately octahedral geometry (Figures 2.5 and 2.6); in solution they behave as strong electrophiles, polymerizing THF and slowly decomposing in other coordinating solvents.



Scheme 2.4. Oxidation of  $[NaIr(cod)(ONO^{tBu})]_2$ , 4, to  $Ir^{III}$  species.

Treatment of **7** with two equivalents of triphenylphosphine yielded yellow  $trans-(ONO^{tBu})$ Ir-(PPh<sub>3</sub>)<sub>2</sub>OTf (**8**, Equation 2.1). Attempts to displace cyclooctadiene from **7** with triethylphosphine or

Figure 2.4. Crystal structure of 5. The *tert*-butyl groups have been removed for clarity. Selected bond lengths (Å) and angles (°): Ir1-O1, 2.2701(1); Ir1-O2, 2.2962(1); Ir1-N1, 2.0818(1); Ir2-O1, 2.0808(1); Ir2-O2, 2.0771(1); Ir2-N1, 2.9953(1); O1-Ir1-O2, 68.864(1); N1-Ir1-O1, 76.957(2); N1-Ir1-O2, 75.747(1); O1-Ir2-O2, 76.775(2); Ir1-O1-Ir2, 103.134(2); Ir1-O2-Ir2, 102.367(2).



Figure 2.5. Crystal structure of 6. A benzene solvent molecule and the PF<sub>6</sub> counterion have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-N1, 2.0736(8); Ir1-N2, 2.0456(8); Ir1-O1, 2.0540(7); Ir1-O2, 2.0849(7); N2-C46, 1.1371(12); O1-Ir1-N1, 85.86(3); O1-Ir1-N2, 81.05(3); O2-Ir1-O1, 89.17(3); O2-Ir1-N2, 85.09(3); O1-Ir1-O2, 165.29(3); N1-Ir1-N2, 89.69(3); Ir1-N2-C46, 173.51(8).



Figure 2.6. Crystal structure of 7. The two *tert*-butyl groups *ortho* to the phenoxy moieties have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-O1, 2.0431(6); Ir1-N1, 2.0738(6); Ir1-O2, 2.0836(6); Ir1-O3, 2.1247(6); Ir1-C39, 2.1725(8); Ir1-C40, 2.1865(8); Ir1-C44, 2.2592(8); Ir1-C43, 2.2656(8); O1-Ir1-N1, 84.59(2); O1-Ir1-O2, 163.22(2); N1-Ir1-O2, 88.90(2); O1-Ir1-O3, 80.91(2); N1-Ir1-O3, 87.90(2); O2-Ir1-O3, 83.42(2); O1-Ir1-C39, 121.97(3); N1-Ir1-C39, 95.20(3); O2-Ir1-C39, 73.96(3); O3-Ir1-C39, 157.08(3); O1-Ir1-C40, 84.60(3); N1-Ir1-C40, 90.09(3); O2-Ir1-C40, 110.91(3); O3-Ir1-C40, 165.50(3); C39-Ir1-C40, 37.42(3); O1-Ir1-C44, 110.92(3); N1-Ir1-C44, 164.19(3); O2-Ir1-C44, 75.34(3); O3-Ir1-C44, 91.51(3); C39-Ir1-C44, 79.40(3); C40-Ir1-C44, 94.28(3); O1-Ir1-C43, 77.60(3); N1-Ir1-C43, 159.93(3); O2-Ir1-C43, 110.72(3); O3-Ir1-C43, 98.24(3); C39-Ir1-C43, 86.58(3); C40-Ir1-C43, 79.18(3); C44-Ir1-C43, 35.50(3).



tricyclohexylphosphine led only to decomposition, while the reaction of 7 with tris(*o*-tolyl)phosphine resulted in protonated ligand, perhaps by benzylic C–H activation followed by reductive elimination of phenol. The crystal structure of 8 is show in Figure 2.7.



Exposure of 8 to water, followed by addition of proton sponge at room temperature gave *trans*- $(ONO^{tBu})Ir(PPh_3)_2OH$  (9, Equation 2.2). Both 8 and 9 were converted to the corresponding chloride (10) by heating at 90°C in dichloromethane for several hours or several days, respectively (Equation 2.3). Formation of 10 from 8 or 9 is much faster in the presence of added tetrabutylammonium chloride. The crystal structure of 9 is show in Figure 2.8.

Figure 2.7. Crystal structure of 8. Two benzene solvent molecules, a *tert*-butyl group's methyls, and the phosphine ligands' phenyl groups (except *ipso* carbons) have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-N1, 2.001(3); Ir1-O1, 2.049(2); Ir1-O2, 2.051(2); Ir1-O3, 2.166(2); Ir1-P1, 2.4142(8); Ir1-P2, 2.4165(8); N1-Ir1-O1, 90.68(9); N1-Ir1-O2, 91.55(9); O1-Ir1-O2, 177.70(8); N1-Ir1-O3, 176.28(9); O1-Ir1-O3, 87.33(8); O2-Ir1-O3, 90.41(8); N1-Ir1-P1, 90.90(7); O1-Ir1-P1, 96.69(6); O2-Ir1-P1, 82.71(6); O3-Ir1-P1, 86.22(6); N1-Ir1-P2, 88.06(7); O1-Ir1-P2, 81.27(6); O2-Ir1-P2, 99.37(6); O3-Ir1-P2, 94.74(6); P1-Ir1-P2, 177.70(3).





All three complexes (8, 9, and 10) react with proton sponge to give the hydride  $(ONO^{tBu})$ Ir-(PPh<sub>3</sub>)<sub>2</sub>H (11). The reaction of 8 takes place over several days at room temperature or in an hour at 90°C, while 9 and 10 react more slowly at 90°C. The crystal structure of 11 is show in Figure 2.9.

The proposed mechanism for this transformation is single-electron transfer followed by H-atom abstraction (Scheme 2.5); the oxidized proton sponge byproduct shown was observed (quantitatively)
Figure 2.8. Crystal structure of 9. The *tert*-butyl groups have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-N1, 2.0395(14); Ir1-O3, 2.0561(13); Ir1-O1, 2.0624(11); Ir1-O2, 2.0686(11); Ir1-P1, 2.3654(5); Ir1-P2, 2.3920(5); N1-Ir1-O3, 179.30(6); N1-Ir1-O1, 89.78(5); O3-Ir1-O1, 90.03(5); N1-Ir1-O2, 89.99(5); O3-Ir1-O2, 90.22(5); O1-Ir1-O2, 178.69(5); N1-Ir1-P1, 97.67(4); O3-Ir1-P1, 83.02(4); O1-Ir1-P1, 95.33(4); O2-Ir1-P1, 83.43(4); N1-Ir1-P2, 90.84(4); O3-Ir1-P2, 88.46(4); O1-Ir1-P2, 81.46(4); O2-Ir1-P2, 99.83(4); P1-Ir1-P2, 170.911(15).



Figure 2.9. Crystal structure of 11. A pentane solvent molecule and the *tert*-butyl groups have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-O1, 2.0663(11); Ir1-O2, 2.0764(11); Ir1-N1, 2.1020(16); Ir1-P2, 2.3229(5); Ir1-P1, 2.3320(5); Ir1-H1, 1.70(2); O1-Ir1-O2, 176.19(5); O1-Ir1-N1, 87.97(5); O2-Ir1-N1, 88.25(5); O1-Ir1-P2, 86.17(4); O2-Ir1-P2, 94.68(3); N1-Ir1-P2, 95.82(4); O1-Ir1-P1, 96.13(4); O2-Ir1-P1, 83.91(3); N1-Ir1-P1, 97.67(4); P2-Ir1-P1, 166.384(19); O1-Ir1-H1, 95.6(6); O2-Ir1-H1, 88.2(6); N1-Ir1-H1, 176.3(7); P2-Ir1-H1, 85.7(7); P1-Ir1-H1, 80.7(7).



by NMR. A related reaction of proton sponge with an Ir<sup>III</sup> complex has previously been reported [11]. In further support of this proposal, **11** was also obtained by treatment of **8** with cobaltocene (a oneelectron donor) and the H atom donor 9,10-dihydroanthracene (DHA), or by heating **8** with sodium hydride. **11** can also be obtained from the reaction of **8** with lithium methoxide or diethylzinc, presumably via  $\beta$ -hydride elimination from an iridium-methoxy [12] or iridium-ethyl intermediate, respectively. The two latter routes give **11** most cleanly; in the reactions with proton sponge, we were unable to separate **11** from the byproducts.



Scheme 2.5. Synthetic routes to (ONO<sup>tBu</sup>)Ir(PPh<sub>3</sub>)<sub>2</sub>H, 11.

Treatment of **8** with dimethylzinc yielded the water-stable methyl complex  $(ONO^{tBu})Ir(PPh_3)_2Me$ (**12**). Oxidation of **12** with I<sub>2</sub> yields the iodide  $(ONO^{tBu})Ir(PPh_3)_2I$  (**13**) and methyl iodide (Scheme 2.6).



Scheme 2.6. Methylation to  $(ONO^{tBu})Ir(PPh_3)_2Me$ , 12, and subsequent functionalization with  $I_2$  to  $(ONO^{tBu})Ir(PPh_3)_2I$ , 13.

Crystal structures for complexes 8, 9, 11, 12, and 13 all exhibit closely analogous octahedral geometries. The structures of 12 and 13 are shown in Figures 2.10 and 2.11.

Unlike 8, 12 reacts cleanly with triethylphosphine to give the analogous  $PEt_3$  complex (14,

**Figure 2.10.** Crystal structure of **12.** Only *ipso* carbon atoms of the phenyl groups on phosphorus are shown. Selected atom distances (Å) and angles (°): Ir-O1, 2.0901(1); Ir-O2, 2.0700(1); Ir-C74, 2.0952(1); Ir-N, 2.1042(1); Ir-P1, 2.3449(1); Ir-P2, 2.3895(1); O1-Ir-O2, 176.495(3); P1-Ir-P2, 172.872(2); N-Ir-C74, 175.671(3); C74-Ir-O1, 95.588(2); C74-Ir-O2, 87.799(2); C74-Ir-P1, 85.584(2); C74-Ir-P2, 87.309(2); O1-Ir-P1, 82.692(2); O1-Ir-P2, 98.559(2); O2-Ir-P1, 96.698(2); O2-Ir-P2, 82.473(2); N-Ir-O1, 88.429(2); N-Ir-O2, 88.212(2); N-Ir-P1, 96.553(2); N-Ir-P2, 90.503(2).



Figure 2.11. Crystal structure of 13. Two pentane solvent molecules and the *tert*-butyl groups have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-N1, 2.040(3); Ir1-O2, 2.066(2); Ir1-O1, 2.076(2); Ir1-P2, 2.4233(10); Ir1-P1, 2.4247(11); Ir1-I2, 2.7013(3); N1-Ir1-O2, 89.52(10); N1-Ir1-O1, 88.88(10); O2-Ir1-O1, 178.36(9); N1-Ir1-P2, 89.69(9); O2-Ir1-P2, 78.59(8); O1-Ir1-P2, 101.03(8); N1-Ir1-P1, 89.04(9); O2-Ir1-P1, 102.10(8); O1-Ir1-P1, 78.25(8); P2-Ir1-P1, 178.55(3); N1-Ir1-I2, 179.19(9); O2-Ir1-I2, 90.56(6); O1-Ir1-I2, 91.05(7); P2-Ir1-I2, 91.12(2); P1-Ir1-I2, 90.15(2).



Scheme 2.7). 14 appears to be more thermally stable than 12, only slowly decomposing at temperatures above 120°C. It reacts similarly with  $I_2$ , giving methyl iodide and  $(ONO^{tBu})Ir(PEt_3)_2I$  (15). Both 14 (Figure 2.12) and 15 (Figure 2.13) were characterized crystallographically. Iodide complex 15 is unstable in methylene chloride, converting to the analogous chloride over several days at room temperature. Such behavior was not observed with the PPh<sub>3</sub> analogue 13.



Scheme 2.7. Synthesis of  $(ONO^{tBu}Ir(PEt_3)_2 \text{ complexes.})$ 

Figure 2.12. Crystal structure of 14. The ethyl groups of one phosphine ligand have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-O2, 2.0674(11); Ir1-O1, 2.0702(11); Ir1-N1, 2.1050(14); Ir1-C50, 2.1154(17); Ir1-P2, 2.3479(5); Ir1-P1, 2.3514(5); O2-Ir1-O1, 178.26(5); O2-Ir1-N1, 88.65(5); O1-Ir1-N1, 89.83(5); O2-Ir1-C50, 91.12(6); O1-Ir1-C50, 90.42(6); N1-Ir1-C50, 178.40(6); O2-Ir1-P2, 84.03(4); O1-Ir1-P2, 95.23(4); N1-Ir1-P2, 93.93(4); C50-Ir1-P2, 87.61(5); O2-Ir1-P1, 97.78(4); O1-Ir1-P1, 83.10(4); N1-Ir1-P1, 91.40(4); C50-Ir1-P1, 87.07(5); P2-Ir1-P1, 174.416(16).



In both  $I_2$  oxidations a dark blue color is observed over much of the course of the reaction, even though the starting complexes and the products are all yellow. Cyclic voltammetry experiments show quasi-reversible oxidations at 20 and 780 mV for **12** and reversible oxidations at -100 and Figure 2.13. Crystal structure of 15. The ethyl groups of the phosphine ligands have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-N1, 2.0619(13); Ir1-O2, 2.0648(11); Ir1-O1, 2.0661(11); Ir1-C(50), 2.148(7); Ir1-P1, 2.3711(4); Ir1-P2, 2.3722(4); Ir1-I2, 2.6625(3); N1-Ir1-O2, 89.86(5); N1-Ir1-O1, 88.67(5); O2-Ir1-O1, 178.36(5); N1-Ir1-C(50), 177.12(15); O2-Ir1-C(50), 89.65(17); O1-Ir1-C(50), 91.86(17); N1-Ir1-P1, 93.81(4); O2-Ir1-P1, 95.64(3); O1-Ir1-P1, 83.74(3); C(50)-Ir1-P1, 89.06(15); N1-Ir1-P2, 91.30(4); O2-Ir1-P2, 82.36(3); O1-Ir1-P2, 98.40(3); C(5)-Ir1-P2, 85.82(15); P1-Ir1-P2, 174.510(14); N1-Ir1-I2, 178.40(4); O2-Ir1-I2, 91.65(3); O1-Ir1-I2, 89.83(3); C(50)-Ir1-I2, 3.05(16); P1-Ir1-I2, 86.571(11); P2-Ir1-I2, 88.374(11).



840 mV for 14 both vs. ferrocene (Figure 2.14). The reaction of 14 with  $AgPF_6$  gave dark blue  $[(ONO^{tBu})Ir(PEt_3)_2Me]PF_6$  (16, Scheme 2.7), characterized by a crystal structure and an EPR spectrum (Figure 2.15) that are very similar to those of the (relatively few) organometallic  $Ir^{IV}$  species reported [13]. 16 could be reduced back to 14 with either cobaltocene or methyllithium; furthermore, treatment of 16 with tetrabutylammonium iodide gave MeI and some 15. All of this suggests that the reaction of 14 (or 12) with  $I_2$  begins with a single electron transfer to generate an intermediate cationic  $Ir^{IV}$  -Me species, which undergoes  $S_N 2$  attack by  $\Gamma$  at the Ir–C bond. The CV data suggest that further oxidization of 16 might be possible, perhaps even to an  $Ir^V$ -methyl complex, but no such species has yet been isolated or otherwise identified. (The close similarity of the second potentials, in contrast to the first, may indicate that the second wave corresponds to oxidation of the ONO<sup>tBu</sup> ligand rather than at Ir.) The crystal structure of 16 is show in Figure 2.16).

# 2.3.3 C-H Activation by Ir<sup>III</sup>(ONO<sup>tBu</sup>) Complexes

In benzene solution,  $(ONO^{tBu})Ir(PPh_3)_2Me$  converts over the course of several hours at 65°C to the analogous phenyl complex  $(ONO^{tBu})Ir(PPh_3)_2Ph$  (17), with evolution of methane. The benzene solution of 17 reacts further over the course of several weeks at 65°C to give a cyclometalated product,  $(ONO^{tBu})Ir(PPh_3)[\kappa^2-PPh_2(o-C_6H_4)]$  (18, Equation 2.4).

Figure 2.14. Cyclic voltammetry of 14, carried out in the air at room temperature. The solvent was dichloromethane with 0.1 M tetrabutylammonium tetrafluoroborate added as the electrolyte. Multiple runs were made with scan rates from 50 to 400 mV/s. Quasi-reversibility is seen in the form of a following chemical step. The dip at 0.3 V is an artifact.



**Figure 2.15.** EPR spectrum of  $[(ONO^{tBu})Ir(PEt_3)_2Me]PF_6$ , **16**, in dichloromethane at 20 K.



Figure 2.16. Crystal structure of one of the molecules of 16 in the unit cell. The unit cell has four iridiumcontaining molecules total; this figure only shows one of them. In addition, ethyl groups on the phosphine ligands, as well as the six benzene molecules per unit cell, have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-O2A, 1.994(5); Ir1-O1A, 2.011(5); Ir1-C50A, 2.101(8); Ir1-N1A, 2.129(7); Ir1-P2A, 2.400(2); Ir1-P1A, 2.418(2); O2A-Ir1-O1A, 173.5(2); O2A-Ir1-C50A, 94.2(3); O1A-Ir1-C50A, 92.3(3); O2A-Ir1-N1A, 87.4(2); O1A-Ir1-N1A, 86.1(2); C50A-Ir1-N1A, 177.4(3); O2A-Ir1-P2A, 82.62(17); O1A-Ir1-P2A, 98.06(18); C50A-Ir1-P2A, 84.4(2); N1A-Ir1-P2A, 93.78(18); O2A-Ir1-P1A, 98.16(17); O1A-Ir1-P1A, 81.81(18); C50A-Ir1-P1A, 89.8(2); N1A-Ir1-P1A, 91.96(18); P2A-Ir1-P1A, 174.24(8).





When **17** is isolated, redissolved in a solvent other than benzene (such as p-xylene), and heated to 65°C, conversion to **18** is complete within a few days. Both **17** (Figure 2.17 and **18** (Figure 2.18) were characterized crystallographically.

Thermolysis of **12** in  $C_6D_6$  yields  $CH_4$  as the only detectable methane isotopologue, and mass spectrometry of the resulting isolated phenyl product **17** shows incorporation of six D atoms (Equation 2.5). In contrast, heating  $(ONO^{tBu})Ir[P(C_6D_5)_3]_2(CH_3)$  (**12**- $d_{30}$ ) in  $C_6D_6$  yields only  $CH_3D$ ; this reaction is slower than that of all-protio-**12**, exhibiting a KIE of **4** 2.20. The PEt<sub>3</sub> analogue **14** reacts very slowly in  $C_6H_6$  or  $C_6D_6$ , requiring several weeks at 120°C to give  $(ONO^{tBu})Ir(PEt_3)_2Ph$ and  $CH_4$  or  $CH_3D$ , respectively.

Figure 2.17. Crystal structure of 17. A benzene and a pentane solvent molecule, as well as the phosphine phenyl groups, have been removed for clarity. The molecule is symmetric about the iridium center. Selected atom distances (Å) and angles (°): Ir1-O1, 2.0744(12); Ir1-C40, 2.074(3); Ir1-N1, 2.103(2); Ir1-P1, 2.3921(6); O1-Ir1-C40, 90.05(4); O1-Ir1-O1', 179.91(8); C40-Ir1-O1', 90.04(4); O1-Ir1-N1, 89.95(4); C40-Ir1-N1, 180.0; O1'-Ir1-N1, 89.96(4); O1-Ir1-P1', 97.70(4); C40-Ir1-P1', 88.831(13); O1'-Ir1-P1', 82.30(4); N1-Ir1-P1, 91.171(13); P1'-Ir1-P1; 177.66(3).



**Figure 2.18.** Crystal structure of **18**. A dodecane solvent molecule and parts of several phenyl and *tert*-butyl groups have been removed for clarity. Selected atom distances (Å) and angles (°): Ir-O1, 2.0696(1); Ir-O2, 2.0612(1); Ir-C46, 2.0669(1); Ir-N, 2.1156(1); Ir-P4, 2.3462(1); Ir-P5, 2.3483(1); O1-Ir-O2, 174.874(3); P4-Ir-P5, 164.008(2); N-Ir-C46, 167.055(4); C46-Ir-O1, 100.779(3); C46-Ir-O2, 80.655(3); C46-Ir-P4, 95.708(2); C46-Ir-P5, 68.499(2); O1-Ir-P4, 85.316(3); O1-Ir-P5, 94.944(2); O2-Ir-P4, 99.475(2); O2-Ir-P5, 80.959(3); N-Ir-O1, 88.656(3); N-Ir-O2, 89.198(3); N-Ir-P4, 93.867(3); N-Ir-P5, 102.125(3).





Thermolysis of **12** at 65°C in methylene chloride, THF, ether, or *p*-xylene leads directly to **18** (Equation 2.6). These transformations require less than one day for complete conversion (in methylene chloride or *p*-xylene), comparable to the time needed for conversion of **12** to **17** and much faster than the conversion of **17** to **18** in benzene. Reaction of **12** in toluene at 65°C proceeds similarly to that in benzene; although a single pure compound could not be isolated, the mass spectrum of the mixture is consistent with formation of an  $Ir^{III}$  tolyl compound,  $(ONO^{tBu})Ir(PPh_3)_2(C_6H_4CH_3)$ . The <sup>31</sup>P NMR shows two strong signals of roughly equal intensity with shifts close to that of phenyl compound **17**, suggesting the formation of two isomers, presumably *meta* and *para* (since *p*-xylene is unreactive); a much weaker nearby signal may indicate a small amount of the *ortho* isomer.



Although 12 is insoluble in acetonitrile, thermolysis in methylene chloride containing a small amount of acetonitrile affords a mixture of 18 and a product resulting from C–H activation of acetonitrile,  $[(ONO^{tBu})Ir(PPh_3)(CH_2CN)]_2$  (19); with  $CD_3CN$ ,  $CH_4$  is the only methane isotopologue produced (Equation 2.7). 19 has the dimeric structure shown in Figure 2.19, where coordination of N from the (CH<sub>2</sub>CN) group bonded to each Ir has displaced a PPh<sub>3</sub> ligand from the other. Although two <sup>1</sup>H NMR signals would be expected for the (CH<sub>2</sub>CN) methylene protons, which are diastereotopic in the solid-state structure, only one is observed; this could result from either accidental degeneracy or dissociation of the dimeric structure in solution.



Figure 2.19. Crystal structure of 19 [14]. A benzene solvent molecule, phosphine phenyl, and (ONO) tert-butyl groups have been removed for clarity. Selected atom distances (Å) and angles (°): Ir1-O1, 2.0190(2); Ir1-O2, 2.0883(2); Ir1-C104, 2.1472(2); Ir1-N1, 2.0758(2); Ir1-N4, 2.0882(2); Ir1-P1, 2.2654(2); N3-C103, 1.1271(1); C103-C104, 1.4380(1); N4-C102, 1.1278(1); C102-C101, 1.4482(2); Ir2-O3, 2.0912(2); Ir2-O4, 2.0396(2); Ir2-C101, 2.1740(3); Ir2-N2, 2.0854(3); Ir2-N3, 2.1290(2); Ir2-P2, 2.2574(2); O1-Ir1-O2, 173.203(10); N4-Ir1-P1, 173.670(9); N1-Ir1-C104, 170.591(10); C104-Ir1-O1, 81.941(8); C104-Ir1-O2, 98.236(8); C104-Ir1-N4, 86.476(8); C104-Ir1-P1, 90.036(7); O1-Ir1-N4, 88.426(8); O1-Ir1-P1, 96.321(8); O2-Ir1-N4, 84.807(8); O2-Ir1-P1, 90.475(8); N1-Ir1-O1, 89.793(8); N1-Ir1-O2, 89.439(8); N1-Ir1-N4, 88.823(8); N1-Ir1-P1, 95.360(8); Ir1-N4-C102, 156.881(14); N4-C102-C101, 171.704(16); C102-C101-Ir2, 104.11(1); Ir2-N3-C103, 156.797(13); N3-C103-C104, 172.115(16); C103-C104-Ir1, 105.731(10); O3-Ir2-O4, 174.306(10); N3-Ir2-P2, 171.891(9); N2-Ir2-C101, 172.156(10); C101-Ir2-O3, 96.853(8); C101-Ir2-O4, 84.460(8); C101-Ir2-N3, 85.543(7); C101-Ir2-P2, 88.633(7); O3-Ir2-N3, 85.175(8); O3-Ir2-P2, 89.930(7); O4-Ir2-N3, 89.412(8); O4-Ir2-P2, 95.646(8); N2-Ir2-O3, 89.263(8); N2-Ir2-O4, 88.981(8); N2-Ir2-N3, 90.101(8); N2-Ir2-P2, 96.309(8).



A plausible mechanism for the chemistry of 12 in benzene is shown in Scheme 2.8. The sequence of product formation (17 and 18 being preferred kinetically and thermodynamically, respectively [15]) would seem to suggest that the first C–H activation is the intermolecular reaction with benzene. But that is excluded by the isotopic labeling results. The H atom that departs with methane clearly comes from a PPh<sub>3</sub> ligand, not solvent benzene, so PPh<sub>3</sub> must be the site of the first C–H activation, even though the corresponding product 18 does not appear at all until much later. We propose therefore that dissociation of one PPh<sub>3</sub> ligand gives coordinatively unsaturated **A**, followed by intramolecular C–H activation and loss of methane to generate cyclometalated intermediate C. In benzene solution coordination of PPh<sub>3</sub> to **C** is not competitive; instead **C** reacts with benzene to give 17 as initial observed product. Subsequent conversion to the thermodynamic product 18 is much slower.



Scheme 2.8. Proposed mechanism for the transformation of 12 in benzene to the kinetic product 17 and the thermodynamic product 18.

C-H activation is shown in Scheme 2.8 as proceeding *via* oxidative addition to give an  $\mathrm{Ir}^{\mathrm{V}}$  intermediate, a mechanism that has been supported by both experiment [16] and calculations [17] for the above-mentioned [15] Cp\* system. It seems reasonable that similar considerations would apply here as well; but an alternative pathway, such as  $\sigma$ -bond metathesis, cannot be excluded. In any case, conversion of **A** to **C** must be irreversible, as no multiple H/D exchange is observed, whereas conversion of **C** to **F** must be reversible, since **17** eventually reverts to **18**.

The fact that products are obtained from solvent activation with toluene but not p-xylene suggests that C-H activation ortho to a methyl substituent is sterically inhibited. As a consequence, in the latter solvent **C** (or a  $\pi$ -arene adduct analogous to **D**) has no alternative but to bind PPh<sub>3</sub> and **18** forms directly, as it does in solvents (dichloromethane, ether, THF) that are not susceptible to C-H activation at all. In acetonitrile the two pathways are competitive. The reaction of **14** is much slower, presumably because PEt<sub>3</sub> dissociates much less readily, and leads only to a phenyl product, indicating that cyclometalation of PEt<sub>3</sub> does not take place.

### 2.3.4 Kinetics of C–H Activation

The transformation of **12** to **17** and/or **18** is readily followed by <sup>31</sup>P NMR, as each of the species has a distinct spectrum. In early experiments results were not always highly reproducible; most probably this is due to oxidation of small amounts of PPh<sub>3</sub> by adventitious impurities, which could effect significant acceleration; indeed, deliberate addition of oxidants such as chloranil and dioxygen did speed up conversion of **12** considerably. However, reasonably reproducible rates ( $\pm 15\%$ ) could be achieved by careful attention to purification of starting complex and solvent as well as exclusion of air.

The somewhat simplified mechanism shown in Scheme 2.9 may be used for analysis; it leaves out the (unobserved) intermediates **B** (which will rapidly convert to **C**) and **D** and **E** (which are presumed to be in rapid equilibrium with **C** and **F**); none of these should have any kinetic consequences. Three transformations will be considered in turn: (1) conversion of **12** to **17** in benzene; (2) conversion of **12** to **18** in *p*-xylene; and (3) conversion of **17** to **18** in benzene or *p*-xylene.

The first of these may be analyzed in terms of reversible dissociation of PPh<sub>3</sub> (henceforth abbreviated as L) followed by rate-determining C–H activation (the  $k_2$  step). Since the conversion of **A** to **C** is irreversible (*vide supra*), no buildup of any intermediate is observed, and formation of **17** is essentially complete before any **18** is observed. In this simplified framework, we can treat the dissociation of L from **12** as a fast pre-equilibrium and the intramolecular C–H activation of L as rate-determining, giving us  $K_1 = [\mathbf{A}][\mathbf{L}]/[\mathbf{12}]$ . Thus the rate law would be  $-d[\mathbf{12}]/dt = d[\mathbf{17}]/dt = k2[\mathbf{A}] = (k_2K_1[\mathbf{12}])/[\mathbf{L}]$ , and the rate should be cleanly first order in **12** and inverse-first-order in L. There is a potential complication if no extra L is added: [L] will be governed by both  $K_1$  and  $K_4$ , so if these two equilibrium constants were significantly different, [L] would vary



Scheme 2.9. Simplified version of Scheme 2.8, used for kinetic analysis.

in a complex manner as conversion of **12** to **17** proceeds, and the disappearance of **12** or appearance of **17** might not follow clean first-order kinetics. Nonetheless, it does: a good exponential fit is achieved (Figure 2.20, left), with  $k_{obs} = 1.8(3) \times 10^{-4} \text{ s}^{-1}$  (equivalent to a half-life of about an hour), so any difference in K values is small enough to neglect. The **12**- $d_{30}$  ((ONO<sup>*t*Bu</sup>)Ir[P(C<sub>6</sub>D<sub>5</sub>)<sub>3</sub>]<sub>2</sub>Me) isotopologue behaves similarly, yielding  $k_{obs} = 4.4(6) \times 10^{-5} \text{ s}^{-1}$  and hence KIE = 4(1) (Figure 2.20, right), consistent with the assignment of C–H activation of L as rate-determining.

**Figure 2.20.** Left: kinetics of conversion of **12** to **17** in  $C_6D_6$  at 65°C. Right: kinetics of conversion of **12**- $d_{30}$  ((ONO<sup>*t*Bu</sup>)Ir[P( $C_6D_5$ )\_3]<sub>2</sub>Me) to **17**- $d_{36}$  ((ONO<sup>*t*Bu</sup>)Ir[P( $C_6D_5$ )\_3]<sub>2</sub>C<sub>6</sub>D<sub>5</sub>) in  $C_6D_6$  at 65°C.



As expected, the addition of extra L slows the reaction significantly; a plot of  $1/k_{obs}$  is linear in [L] (Figure 2.21). In principle, at sufficiently high [L] some **18** should form directly in competition with **17**; in practice, such conditions are probably not reachable (and conversion of **12** would become extremely slow anyway).

Figure 2.21. Dependence of the reciprocal of the rate of conversion of 12 to 17 on the amount of added triphenylphosphine. See Section 2.5.2 for details on how this plot was constructed.



The rate law for direct conversion of **12** to **18** in *p*-xylene should be identical to the above, and the reaction does exhibit clean first-order kinetics, at a rate  $(k_{obs} = 8(1) \times 10^{-5} \text{ s}^{-1})$  about a factor of 2 slower than that for **12** to **17**. There are several possible explanations for the discrepancy. First, the values of  $K_1$  and  $k_2$  need not be identical to those in benzene (though they would not be expected to differ very much). Second, intermediate **C** may be complexed by *p*-xylene to give an analogue of intermediate  $\mathbf{D}$ , which in this case (in contrast to benzene) would not lead to any productive reaction, but would reduce the concentration of  $\mathbf{C}$  and hence the rate of formation of  $\mathbf{18}$ . However, any substantial (i.e. sufficient to account for the entire factor of 2) concentration of a new intermediate should have been detectable by NMR. Finally (and perhaps most likely), it may be that agreement within a factor of 2 (especially on changing solvent) is as good as can be expected, given the reproducibility considerations discussed earlier.

As noted above, the conversion of **17** to **18** is much slower in benzene than in *p*-xylene, taking place over weeks or days, respectively (Figure 2.22). This observation is readily explained by Scheme 2.9: the concentration of **C**, the precursor to **18**, will be inversely related to the concentration of benzene. The rate law for that mechanism can be derived by using the steady-state approximation for *both* **C** and **F**, both of which should be present in low concentration and in rapid equilibrium with one another. This is most simply accomplished by defining a dummy variable  $[\mathbf{X}] = [\mathbf{C}] + [\mathbf{F}]$ . For steady-state in  $[\mathbf{X}]$ :  $0 = d[\mathbf{X}]/dt = k_{-4}[\mathbf{17}] - k_4[\mathbf{F}][\mathbf{L}] - k_5[\mathbf{C}][\mathbf{L}]$ . Substituting  $[\mathbf{F}] = K_3[\mathbf{C}][\text{PhH}]$  gives  $k_{-4}[\mathbf{17}] - k_4[\mathbf{F}][\mathbf{L}] - k_5[\mathbf{C}][\mathbf{L}] = k_{-4}[\mathbf{17}] - K_3k_4[\mathbf{C}][\text{PhH}][\mathbf{L}] - k_5[\mathbf{C}][\mathbf{L}] = 0$ ; hence  $[\mathbf{C}] = (k_{-4}[\mathbf{17}])/(k_5[\mathbf{L}] + K_3k_4[\text{PhH}][\mathbf{L}])$ . Hence the rate law for the conversion is  $-d[\mathbf{17}]/dt =$  $d[\mathbf{18}]/dt = k_5[\mathbf{C}][\mathbf{L}] = (k_{-4}k_5[\mathbf{17}])/(k_5 + K_3k_4[\text{PhH}])$ . In benzene solution the reaction should be first-order in **17** and independent of [L]; both were observed. In *p*-xylene, on the other hand, [PhH] is continuously increasing as **17** is consumed, so first-order kinetics (which *are* observed) would not be expected *unless*  $k_5$  is large compared to  $k_4K_3$ [PhH] over the course of the reaction.





We can test this for self-consistency with the observed rate constants, again assuming that there is little difference in parameters between benzene and *p*-xylene reactions. For conversion of **17** to **18** in benzene,  $k_{obs} = 4.2(6) \times 10^{-7} \text{ s}^{-1}$ . Since no direct formation of **18** from **12** was observed,  $k_5$  must be small compared to  $k_4K_3$ [PhH], so that value of  $k_{obs}$  is approximately equal to  $k_{-4}k_5/k_4K_3$ [PhH]. For the reaction in *p*-xylene,  $k_{obs} = 2.9(4) \times 10^{-6} \text{ s}^{-1}$ ; if our assumption that  $k_5$  is large compared to  $k_4K_3$ [PhH] is correct, that value of  $k_{obs} = k_{-4}$ . Substituting this value into

the above expression, we get  $k_5/k_4K_3$ [PhH] = 0.13, so  $k_5$  is not completely negligible compared to  $k_4K_3$ [PhH], but small enough (within the limits of reproducibility as well as the assumption of solvent-independent parameters) to validate the approximation for  $k_{obs}$  in benzene. Furthermore, since for neat benzene [PhH]  $\approx 11$  M,  $k_5/k_4K_3 = 1.4$  M. For the reaction in *p*-xylene, the starting [17] = the maximum [PhH] = 8.8 mM and the minimum value of  $k_5/k_4K_3$ [PhH] = 160, so the assumption required to account for first-order kinetics is valid as well. Accordingly, the kinetics appear completely consistent with the proposed mechanism.

# 2.4 Conclusions

The ONO ligand provides a versatile framework for synthesis of a wide variety of  $Ir^{I}$  and  $Ir^{III}$  complexes. Using this framework, two key steps in a scheme for functionalization of hydrocarbons have been demonstrated. Conversion of the Ir-Me bond in complexes **12** and **14** to MeI is effected by addition of  $I_2$ ; there is evidence that the reaction proceeds *via* one-electron oxidation to an (isolable)  $Ir^{IV}$  methyl intermediate. Triphenylphosphine complex **12** is able to activate C-H bonds in benzene (and toluene) under quite mild conditions; the mechanism follows an unusual pathway in which the first C-H activation is intramolecular, but the product of that process, although thermodynamically preferred, is kinetically disfavored with respect to the intermolecular benzene activation product. Unfortunately the (ONO)Ir<sup>III</sup> system is not sufficiently reactive to activate nonaromatic C-H bonds (except for acetonitrile).

# 2.5 Supporting Details

### 2.5.1 Experimental Section

### 2.5.1.1 General Methods

All compounds were prepared in a nitrogen-filled glovebox unless otherwise specified. Reactions taking place in dichloromethane at 90°C were conducted in either sealed glass bombs or J-Young NMR tubes. Solvents in the glovebox were dried using the Grubbs method [18]. All NMR solvents were purchased from Cambridge Isotope Laboratories, Inc., (except for CDCl<sub>3</sub>) filtered through alumina, and stored over 4 Å molecular sieves. POCl<sub>3</sub> was purchased from Acros Organics. 2,6-dibromopyridine, nBuLi, tBuLi, 4-tert-butylpyridine, [FeCp<sub>2</sub>][PF<sub>6</sub>], indene, N,N-dimethylaminoethanol, PPh<sub>3</sub>, propylene, proton sponge, AgPF<sub>6</sub>, AgOTf, 15-crown-5, and NaH were purchased from Aldrich. H<sub>2</sub>O<sub>2</sub> was purchased from EMD. [Ir(cod)Cl]<sub>2</sub> and Pd(PPh<sub>3</sub>)<sub>4</sub> were purchased from Strem. The synthetic route towards the ligand H<sub>2</sub>(ONO) closely follows a previously described procedure [9]. <sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, and <sup>31</sup>P NMR spectra were recorded on Varian Mercury 300 MHz NMR spectrometers. X-ray data were collected using a Bruker KAPPA APEX II diffractometer.

#### 2.5.1.2 Synthesis of 4-tert-Butylpyridine-N-oxide

Following a published procedure [19], 4-*tert*-butylpyridine (18.0 mL, 16.6 g, 123 mmol) was mixed with 135 mL of glacial acetic acid and 100 mL of hydrogen peroxide (30% in water) in a 1 L roundbottom flask under air. After refluxing for 4 h, 100 mL of additional hydrogen peroxide (30% in water) was added, and the mixture was refluxed overnight. Then 200 mL of the solvent was removed by distillation, and 100 mL water was added and then removed by distillation as well. The remaining solution was neutralized with sodium carbonate. The organic layer was extracted with methylene chloride, filtered, and evaporated to dryness to yield white crystals (which gave a yellow solution in  $CH_2Cl_2$ ). Isolated yield: 15.3 g, 101 mmol, 82%. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.31 (s, 9H,  $C(CH_3)_3$ ), 7.26 (d, 2H, <sup>3</sup>J = 7.2 Hz, aryl-H), 8.15 (d, 2H, <sup>3</sup>J = 7.5 Hz, aryl-H). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  30.5 (C(CH<sub>3</sub>)<sub>3</sub>), 34.6 (C(CH<sub>3</sub>)<sub>3</sub>), 123.1, 138.6, 151.2 (aryl).

### 2.5.1.3 Synthesis of 2-Chloro-4-tert-butylpyridine

In a 250 mL round-bottom flask open to the air, 4-*tert*-butylpyridine-*N*-oxide (15.3 g, 101 mmol) was dissolved in 61 mL of neat POCl<sub>3</sub>. The mixture was allowed to reflux under argon for 12 to 16 h (refluxing can also be done under air, but the yield is somewhat lower). Excess POCl<sub>3</sub> was removed by distillation, and the remaining liquid was washed with a saturated aqueous solution of sodium carbonate. The organic layer was extracted with ether, filtered, and evaporated to dryness, yielding a dark red oil (13.5 g, 79.3 mmol, 79% yield). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.26 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 7.16 (dd, 1H, <sup>3</sup>J = 5.4 Hz, <sup>4</sup>J = 1.8 Hz, aryl-H), 7.25 (d, 1H, <sup>4</sup>J = 1.8 Hz, aryl-H), 8.23 (dd, 1H, <sup>3</sup>J = 5.7 Hz, <sup>5</sup>J = 0.6 Hz, aryl-H). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  30.3 (C(CH<sub>3</sub>)<sub>3</sub>), 35.0 (C(CH<sub>3</sub>)<sub>3</sub>), 119.7, 121.3, 149.4, 151.7, 163.5 (aryl).

### 2.5.1.4 Synthesis of 2-Chloro-4-tert-butylpyridine-N-oxide

In a 1 L round-bottom flask, 2-chloro-4-*tert*-butylpyridine (13.5 g, 79.3 mmol) was mixed with 100 mL of glacial acetic acid and 80 mL of hydrogen peroxide (30% in water). After refluxing for 4 h under air, 80 mL of additional hydrogen peroxide (30% in water) was added and the mixture was refluxed overnight. Then 200 mL of the solvent was removed by distillation, and 100 mL of water was added and then distilled off as well. The remaining solution was neutralized with sodium carbonate. The organic layer was extracted with methylene chloride, filtered, and evaporated to dryness to yield yellow crystals (10.3 g, 55.3 mmol, 70% yield). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.31 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 7.19 (dd, 1H, <sup>3</sup>J = 6.6 Hz, <sup>4</sup>J = 3.0 Hz, aryl-H), 7.44 (d, 1H, <sup>4</sup>J = 2.7 Hz, aryl-H), 8.27 (dd, 1H, <sup>3</sup>J = 6.6 Hz, <sup>5</sup>J = 0.6 Hz, aryl-H). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  30.4 (C(CH<sub>3</sub>)<sub>3</sub>), 34.7 (C(CH<sub>3</sub>)<sub>3</sub>), 121.3, 124.1, 139.8, 151.3 (aryl).

#### 2.5.1.5 Synthesis of 2,6-Dichloro-4-tert-butylpyridine

In a 250 mL round-bottom flask open to the air, 2-chloro-4-*tert*-butylpyridine-N-oxide (15.3 g, 101 mmol) was dissolved in 40 mL of neat POCl<sub>3</sub>. The mixture was allowed to reflux under argon for 12 to 16 h. Excess POCl<sub>3</sub> was removed by distillation, and the remaining liquid was washed with a saturated aqueous solution of sodium carbonate. The organic layer was extracted with ether, filtered, and evaporated to dryness, yielding a thick black oil. This oil was subjected to column chromatography over silica (95:5 hexanes/ethyl acetate), affording brown crystals after evaporation of solvent. The crystals were washed with hexanes, giving white 2,6-dichloro-4-*tert*-butylpyridine (5.57 g, 27.3 mmol, 49% yield; yield over four steps from 4-*tert*-butylpyridine: 22%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.30 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 7.23 (s, 2H, aryl-H). <sup>13</sup>C{<sup>1</sup>H} NMR (75.5 MHz, CDCl<sub>3</sub>):  $\delta$  30.3 (C(CH<sub>3</sub>)<sub>3</sub>), 35.4 (C(CH<sub>3</sub>)<sub>3</sub>), 120.2, 150.6, 166.3 (aryl).

#### 2.5.1.6 Synthesis of O-Methoxymethyl-2-bromo-4,6-di-tert-butylphenoxide

Bromine (3.7 mL, 12 g, 73 mmol) was added via syringe to a solution of 2,4-di-tert-butylphenol (15 g, 73 mmol) in  $CH_2Cl_2$  (200 mL). The brown color of  $Br_2$  disappeared upon addition. GC-MS analysis after 5 min shows only the presence of the desired brominated  $product(M^+ = 284 \text{ and } 286)$ . The organic mixture was washed with water, then dried over  $MgSO_4$ , and filtered. Removal of volatile material by rotary evaporation gave a golden oil which solidified after placing under high vacuum (< 1 mTorr). This material (4,6-di-*tert*-butyl-2-bromophenol) was dissolved in dry THF (200 mL) under argon, and was deprotonated with NaH (1.92 g, 80 mmol). After the addition of NaH the reaction mixture was stirred for 1 h at room temperature; then MOMCl (6.1 mL, 6.5 g, 80 mmol) was added via syringe. The reaction mixture was stirred at room temperature for 9 h. Water was added and the mixture was concentrated under vacuum. The desired product was extracted with  $CH_2Cl_2$  (three times); the combined organic fractions were dried over MgSO<sub>4</sub>, filtered, and dried under high vacuum overnight to give 23.5 g (98% yield over two steps) of O-methoxymethyl-2-bromo-4,6-di-*tert*-butylphenoxide as a golden oil. <sup>1</sup>H NMR (300 MHz,  $CDCl_3$ ):  $\delta$  1.30 (s, 9H,  $C(CH_3)_3$ ), 1.44 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 3.70 (s, 3H, OCH<sub>3</sub>), 5.23 (s, 2H, OCH<sub>2</sub>O), 7.32 (d, 2H, aryl-H), 7.41 (d, 2H, aryl-H). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  31.0 (C(CH<sub>3</sub>)<sub>3</sub>), 31.5 (C(CH<sub>3</sub>)<sub>3</sub>), 34.8 (C(CH<sub>3</sub>)<sub>3</sub>), 36.1 (C(CH<sub>3</sub>)<sub>3</sub>), 57.9 (OCH<sub>3</sub>), 99.5 (OCH<sub>2</sub>O), 117.7, 124.1, 128.9, 144.6, 147.8, 150.7 (aryl). MS FAB+:  $328 (M^+)$ .

### 2.5.1.7 Synthesis of MOM<sub>2</sub>(ONO)

A mixture of *O*-Methoxymethyl-2-bromo-4,6-di-*tert*-butylphenoxide (5.19 g, 15.8 mmol) and THF (25 mL) in a Schlenk tube fitted with a screw-in Teflon stopper was frozen in a cold well, along with a solution of *t*BuLi (2.13 g, 33.3 mmol, 2.1 eq) in hexanes (10 mL), in an inert atmosphere

glove box. Both solutions were taken out of the box, and the tBuLi solution was added to the solution of O-Methoxymethyl-2-bromo-4,6-di-tert-butylphenoxide while allowing the latter to thaw. The mixture was stirred for 1 h while allowing it to reach room temperature. ZnCl<sub>2</sub> (1.51 g, 7.12 mmol, 0.70 eq) was added with the aid of THF. After stirring the reaction mixture for 30 minutes, 1,3-dibromobenzene (1.69 g, 7.12 mmol, 0.45 eq) and  $Pd(PPh_3)_4$  (188.4 mg, 0.163 mmol, 0.01 eq) were added with the aid of some THF. The reaction vessel was placed in an oil bath preheated to 75°C and stirred for 16 h, then allowed to cool to room temperature and quenched with water. Volatile materials were removed under vacuum and water was added. This mixture was extracted with Et<sub>2</sub>O (three times). The combined organics were dried over MgSO<sub>4</sub>, filtered, and concentrated by rotary evaporation. The resulting residue was suspended in MeOH cooled to  $-25^{\circ}$ C. The resulting white precipitate was collected by filtration through a sintered glass funnel, washed with cold MeOH, and immediately used for the synthesis of  $H_2(ONO)$ . <sup>1</sup>H NMR (300 MHz,  $CDCl_3$ ):  $\delta$  1.37 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.51 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 3.41 (s, 6H, OCH<sub>3</sub>), 4.64 (s, 4H, OCH<sub>2</sub>O), 7.45 (d, 2H, aryl-H), 7.61 (d, 2H, aryl-H), 7.68 – 7.80 (m, 3H,  $\rm NC_5H_3).$   $^{13}\rm C\{^1H\}$  NMR (75.4 MHz,  $\rm CDCl_3):$   $\delta$  31.1  $(C(CH_3)_3), 31.6 (C(CH_3)_3), 34.8 (C(CH_3)_3), 35.6 (C(CH_3)_3), 57.6 (OCH_3), 99.7 (OCH_2O), 123.2, 0.5 (OCH_3), 0.5$ 125.2, 126.7, 134.1, 136.1, 142.5, 146.1, 151.5, 158.4 (aryl).

# Synthesis of $H_2(ONO)$

Compound MOM<sub>2</sub>(ONO) was suspended in 25 mL of MeOH, and 25 mL of concentrated HCl was added. This mixture was heated at 80°C for 5 h. After cooling, volatile materials were removed under vacuum yielding 3.45 g (0.70 mmol, 90% based on *O*-Methoxymethyl-2-bromo-4,6-di-*tert*-butylphenoxide) of H<sub>2</sub>(ONO) as a white powder. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.39 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.48 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 7.46 (d, 2H, aryl-H), 7.51 (d, 2H, aryl-H), 7.67 (d, 2H,  $3_5-NC_5H-H_2$ ), 8.01 (t, 1H, 4-NC<sub>5</sub>H<sub>2</sub>-H), 10.59 (s, 2H, OH). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  29.8 (C(CH<sub>3</sub>)<sub>3</sub>), 31.8 (C(CH<sub>3</sub>)<sub>3</sub>), 34.6 (C(CH<sub>3</sub>)<sub>3</sub>), 35.6 (C(CH<sub>3</sub>)<sub>3</sub>), 120.5, 121.3, 123.0, 126.4, 137.5, 140.0, 141.5, 153.3, 157.6 (aryl). HR-MS: C<sub>33</sub>H<sub>45</sub>O<sub>2</sub>N: Calculated: 487.3450. Measured: 487.3446.

# 2.5.1.8 Synthesis of $MOM_2(ONO^{tBu})$

*O*-Methoxymethyl-2-bromo-4,6-di-*tert*-butylphenoxide (6.15 g, 18.7 mmol), was dissolved in 60 mL of THF. *tert*-butyllithium (2.52 g, 39.4 mmol) was dissolved in 27 mL of pentane and added to the solution of *O*-methoxymethyl-2-bromo-4,6-di-*tert*-butylphenoxide at  $-78^{\circ}$ C. The mixture was allowed to warm to room temperature and stirred for 1 h. A suspension of ZnCl<sub>2</sub> (1.80 g, 13.2 mmol) in THF was then added, and the mixture stirred for another 30 min. A solution of 2,6-dichloro-4-*tert*-butylpyridine (1.72 g, 8.42 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (218 mg, 189  $\mu$ mol) in THF was added, the reaction vessel was transferred to a preheated 75°C oil bath, and the mixture was stirred for 16 h. The

mixture was quenched with 10 mL of water, and the volatiles were removed by rotary evaporation. Another 70 mL of water was then added, and the organic layer was extracted three times with ether, dried with MgSO<sub>4</sub>, and evaporated to dryness, giving a white powder, which was purified by washing with cold methanol (2.67 g, 4.23 mmol, 50.3% yield). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.35 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.37 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 1.49 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 3.38 (s, 6H, OCH<sub>3</sub>) 4.60 (s, 4H, OCH<sub>2</sub>O), 7.42 (d, 2H, <sup>4</sup>J = 2.6 Hz, aryl-H), 7.56 (d, 2H, <sup>4</sup>J = 2.6 Hz, aryl-H), 7.66 (s, 2H, NC<sub>5</sub>H<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  30.6, 30.9, 31.4, 34.6, 34.9, 35.4 (C(CH<sub>3</sub>)<sub>3</sub>), 57.3 (OCH<sub>3</sub>), 99.3 (OCH<sub>2</sub>O), 120.4, 124.8, 126.6, 134.3, 142.2, 145.8, 151.3, 158.0, 159.7 (aryl).

## 2.5.1.9 Synthesis of $H_2(ONO^{tBu})$

 $MOM_2(ONO^{tBu})$  (2.67 g, 4.23 mmol) was suspended in a mixture of methanol (40 mL) and concentrated HCl (40 mL) and heated at 80°C for 6 h. The suspension was then cooled to 0°C and filtered, and the precipitate, a white powder, was washed with cold MeOH to afford H<sub>2</sub>(ONO<sup>tBu</sup>) (1.71 g, 3.14 mmol, 74% yield). <sup>1</sup>H NMR (300 MHz,  $d_8$ -THF):  $\delta$  1.36 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.46 (br, 27H, C(CH<sub>3</sub>)<sub>3</sub>), 7.42 (d, 2H, <sup>4</sup>J = 2.4 Hz, aryl-H), 7.53 (d, 2H, <sup>4</sup>J = 2.7 Hz, aryl-H), 7.81 (s, 2H, NC<sub>5</sub>H<sub>2</sub>), 10 (br s, concentration dependent, 2H, OH). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  29.6, 30.6, 31.6, 34.4, 35.3, 35.5 (C(CH<sub>3</sub>)<sub>3</sub>), 117.7, 121.7, 122.6, 126.0, 137.2, 141.2, 153.0, 157.2, 164.1 (aryl). MS FAB+: 543.4052 (M<sup>+</sup>). Analysis calculated for C<sub>37</sub>H<sub>53</sub>NO<sub>2</sub>: C, 81.72; H, 9.82; N, 2.58. Found: C, 81.57; H, 10.06; N, 2.55.

### 2.5.1.10 Synthesis of Na[Ir(cod)ONO], 1

H<sub>2</sub>(ONO) (91.2 mg, 187 μmol) was dissolved in 10 mL of THF, and an excess of NaH (24.6 mg, 1.03 mmol) was added. The yellow suspension first turned orange and then yellow again, with vigorous evolution of H<sub>2</sub>. The suspension was allowed to stir for one hour, after which it was filtered through Celite and added to a stirring solution of  $[Ir(cod)Cl]_2$  (60.0 mg, 89.3 μmol) in 5 mL of THF. After 30 min of stirring the solution was filtered and pumped down, giving **1** as a red powder. Residual solvent was removed by trituration with benzene followed by overnight evacuation under high vacuum. Isolated yield was 148.3 mg (183.3 μmol, 98.0%); the yield was quantitative by NMR. <sup>1</sup>H NMR (300 MHz,  $d_8$ -THF):  $\delta$  0.84 (m, 4H, sp<sup>3</sup> on cod), 1.32 (s, 18H, 2 *t*Bu on ligand phenolate), 1.49 (s, 18H, 2 *t*Bu on ligand phenolate), 1.68 (br m, 4H, sp<sup>3</sup> on cod), 2.99 (br d, 4H, J = 2.7 Hz, sp<sup>2</sup> on cod), 7.19 (d, 2H, <sup>4</sup>J = 2.7 Hz, ligand aryl), 7.24 (d, 2H, <sup>4</sup>J = 2.6 Hz, ligand aryl), 7.26 (br s, 2H, ligand aryl), 7.66 (t, 1H, <sup>3</sup>J = 8.0 Hz, ligand pyridine 4-position). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz,  $d_8$ -THF):  $\delta$  14.6, 23.4, 31.5, 32.5, 32.8, 34.7, 36.2, 49.7, 121.3, 123.8, 125.0, 131.9, 135.7, 137.2, 139.2, 159.4, 166.9. MS FAB+: 786.3856 (M<sup>+</sup>-Na).

### 2.5.1.11 Synthesis of Pyridine-Activated Complex 3

Na[Ir(cod)(ONO)] (1) (85.1 mg, 105  $\mu$ mol) was dissolved in 1 mL of C<sub>6</sub>H<sub>6</sub>. 15-Crown-5 (21  $\mu$ L, 106  $\mu$ mol) was mixed in, and the solution was allowed to sit undisturbed for several days. Orange crystals formed and were shown crystallographically to consist of **3**. A pure (by NMR) sample was obtained by washing with C<sub>6</sub>H<sub>6</sub>, redissolving in THF, and drying under vacuum. Isolated yield: 82.7 mg (79.8  $\mu$ mol, 75.9%). <sup>1</sup>H NMR (500 MHz,  $d_8$ -THF):  $\delta$  1.35 (s, 9H, tBu on ligand phenolate), 1.42 (s, 9H, tBu on ligand phenolate), 1.51 (br s, 18H, 2 tBu on ligand phenolate), 1.77 (br, 4H, sp<sup>3</sup> on cod), 2.18 (br, 4H, sp<sup>3</sup> on cod), 3.29 (br, 2H, sp<sup>2</sup> on cod), 3.37 (s, 20H, crown ether), 4.46 (br, 2H, sp<sup>2</sup> on cod), 7.24 (d, 1H, <sup>4</sup>J = 2.6 Hz, ligand aryl), 7.25 (d, 1H, <sup>4</sup>J = 2.4 Hz, ligand aryl), 7.48 (d, 1H, <sup>3</sup>J = 8.4 Hz, ligand aryl), 7.78 (d, 1H, <sup>4</sup>J = 2.4 Hz, ligand aryl), 7.91 (d, 1H, <sup>3</sup>J = 8.2 Hz, ligand aryl), 8.45 (d, 1H, <sup>4</sup>J = 2.6 Hz, ligand aryl), 18.14 (s, 1H, ligand phenol). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz,  $d_8$ -THF):  $\delta$  30.4, 31.1, 31.6, 32.4, 32.9, 33.9, 35.1, 35.4, 36.1, 36.4, 45.1, 70.2, 74.4, 112.5, 120.2, 120.8, 123.0, 124.3, 124.4, 126.9, 135.0, 137.4, 138.5, 138.8, 146.5, 149.7, 152.6, 153.2, 159.7, 162.7.

### 2.5.1.12 Synthesis of $[NaIr(cod)(ONO^{tBu})]_2$ , 4

 $H_2(ONO^{tBu})$  (246.8 mg, 453.8 µmol) was dissolved in 10 mL of THF, and an excess of NaH (64.8 mg, 2.70 mmol) was added. The light yellow solution first turned orange and then yellow again, with vigorous evolution of H<sub>2</sub>. The suspension was allowed to stir for an hour, after which it was filtered through Celite.  $[Ir(cod)Cl]_2$  (145.2 mg, 216.2  $\mu$ mol) was dissolved in THF and slowly added to the stirring solution of  $Na_2(ONO^{tBu})$  in order to prevent formation of overmetalated  $[Ir(cod)]_2(ONO^{tBu})$ , 5. After an hour of stirring the solvent was removed in vacuo, redissolved in hexanes, and filtered, and the solvent removed *in vacuo* again, giving 4 THF as a red solid with a glassy appearance. The residual THF was removed by adding more hexanes and evacuating to give 4. 4 THF is very soluble in hexanes, whereas 4 is much less so; consequently impurities in 4 can be removed with a hexanes wash. Crystals were obtained by allowing a pentane solution of 4. THF or 4 to evaporate. Isolated yield was 326.4 mg (188.6  $\mu$ mol, 87.2%). <sup>1</sup>H NMR (300 MHz,  $d_8$ -THF):  $\delta$  0.83 (br d, 16H, <sup>2</sup>J = 7.5 Hz, sp<sup>3</sup> on 2 cod), 1.33 (s, 36H, 4 tBu on ligand phenolate), 1.37 (s, 18H, 2 tBu on ligand pyridine), 1.49 (s, 36H, 4 tBu on ligand phenolate), 2.97 (br s, 8H, sp<sup>2</sup> on 2 cod), 7.19 (d, 4H,  ${}^{4}J = 2.7$  Hz, 2 ligand phenolate aryl), 7.23 (d, 4H,  ${}^{4}J = 3.0$  Hz, 2 ligand phenolate aryl), 7.25 (s, 4H, 2 ligand pyridine aryl).  ${}^{13}C{}^{1H}$  NMR (75.4 MHz,  $d_8$ -THF):  $\delta$  31.6, 32.1, 33.1, 33.5, 35.4, 36.2, 36.9, 50.3, 119.2, 124.4, 125.4, 133.0, 136.2, 139.6, 159.6, 161.2, 167.7. MS FAB+: 842.4478 ( $[Ir(cod)(ONO^{tBu})]$  $(M^+-Na)$ . Analysis calculated for  $C_{90}H_{126}Ir_2N_2Na_2O_4$ : C, 62.47; H, 7.34; N, 1.62. Found: C, 62.26; H, 7.52; N, 1.35.

#### 2.5.1.13 Reaction of 4 with CO

 $[NaIr(cod)(ONO^{tBu})]_2$  (179.4 mg, 103.7  $\mu$ mol) was dissolved in THF in a Schlenk flask. The solution was cooled to  $-78^{\circ}$ C, and an atmosphere of CO (about 5 mmol) was introduced into the headspace. The solution was then brought back to room temperature and allowed to stir overnight. Afterward, the solution was pumped down, yielding a yellow-brown solid with IR stretching frequencies at 2057, 2030, and 1977 cm<sup>-1</sup>. This solid was reintroduced into the glovebox, redissolved in pentane, and filtered. Allowing the pentane solution to slowly evaporate yielded brown crystals. X-ray diffraction of the crystals revealed their identity to be  $Ir_4(CO)_{12}$ , consistent with the aforementioned IR stretching frequencies.

### 2.5.1.14 Reaction of 4 with H<sub>2</sub>

 $[NaIr(cod)(ONO^{tBu})]_2$  (10.2 mg, 5.89  $\mu$ mol) was dissolved in 0.7 mL of  $d_8$ -THF in a J-Young NMR tube. Two drops of benzene were added as an internal standard. The headspace was then charged with 2.9 atm H<sub>2</sub>, and the NMR tube continuously inverted for mixing. After 11 h, the solution color had lightened considerably, and an iridium mirror had deposited. <sup>1</sup>H NMR showed quantitative conversion to the protonated ligand H<sub>2</sub>(ONO<sup>tBu</sup>).

## 2.5.1.15 Synthesis of $[Ir(cod)]_2(ONO^{tBu})$ , 5

H<sub>2</sub>(ONO<sup>*t*Bu</sup>) (57.6 mg, 106 μmol) was dissolved in 5 mL of THF, and an excess of NaH (30.2 mg, 1.26 mmol) was added. The yellow suspension first turned orange and then yellow again, with vigorous evolution of H<sub>2</sub>. The suspension was allowed to stir for an hour, after which it was filtered through Celite. A 5 mL THF solution of  $[Ir(cod)Cl]_2$  (71.1 mg, 107 μmol) was then added while stirring. After 1 h of stirring, the solvent was removed *in vacuo*; and the orange compound was redissolved in pentane and filtered. The solvent was then removed *in vacuo* again, giving **5** as an orange powder. Crystals were obtained by allowing a pentane solution to evaporate. Yield was 119.3 mg (104 μmol, 98.6%). <sup>1</sup>H NMR (300 MHz, *d*<sub>8</sub>-THF):  $\delta$  0.81 (br d, 16H, <sup>2</sup>J = 6.9 Hz, sp<sup>3</sup> on 2 cod), 1.39 (s, 18H, 2 *t*Bu on ligand phenolate), 1.52 (s, 9H, *t*Bu on ligand pyridine), 1.58 (s, 18H, 2 *t*Bu on ligand phenolate), 3.08 (br s, 8H, sp<sup>2</sup> on 2 cod), 7.51 (br d, 4H, J = 5.4 Hz, 2 ligand phenolate aryl), 7.82 (s, 2H, ligand pyridine aryl). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, *d*<sub>8</sub>-THF): 15.2, 24.1, 31.0, 31.6, 32.65, 32.75, 33.4, 35.1, 35.8, 35.9, 36.9, 38.3, 56.1, 121.7, 124.9, 130.0, 134.9, 139.2, 141.8, 159.3, 163.1, 163.6. MS FAB+: 1141.5018 (M<sup>+</sup> with <sup>191</sup>Ir), 843.4935 ([Ir(cod)(ONO<sup>*t*Bu</sup>)]<sup>+</sup>). Analysis calculated for C<sub>53</sub>H<sub>75</sub>Ir<sub>2</sub>NO<sub>2</sub>: C, 55.71; H, 6.62; N, 1.23. Found: C, 54.81; H, 6.77; N, 1.12.

Alternatively,  $[NaIr(cod)(ONO^{tBu})]_2$  (15 mg, 9  $\mu$ mol) was dissolved in 1 mL of THF.  $[Ir(cod)Cl]_2$  (6 mg, 9  $\mu$ mol) was dissolved in 2 mL of THF and added. After two hours the solution was the solvent was removed *in vacuo*, redissolved in pentane, and filtered, and the solvent removed *in vacuo* again,

giving 5 (20 mg, 18  $\mu$ mol, 100% yield) as an orange powder. Characterization data were as reported above.

# 2.5.1.16 Synthesis of $[(ONO^{tBu})Ir(cod)(MeCN)][PF_6]$ , 6

[NaIr(cod)(ONO<sup>tBu</sup>)]<sub>2</sub> (106.3 mg, 61.4 µmol) was dissolved in 10 mL of THF. A solution of AgPF<sub>6</sub> (59.4 mg, 235 µmol) in acetonitrile was added, resulting in the mixture immediately turning black. The solution was allowed to stir overnight. Afterward, the solvent was removed *in vacuo*, and the black solid redissolved in benzene, filtered, and lyophilized to give **6** as a yellow powder. This complex was recrystallized by layering pentane onto a benzene solution. Yield after recrystallization was 93.0 mg (90.4 µmol, 73.6%). <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>CN):  $\delta$  1.37 (s, 18H, 2 *t*Bu on ligand phenolate), 1.45 (s, 9H, *t*Bu on ligand pyridine), 1.53 (s, 18H, 2 *t*Bu on ligand phenolate), 2.26 (m, 4H, sp<sup>3</sup> on cod), 2.42 (s, 3H, MeCN ligand), 2.75 (br s, 2H, sp<sup>3</sup> on cod), 4.31 (br s, 2H, sp<sup>3</sup> on cod), 5.45 (m, 2H, sp<sup>2</sup> on cod), 6.65 (m, 2H, sp<sup>2</sup> on cod), 7.41 (two overlapping peaks, s, 4H, 2 ligand phenolate aryl), 7.70 (s, 2H, ligand pyridine aryl). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  1.3, 28.0, 29.3, 29.4, 30.3, 31.2, 33.9, 34.4, 35.5, 100.2, 113.9, 119.9, 120.6, 123.2, 125.8, 126.4, 139.4, 140.7, 154.3, 161.8, 162.1. <sup>19</sup>F{<sup>13</sup>C} NMR (282 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -71.1 (d, <sup>1</sup>*J*<sub>PF</sub> = 711 Hz). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -143.2 (septet, <sup>1</sup>*J*<sub>PF</sub> = 711 Hz). MS FAB+: 842.4472 ([Ir(cod)(ONO<sup>tBu</sup>)]<sup>+</sup>). Analysis calculated for C<sub>47</sub>H<sub>66</sub>F<sub>6</sub>IrN<sub>2</sub>O<sub>2</sub>P · C<sub>6</sub>H<sub>6</sub>: C, 57.54; H, 6.56; N, 2.53. Found: C, 57.06; H, 6.48; N, 2.42.

Alternatively,  $[NaIr(cod)(ONO^{tBu})]_2$  (103.9 mg, 60.0  $\mu$ mol) was dissolved in 10 mL of THF. A suspension of  $[FeCp_2][PF_6]$  (75.6 mg, 228  $\mu$ mol) in acetonitrile was added, the solution was allowed to stir overnight, the solvent was removed *in vacuo*, and the solid redissolved in benzene, filtered, and lyophilized to give **6**. Yield after recrystallization (as above) was 98.7 mg (96.0  $\mu$ mol, 79.9%). Characterization data were as reported above.

### 2.5.1.17 Synthesis of (ONO<sup>tBu</sup>)Ir(cod)OTf, 7

 $[NaIr(cod)(ONO^{tBu})]_2$  (310.0 mg, 179.1 µmol) and AgOTf (175.7 mg, 683.8 µmol) were each dissolved in about 10 mL of benzene. The AgOTf solution was then added dropwise to the stirring solution of **4**. The mixture immediately turned black and was allowed to stir overnight. It was then filtered, pumped down, and washed with pentane, yielding  $(ONO^{tBu})Ir(cod)OTf$ , **7** (259 mg, 261 µmol, 76% yield). Since **7** has limited solubility in benzene (about 10 mg/mL), it can be purified by washing with benzene. Crystals were obtained by layering a saturated benzene solution with pentane. <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  0.93 (s, 9H, tBu on ligand pyridine), 1.19 (br s, 8H, sp<sup>3</sup> on cod), 1.42 (s, 18H, 2 tBu on ligand phenolate), 1.74 (s, 18H, 2 tBu on ligand phenolate), 2.42 (br s, 2H, sp<sup>2</sup> on cod), 4.62 (m, 2H, sp<sup>2</sup> on cod), 7.35 (s, 2H, ligand pyridine aryl), 7.45 (d, 2H, <sup>4</sup>J = 2.7 Hz, ligand phenolate aryl), 7.58 (d, 2H, <sup>4</sup>J = 2.7 Hz, ligand phenolate aryl). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  27.4, 29.5, 30.0, 30.7, 31.4, 34.0, 34.2, 35.7, 90.7, 112.8, 120.6, 123.3, 125.9, 126.2, 139.1, 139.6, 153.2, 160.9, 161.2. <sup>19</sup>F{<sup>13</sup>C} NMR (282 MHz,  $C_6D_6$ ):  $\delta$  -77.6. MS FAB+: 991.5552 (M<sup>+</sup>), 858.5524 ([(ONO<sup>tBu</sup>)Ir(cod)]<sup>+</sup>). Analysis calculated for  $C_{46}H_{63}F_3IrNO_5PS$ : C, 55.74; H, 6.41; N, 1.41. Found: C, 55.51; H, 6.36; N, 1.38.

### 2.5.1.18 Synthesis of (ONO<sup>tBu</sup>)Ir(PPh<sub>3</sub>)<sub>2</sub>OTf, 8

7 (89.4 mg, 90.2  $\mu$ mol) and PPh<sub>3</sub> (47.3 mg, 180  $\mu$ mol) were each dissolved in benzene and mixed together. The mixture was stirred at 90°C for at least 3 h, filtered, and then lyophilized. **8** (117.6 mg, 83.5  $\mu$ mol, 92.6% yield) was formed as a yellow powder, soluble in benzene and slightly soluble in pentane (about 1 mg/mL). **8** is stable for several days at 90°C with little decomposition. <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  0.94 (s, 9H, tBu on ligand pyridine), 1.25 (s, 18H, 2 tBu on ligand phenolate), 1.35 (s, 18H, 2 tBu on ligand phenolate), 6.52 (s, 2H, ligand pyridine aryl), 6.68 (d, 2H, <sup>4</sup>J = 2.4 Hz, ligand phenolate aryl), 6.87 (br s, 12H, triphenylphosphines), 7.16 (br s, 6H, triphenylphosphines), 7.18 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl), 7.63 (br s, 12H, triphenylphosphines). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  29.6, 29.7, 29.9, 31.2, 33.6, 35.7, 119.4, 123.2, 125.0, 125.6, 126 – 128 (may be obscured by C<sub>6</sub>D<sub>6</sub>), 129.6, 134.0, 135.1 (br), 136.7, 140.7, 141.1. <sup>19</sup>F{<sup>13</sup>C} NMR (282 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -76.4. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -17.2. MS FAB+: 1258.5423 ([Ir(PPh<sub>3</sub>)<sub>2</sub>(ONO<sup>tBu</sup>)]<sup>+</sup>), 1145.3984 ([Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)(OTf)]<sup>+</sup>), 996.4537 ([Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)]<sup>+</sup>). Analysis calculated for C<sub>74</sub>H<sub>81</sub>F<sub>3</sub>IrNO<sub>5</sub>P<sub>2</sub>S: C, 63.14; H, 5.80; N, 1.00. Found: C, 63.24; H, 5.95; N, 0.87.

# 2.5.1.19 Synthesis of (ONO<sup>tBu</sup>)Ir(PPh<sub>3</sub>)<sub>2</sub>OH, 9

**8** (20.8 mg, 14.7 μmol) was dissolved in benzene, and 2 μL of H<sub>2</sub>O was added *via* a microliter syringe. The mixture was stirred for one hour, after which proton sponge (3.6 mg, 17 μmol) dissolved in benzene was added. A precipitate was immediately observed, and the mixture was stirred for four hours, pumped down, redissolved in benzene, filtered, and lyophilized, giving **9** (18.8 mg, 14.7 μmol, quantitative yield) as a yellow powder. **9** is slightly soluble in pentane (about 3 mg/mL) and was crystallized by letting a pentane solution evaporate. <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  –1.63 (s, <sup>1</sup>H, IrOH), 1.05 (br, 27H, 2 *t*Bu on ligand phenolate, *t*Bu on ligand pyridine), 1.34 (s, 18H, 2 *t*Bu on ligand phenolate), 6.75 (br, 4H, 2 ligand phenolate aryl), 6.8 – 7.2 (many broad overlapping peaks, 30H, triphenylphosphines), 7.38 (br s, 2H, ligand pyridine aryl). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  –23.2. MS FAB+: 1275.5450 ([Ir(PPh<sub>3</sub>)<sub>2</sub>(ONO<sup>*t*Bu</sup>)OH]<sup>+</sup>), 1258.5423 ([Ir(PPh<sub>3</sub>)<sub>2</sub>(ONO<sup>*t*Bu</sup>)OH]<sup>+</sup>). Analysis calculated for C<sub>73</sub>H<sub>82</sub>IrNO<sub>3</sub>P<sub>2</sub>: C, 68.73; H, 6.48; N, 1.10. Found: C, 68.71; H, 6.66; N, 1.10.

# $\textbf{2.5.1.20} \quad \textbf{Synthesis of (ONO^{tBu})Ir(PPh_3)_2Cl, 10}$

8 (39.0 mg, 27.7  $\mu$ mol) was dissolved in 3 mL of dichloromethane and heated to 90°C for five hours. The solution was then pumped down, redissolved in benzene, filtered, and lyophilized, giving 10 (35.4 mg, 27.4  $\mu$ mol, 98.7% yield) as a yellow powder. <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  0.79 (s, 18H, 2 *t*Bu on ligand phenolate), 1.12 (s, 9H, *t*Bu on ligand pyridine), 1.27 (s, 18H, 2 *t*Bu on ligand phenolate), 6.50 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl), 6.65 (s, 2H, ligand pyridine aryl), 6.93 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl), 6.9 – 7.3 (many broad overlapping peaks, 30H, triphenylphosphines). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  29.6, 30.4, 31.9, 34.3, 34.9, 35.7, 120.2, 124.5, 125.1, 126.1, 127.4 (br), 127.8 (br), 128.3 (br), 129.7 (br), 133.7 (br), 136.3 (br), 136.8, 141.0, 155.7, 159.1, 170.1. <sup>31</sup>P{<sup>1</sup>H} NMR (121 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  -25.1. MS FAB+: 1294.5082 ([Ir(PPh<sub>3</sub>)<sub>2</sub>(ONO<sup>*t*Bu</sup>)Cl]<sup>+</sup>), 1257.5300 ([Ir(PPh<sub>3</sub>)<sub>2</sub>(ONO<sup>*t*Bu</sup>)]<sup>+</sup>), 1031.3262 ([Ir(PPh<sub>3</sub>)(ONO<sup>*t*Bu</sup>)Cl]<sup>+</sup>). Analysis calculated for C<sub>73</sub>H<sub>81</sub>ClIrNO<sub>2</sub>P<sub>2</sub>: C, 67.75; H, 6.31; N, 1.08. Found: C, 68.60; H, 6.84; N, 1.07.

# 2.5.1.21 Synthesis of $(ONO^{tBu})Ir(PPh_3)_2H$ , 11

LiOMe (3.9 mg, 0.10 mmol) was dissolved in methanol, and 8 (67.2 mg, 47.7  $\mu$ mol) was added while stirring. A light yellow filtrate formed overnight and was filtered out. When benzene was added to this filtrate, a black precipitate immediately formed, which was also filtered out. The remaining yellow solution was lyophilized, giving (ONO<sup>tBu</sup>)Ir(PPh<sub>3</sub>)<sub>2</sub>H, **11** (37.6 mg, 29.9  $\mu$ mol, 62.5% yield), as a yellow powder. <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  –15.4 (t, 1H, <sup>2</sup>J<sub>PH</sub> = 17.8 Hz, IrH), 0.79 (s, 18H, 2 tBu on ligand phenolate), 1.17 (s, 9H, tBu on ligand pyridine), 1.41 (s, 18H, 2 tBu on ligand phenolate), 6.8 – 7.4 (many broad overlapping peaks, 36H, ligand aryl, triphenylphosphine aryl). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  28.4, 30.0, 31.7, 33.7, 34.2, 34.9, 118.6, 123.5, 124.9, 126-128 (may be obscured by C<sub>6</sub>D<sub>6</sub>), 128.9 (br), 134.3 (br), 135.2, 154.1, 158.0, 170.3. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  9.8. MS FAB+: 1260.5502 ([Ir(PPh<sub>3</sub>)<sub>2</sub>(ONO<sup>tBu</sup>)H<sub>2</sub>]<sup>+</sup>), 997.4542 ([Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)H]<sup>+</sup>).

11 was also obtained from the following reactions, although in most cases it was observed only by NMR and could not be isolated cleanly:

- 8 (25.7 mg, 18.3 μmol) and proton sponge (3.8 mg, 17.7 μmol) were dissolved in benzene and mixed. The solution was heated to 90°C for 24 h. It was then pumped down, redissolved in pentane, filtered, and pumped down again. The yield of 11 was nearly quantitative (by NMR).
- 8 (11.3 mg, 7.2 μmol) and dihydroanthracene (1.3 mg, 7.2 μmol) were dissolved in C<sub>6</sub>D<sub>6</sub> and mixed. CoCp<sub>2</sub> (1.4 mg, 7.4 μmol) dissolved in C<sub>6</sub>D<sub>6</sub> was then added, and the entire mixture transferred to a J-Young NMR tube. After stirring for one hour, NMR revealed the formation of **11** as the major product.
- 8 (16.7 mg, 10.7 μmol) was dissolved in approximately 1 mL of C<sub>6</sub>D<sub>6</sub> in a J-Young NMR tube, and an excess of solid NaH (30 mg, 1 mmol) was added. The NMR tube was heated to 90°C, and the reaction was followed by NMR; after 26 h the reaction was complete. The solution was then removed, filtered, and pumped down. Isolated yield was 11.8 mg, 9.4 μmol, 88%.

8 (38.4 mg, 27.3 μmol) was dissolved in approximately 5 mL of benzene, and ZnEt<sub>2</sub> (1.5 μL, 14 μmol) was added *via* a microliter syringe. The stirring solution first turned red and then yellow and was allowed to stir overnight. The solution was then pumped down, redissolved in pentane, filtered, and pumped down again to form **11** as a clean solid.

# 2.5.1.22 Synthesis of $(ONO^{tBu})Ir(PPh_3)_2Me$ , 12

8 (203.8 mg, 144.8 µmol) was dissolved in benzene, and  $\text{ZnMe}_2$  (6.2 µL, 90 µmol) was added *via* a microliter syringe. The solution was stirred at room temperature overnight, filtered, and then lyophilized. **12** (182.6 mg, 143.4 µmol, 99.0% yield) was formed as a yellow powder, soluble in benzene and slightly soluble in pentane, and could be recrystallized by layering pentane on a benzene solution. <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  1.13 (s, 9H, *t*Bu on ligand pyridine), 1.18 (s, 18H, 2 *t*Bu on ligand phenolate), 1.40 (s, 18H, 2 *t*Bu on ligand phenolate), 3.03 (t, 3H, <sup>3</sup>J<sub>PH</sub> = 6.1 Hz, IrMe), 6.82 (d, 2H, <sup>4</sup>J = 2.4 Hz, ligand phenolate aryl), 6.89 (br s, 12H, triphenylphosphines), 6.92 (s, 2H, ligand pyridine aryl), 7.19 (d, 2H, <sup>4</sup>J = 2.6 Hz, ligand phenolate aryl), 7.16 (br s, 6H, triphenylphosphines), 7.46 (br s, 12H, triphenylphosphines). <sup>13</sup>C{<sup>1</sup>H} NMR (75.4 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  -31.4 (t, <sup>2</sup>J<sub>PC</sub> = 8.6 Hz), 29.3, 29.9, 31.3, 33.6, 34.3, 35.1, 119.4, 123.3, 125.9, 126.1, 127.1, 128.7, 134.7 (br), 135.1, 140.3, 153.9, 157.8, 170.4. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -14.6. MS FAB+: 1273.4640 (M<sup>+</sup>), 1011.4714 ([Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)(Me)]<sup>+</sup>), 995.3394 ([Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)]<sup>+</sup>). Analysis calculated for C<sub>74</sub>H<sub>84</sub>IrNO<sub>2</sub>P<sub>2</sub>: C, 69.78; H, 6.65; N, 1.10. Found: C, 69.81; H, 6.53; N, 1.05.

# 2.5.1.23 Synthesis of $(ONO^{tBu})Ir(PPh_3)_2I$ , 13

8 (10.5 mg, 8.24 µmol) and I<sub>2</sub> (2.1 mg, 8.3 µmol) were each dissolved in benzene and mixed together. The mixture was stirred at room temperature for at least 3 h, filtered, and then lyophilized. **13** (10.8 mg, 7.80 µmol, 94.6% yield) was formed as a yellow, pentane-soluble powder, although impurities can give it a green color. Crystals were obtained by allowing a pentane solution to evaporate. <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  0.90 (s, 18H, 2 *t*Bu on ligand phenolate), 1.15 (s, 9H, *t*Bu on ligand pyridine), 1.28 (s, 18H, 2 *t*Bu on ligand phenolate), 6.52 (d, 2H, <sup>4</sup>J = 2.6 Hz, ligand phenolate aryl), 6.70 (s, 2H, ligand pyridine aryl), 6.96 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl), 7.08 (br s, 12H, triphenylphosphines), 7.21 (br s, 12H, triphenylphosphines), 8.16 (br s, 6H, triphenylphosphines). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  30.3, 30.4, 31.8, 34.3, 34.9, 35.7, 120.5, 124.8, 125.1, 126.6, 127.4 (br), 129.8 (br), 133.7 (br), 136.9, 137.3 (br), 141.2, 154.8, 159.2, 170.4. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -29.1. MS FAB+: 1386.5627 (M<sup>+</sup>), 1123.3712 ([Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)(I)]<sup>+</sup>).

# 2.5.1.24 Synthesis of $(ONO^{tBu})Ir(PEt_3)_2Me$ , 14

12 (79.4 mg, 62.3  $\mu$ mol) was dissolved in 5 mL of benzene, and PEt<sub>3</sub> (20  $\mu$ L, 136  $\mu$ mol) was added. The solution was allowed to stir for seven hours, after which the benzene and excess PEt<sub>3</sub> were removed by lyophilization. The yellow powder obtained was redissolved in 5 mL of dichloromethane, and [Rh(cod)<sub>2</sub>]OTf (30.5 mg, 62.7  $\mu$ mol) dissolved in 3 mL of acetonitrile was added to complex residual PEt<sub>3</sub>. The solution was allowed to stir for three hours. Afterward, it was pumped down, and the resulting **14** was redissolved in hexanes, filtered to remove the byproducts and impurities, and pumped down again. Isolated yield was 51.4 mg (52.2  $\mu$ mol, 83.7%). Crystals were obtained by allowing a pentane solution to evaporate. <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  0.75 (m, 18H, 6 P–CH<sub>2</sub>–CH<sub>3</sub>), 1.16 (s, 9H, tBu on ligand pyridine), 1.46 (s, 18H, 2 tBu on ligand phenolate), 1.65 (m, 33H, 2 tBu on ligand phenolate, 6 P–CH<sub>2</sub>–CH<sub>3</sub>, IrMe), 7.34 (d, 2H, <sup>4</sup>J = 2.6 Hz, ligand phenolate aryl), 7.43 (s, 2H, ligand pyridine aryl), 7.53 (d, 2H, <sup>4</sup>J = 2.6 Hz, ligand phenolate aryl). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  –33.4 (t, J<sub>CP</sub> = 8.2 Hz), 8.1 (t, J<sub>CP</sub> = 1.5 Hz), 13.3 (t, J<sub>CP</sub> = 14.3 Hz), 30.6, 31.3, 32.4, 34.4, 35.3, 36.3, 118.7, 124.0, 125.6, 128.1, 136.2, 140.6, 156.3, 159.3, 172.9 (t, J = 2.2 Hz). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  –19.2. MS FAB+: 985.5609 (M<sup>+</sup>), 867.4800 ([Ir(PEt<sub>3</sub>)(ONO<sup>tBu</sup>)(Me)]<sup>+</sup>). Analysis calculated for C<sub>50</sub>H<sub>84</sub>IrNO<sub>2</sub>P<sub>2</sub>: C, 60.95; H, 8.59; N, 1.42. Found: C, 61.18; H, 8.32; N, 1.45.

# 2.5.1.25 Synthesis of $(ONO^{tBu})Ir(PEt_3)_2I$ , 15

14 (11.8 mg, 12.0  $\mu$ mol) and I2 (3.0 mg, 12.0  $\mu$ mol) were each dissolved in benzene and mixed together. The mixture was stirred at room temperature for 5 h, filtered, and then lyophilized. 15 was formed as a yellow, pentane-soluble powder. Crystals were obtained by allowing a pentane solution to evaporate. <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  0.74 (m, 18H, 6 P–CH<sub>2</sub>–CH<sub>3</sub>), 1.09 (s, 9H, tBu on ligand pyridine), 1.42 (s, 18H, 2 tBu on ligand phenolate), 1.71 (s, 18H, 2 tBu on ligand phenolate), 1.96 (m, 12H, 6 P–CH<sub>2</sub>–CH<sub>3</sub>), 7.36 (s, 2H, ligand phenolate aryl), 7.37 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl), 7.46 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  8.4 (t,  $J_{CP} = 1.6$  Hz), 15.0 (t,  $J_{CP} = 15.3$  Hz), 30.0, 31.0, 31.9, 34.1, 34.9, 35.8, 118.8, 124.5, 124.7, 126.5, 137.2, 141.3, 156.3 (t,  $J_{CP} = 1.4$  Hz), 159.9, 171.7 (t,  $J_{CP} = 2.2$  Hz). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  –26.3.

The reaction of 14 and I<sub>2</sub> in dichloromethane gives a new species along with 15 and MeI; over the course of four days all of the 15 is converted to the new species. Crystals were obtained after the contents of the NMR tube were allowed to evaporate. X-ray crystallography, NMR, and MS support identification of this compound as the analogous chloride,  $(ONO^{tBu})Ir(PEt_3)_2Cl.$ <sup>1</sup>H NMR (300 MHz,  $CD_2Cl_2$ ):  $\delta$  0.74 (m, 18H, 6 P– $CH_2-CH_3$ ), 1.01 (m, 12H, 6 P– $CH_2-CH_3$ ), 1.33 (s, 18H, 2 tBu on ligand phenolate), 1.37 (s, 18H, 2 tBu on ligand phenolate), 1.38 (s, 9H, tBu on ligand pyridine), 7.11 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl), 7.26 (d, 2H, <sup>4</sup>J = 2.5 Hz, ligand phenolate aryl), 7.31 (s, 2H, ligand pyridine aryl). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz,  $CD_2Cl_2$ ):  $\delta$  7.7, 13.0 (t,  $J_{CP} = 15.1$  Hz), 30.5, 30.6, 31.9, 34.4, 35.5, 35.9, 119.4, 124.6, 124.8, 126.6, 137.6, 140.3, 157.0, 160.5, 171.7. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz,  $CD_2Cl_2$ ):  $\delta$  –20.7. MS FAB+ 970.5417 ([Ir(PEt\_3)\_2(ONO^{tBu})]^+), 887.3802 ([Ir(PEt\_3)(ONO^{tBu})(Cl)]^+), 852.4370 ([Ir(PEt\_3)(ONO^{tBu})]^+).

# 2.5.1.26 Synthesis of $[(ONO^{tBu})Ir(PEt_3)_2Me]PF_6$ , 16

14 (31.8 mg, 32.3  $\mu$ mol) was dissolved in dichloromethane, and a dichloromethane suspension of AgPF<sub>6</sub> (8.1 mg, 32  $\mu$ mol) was added. The mixture was allowed to stir for one hour before being pumped down. It was then redissolved in a small amount of benzene and filtered. The solution was then layered with pentane and allowed to sit overnight. Dark blue needle-like crystals of  $16\cdot 2 C_6 H_6$  (39.1 mg, 30.4  $\mu$ mol, 94.1% yield) were recovered. <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  -3.1 (very broad), -2.0 (broad), 0.73, 3.99, 12.0 (very broad). <sup>19</sup>F{<sup>13</sup>C} NMR (282 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  -73.8 (d, <sup>1</sup>J<sub>PF</sub> = 710 Hz). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  -144.7 (septet, <sup>1</sup>J<sub>PF</sub> = 710 Hz). MS FAB+: 985.5561 (M<sup>+</sup>), 867.4697 ([Ir(PEt<sub>3</sub>)(ONO<sup>tBu</sup>)(Me)]<sup>+</sup>).

### 2.5.1.27 Synthesis of (ONO<sup>tBu</sup>)Ir(PPh<sub>3</sub>)<sub>2</sub>Ph, 17

12 (20.4 mg, 16.0  $\mu$ mol) was dissolved in 10 mL of benzene and stirred in a 65°C oil bath for 24 h. The solution was reintroduced into the glovebox, and the solvent was removed. The residue was redissolved in pentane and filtered, and the solution pumped down to obtain 17 (20.9 mg, 15.6  $\mu$ mol, 98% yield). Crystals were obtained by allowing a pentane solution to evaporate. <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  0.70 (s, 18H, 2 *t*Bu on ligand phenolate), 1.20 (s, 9H, *t*Bu on ligand pyridine), 1.43 (s, 18H, 2 *t*Bu on ligand phenolate), 5.83 (br s, 2H, IrPh), 6.54 (br s, 1H, IrPh), 6.62 (d, 2H, <sup>4</sup>J = 2.7 Hz, ligand phenolate aryl), 6.78 (s, 2H, ligand pyridine aryl), 6.8 – 7.1 (multiple broad peaks, 30H, triphenylphosphines), 7.16 (d, 2H, <sup>4</sup>J = 2.6 Hz, ligand phenolate aryl), 7.29 (br s, 2H, IrPh). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  30.3, 30.6, 32.2, 34.2, 34.4, 35.9, 120.4, 123.6, 124.1, 125.6, 125.9, 126.9, 127.0, 129.6, 129.7, 133.3 (br), 135.7, 136.5 (br), 141.2, 145.9, 155.3, 157.7, 171.5. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  -13.2.

#### 2.5.1.28 Reaction of 12 with Toluene

12 (7.8 mg, 6.1 µmol) was dissolved in 700 µL of toluene- $d_8$  in a J-Young NMR tube. The tube was heated at 65°C and periodically monitored by <sup>1</sup>H NMR until all starting material signals had disappeared, which took six days; the final <sup>1</sup>H NMR spectrum was complex. The mass spectrum of the solid obtained by evaporation exhibited a signal indicating the presence of the analogous tolyl complex (1094.5436, [Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)(C<sub>6</sub>D<sub>4</sub>CD<sub>3</sub>]<sup>+</sup>, [M–PPh<sub>3</sub>]<sup>+</sup>), while the <sup>31</sup>P{<sup>1</sup>H} NMR of the dissolved solid showed two approximately equal signals at  $\delta$  –12.2 and –12.3, tentatively assigned to meta and para isomers. A much weaker signal at –12.8 may indicate formation of a very small amount of ortho isomer. Isolation of a pure product was not achieved.

# 2.5.1.29 Synthesis of $(ONO^{tBu})Ir(PPh_3)[\kappa^2 - (o-C_6H_4)PPh_2]$ , 18

12 (8.2 mg, 6.4  $\mu$ mol) was dissolved in 1 mL of CD<sub>2</sub>Cl<sub>2</sub> in a J-Young NMR tube and submerged in a 65°C oil bath for 21 h. After NMR confirmation that the reaction was complete, the solvent was removed to obtain 18 (7.7 mg, 6.1  $\mu$ mol, 95% isolated yield). Crystals were obtained by allowing a pentane solution to evaporate. <sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  0.47 (s, 18H, 2 *t*Bu on ligand phenolate), 1.27 (s, 18H, 2 *t*Bu on ligand phenolate), 1.34 (s, 9H, tBu on ligand pyridine), 6.64 (m, 4H, triphenylphosphines), 6.9 – 7.4 (many multiplets, 23H, triphenylphosphines), 7.50 (dd, <sup>3</sup>J = 4.4 Hz, <sup>3</sup>J = 6.6 Hz, 2H, triphenylphosphines). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  29.58, 30.76, 32.11, 34.24, 35.27, 35.32, 119.51, 119.69, 122.48, 122.55, 123.83, 124.00, 125.60, 125.77, 128.32, 128.39, 129.03, 129.54, 133.76, 133.83, 136.03, 139.93, 140.51, 140.61, 152.80, 153.23, 154.77, 159.36, 170.44. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  -69.5 (d, <sup>2</sup>J<sub>PP</sub> = 448 Hz), -2.5 (d, <sup>2</sup>J<sub>PP</sub> = 448 Hz). MS FAB+: 1257.5292 (M<sup>+</sup>), 995.4405 ([Ir(PPh<sub>3</sub>)(ONO<sup>tBu</sup>)]<sup>+</sup>).

# 2.5.1.30 Synthesis of $[(ONO^{tBu})Ir(PPh_3)(CH_2CN)]_2$ , 19

12 (13.1 mg, 10.3 µmol) was dissolved in 1 mL of  $CD_2Cl_2$  in a J-Young NMR tube, and 40 µL of acetonitrile was added. The tube was then submerged in a 65°C oil bath for 72 h. After NMR confirmation that the reaction had completed,  $[Rh(cod)_2]OTf$  (2.6 mg, 5.3 µmol) dissolved in 1 mL of acetonitrile was added. The solution was allowed to stir for three hours. Afterward, it was pumped down, and the resulting **19** was redissolved in hexanes, filtered to remove the byproducts and impurities, and pumped down again. Crystals were obtained by allowing a pentane solution to evaporate. Isolated yield was 91% (9.7 mg, 4.7 µmol). <sup>1</sup>H NMR (500 MHz,  $CD_2Cl_2$ ):  $\delta$  1.23 (s, 9H, 2 tBu on ligand), 1.25 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.43 (s, 9H, 2 tBu on ligand), 1.44 (s, 9H, 2 tBu on ligand), 1.55 (s, 9H, 2 tBu on ligand), 1.57 (s, 2H, Ir-CH<sub>2</sub>-CN), 6.4-6.5 (m, 3H, triphenylphosphine), 6.7-6.8 (m, 3H, triphenylphosphine), 6.9-7.1 (m, 6H, triphenylphosphine), 7.2-7.5 (m, 6H, triphenylphosphine), 7.6-7.8 (m, 2H, triphenylphosphine), 7.9-8.1 (m, <sup>1</sup>H, triphenylphosphine). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  3.4, 30.1, 30.3, 30.5, 31.9, 32.2, 34.2, 34.6, 35.2, 35.7, 35.9, 116.0, 118.0, 120.2, 122.5,

#### 2.5.1.31 Kinetic Experiments

Kinetic experiments were carried out with 8.8 mM solutions of **12** or **14**. In a typical example, 7.8 mg (6.1  $\mu$ mol) **12** was dissolved in 700  $\mu$ L of C<sub>6</sub>D<sub>6</sub> inside a nitrogen-filled glovebox, and the solution was transferred to a J-Young NMR tube. The NMR tube was then removed from the glovebox and fully submerged in a 65°C ethylene glycol bath. The reactions were periodically halted by transferring the

Entry <sup>a</sup>	eq $\mathrm{PPh}_3^{\ b}$	$[\mathrm{PPh}_3]^c$	$k^d_{ m obs}$	$R^2$
a	0.000	0	$2.18\times10^{-4}$	0.9937
b	0.125	1.1	$1.54 \times 10^{-5}$	0.9965
c	0.250	2.2	$1.19  imes 10^{-5}$	0.9842
d	0.375	3.3	$6.27  imes 10^{-6}$	0.9964
е	0.500	4.4	$5.28 \times 10^{-6}$	0.9910
f	0.500	4.4	$5.77 \times 10^{-6}$	0.9921
g	0.625	5.4	$4.14\times10^{-6}$	0.9877
h	0.750	6.5	$2.58\times10^{-6}$	0.9768
i	0.750	6.5	$3.14 \times 10^{-6}$	0.9912
j	0.875	7.6	$2.32\times10^{-6}$	0.9904
k	1.000	8.7	$1.88 \times 10^{-6}$	0.9821
1	1.125	9.8	$1.90 \times 10^{-6}$	0.9558
m	1.250	10.9	$1.70 \times 10^{-6}$	0.9777

**Table 2.1.** Summary of the results of Figure 2.23, used to create Figure 2.21. a) The particular run is detailed in the corresponding section in Figure 2.23; b) equivalents of PPh<sub>3</sub> added; c) concentration of added PPh<sub>3</sub> in mM. d) the  $k_{obs}$  value, in s<sup>-1</sup>, calculated by fitting the curve to the first-order rate equation  $[\mathbf{12}] = [\mathbf{12}]_0 \exp(-k_{obs}t)$ .

NMR tube into an ice bath before NMR measurements. The progress of the reactions were measured by <sup>31</sup>P NMR integration, with NOE turned off and the d1 time set to 22.895 s (**12** has the longest relaxation time, 4.579 s, of all the relevant iridium compounds). For PPh<sub>3</sub> inhibition experiments, the Ir complex was mixed with various amounts of a 20 mg/mL stock solution of PPh<sub>3</sub> in  $C_6D_6$ , and additional  $C_6D_6$  was added to bring the volume up to 700  $\mu$ L.

### 2.5.2 Kinetics Details

Figure 2.21 was constructed from the data in table 2.1. The entries in this table were obtained from individual runs detailed in Figure 2.23.

### 2.5.3 Crystallographic Data

Crystallographic data for the complexes 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, and  $(ONO^{tBu})Ir(PEt_3)_2Cl$  are found in the following tables 2.2, 2.3, 2.4, 2.5, and 2.6.

### 2.6 Acknowledgments

We thank Dr. Michael W. Day and Lawrence M. Henling (Caltech) for X-ray crystallographic studies. The Bruker KAPPA APEXII X-ray diffractometer was purchased *via* an NSF CRIF:MU award to the California Institute of Technology, CHE-0639094. This work was supported by BP in the  $MC_2$  and  $XC_2$  programs.

 $\begin{array}{l} \textbf{Figure 2.23. Conversion of 12 to 17-} d_6 \text{ in } C_6 D_6 \text{ with varying amounts of extra PPh_3 added. } [12]_0 = 8.7 \text{ mM.} \\ \textbf{a)} \ [\text{PPh}_3]_0 = 0 \text{ mM, b)} \ [\text{PPh}_3]_0 = 1.1 \text{ mM, c}) \ [\text{PPh}_3]_0 = 2.2 \text{ mM, d}) \ [\text{PPh}_3]_0 = 3.3 \text{ mM, e}) \ [\text{PPh}_3]_0 = 4.4 \text{ mM, } \\ \textbf{f)} \ [\text{PPh}_3]_0 = 4.4 \text{ mM, g}) \ [\text{PPh}_3]_0 = 5.4 \text{ mM, h}) \ [\text{PPh}_3]_0 = 6.5 \text{ mM, i}) \ [\text{PPh}_3]_0 = 6.5 \text{ mM, j}) \ [\text{PPh}_3]_0 = 7.6 \text{ mM, k}) \ [\text{PPh}_3]_0 = 8.7 \text{ mM, l}) \ [\text{PPh}_3]_0 = 9.8 \text{ mM, m}) \ [\text{PPh}_3]_0 = 10.9 \text{ mM.} \end{array}$ 



	4	5	6	7
Empirical for- mula	$\begin{array}{c} C_{90}H_{126}N_2O_4Ir_2\\ \cdot 2\mathrm{Na}\cdot\mathrm{C}_4H_{10}O\end{array}$	$\mathrm{C}_{53}\mathrm{H}_{75}\mathrm{NO}_{2}\mathrm{Ir}_{2}$	$\begin{array}{c} [{\rm C}_{47}{\rm H}_{66}{\rm N}_{2}{\rm O}_{2}{\rm Ir}] \\ [{\rm PF}_{6}]\cdot{\rm C}_{6}{\rm H}_{6} \end{array}$	$\begin{array}{c} \rm C_{46}H_{63}F_{3}NO_{5}SIr\\ \cdot 1.5(\rm C_{6}H_{6}) \end{array}$
Formula weight	1804.43	1142.54	1106.30	1108.40
Crystal struc- ture	Monoclinic	Monoclinic	Triclinic	Triclinic
Lattice parameters				
a (Å)	29.8716(11)	9.5497(4)	11.0592(5)	11.7099(4)
b (Å)	14.4205(5)	22.3182(9)	11.8291(5)	13.1880(5)
c (Å)	24.4163(15)	22.9384(10)	20.4215(9)	17.2153(6)
$\alpha$ (°)	90	90	105.154(2)	86.059(2)
$\beta$ (°)	123.7310(10)	92.086(2)	97.156(2)	72.263(2)
$\gamma$ (°)	90	90	95.370(2)	87.034(2)
Volume $(Å^3)$	8747.0(7)	4885.7(4)	2536.27(19)	2524.87(16)
Space group	C2/c	$P2_1/n$	P1	P1
Z value	4	4	2	2
$ ho_{ m calc}~({ m g/cm^3})$	1.370	1.553	1.449	1.458
$\mu \ (\mathrm{mm}^{-1})$	3.100	5.481	2.727	2.744
Temperature (K)	100(2)	100(2)	100(2)	100(2)
$\theta$ range (°)	1.66 to 35.19	1.82 to 35.82	1.80 to 40.84	1.55 to 43.59
No. obs. $(I > 2\sigma(I))$	15255	19264	26070	34153
No. parameters	485	533	874	883
Goodness of fit <sup>*</sup>	3.747	1.885	1.957	1.536
Max. shift in cy- cle	0.003	0.007	0.016	0.015
$\begin{array}{ll} \text{Residuals}^*: & R, \\ R_w \end{array}$	0.0314; 0.0719	0.0355; 0.0535	0.0206; 0.0392	0.0221; 0.0381
Absorption cor- rection	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents
$\max/\min$	0.7469; 0.5672	0.7470; 0.5076	0.7480; 0.5945	0.7486; 0.6139
Largest peak & hole $(e^-/Å^3)$	2.370; -1.617	2.894; -2.135	2.557; -1.524	2.541; -1.556

**Table 2.2.** \*  $R = \frac{\sum_{hkl} ||F_{obs}| - |F_{calc}||}{\sum_{hkl} |F_{obs}|}; R_w = \sqrt{\frac{\sum_{hkl} w(|F_{obs}| - |F_{calc}|)^2}{\sum_{hkl} wF_{obs}^2}}, w = 1/\sigma^2(F_{obs}); \text{ GOF} =$ 

$$\sqrt{\frac{\sum_{hkl} w(|F_{obs}| - |F_{calc}|)^2}{n_{data} - n_{vari}}}.$$

	8	9	10	11
Empirical for-	$\mathrm{C}_{74}\mathrm{H}_{81}\mathrm{F}_{3}\mathrm{NO}_{5}\mathrm{P}_{2}$	$\mathrm{C}_{73}\mathrm{H}_{82}\mathrm{NO}_{3}\mathrm{P}_{2}\mathrm{Ir}$	$\mathrm{C}_{73}\mathrm{H}_{81}\mathrm{NO}_{2}\mathrm{P}_{2}\mathrm{Cl}$	$\mathrm{C}_{73}\mathrm{H}_{82}\mathrm{NO}_{2}\mathrm{P}_{2}\mathrm{Ir}$
mula	$\operatorname{SIr} \cdot 0.53(\mathrm{C}_{5}\mathrm{H}_{12})$		$\mathrm{Ir} \cdot 5(\mathrm{CH}_2\mathrm{Cl}_2)$	$\cdot \mathrm{C}_{5}\mathrm{H}_{12}$
Formula woight	$1.47(C_6H_6)$	1975 54	1718 61	1221 68
Crystal strug	1000.04 Monoclinic	1270.04 Monoelinie	Monoelinie	1551.00 Monoclinia
ture		Monochine	Monochine	
Lattice parame-				
ters				
a (Å)	12.9942(5)	13.0223(4)	19.3956(9)	16.8289(8)
b (Å)	22.9825(9)	21.0636(7)	13.1877(6)	23.8694(10)
c (Å)	25.8969(9)	22.7792(8)	31.5557(15)	17.4749(8)
$\alpha$ (°)	90	90	90	90
$\beta$ (°)	103.513(2)	99.1960(10)	106.611(2)	102.373(2)
$\gamma$ (°)	90	90	90	90
Volume (Å <sup>3</sup> )	7519.7(5)	6167.9(4)	7734.6(6)	6856.5(5)
Space group	$P2_1/n$	$P2_1/n$	$P2_{1}/c$	$P2_1/n$
Z value	4	4	4	4
$ ho_{ m calc}~({ m g/cm^3})$	1.379	1.374	1.476	1.290
$\mu \ (\mathrm{mm}^{-1})$	1.906	2.265	2.194	2.040
Temperature	100(2)	100(2)	100(2)	100(2)
(K)				
$\theta$ range (°)	1.84 to $31.76$	2.41 to $29.67$	1.35 to 37.99	1.47 to $33.55$
No. obs. $(I > Q_{-}(I))$	18398	14018	32658	19762
$2\sigma(I)$	066	1040	071	1086
No. parameters	900	1049	0/1	2 1 4 0
Goodness of int	2.750	1.713	2.132	2.140
cle	0.002	0.004	0.011	0.004
Residuals*: $R$ ,	0.0463; 0.0958	0.0238; 0.0373	0.0340; 0.0589	0.0310; 0.0519
$R_w$		,	,	,
Absorption cor-	Semi-empirical	Semi-empirical	Semi-empirical	Semi-empirical
rection	from equivalents	from equivalents	from equivalents	from equivalents
$\max/\min$	0.7463; 0.6010	0.7459; 0.6381	0.7474; 0.6430	0.7466; 0.6219
Largest peak & hole $(e^-/Å^3)$	3.915; -2.838	2.894; -0.696	3.136; -2.303	2.907; -2.314

	12	13	14	15
Empirical for- mula	$\mathrm{C}_{74}\mathrm{H}_{84}\mathrm{NO}_{2}\mathrm{P}_{2}\mathrm{Ir}$	$\begin{array}{c} \mathbf{C}_{73}\mathbf{H}_{81}\mathbf{INO}_{2}\mathbf{P}_{2}\mathbf{Ir}\\ \cdot 2\left(\mathbf{C}_{5}\mathbf{H}_{12}\right)\end{array}$	$\mathrm{C}_{50}\mathrm{H}_{84}\mathrm{NO}_{2}\mathrm{P}_{2}\mathrm{Ir}$	$\begin{array}{c} 0.67(C_{49}H_{80}INO_{2}P_{2}Ir);\\ 0.33(C_{50}H_{83}NO_{2}P_{2}Ir) \end{array}$
Formula weight	1273.56	1529.72	985.32	1097.19
Crystal struc- ture	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Lattice parameters				
a (Å)	13.1981(7)	14.4250(5)	12.2897(7)	12.2460(6)
b (Å)	20.9991(9)	19.4180(6)	35.3664(19)	35.7358(18)
c (Å)	22.8801(12)	26.3735(9)	11.4244(6)	11.4544(6)
$\alpha$ (°)	90	90	90	90
$\beta$ (°)	100.388(3)	99.362(2)	93.830(2)	93.490(2)
$\gamma$ (°)	90	90	90	90
Volume $(Å^3)$	6237.2(5)	7288.9(4)	4954.4(5)	6856.5(5)
Space group	$P2_1/n$	$P2_{1}/c$	$P2_{1}/c$	$P2_{1}/c$
Z value	4	4	4	4
$ ho_{ m calc}~({ m g/cm^3})$	1.356	1.394	1.321	1.457
$\mu \; (\mathrm{mm}^{-1})$	2.239	2.346	2.796	3.386
Temperature	100(2)	100(2)	100(2)	100(2)
(K)				
$\theta$ range (°)	1.66 to 29.33	1.57 to $28.67$	1.76 to 27.89	1.87 to $40.01$
No. obs. $(I > 2\sigma(I))$	10617	15318	10841	25951
No. parameters	737	848	527	537
Goodness of fit*	1.268	2.742	1.824	1.448
Max. shift in cy- cle	0.003	0.002	0.003	0.010
$\begin{array}{ll} \text{Residuals}^*: & R, \\ R_w \end{array}$	0.0387; 0.0478	0.0482; 0.0750	0.0188; 0.0366	0.0344; 0.0620
Absorption cor- rection	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents
$\max/\min$	0.7459; 0.6362	0.4314; 0.3230	0.7456; 0.6727	0.7479; 0.6295
Largest peak & hole $(e^-/Å^3)$	1.724; -1.487	1.880; -2.150	0.633; -0.778	2.448; -2.844

**Table 2.4.** \* 
$$R = \frac{\sum_{hkl} ||F_{obs}| - |F_{calc}||}{\sum_{hkl} |F_{obs}|}; R_w = \sqrt{\frac{\sum_{hkl} w(|F_{obs}| - |F_{calc}|)^2}{\sum_{hkl} wF_{obs}^2}}, w = 1/\sigma^2(F_{obs}); \text{ GOF} = \sqrt{\frac{\sum_{hkl} w(|F_{obs}| - |F_{calc}|)^2}{\sum_{hkl} wF_{obs}^2}}$$

$$\sqrt{rac{\sum_{hkl} w(|F_{obs}| - |F_{calc}|)^2}{n_{data} - n_{vari}}}.$$

	16	17	18	19
Empirical for- mula	$\begin{array}{c} [{\rm C}_{50}{\rm H}_{84}{\rm NO}_2{\rm P}_2{\rm Ir}] \\ [{\rm PF}_6]\cdot 1.5({\rm C}_6{\rm H}_6) \end{array}$	$\frac{\mathrm{C}_{79}\mathrm{H}_{86}\mathrm{NO}_{2}\mathrm{P}_{2}\mathrm{Ir}}{\cdot 2\left(\mathrm{C}_{6}\mathrm{H}_{6}\right)}$	$\mathrm{C}_{73}\mathrm{H}_{80}\mathrm{NO}_{2}\mathrm{P}_{2}\mathrm{Ir}$	$ \begin{array}{ c c } C_{114}H_{136}Li_2N_4O_4\\ P_2Ir_2 \end{array} $
Formula weight	1249.08	745.92	1257.52	2086.49
Crystal struc- ture	Triclinic	Orthorhombic	Monoclinic	Triclinic
Lattice parameters				
a (Å)	21.3366(12)	16.0771(8)	41.3489(19)	16.4557(8)
b (Å)	21.4842(13)	20.5290(10	18.8871(9)	17.2824(8)
c (Å)	26.6266(15)	23.1672(11)	20.6067(9)	21.7560(10)
$\alpha$ (°)	81.836(4)	90	90	93.951(2)
$\beta$ (°)	85.844(3)	90	111.731(2)	96.184(3)
$\gamma$ (°)	89.459(4)	90	90	101.190(3)
Volume (Å <sup>3</sup> )	12050.2(12)	7646.3(6)	14949.3(12)	6008.7(5)
Space group	P1	Pbcn	C2/c	P1
Z value	8	8	8	2
$ ho_{ m calc}~({ m g/cm^3})$	1.377	1.296	1.117	1.153
$\mu \ (\mathrm{mm}^{-1})$	2.354	1.837	1.867	2.284
Temperature	100(2)	100(2)	100(2)	100(2)
(K)				
$\theta$ range (°)	1.66 to 27.99	1.76 to 37.38	1.47 to $32.01$	2.34 to 34.09
No. obs. $(I > 2\sigma(I))$	37498	13314	20406	30107
No. parameters	2386	417	758	1176
Goodness of fit*	1.780	3.326	2.133	2.866
Max. shift in cy- cle	0.003	0.001	0.008	0.007
$\begin{array}{ll} \text{Residuals}^*: & R, \\ R_w \end{array}$	0.0739; 0.1072	0.0443; 0.0804	0.0311; 0.0569	0.0335; 0.0589
Absorption cor- rection	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents
$\max/\min$	0.8340; 0.6254	0.7473;  0.6479	0.7463; 0.6478	0.7461; 0.6684
Largest peak & hole $(e^-/Å^3)$	2.889; -2.188	4.097; -2.794	1.457; -0.873	1.933; -1.882

**Table 2.5.** \*  $R = \frac{\sum_{hkl} ||F_{obs}| - |F_{calc}||}{\sum_{hkl} |F_{obs}|}; R_w = \sqrt{\frac{\sum_{hkl} w(|F_{obs}| - |F_{calc}|)^2}{\sum_{hkl} wF_{obs}^2}}, w = 1/\sigma^2(F_{obs}); \text{ GOF} =$ 

$$\sqrt{\frac{\sum_{hkl} w(|F_{\rm obs}| - |F_{\rm calc}|)^2}{n_{\rm data} - n_{\rm vari}}}.$$

	$(ONO^{tBu})Ir(PEt_3)_2Cl$		
Empirical for-	$\mathrm{C}_{49}\mathrm{H}_{81}\mathrm{ClNO}_{2}\mathrm{P}_{2}\mathrm{Ir}$		
mula			
Formula weight	1005.74		
Crystal struc-	Monoclinic		
ture			
Lattice parame-			
ters			
a (A)	12.2623(6)		
b (A)	35.4340(17)		
c (A)	11.3773(6)		
$\alpha$ (°)	90		
$\beta$ (°)	93.368(2)		
$\gamma$ (°)	90		
Volume (Å <sup>3</sup> )	4934.9(4)		
Space group	$P2_{1}/c$		
Z value	4		
$ ho_{ m calc}~({ m g/cm^3})$	1.354		
$\mu \ (\mathrm{mm}^{-1})$	2.861		
Temperature	100(2)		
(K)			
$\theta$ range (°)	1.88 to 39.87		
No. obs. $(I >$	26158		
$2\sigma(I))$			
No. parameters	526		
Goodness of fit*	2.079		
Max. shift in cy-	0.003		
cle			
Residuals*: $R$ ,	0.0371; 0.0602		
$R_w$	G · · · 1		
Absorption cor-	from equivalents		
max/min	$0.7478 \cdot 0.5515$		
Largest peak fr	2623 - 2021		
hole $(e^{-}/Å^{3})$	2.020, -2.901		
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 $Cp^*(OTf)Ir(PPh_3)Me$  in  $CH_2Cl_2$ , reacts with benzene to form  $Cp^*(OTf)Ir(PPh_3)Ph$ . Here however the intermolecular activation product is thermodynamically preferred; probably the difference between the two systems is primarily of steric origin, as both include ligands (*tert*butyl substituents on ONO; the large  $Cp^*$  group) that can lead to severe crowding.

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# Chapter 3

# DFT virtual screening identifies rhodium-amidinate complexes as active homogeneous catalysts for methane to methanol oxidation

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## 3.1 Abstract

In the search for new organometallic catalysts for the low temperature selective conversion of  $CH_4$  to  $CH_3OH$ , we apply quantum mechanical virtual screening to select the optimum combination of ligand and solvent on rhodium to achieve low barriers for  $CH_4$  activation and functionalization to recommend for experimental validation. We report quantum mechanical predictions (including implicit and explicit solvation) of the mechanisms for various bidentate and tridentate  $Rh^{III}$  complexes to catalytically activate and functionalize methane, using trifluoroacetic acid (TFAH) or water as a solvent. Our most notable results include the design of a  $Rh^{III}(NN^F)$  (( $NN^F = bis(N-pentafluorophenyl$ ) pentafluorobenzylamidinate) complex, with a methane activation transition state barrier of  $\Delta G^{\ddagger} = 27.6$  kcal/mol in TFAH, and a  $Rh^{III}(bisq)$  ((bisq) = bis(quinolinyl)benzene) complex, with a methane activation transition state barrier of  $\Delta G^{\ddagger} = 33.4$  kcal/mol in TFAH. To close the catalytic cycle, the functionalization of methylrhodium intermediates was also investigated, involving carbon-oxygen bond formation *via*  $S_N 2$  attack by solvent, or  $S_R 2$  attack by a vanadium oxo. In addition, we have found a correlation between  $CH_4$  activation barriers and rhodium-methyl bond energies that allow us to predict the activation transition state energies for future ligands as well.

## 3.2 Introduction

The facile, selective, and direct conversion of methane into methanol has long been a goal of industrial chemists [1]. Molecular compounds in solution have long been investigated as potential catalysts for this transformation, as they are typically well-defined, easy to characterize and model, and operate under relatively mild conditions. Whereas much previous work has been done on Pt and Pd catalysts [2, 3], in this chapter we focus on rhodium due to its well-documented nature as an effective C–H activating metal [4] and whose lower electronegativity may allow it to avoid poisoning by coordinating media.

Our initial calculations found that using neutral tridentate pincer ligands  $(L_3)$  resulted in neutral  $L_3Rh(TFA)_3$  resting states. In order for such complexes to activate methane, a TFA ligand must be both protonated and removed to create an open coordination site. The frequent result was that the overall methane activation energy (i.e. energy of the transition state minus energy of the resting state) was too high to be feasible. Thus, to provide the best candidates for experiments, we shifted our attention to bidentate and monoanionic ligands, which are expected to favor Rh<sup>III</sup> states that would incorporate a labile, protonated TFAH solvent molecule, thus removing the extra energy penalty for protonation. Bidentate and tridentate ligands were chosen to facilitate redox processes which interconvert square-planar and octahedral coordination environments. Thus we initially examined four classes of ligands that we thought might be prove effective while likely not too hard to synthesize:

- bis(*N*-phenyl)benzylamidinate (NN);
- (*N*-phenyl)acetaldiminyl quinolate (ONN);
- bis(pyridyl)(m) ethanesulfonate  $(DP\frac{M}{E}S);$
- bis(pyrrolyl)quinolinyl phosphine (PN);

and two solvents: water and trifluoroacetic acid, due to their pH range and oxidative stability. We then embarked on quantum mechanical (QM) virtual screening to select the optimum combinations of ligand and solvent to recommend for experimental validation. Here we used density functional theory (DFT) at the B3LYP and M06 levels, including both implicit and explicit solvation, for systematic searches over possible reactions mechanisms for  $CH_4$  activation and for functionalization.

We found that rhodium complexed with the bidentate bis(N-phenyl) benzylamidinate (NN) ligand was the most promising in our initial screen. We then designed a new ligand, bis(N-pentafluorophenyl) pentafluorobenzylamidinate (NN<sup>F</sup>), essentially an electron-poor version of (NN), that we found to be even more promising, with lower transition state barriers for both methane activation and Rh-Me functionalization. In addition, we also designed more and less electron-donating variations of the (ONN) ligand; and broadened our investigation to a fifth ligand class, bis(quinolinyl)benzene(bisq), that was expected to have further reduced functionalization barriers. Our efforts culminated in two complexes,

- Rh<sup>III</sup>(bis(*N*-pentafluorophenyl) pentafluorobenzylamidinate), denoted as Rh<sup>III</sup>(NN<sup>F</sup>); and
- Rh<sup>III</sup>(bis(quinolinyl) benzene), denoted as Rh<sup>III</sup>(bisq);

that can catalytically activate and functionalize methane, using TFAH or water as a solvent. The first case,  $\mathrm{Rh}^{\mathrm{III}}(\mathrm{NN}^{\mathrm{F}})$ , leads to a transition state barrier of  $\Delta G^{\ddagger} = 27.6$  kcal/mol at 298 K for methane activation in TFAH (35.0 kcal/mol in water), the lowest we have found using  $\mathrm{Rh}^{\mathrm{III}}$ . The barrier for functionalization is  $\Delta G^{\ddagger} = 36.8$  kcal/mol at 298 K for TFAH (29.7 kcal/mol in water). The second case,  $\mathrm{Rh}^{\mathrm{III}}(\mathrm{bisq})$ , leads to a transition state barrier of  $\Delta G^{\ddagger} = 33.4$  kcal/mol at 298 K for methane activation in TFAH, and  $\Delta G^{\ddagger} = 32.0$  kcal/mol at 298 K for Rh–Me functionalization in TFAH, also among the lowest we have found using  $\mathrm{Rh}^{\mathrm{III}}$ . For  $\mathrm{Rh}^{\mathrm{III}}$  complexes with neutral transition states, we find that increasing the electron-withdrawing nature of the ligands decreases barriers for both activation and functionalization. Thus, the only condition opposing even less donating ligands (i.e. lower barriers) is catalyst stability.

This chapter should be of great interest to experimentalists who can now focus on these two ligands in TFAH and water to validate and further optimize these systems.

#### **3.3** Materials and Methods

All quantum mechanical calculations were carried out using the Jaguar software version 7.6 developed by Schrödinger Inc. [5]. Geometry optimizations were carried out on initial guess structures, and vibrational frequencies were calculated to confirm the optimized geometries as intermediates or transition states and to construct a free energy profile. Solvation energies were calculated using the PBF Poisson-Boltzmann implicit continuum solvation model [6] in Jaguar, with a dielectric constant of 8.55 and a probe radius of 2.451 Å for TFAH and 80.37 and 1.40 Å for water. Explicit waters were added into the calculations of aqueous  $Rh(NN^F)$  (two explicit waters per aqua ligand) for more accurate solvation modeling.

Geometry optimization and vibrational data were calculated using the B3LYP density functional [7] with a smaller basis set, whereas single point gas-phase and solvated energies were calculated using the M06 functional [8] and a larger basis set. Here the "smaller basis set" consists of a modified double- $\zeta$  Los Alamos basis set and pseudopotential [9] that includes f functions for rhodium [10], and the 6-31G<sup>\*\*</sup> basis set [11] for the other atoms; whereas the "larger basis set" consists of the triple- $\zeta$  Los Alamos basis set and pseudopotential (LACV3P<sup>\*\*</sup>++) modified to include f functions and diffuse functions for rhodium, and the 6-311G<sup>\*\*</sup> ++ basis set [12] for the other atoms. For orbital analysis, the Pipek-Mezey localization procedure was used [13].

Rather than specify a particular chemical oxidant, we adopted a consistent electrostatic potential for electrons to determine the free energy changes of redox reactions. A value of 1.23 V vs. SHE, the standard potential for the reduction of oxygen at pH = 0 and 25°C ( $O_2(g) + 4 H^+(aq) + 4e^-(aq) \rightarrow 2H_2O(\ell)$ ), was adopted for models in trifluoroacetic acid. For water, the pH was taken as 7 and the potential thus reduced to 0.817 V; this was calculated using the equation  $E = E^\circ - \Delta G/n\mathcal{F}$  where  $\mathcal{F}$  is Faraday's constant and  $\Delta G = kT \ln Q = kT \cdot pH \cdot \ln 10$ . The free energy of the electron was then calculated using the equation  $G = -\mathcal{F}(E + 4.28 \text{ V})$  where 4.28 V represents the absolute potential of the SHE reference, yielding electron free energies of -127.1 and -117.5 kcal/mol, respectively [14]. The free energy of the proton was taken as -260 kcal/mol in TFAH and -279.80 kcal/mol in pH = 7 water [15]. The free energy for each molecular species in solution was calculated using the formula

$$G = E_{\text{gas}} + \Delta G_{\text{solv}} + \text{ZPE} + H_{\text{vib}} + 6kT - T[S_{\text{vib}} + 0.54(S_{\text{trans}} + S_{\text{rot}} - 14.3 \text{ e.u.}) + 7.98 \text{ e.u.}]$$

where the last term is an empirical approximation for the change in the translational and rotational entropy of the molecule between the gas phase and the solution phase (due to the finite librational frequencies) derived from Wertz [16]. For gas phase molecules (methane, methanol at 498.15 K, and for the purposes of this study methyl trifluoroacetate), we assumed that equilibration between the dissolved gas and the headspace occurred at a much faster timescale than the reactions in question; leading to  $\Delta G_{\text{gas}\to\text{solv}} = 0$ . Thus, the free energy of such gas molecules can be simply calculated using the formula

$$G = G_{\text{gas}} = E_{\text{gas}} + \text{ZPE} + H_{\text{tot}} - TS_{\text{tot}}$$

We simulated methanol in the gas phase at 498.15 K and the solution phase at room temperature by adding the empirical hydration free energy of -3.2 kcal/mol [17] to the gas phase free energy.

For pure liquids (e.g., trifluoroacetic acid and water), the Gibbs free energy was calculated using the formula

$$G_{\text{liquid}} = E_{\text{gas}} + \text{ZPE} + H_{\text{tot}} - TS_{\text{tot}} + \Delta G_{\text{gas} \rightarrow \text{liquid}}$$

where  $\Delta G_{\text{gas} \rightarrow \text{liquid}} = G_{\text{liquid}} - G_{\text{gas}}$  (1 atm) is the free energy of condensation to liquid from 1 atm gas. We can solve for this by noting that

$$\Delta G_{\rm gas \to liquid} = \Delta G_{\rm exp} + \Delta G_{\rm gas \to solv}$$

where  $\Delta G_{\exp} = G_{gas}(P) - G_{gas}(1 \text{ atm})$  is the expansion of the gas from 1 atm to the vapor pressure P, and  $\Delta G_{gas \rightarrow solv}$  is the condensation of gas to liquid. Since a liquid is by definition at equilibrium

Tomporatura	Trifl	uoroacetic	acid	Water			
remperature	A	В	С	А	В	С	
298.15 K	3.33963	1267.252	-52.958	5.40221	1838.675	-31.737	
$323.15 {\rm K}$	3.33963	1267.252	-52.958	5.20389	1733.926	-39.485	
$348.15 { m K}$	3.33963	1267.252	-52.958	5.07680	1659.793	-45.854	
$373.15 { m K}$	3.33963	1267.252	-52.958	5.08354	1663.125	-45.622	
$398.15 { m K}$	3.33963	1267.252	-52.958	3.55959	643.748	-198.043	
$423.15 {\rm K}$	3.33963	1267.252	-52.958	3.55959	643.748	-198.043	
448.15 K	3.33963	1267.252	-52.958	3.55959	643.748	-198.043	
$473.15 { m K}$	3.33963	1267.252	-52.958	3.55959	643.748	-198.043	
$498.15 { m K}$	3.33963	1267.252	-52.958	3.55959	643.748	-198.043	

Table 3.1. Antoine equation parameters used for trifluoroacetic acid and water at each temperature point investigated. Numbers taken from [18] and are set such that P will be measured in bar.

with its vapor pressure,  $\Delta G_{\text{gas} \rightarrow \text{solv}} = 0$ , and we thus have

$$\Delta G_{\text{gas}\to\text{liquid}} = G_{\text{gas}}(P) - G_{\text{gas}}(1 \text{ atm}) = RT \ln\left(\frac{P}{1 \text{ atm}}\right).$$

We can find the vapor pressure P at a given temperature using the Antoine Equation:

$$\log_{10} P = A - \frac{B}{C+T},$$

where the empirical parameters A, B, and C vary with the solvent and temperature range and were taken from table 3.1. Calculations were performed at nine temperature levels spaced by 25 K from 298.15 K to 498.15 K.

The  $S_R 2$  attack involving  $OV^V Cl_3$  converts two singlets to two doublets, and hence the transition states feature spin contamination ( $S^2 > 0$ ) while representing an overall singlet. Structures that did not feature such spin contamination were considered to be transition states for an alternative  $S_N 2$ attack that forms  $MeOV^{III}Cl_3^-$  and a  $Rh^I$  species, all of which were higher in energy.

#### **3.4** Results

The most common oxidation state of rhodium is +III, but oxidation states from 0 to +VI have been observed [19]. While previous work has focused on the C–H activation ability of Rh<sup>I</sup> [3]b, our current results center on a Rh<sup>III</sup> resting state. This is due to the requirement that the desired process operate above the CH<sub>4</sub>/CH<sub>3</sub>OH redox couple (0.59 V vs. SHE at pH = 0) and below the reduction potential of O<sub>2</sub> in the reaction conditions, which favor higher oxidation states.

Scheme 3.1 shows hypothetical catalytic cycles for the activation and functionalization of methane. Starting from an inorganic  $Rh^{III}$  resting state (1), we investigated the C–H activation of methane

following the displacement of a TFAH solvent molecule  $(2^{\ddagger})$  to form a Rh<sup>III</sup>-methyl organometallic species (3). Starting with (3), there are several pathways to functionalization:

- 1. III-I:  $S_N 2$  attack (4<sup>‡</sup>) by the conjugate base of the solvent to form methyl trifluoroacetate and a Rh<sup>I</sup> species (5), which is reoxidized to the inorganic Rh<sup>III</sup> resting state (1). In all cases investigated we found that this  $S_N 2$  attack occurs on a five-coordinate Rh complex, with the neutral solvent *trans* to the methyl group dissociated in the transition state. This is consistent with previous work by Goldberg et al. implicating five-coordinate platinum intermediates [20];
- 2. III-II: S<sub>R</sub>2 attack (6<sup>‡</sup>) by a metal-oxo species to form a metal-methoxy species and a Rh<sup>II</sup> species (7) via methyl radical transfer. Both of these are then reoxidized by one electron, to the metal-oxo species and methanol and to the inorganic Rh<sup>III</sup> resting state (1), respectively. Here, OVCl<sub>3</sub> was used as a model metal-oxo capable of one-electron reduction, even though it would likely hydrolyze in these solvents. We are developing stable metal oxo reagents optimized for this reaction mechanism [21] and use OVCl<sub>3</sub> here as a computationally simple model. The S<sub>R</sub>2 transition state for Rh(NN) involves a five-coordinate Rh complex as well. For the Rh(NN<sup>F</sup>) case, the transition states retain weak interactions with the neutral *trans* ligand, with an elongated Rh–O bond distance of 2.472 Å for TFAH and 2.228 Å for water. This is presumably due to the increased electrophilicity of the metal center in the Rh(NN<sup>F</sup>) complexes;
- 3. III-IV-II: Oxidation to a Rh<sup>IV</sup> species (8) followed by S<sub>N</sub>2 attack (9<sup>‡</sup>) generating a Rh<sup>II</sup> species (7), which is then further oxidized back to the Rh<sup>III</sup> resting state (1). This route was only investigated for the Rh(NN<sup>x</sup>) and Rh(DP<sup>M</sup><sub>E</sub>S) complexes, which had both kinetically accessible activation transition states and thermodynamically accessible Rh<sup>IV</sup> intermediates. In all cases investigated we found that this S<sub>N</sub>2 attack occurs on a six-coordinate Rh complex, presumably due to the increased electrophilicity of the Rh<sup>IV</sup> center. The six-coordinate Rh complexes have elongated Rh−O bond distances to the neutral *trans* ligand (e.g., 2.377 Å for Rh(NN), 2.379 Å for Rh(NN<sup>F</sup>), and 2.255 Å for Rh(NN<sup>F</sup>) in water).

In all cases, the energy of reoxidation was calculated assuming a potential of 1.23 V vs. SHE, i.e. with  $O_2$  as the terminal oxidant. However, in practice it may be necessary to use intermediate oxidants as well, although that is beyond the scope of this study.

A system which can proceed around any of these cycles with a global activation barrier below approximately 36 kcal/mol at 200°C is of academic interest, as transition state theory gives a turnover frequency (TOF) of roughly 1 hr<sup>-1</sup> at 1 atm CH<sub>4</sub> for such a process. Achieving an industrially relevant TOF on the order of 1 s<sup>-1</sup> requires a global barrier of 29 kcal/mol, although greater pressures of CH<sub>4</sub> would increase this limit [22].

We screened complexes of rhodium with the following ligands, as depicted in Figure 3.1:



Scheme 3.1. Hypothetical catalytic cycle for the activation and functionalization of methane. This shows several potential routes, including III-I (red), III-II (blue), and III-IV-II (green), which are further described in the text. In addition, a fourth possibility, I-III (purple), involves the direct C–H activation  $(10^{\ddagger})$  by a Rh<sup>II</sup> species (5) to a Rh<sup>III</sup> hydride methyl (11). However, given the oxidizing nature of the reaction conditions, we do not anticipate this to be a fruitful pathway, as any catalytic cycle involving a Rh<sup>I-</sup>(III) cycle would likely suffer from the fact that oxidation of 5 to 1 would act as a thermodynamic sink. Hence, this last option was not pursued to the same extent in this investigation.

- the bis (N-phenyl)benzylamidinate (NN) ligand and its fluorinated analogue (NN F);
- the (*N*-phenyl)acetaldiminyl quinolate (ONN) ligand and its related (ONN<sup>F</sup>) and (ONN<sup>NMe<sub>2</sub></sup>) ligands;
- the bis(pyridyl)methanesulfonate (DPMS) and bis(pyridyl)ethanesulfonate (DPES) ligands;
- the bis(pyrrolyl)quinolinyl phosphine (PN) ligand; and
- the bis(quinolinyl)benzene (bisq) ligand, its di- and tetrafluorinated analogues (bisq<sup>F<sub>2</sub></sup>) and (bisq<sup>F<sub>4</sub></sup>), and its di- and tetramethylated analogues (bisq<sup>Me<sub>2</sub></sup>) and (bisq<sup>Me<sub>4</sub></sup>).

Figure 3.1. The rhodium-ligand complexes screened. For each complex, the  $Rh^{I}$  form in TFAH is shown here, but full catalytic cycles were computed. The best kinetics were predicted for the  $Rh(NN^{F})$  and Rh(bisq) complexes.



For each of these ligands complexed with rhodium, we generated catalytic cycles in the template of Scheme 3.1. For the (DPMS), (PN), and (ONN<sup>x</sup>) family of ligands, we found that either the methane activation energy or the methyl functionalization energy (or both) were too high for effective catalysis (Table 3.2). However, we found lower numbers for the (NN<sup>x</sup>) family of ligands, on which we have decided to focus our discussion.

#### 3.4.1 The Rh(NN) complexes in TFAH

Scheme 3.2 shows the calculated free energies of Rh(NN) complexes in trifluoroacetic acid solvent. Note that all free energies are referenced to the resting state,  $[(NN)Rh^{III}(TFA)_4]^{2-}(H^+_{ax})_2$ , which is highlighted by a purple box. Hence, although the resting complex is regenerated at the end of the catalytic cycle, the new free energy is -13.7 kcal/mol at 298 K, because this is the energy change of the overall equation  $CH_4 + TFAH \longrightarrow TFA-Me + 2H^+ + 2e^-$ ; and thus all energies at the second cycle would be -13.7 kcal/mol lower.

Oxidation of the inorganic  $Rh^{I}$  species to inorganic  $Rh^{III}$  species is highly favorable, from 40 to 50 kcal/mol downhill, depending on the temperature and the charge of the species. We conclude that



Scheme 3.2. (a) Activation of methane using Rh(NN) complexes in TFAH; and (b) the subsequent functionalization. Red denotes the III-I functionalization pathway; blue the III-II pathway, and green the III-IV-II pathway. Free energies (kcal/mol) are referenced to the resting state,  $[(NN)Rh^{III}(TFA)_4]^{2-}(H^+_{ax})_2$ . The resting state is highlighted by a purple box, and the key methyl intermediate,  $[(NN)Rh^{III}(Me_{ax})(TFA)_3]^{2-}(H^+_{ax})(H^+_{eq})$ , is highlighted by a yellow box.

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TS type	TS	Rh(NN)	$Rh(NN^F)$	Rh(ONN)	$\operatorname{Rh}(\operatorname{ONN}^{\mathrm{F}})$	$\operatorname{Rh}(\operatorname{ONN}^{\operatorname{NMe}_2})$	Rh(DPMS)	Rh(DPES)
Activa-	${\rm Me}_{\rm ax}$	32.6/34.8	27.6/29.6	37.2/39.8	35.8/37.8	38.7/41.2	38.0/40.2	41.0/44.0
tion	$Me_{eq}$	38.3/40.4	33.7/36.3	37.9/40.7	38.1/40.1	40.0/42.9	33.9/36.2	35.6/38.4
Functio-	(III-I)	54.8/60.3	42.7/48.2	44.2/49.3	41.7/45.8	46.7/52.6	46.6/51.3	53.8/59.3
naliza-	(III-II)	43.2/44.2	38.1/40.0	40.4/42.5	39.1/40.8	41.4/43.4	41.0/41.6	45.5/47.4
tion	(III-IV-II)	42.2/48.6	36.8/43.6	N/A	N/A	N/A	49.3/56.3	49.9/57.1
TS type	TS	Rh(PN)	Rh(bisq)	$\mathrm{Rh}(\mathrm{bisq}^{\mathrm{F}_2})$	$\operatorname{Rh}(\operatorname{bisq}^{F_4})$	$Rh(bisq^{Me_2})$	$Rh(bisq^{Me_4})$	
Activa-	${\rm Me}_{\rm ax}$	40.1/43.0	38.3/40.7	39.3/42.4	40.4/43.0	38.8/41.9	40.7/44.4	•
tion	$Me_{eq}$	35.0/37.7	33.4/35.8	36.4/39.4	38.2/40.9	32.8/35.9	34.3/37.5	
Functiona	- (III-I)	38.3/43.8	31.8/37.8	32.3/38.4	30.2/35.0	35.0/41.9	38.0/45.5	-
lization	(III-II)	47.7/56.9	32.0/33.7	31.8/33.6	33.7/35.3	35.7/38.3	38.9/42.0	

**Table 3.2.** Lowest activation and functionalization energies for each series of Rh-ligand complexes in TFAH. Detailed cycles for the  $(NN^x)$  family of ligands are found in Schemes 3.2 and 3.3. Detailed cycles for the  $(ONN^x)$  family of ligands are found in Schemes 3.9 through 3.11. Detailed cycles for the  $(DP\frac{M}{E}S)$  family of ligands are found in Schemes 3.12 through 3.14. Detailed cycles for the (PN) ligand are found in Schemes 3.15 and 3.16. Detailed cycles for the  $(bisq^x)$  family of ligands are found in Schemes 3.17 through 3.20. For each entry, the first number is at 298 K and the second at 498 K. Not all III-IV-II transition states were calculated. All free energies in kcal/mol.

the III-I  $S_N^2$  attack pathway is not likely. Indeed, the activation barrier for this is a prohibitively high 54.8 kcal/mol at room temperature (Figure 3.2b). In addition, we also conclude that a I-III pathway involving methane activation by  $Rh^I$  is not likely due to the oxidation potential of the  $Rh^I$ species.

The remaining viable pathways all involve methane activation by the inorganic Rh<sup>III</sup>(NN) complex to form a Rh<sup>III</sup>(NN)–Me species. We were initially gratified to see that thermodynamically the methyl species is not very endergonic. We were even more intrigued to find that the methane activation transition state barrier is only 32.6 kcal/mol at 298 K (Figure 3.2a), making it the most accessible barrier that we had found for Rh<sup>III</sup> complexes in TFAH (Table 3.2).

In contrast, neither the III-II (Figure 3.2c) nor the III-IV-II (Figure 3.2d) functionalization pathways seemed as promising. Although further oxidation to a  $Rh^{IV}(NN)$ —Me species was roughly thermoneutral, the barrier to reductive functionalization was 42.2 kcal/mol. The oxidation from  $Rh^{III}$  to  $Rh^{IV}$  was effective in lowering the global  $S_N^2$  barrier from 54.8 to 42.2 kcal/mol. To explain the high functionalization barrier for  $S_N^2$  attack, we note that this may be due to the high energy or low chemical activity of trifluoroacetate ion in solution. Since TFA<sup>-</sup> is necessary as the attacking nucleophile, a higher pH may be employed to lower this barrier before a deprotonated intermediate becomes the new resting state.

Due to the unusually low barrier for methane activation, we did not want to dismiss this ligand framework. Rather, our efforts focused on how potential modifications on the (NN) ligand might lower the functionalization barrier. Reasoning that a more electronegative ligand may inductively increase the electrophilicity of the rhodium-methyl bond and make nucleophilic attack more likely, we decided to investigate Rh complexes with the fluorinated analogue bis(N-pentafluorophenyl) pentafluorobenzylamidinate (NN<sup>F</sup>) ligand.

 $\begin{array}{l} \textbf{Figure 3.2.} \ Rh(NN) \ transition \ state \ structures. (a) \ methane \ activation: \ Rh1-C36 \ 2.273 \ \text{\AA}, \ C36-H19 \ 1.365 \\ \text{\AA}, \ H19-O10 \ 1.321 \ \text{\AA}, \ Rh1-C36-H19 \ 64.624^{\circ}, \ C36-H19-O10 \ 155.492^{\circ}. (b) \ Rh(III-I) \ S_N^2 \ attack: \ Rh1-C60 \ 2.431 \\ \text{\AA}, \ C60-O65 \ 1.936 \ \text{\AA}, \ Rh1-C60-O65 \ 176.680^{\circ}, \ Rh1-O53 \ 3.473 \ \text{\AA}. (c) \ Rh(III-II) \ S_N^2 \ attack: \ Rh1-C60 \ 2.368 \\ \text{\AA}C60-O65 \ 1.995 \ \text{\AA}, \ Rh1-C60-O65 \ 175.541^{\circ}, \ Rh1-O53 \ 3.171 \ \text{\AA}. (d) \ Rh(III-IV-II) \ S_N^2 \ attack: \ Rh1-C60 \ 2.138 \\ \text{\AA}, \ C60-O64 \ 2.263 \ \text{\AA}, \ Rh1-O53 \ 2.377 \ \text{\AA}, \ Rh1-C60-O64 \ 168.802^{\circ}, \ C60-Rh1-O53 \ 164.984^{\circ}. \end{array}$ 



# 3.4.2 The $Rh(NN^F)$ complexes in TFAH

Compared to the analogous Rh(NN) complexes, the fluorinated  $Rh(NN^F)$  complexes (Scheme 3.3) show some marked differences in free energies. Many of these differences can be attributed to the much higher electron-withdrawing character of the  $(NN^F)$  ligand. For instance, the  $Rh^I(NN^F)$  species is 13.3 kcal/mol more stable to oxidation than the corresponding  $Rh^I(NN)$  species. In the same way, the  $S_N 2$  functionalization barrier on the III-I path is 12.1 kcal/mol lower. This is due to the highly electron-withdrawing  $(NN^F)$  ligand, which stabilizes lower oxidation states. Unfortunately, this effect is not sufficiently large for us to consider the III-I or I-III pathways. Other thermodynamic effects of fluorine atom substitution include increased acidity of all the complexes (i.e. stabilization of the anionic species by 4-8 kcal/mol), an increased stabilization of the  $Rh^{III}$ –Me species (by about 8 kcal/mol), and a decreased stabilization of the  $Rh^{IV}$ –Me species (by about 20 kcal/mol relative to  $Rh^{III}$ –Me.)

The barrier for methane activation, already relatively low for the Rh(NN) case, was even lower for the Rh(NN<sup>F</sup>) case, at only 28.7 kcal/mol at 298 K (Figure 3.3a). However, the real test of the utility of the (NN<sup>F</sup>) ligand is its effectiveness in aiding the functionalization step. It lowers the global III-I  $S_N^2$  barrier from 54.8 to 42.7 kcal/mol and the isolated  $S_N^2$  barrier (from the Rh<sup>III</sup>-Me intermediate) to 40.8 from 45.1 kcal/mol (Figure 3.3b). It raises the neutral III-IV-II  $S_N^2$  barrier by raising the Rh<sup>IV</sup> intermediate energy. Hence, we put our hopes into the (NN<sup>F</sup>) ligand lowering the barrier for a net anionic III-IV-II  $S_N^2$  or a III-II  $S_R^2$  attack (Figure 3.3c,d). And indeed it does: the new global  $S_N^2$  and  $S_R^2$  barriers of 36.8 and 38.1 kcal/mol, respectively, approach the target values.

# 3.4.3 The $Rh(NN^F)$ complexes in water

Another method that may lower transition state barriers is switching the solvent, and therefore the nucleophile, to water. This has the practical advantage that any commercialized process will have greater simplicity if carried out in water as opposed to a strong acid. Hence, we investigated the same  $Rh(NN^F)$  complexes in water.

The thermodynamic profile for  $Rh(NN^F)$  complexes in water (Scheme 3.4) is very promising: the  $Rh^{III}(NN^F)$ -methyl,  $Rh^{IV}(NN^F)$ -methyl, and  $Rh^{II}(NN^F)$  species are all stabilized relative to the inorganic  $Rh^{III}(NN^F)$  reference state. Hence, whereas for the TFAH solvent case a thermodynamic barrier must be climbed in each catalytic step, in water each step is either thermodynamically downhill or approximately neutral.

In Scheme 3.4, all energies are referenced to the lowest inorganic  $\mathrm{Rh}^{\mathrm{III}}$  state,  $[(\mathrm{NN}^{\mathrm{F}})\mathrm{Rh}^{\mathrm{III}}$ - $(\mathrm{OH})_4]^{2-}(\mathrm{H}^+_{\mathrm{ax}})(\mathrm{H}^+_{\mathrm{eq}})$ , which is highlighted by a purple box. This is to keep consistent with the practices in Schemes 3.2 and 3.3, where the lowest inorganic  $\mathrm{Rh}^{\mathrm{III}}$  state is also the resting state. However, in this case the organometallic  $\mathrm{Rh}^{\mathrm{III}}(\mathrm{NN}^{\mathrm{F}})$ -methyl complexes are stabilized to such an



Scheme 3.3. (a) Activation of methane using  $Rh(NN^F)$  complexes in TFAH; and (b) the subsequent functionalization. Red denotes the III-I functionalization pathway; blue the III-II pathway, and green the III-IV-II pathway. Free energies (kcal/mol) are referenced to the resting state,  $[(NN^F)Rh^{III}(TFA)_4]^{2-}(H^+_{ax})_2$ . The resting state is highlighted by a purple box, and the key methyl intermediate,  $[(NN^F)Rh^{III}(Me_{ax})(TFA)_3]^{2-}(H^+_{ax})$ , is highlighted by a yellow box.

 $\begin{array}{l} {\bf Figure ~ 3.3.~Rh(NN^F)~transition~state~structures.~(a)~methane~activation:~Rh1-C61~2.267~Å,~C61-H19~1.365\\ {\rm \mathring{A},~H19-O10~1.321~\mathring{A},~Rh1-C61-H19~63.875^\circ,~C61-H19-O10~157.549^\circ.~(b)~Rh(III-I)~S_N2~attack:~Rh1-C60~2.368\\ {\rm \mathring{A},~C60-O65~2.021~\mathring{A},~Rh1-C60-O65~176.330^\circ,~Rh1-O53~3.265~\mathring{A}.~(c)~Rh(III-II)~S_R2~attack:~Rh1-C60~2.399\\ {\rm \mathring{A}C60-O65~1.935~\mathring{A},~Rh1-O53~2.472~\mathring{A},~Rh1-C60-O65~172.164^\circ,~C60-Rh1-O53~168.496^\circ.~(d)~Rh(III-II)\\ {\rm S_N2~attack:~Rh1-C60~2.259~\mathring{A},~C60-O64~2.156~\mathring{A},~Rh1-O53~2.379~\mathring{A},~Rh1-C60-O64~159.539^\circ,~C60-Rh1-O53~169.220^\circ. \end{array}$ 





Scheme 3.4. Thermodynamic profile for the activation and functionalization of methane using Rh(NN<sup>F</sup>) complexes in water. This chart is meant to be read from left to right; the first row contains the pathway through neutral species and the second row through anionic species. Red denotes the III-I functionalization pathway; blue the III-II, and green the III-IV-II pathway. All free energies (kcal/mol) are at pH = 7 and referenced to the lowest inorganic Rh<sup>III</sup> state,  $[(NN^F)Rh^{III}(OH)_4]^{2-}(H^+_{ax})(H^+_{eq})$ , highlighted by a purple box; whereas the key methyl intermediate and true resting state,  $[(NN^F)Rh^{III}(Me_{eq})(OH)_3]^{2-}(H^+_{ax})_2$ , is highlighted by a yellow box.

extent that the true resting state is now  $[(NN^F)Rh^{III}(Me_{eq})(OH)_3]^{2-}(H_{ax}^+)_2$ , which is highlighted by a yellow box and is analogous to the key methyl intermediate referenced in Schemes 3.2 and 3.3. The practical consequence is that the barrier to  $CH_4$  activation is properly referenced to the lowest inorganic  $Rh^{III}$  state, whereas the barrier to methyl group functionalization ought to be referenced to the true resting state.

Having verified that the  $Rh(NN^F)$  catalytic system in water was thermodynamically feasible, we sought accessible transition states for both the methane activation and functionalization steps. For methane activation, we began by assuming that the activation would take place *via* electrophilic substitution with a *cis* hydroxo ligand acting as a proton acceptor (Scheme 3.5). We then found transition states, starting from both neutral and anionic species, with the methane and the interacting hydroxo in every possible configuration with respect to the  $(NN^F)$  ligand. Our lowest transition state barrier of 35.0 kcal/mol at 298 K occurs with the methyl group forming in the axial position, donating its extra proton to an equatorial hydroxo ligand and *trans* to an axial hydroxo ligand (Figure 3.4a). This is significantly higher than in the TFAH solvent case, but still within the limits of feasibility. We examined the possible role of a concerted reaction with a bridging water molecule, but we did not see a decrease in the transition state energy.



Scheme 3.5. Transition states for the activation of methane using  $Rh(NN^F)$  complexes in water. Chart is meant to be read from top to bottom; the left side contains the pathway through neutral species and the right side through anionic species. All free energies are in kcal/mol and referenced to the lowest inorganic  $Rh^{III}$  state.

Following the activation of methane, the other transition state that needed to be calculated was for the functionalization of the rhodium-methyl bond. We investigated the functionalization through

 $\begin{array}{l} \textbf{Figure 3.4.} \ Rh(NN^{\rm F}) \ in water transition state structures. (a) methane activation: Rh1-C66 2.296 Å, C66-H65 1.383 Å, H65-O5 1.271 Å, Rh1-C66-H65 55.587°, C66-H65-O5 161.845°. (b) Rh(III-I) S_N2 attack: Rh1-C64 2.698 Å, C64-O67 1.803 Å, O67-H68 1.043 Å, H68-O47 1.516 Å, O47-H53 1.001 Å, H53-O5 1.718 Å, Rh1-C60-O65 148.135°, Rh1-O54 3.265 Å. (c) Rh(III-II) S_R2 attack: Rh1-C65 2.371 ÅC65-O68 2.010 Å, Rh1-O55 2.228 Å, Rh1-C65-O68 164.320°, C65-Rh1-O55 169.736°. (d) Rh(III-IV-II) S_N2 attack: Rh1-C64 2.526 Å, C64-O67 1.930 Å, O67-H68 1.033 Å, H68-O46 1.503 Å, O46-H51 1.008 Å, H51-O47 1.594 Å, O47-H3 0.981 Å, H3-O5 1.901 Å, Rh1-O54 2.255 Å, Rh1-C64-O67 171.136°, C64-Rh1-O54 167.491°. \end{array}$ 



the III-I, III-II, and III-IV-II routes (Schemes 3.6, 3.7, and 3.8, respectively). For each route, we restricted our investigation to activations from rhodium species with axial methyl groups, since (as in the TFAH case) the axial isomer is preferentially formed during the activation step.

$[(NN^{F})(Rh^{III})(CH_3)(OH)_3]^2(H^+)_2 \\ ( \underset{N}{\overset{CH_3}{\underset{OH_2}{OH_2}}} \underset{OH_2}{\overset{H_2OH_2}{\underset{OH_2}{\overset{H_2OH_2}{\overset{H_2OH_2}{\overset{H_2OH_2}{\overset{H_2OH_2}{\overset{H_2OH_2}{\overset{H_2OH_2}}}} )$	$\begin{bmatrix} H_{-} OH \\ HO \\ HO \\ H_{-} H \\ CH_{3} OH \\ CH_{3} OH \\ N \\ \bullet OH_{2} \end{bmatrix}^{\ddagger}$	$\begin{array}{c} C_{6}F_{5} \\ \hline C_{6}F_{5}-N \stackrel{(h)}{\frown} N-C_{6}F_{5} \\ \hline C_{1}C_{1}OH \\ -CH_{3}OH \\ H_{2}O \\ OH_{2} \end{array}$	$[(\mathbf{NN}^{F})(\mathbf{Rh}^{III})(\mathbf{CH}_{3})(\mathbf{OH})_{3}]^{2^{*}}(\mathbf{H}^{*}) \\ ( \begin{array}{c} CH_{3} \\ $	$\begin{bmatrix} H & OH \\ H & H \\ CH_3 & OH \\ CH_3 & OH \\ N & \Theta \\ N & OH \end{bmatrix}^{\ddagger}$	$\begin{array}{c} C_6F_5\\ \hline C_6F_5-N \swarrow N-C_6F_5\\ \hline -CH_3OH \\ H_2O \\ H_2O \\ \end{array} \\ \begin{array}{c} C_6F_5-N \swarrow N-C_6F_5\\ \hline Ph \\ H_2O \\ OH \\ \end{array}$
(Me ax, OH eq)	<b>Rh III-I TS</b>	[(NN <sup>F</sup> )(Rh <sup>I</sup> )(OH) <sub>2</sub> ] <sup>2-</sup> (H <sup>+</sup> ) <sub>2</sub>	<b>(Me ax, H<sub>2</sub>O ax)</b>	<b>Rh III-I TS</b>	<b>[(NN<sup>F</sup>)(Rh<sup>I</sup>)(OH)<sub>2</sub>]<sup>2-</sup>(H<sup>+</sup>)</b>
G (298K) = 0.6	G (298K) = 51.6	G (298K) = 14.1	G (298K) = 5.0	G (298K) = 60.7	G (298K) = 10.8
G (498K) = 1.9	G (498K) = 55.8	G (498K) = 8.0	G (498K) = 6.4	G (498K) = 66.1	G (498K) = 7.2

Scheme 3.6. Transition states for the III-I functionalization pathway via  $S_N^2$  attack in water. The left side is the pathway through neutral species and the right side through anionic species. All free energies are in kcal/mol and referenced to the resting state,  $[(NN^F)Rh^{III}(Me_{eq})(OH)_3]^{2-}(H^+_{ax})_2$ .

For the III-I route, we required an aqua ligand to be the leaving group *trans* to the methyl, limiting us to only two possible transition states: a neutral transition complex (Scheme 3.6, left) and an anionic complex (Scheme 3.6, right). Although the neutral transition state (Figure 3.4b) is somewhat lower in energy, we found that in both cases the activation energy for this pathway is prohibitively high.

For the III-II route (Scheme 3.7), we no longer needed require the leaving group *trans* to the Rh<sup>III</sup>methyl to be an aqua ligand. Hence we performed calculations on four different potential transition states, starting with two isomers of neutral  $[(NN^F)Rh^{III}(Me_{ax})(OH)_3]^{2-}(H^+)_2$  (Scheme 3.7, upper left) and two isomers of anionic  $[(NN^F)Rh^{III}(Me_{ax})(OH)_3]^{2-}(H^+)$  (Scheme 3.7, upper right). We found that this S<sub>R</sub>2 pathway was even more facile, with all barriers in the 30s (Scheme 3.7, middle) and the lowest barrier being 31.7 kcal/mol for OVCl<sub>3</sub> attack on a neutral species with an axial methyl ligand, which is shown in detail in Figure 3.4c.

For the III-IV-II route (Scheme 3.8), a good leaving group *trans* to the Rh<sup>III</sup>-methyl once again became important. Hence, we were limited to only investigating one possible transition state, shown in detail in Figure 3.4d. We found the activation energy for this process to be approximately equal to that of the methane activation step.

Hence, we conclude that for the  $Rh(NN^F)$  catalytic system in water, both III-IV-II  $S_N^2$  and III-II  $S_R^2$  are viable pathways for functionalization, whereas the III-I  $S_N^2$  pathway is still too high in energy. This is similar to the case in TFAH, except that the relative ease of activation *vis-à-vis* functionalization has now been reversed.

#### 3.4.4 The $Rh(ONN^x)$ family of complexes in TFAH

Schemes 3.9, 3.10, and 3.11 depict the catalytic cycle for the activation and functionalization of methane using Rh(ONN),  $Rh(ONN^{F})$ , and  $Rh(ONN^{NMe_2})$  complexes in TFAH, respectively. In all



Scheme 3.7. Transition states for the III-II functionalization pathway via  $S_R 2$  attack in water. This chart is meant to be read from top to bottom; the left side contains the pathway through neutral species and the right side through anionic species. All free energies are in kcal/mol and referenced to the resting state,  $[(NN^F)Rh^{III}(Me_{eq})(OH)_3]^{2-}(H^+_{ax})_2$ .



Scheme 3.8. Transition state for the III-IV-II functionalization pathway via  $S_N 2$  attack in water. All free energies are in kcal/mol and referenced to the resting state,  $[(NN^F)Rh^{III}(Me_{eq})(OH)_3]^{2-}(H^+_{ax})_2$ .

cases, the resting state contains an axial TFAH ligand and equatorial TFA ligands, but the activation transition state which involves an axial methyl group is slightly lower in energy than the transition state which involves an equatorial methyl group. The methane activation energy for Rh(ONN) is 37.2 kcal/mol at 298 K, which is somewhat too high for promising catalysis. Switching to  $Rh(ONN^{F})$  decreases this activation energy slightly to 35.8 kcal/mol, whereas using  $Rh(ONN^{NMe_2})$  raises it to 38.7 kcal/mol.



Scheme 3.9. Catalytic cycle for the activation and functionalization of methane using Rh(ONN) complexes in TFAH. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.

The  $\operatorname{Rh}^{\operatorname{III}}(\operatorname{ONN}^x)$ -Me species investigated have a methyl group axial to the (ONN<sup>x</sup>) plane; any isomer with an equatorial methyl group would likely be less stable due to the *trans* effect of the (ONN<sup>x</sup>)'s quinoline nitrogen. The  $\operatorname{Rh}^{\operatorname{III}}(\operatorname{ONN}^x)$ -Me species are slightly endergonic relative to their respective resting states.

In all cases, the III-II  $S_R^2$  pathway is favored over the III-I  $S_N^2$  pathway. For Rh(ONN) the  $S_R^2$  barrier is 40.3 kcal/mol at 298 K; this decreases to 39.2 kcal/mol for Rh(ONN<sup>F</sup>) but increases



Scheme 3.10. Catalytic cycle for the activation and functionalization of methane using  $Rh(ONN^F)$  complexes in TFAH. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.



Scheme 3.11. Catalytic cycle for the activation and functionalization of methane using  $Rh(ONN^{NMe_2})$  complexes in TFAH. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.

to 41.4 kcal/mol for  $Rh(ONN^{NMe_2})$ . The resultant  $Rh^{III}(ONN^x)$  species were all approximately the same (20.5, 20.3, and 20.7 kcal/mol, respectively) in energy relative to their resting states.

#### 3.4.5 The Rh(DPMS) and Rh(DPES) complexes in TFAH

Scheme 3.12 shows the catalytic cycle for the activation and functionalization of methane using Rh(DPMS) complexes in TFAH, with the latter *via* the Rh(III-I), Rh(III-II), and Rh(III-IV-II) pathways. While there is a relatively accessible activation barrier of 33.9 kcal/mol at 298 K, it differs from the activation transition states of the NN<sup>x</sup> and ONN<sup>x</sup> families in that it forms a methyl complex with the methyl group equatorial to the N-Rh-N plane. Interconvertibility with the lower-energy axial methyl complex is assumed given the lability of the sulfonate moiety and the TFAH ligands. Unfortunately, the lowest functionalization barrier found was 41.0 kcal/mol at 298 K for the III-II pathway, which is too high.

The analogous catalytic cycle for Rh(DPES) complexes in TFAH is shown in Scheme 3.13. The energy profile is very similar to that of the Rh(DPMS) complexes; however, the transition states found are typically several kcal/mol higher than their Rh(DPMS) counterparts. This may be due to the extra methyl group rendering the overall ligand more electron donating, destabilizing the formation of a Rh–Me bond and decreasing its electrophilicity for functionalization.

We also investigated Rh<sup>I</sup>(DPMS) species, the results of which are shown in Scheme 3.14. The energy profile appears to be much more favorable, with the highest barrier being the oxidative addition of methane at 26.4 kcal/mol at 298 K. However, under reaction conditions one might expect the oxidative addition of methane by Rh<sup>I</sup>(DPMS) to be outcompeted by Rh<sup>I</sup>(DPMS)'s oxidation to a Rh<sup>III</sup>(DPMS) species, which according to Scheme 3.12 is downhill by 33.0 kcal/mol at 298 K. Therefore, the I-III pathway was not considered to be viable.

#### 3.4.6 The Rh(PN) complexes in TFAH

Scheme 3.15 shows the catalytic cycle for the activation and functionalization of methane using Rh(PN) complexes in TFAH, with the latter *via* the Rh(III-I) and Rh(III-II) pathways. Unfortunately, it appears that the functionalization barriers are too high for effective catalysis with this ligand: the lowest III-I  $S_N 2$  barrier is 38.0 kcal/mol at 298 K and the lowest III-II  $S_R 2$  barrier is 47.7 kcal/mol. Taking into account the additional fact that the activation transition state to produce an axial methyl species is 40.1 kcal/mol high, we conclude that Rh<sup>III</sup>(PN) is not likely to be an effective catalyst for methane oxidation.

We also investigated  $Rh^{I}(PN)$  species, the results of which are shown in Scheme 3.16. As in the case of the Rh(DPMS) complexes, oxidative addition of methane by  $Rh^{I}(PN)$  appears to be more facile, with a barrier of 28.1 kcal/mol at 298 K. Unfortunately, the resultant  $Rh^{III}(PN)(H)(Me)$ 



Scheme 3.12. The activation and functionalization of methane using Rh(DPMS) complexes in TFAH, *via* the Rh(III-I), Rh(III-II), and Rh(III-IV-II) pathways. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.



Scheme 3.13. The activation and functionalization of methane using Rh(DPES) complexes in TFAH, *via* the Rh(III-I), Rh(III-II), and Rh(III-IV-II) pathways. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.



Scheme 3.14. Catalytic cycle for the activation and functionalization of methane using Rh(DPMS) complexes in TFAH, *via* the Rh(I-III) pathway. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.

species are all significantly thermodynamically uphill (at least 22.0 kcal/mol at 298 K). Furthermore, as in the case of the Rh(DPMS) complexes, under reaction conditions one might expect the oxidative addition of methane by Rh<sup>I</sup>(PN) to be outcompeted by Rh<sup>I</sup>(PN)'s oxidation to a Rh<sup>III</sup>(PN) species, which according to Scheme 3.15 is downhill by 23.7 kcal/mol at 298 K. Therefore, the I-III pathway was not further pursued.

#### 3.4.7 The $Rh(bisq^x)$ family of complexes in TFAH

Due to the large in-TFAH Rh–Me functionalization barriers encountered in the other ligands so far (Table 3.2), we designed the bis(quinolinyl) benzene (bisq<sup>x</sup>) family of ligands (Figure 3.1) in the hopes of finding more facile  $S_N 2$  and  $S_R 2$  pathways. These ligands would be expected to be coordinated to rhodium in a *fac*-L<sub>3</sub> manner, with a weak  $\eta^2$ -benzene interaction axial to the N–Rh–N plane. A methyl group would then be expected to be coordinated axial to the N–Rh–N plane as well, due to the weaker *trans* effect of the benzene ring as opposed to the nitrogen donors. The  $\eta^2$ -benzene interaction is also expected to be a better leaving group than TFA/TFAH, thereby lowering both the barrier and thermodynamics of functionalization. Beyond the base (bisq) ligand itself, we also investigated the di- and tetrafluorinated analogues (bisq<sup>F<sub>2</sub></sup>) and (bisq<sup>F<sub>4</sub></sup>), and the di- and tetramethylated analogues (bisq<sup>Me<sub>2</sub></sup>) and (bisq<sup>Me<sub>4</sub></sup>), to see how changing the electronics of the ligand



Scheme 3.15. Catalytic cycle for the activation and functionalization of methane using Rh(PN) complexes in TFAH, *via* the Rh(III-I) and Rh(III-II) pathways. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.



Scheme 3.16. Catalytic cycle for the activation and functionalization of methane using Rh(PN) complexes in TFAH, *via* the Rh(I-III) pathway. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.

might change its associated transition state barriers.

Scheme 3.17 shows the ground states of the various  $Rh^{III}(bisq^x)$  species: the neutral  $Rh^{III}(bisq^x)$ - $(TFA)_3$ , the protonated  $[Rh^{III}(bisq^x)(TFA)_2(TFAH)]^+$  and  $[Rh^{III}(bisq^x)(TFA)_2)]^+$ , and their relative free energies. The first point to note is that, since the  $(bisq^{x})$  ligands are L<sub>3</sub>, activation of methane requires first the protonation of a TFA ligand followed by its removal as TFAH to form an open coordination site. As Scheme 3.17 shows, as we increase the electron-withdrawing groups on  $(bisq^{x})$ , replacing Me with H and H with F, the resultant decrease in electron donation to the central Rh decreases the basicity of the attached TFA ligands and increases the energy of their protonated forms. The second and related point to note is that the true resting state is not consistent for all  $(bisq^x)$ species: the more electron-rich ligands (bisq<sup>Me<sub>2</sub></sup>) and (bisq<sup>Me<sub>4</sub></sup>) have positively-charged resting states, the base ligand (bisq) has both the neutral and a protonated species in even equilibrium, while the less electron-rich ligands ( $bisq^{F_2}$ ) and ( $bisq^{F_4}$ ) prefer to be neutral. However, the energies of all species have been referenced to neutral  $\operatorname{Rh}^{\operatorname{III}}(\operatorname{bisq}^{x})(\operatorname{TFA})_{3}$  for consistency. The final point to note is that the specific protonated resting state for the more electron-rich ligands (bisq<sup>Me<sub>2</sub></sup>) and (bisq<sup>Me<sub>4</sub></sup>) depends on temperature: at 298 K  $[Rh^{III}(bisq^{Me_x})(TFA_{ax})(TFAH_{eq}\cdots TFA_{eq})]^+$  is favored, but at 498 K it is more advantageous to dissociate the TFAH and have  $[Rh^{III}(bisq^{Me_x})(\kappa^1 - TFA_{eq})(\kappa^2 - TFA_{ax, eq})]^+$ instead.

Scheme 3.18 shows the three potential methane activation transition states that may result



**Scheme 3.17.** The inorganic  $\operatorname{Rh}^{\operatorname{III}}(\operatorname{bisq}^{x})(\operatorname{TFA})_{3}$  species and its protonated analogues  $[\operatorname{Rh}^{\operatorname{III}}(\operatorname{bisq}^{x})(\operatorname{TFA})_{2}(\operatorname{TFAH})]^{+}$  and  $[\operatorname{Rh}^{\operatorname{III}}(\operatorname{bisq}^{x})(\operatorname{TFA})_{2})]^{+}$ , along with their relative energies in TFAH. Both protonation and TFAH removal are necessary before methane activation can take place. All free energies are in kcal/mol and referenced to the corresponding  $\operatorname{Rh}^{\operatorname{III}}(\operatorname{bisq}^{x})(\operatorname{TFA})_{3}$  species.

depending on the  $CH_4$  molecule's approach towards the  $[Rh^{III}(bisq^x)(TFA)_2)]^+$ 's open coordination site. The top transition state shows the result of a methane approach to an axial open coordination site, whereas the other two show the result of an equatorial approach, with either the axial or equatorial TFA ligand gaining the methane's proton. The axial approach results in a  $[Rh^{III}-Me_{ax}]^+$ species, whereas the equatorial approaches result in  $[Rh^{III}-Me_{eq}]^+$  species, all of which may be deprotonated to form their neutral analogues. Further oxidation to  $Rh^{IV}$  species is quite uphill; hence the III-IV-II functionalization pathway was not investigated for these rhodium-ligand complexes.

It should be noted that regardless of the specific  $(bisq^x)$  ligand, the lowest energy methane activation transition state is  $[Rh^{III}(bisq^x)(TFA_{ax})(Me_{eq}\cdots H\cdots TFA_{eq})]^{+\ddagger}$ , which involves an equatorial approach for the methane and results in the methyl complex  $[Rh^{III}(bisq^x)(TFA_{ax})(Me_{eq})(TFAH_{eq})]^+$ . However, both the neutral and protonated  $Rh^{III}-Me_{ax}$  species are lower in energy than their equatorial counterparts. We assume that interconversion between the  $Rh^{III}-Me_{eq}$  and  $Rh^{III}-Me_{ax}$  is facile due to the lability of the TFAH and  $\eta^2$ -benzene ligands.

Upon examination of the methane activation transition state energies, it appears that the general trend is that increasing the electron-donating nature of groups on the (bisq) ligand appears to favor lower barriers. This is opposite to that observed in the other ligand families, in which less electron-donating ligands are preferred. However, a comparison of the energies of  $[Rh^{III}(bisq^x)(TFA)-(Me\cdots H\cdots TFA)]^{+\ddagger}$  transition states with that of their protonated  $[Rh^{III}(bisq^x)(TFA)_2(TFAH)]^+$ 

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**Scheme 3.18.** The various methane activation transition states  $[Rh^{III}(bisq^x)(TFA)(Me\cdots H\cdots TFA)]^{+\ddagger}$  and their resultant  $[Rh^{III}(bisq^x)(TFA)(Me)(TFAH)]^+$  products. Ensuing deprotation (in preparation for III-I and III-II functionalization) and oxidation (in preparation for III-IV-II functionalization) are also depicted. Blue denotes the most favored Rh–Me intermediate and red the most favored activation transition state. All free energies are in kcal/mol and referenced to the corresponding Rh<sup>III</sup>(bisq<sup>x</sup>)(TFA)<sub>3</sub> species.

precursors (Scheme 3.17) shows that the decreased activation barriers for more electron-donating ligands is simply due to the decreased energy of protonation of the inorganic  $\text{Rh}^{\text{III}}(\text{bisq}^{x})(\text{TFA})_{3}$  precursors. It should also be noted that for ( $\text{bisq}^{\text{Me}_{2}}$ ) and ( $\text{bisq}^{\text{Me}_{4}}$ ), the energies shown in Scheme 3.18 are not the full transition barriers, since they are not referenced to the ground states of those rhodium-ligand complexes. The true barriers are recorded in Table 3.2.

An examination of the energies of the lowest Rh–Me intermediate for each (bisq<sup>x</sup>) ligand (Scheme 3.18, blue) shows that the relative energy decreases as the electron-withdrawing nature of groups on the (bisq) ligand is increased. This is easily explained by noting that a decrease in the electron-donating power of the (bisq) ligand is expected to increase the rhodium atom's electrophilicity, and thus increase the strength of its bond with the methyl group. Indeed, for (bisq<sup> $F_4$ </sup>) the Rh–Me species is slightly lower (by 0.3 kcal/mol) in energy than its Rh<sup>III</sup>(bisq<sup>x</sup>)(TFA)<sub>3</sub> precursor at 298 K, and is the true resting state. However, this does not change the overall methane activation barrier.

The III-I  $S_N 2$  and III-II  $S_R 2$  functionalization pathways were investigated by searching for transition states resulting from TFA<sup>-</sup>/TFAH or OVCl<sub>3</sub> attack on each Rh–Me species, axial and equatorial, neutral and positively charged; for all five (bisq<sup>x</sup>) ligands. A total of 65 transition state structures were analyzed.

Figure 3.5 shows the functionalization transition states for  $S_N^2$  attack by TFA<sup>-</sup>/TFAH on various Rh–Me intermediates. Both H<sup>+</sup> pre-protonation followed by TFA<sup>-</sup> attack and concerted TFAH attack/deprotonation transition states were investigated. The lowest energy  $S_N^2$  functionalization barrier was found to arise from the attack of a TFA<sup>-</sup> ion on a protonated Rh–Me<sub>ax</sub> species. Not surprisingly, lower barriers were found for Rh<sup>III</sup>(bisq<sup>x</sup>) complexes with less electron-donating ligands. The energies are overall significantly lower than those found with other ligand families, thus confirming our initial hypothesis that a weak  $\eta^2$ -benzene coordinated *trans* to the methyl would facilitate  $S_N^2$  attack. Indeed, barriers of 34.1 kcal/mol and lower at 298 K are found for (bisq) and its fluorinated analogues, thereby establishing the viability of the Rh<sup>III</sup>(bisq<sup>x</sup>) family of complexes as potentially effective catalysts.

Figure 3.6 shows the functionalization transition states for  $S_R^2$  attack by OVCl<sub>3</sub> on both neutral  $Rh^{III}(bisq^x)(Me)(TFA)_2$  and protonated  $[Rh^{III}(bisq^x)(Me)(TFA)(TFAH)]^+$  species, with both axial and equatorial methyl conformations. In most cases the lowest energy  $S_R^2$  functionalization barrier was found to arise from the attack of a OVCl<sub>3</sub> molecule on a neutral  $Rh-Me_{ax}$  species (the lone exception is  $(bisq^{Me4})$ , which prefers a protonated transition state). As in the III-I  $S_N^2$  case, lower barriers were found for  $Rh^{III}(bisq^x)$  complexes with less electron-donating ligands, and overall the barriers were reduced compared to those of other ligand families; although the effect is not as pronounced as for the  $S_N^2$  case, and the tetrafluorinated  $(bisq^{F4})$  version is an outlier. Barriers of 33.4 kcal/mol and lower at 298 K are found for (bisq) and its fluorinated analogues, thereby establishing

**Figure 3.5.** The various  $Rh^{III}(bisq^x)(Me)$  functionalization transition states for the III-I  $S_N^2$  pathway. All transition states resulting from TFA<sup>-</sup>/TFAH attack on each Rh–Me species, axial and equatorial, neutral and positively charged, are shown. The lowest transition state for each  $(bisq^x)$  ligand is shown in red. All free energies are in kcal/mol and referenced to the corresponding  $Rh^{III}(bisq^x)(TFA)_3$  species.



the viability of the III-II pathway as well as the III-I pathway for methyl functionalization of the  $Rh^{III}(bisq^x)$  family of complexes.

**Figure 3.6.** The various  $\text{Rh}^{\text{III}}(\text{bisq}^x)(\text{Me})$  functionalization transition states for the III-II S<sub>R</sub>2 pathway. All transition states resulting from OVCl<sub>3</sub> attack on each Rh–Me species, axial and equatorial, neutral and positively charged, are shown. The lowest transition state for each ( $\text{bisq}^x$ ) ligand is shown in red. All free energies are in kcal/mol and referenced to the corresponding Rh<sup>III</sup>( $\text{bisq}^x$ )(TFA)<sub>3</sub> species.



Scheme 3.19 shows the remainder of the catalytic cycle after either III-I or III-II functionalization, and compares the two functionalization processes. For the III-I pathway,  $S_N^2$  attack by TFA<sup>-</sup>/TFAH results in the formation of the Me–TFA product and Rh<sup>I</sup>(bisq<sup>x</sup>)(TFA)(TFAH), which is reoxidized to the starting complex Rh<sup>III</sup>(bisq<sup>x</sup>)(TFA)<sub>3</sub>. For the III-II pathway,  $S_R^2$  attack by OVCl<sub>3</sub> results in the formation of Me–OVCl<sub>3</sub> and Rh<sup>II</sup>(bisq<sup>x</sup>)(TFA)(TFAH), which are also reoxidized to the starting complex Rh<sup>III</sup>(bisq<sup>x</sup>)(TFA)<sub>3</sub> as well as the product Me–TFA and regenerated OVCl<sub>3</sub>. Either way, the final relative energy of the Rh<sup>III</sup>(bisq<sup>x</sup>)(TFA)<sub>3</sub> complex is –13.7 kcal/mol at 298 K, which represents a completed cycle of the overall reaction CH<sub>4</sub> + TFAH  $\rightarrow$  TFA–Me + 2H<sup>+</sup> + 2e<sup>-</sup>.

Finally, the I-III pathway was also investigated, starting from  $Rh^{I}(bisq^{x})(TFA)(TFAH)$  as an


Scheme 3.19. Comparison of the functionalization of  $Rh^{III}(bisq^x)(Me_{ax})(TFA)_2$ , the lowest Rh-Me species, via the III-I  $S_N 2$  and III-II  $S_R 2$  pathways; and the completion of the catalytic cycle. Only the lowest functionalization transition state is shown for each pathway.

alternative ground state. The results are shown in Scheme 3.20. Although the oxidative addition of methane by  $Rh^{I}(bisq^{x})$  species was feasible with minimum transition states of 27.9-30.6 depending on the particular ligand, the resulting  $Rh^{I}(bisq^{x})(H)(Me)(TFA)$  species are very uphill in energy. Deprotonation to form a  $Rh^{I}$ —Me species was prohibitively uphill both kinetically and thermodynamically. Along with the fact that  $Rh^{I}(bisq^{x})$  species would be less stable than their  $Rh^{III}(bisq^{x})$  analogues at reaction conditions, we did not pursue this route further.



Scheme 3.20. Catalytic cycle for the activation and functionalization of methane using  $Rh(bisq^x)$  complexes in TFAH, via the Rh(I-III) pathway. Blue denotes the resting state and red the most favored pathway. All free energies are in kcal/mol.

By plotting the activation and transition state energies of the various  $Rh^{III}(bisq^x)$  ligands, we can determine the particular ligand with the optimal activity. The results are shown in Figure 3.7, and show convincingly that at both 298 K and 498 K, whether using the III-I or III-II pathway, the base ligand  $Rh^{III}(bisq)$  is the best choice.

In comparing the relative merits of the III-I and III-II pathways, the energies of the two transition states at 298 K are very close, within 1 kcal/mol for each (bisq<sup>x</sup>) ligand (although, as mentioned before, (bisq<sup>F4</sup>) appears to be an outlier). However, the energies are expected to increase at 498 K, due to the increased entropy penalty of bringing an extra TFAH or OVCl<sub>3</sub> to the system. For the III-I S<sub>N</sub>2 pathway, this is a significant penalty of 6.0-6.2 kcal/mol, and may be enough to render functionalization inaccessible. However, for the III-II S<sub>R</sub>2 pathway the entropy penalty is much less at 1.7-2.0 kcal/mol, and both the base (bisq) and fluorinated (bisq<sup>F2</sup>) and (bisq<sup>F4</sup>) have barriers at

**Figure 3.7.** Top: graph of the activation and III-I functionalization transition state energies of the various  $Rh(bisq^x)$  complexes. The best choice at both 298 K and 498 K is the base Rh(bisq) complex. This complex has a maximum barrier of 33.4 kcal/mol at 298 K and 37.8 kcal/mol at 498 K. The rate-determining step is activation at 298 K and functionalization at 498 K. Bottom: graph of the activation and III-II functionalization transition state energies of the various  $Rh(bisq^x)$  complexes. Again, the best choice at both 298 K and 498 K is the base Rh(bisq) complex. This complex has a maximum barrier of 33.4 kcal/mol at 298 K and 498 K. Bottom: graph of the activation and III-II functionalization transition state energies of the various  $Rh(bisq^x)$  complexes. Again, the best choice at both 298 K and 498 K is the base Rh(bisq) complex. This complex has a maximum barrier of 33.4 kcal/mol at 298 K and 35.8 kcal/mol at 498 K. The rate-determining step is methane activation at both temperature points. Both: Blue diamond markers and lines denote transition state energies at 298 K, and red square markers and lines at 498 K. Outline marker shapes denote activation transition states and filled marker shapes denote functionalization transition states. The overall barrier for each particular complex is the greater of the activation and functionalization barriers.



35.3 kcal/mol or below. Thus it appears that the III-II  $S_R 2$  pathway is the best choice for methyl functionalization.

Hence, we conclude that the base Rh(bisq) rhodium-ligand complex is the best choice among the entire Rh(bisq<sup>x</sup>) family, with an overall reaction barrier of 33.4 kcal/mol at 298 K and 35.8 kcal/mol at 498 K, when the III-II  $S_B^2$  functionalization pathway is used.

#### 3.4.8 Product protection and C–H activation

As mentioned in the introduction, a major hurdle that any putative methane to methanol catalytic scheme must overcome arises because the C–H bond dissociation energy of methanol is 9 kcal/mol weaker than that of methane. Preventing the overoxidation of the product is thus a challenge and is the reason we elected to investigate electrophilic metal centers in acidic solvent. Since the transition state of an electrophilic activation involves donation of electron density from the methane C–H  $\sigma$  bond to the metal, a highly electron-withdrawing trifluoroacetate substituent that decreases this  $\sigma$  bond electron density is expected to increase the transition state energy. Thus the highly electronegative trifluoroacetate group of methyl trifluoroacetate withdraws electron density from the methyl C–H bonds, thereby decreasing their ability to donate into the rhodium center and raising activation barriers.

Indeed, we see this effect in explicit calculations with both the (NN) and (NN<sup>F</sup>) ligand sets. Figures 3.8 and 3.9 show the various isomeric transition states for the activation of both methane and methyl trifluoroacetate in TFAH. At 298 K, each transition state for the activation of methane was 3 to 10 kcal/mol lower than the corresponding transition state for the activation of methyl trifluoroacetate (1 atm reference for both). The first two rows of Figure 3.10 show only the lowest energy isomer of each activation, and thus an overall  $\Delta G^{\ddagger}$  (lowest Me–TFA transition state minus lowest CH<sub>4</sub> transition state) of 2.7 kcal/mol is found for (NN) and 5.5 kcal/mol for (NN<sup>F</sup>). The numbers significantly improve to 6.4 and 9.8 kcal/mol at 498 K. This is due to the volatility of Me–TFA, which greatly raises its free energy at 498 K.

In contrast, activation of methanol (1 M reference state) by Rh(NN<sup>F</sup>), shown in Figure 3.11 and summarized in the third row of Figure 3.10, was even lower than that of methane: by 0.3 or 1.8 kcal/mol at 298 K when comparing the lowest CH<sub>3</sub>OH transition state and the lowest CH<sub>4</sub> transition state in TFAH (Figure 3.10, first and second rows); for (NN<sup>F</sup>) in water this gap is larger at 2 to 3 kcal/mol (Figure 3.10, third row). We can explain this by noting that the hydroxyl group in methanol has electron donating properties and hence the donation effect of the C–H  $\sigma$  orbital into the electrophilic metal center is increased, leading to a decreased transition state barrier; however these numbers are lower than the 9 kcal/mol simple BDE difference between the C–H bonds in methanol and comparable to work done by Owen et al. [23].

Product protection studies were also carried out for the Rh(DPMS) and Rh(DPES) complexes,

Figure 3.8. Transition states for the functionalization of methane, Me–TFA, and methanol using Rh(NN) complexes in TFAH. All free energies are in kcal/mol and relative to the lowest energy inorganic state (i.e. right before methane activation).



Figure 3.9. Transition states for the functionalization of methane, Me–TFA, and methanol using  $Rh(NN^F)$  complexes in TFAH. All free energies are in kcal/mol and relative to the lowest energy inorganic state (i.e. right before methane activation).



Figure 3.10. Summary of the data presented in Figures 3.8, 3.9, and 3.11. In each row, the leftmost structure is the lowest-energy activation transition state for methane (1 atm); the center structure is the lowest-energy transition of MeTFA (1 atm, not applicable for the  $H_2O$  case); and the rightmost structure is the lowest-energy transition state for the activation of MeOH (1 atm). All free energies are in kcal/mol and relative to the lowest energy inorganic state (i.e. right before methane activation).



Figure 3.11. Comparison of activation energies for methane (1 atm) and for methanol (1 M at 298 K, 1 atm at 498 K) in the same structure for  $Rh(NN^F)$  complexes in water. In this case, methanol was easier to activate by 2 to 3 kcal/mol. All free energies are in kcal/mol and relative to the lowest energy inorganic state (i.e. right before methane activation).

(NN<sup>F</sup>) ligand in water (neutral species)





the results of which are shown in Figures 3.12 and 3.13, respectively. Modest product protection  $\Delta\Delta G^{\ddagger}$ 's of 1.4 kcal/mol and 2.2 kcal/mol at 298 K were found, but these improve to 5.3 kcal/mol and 6.6 kcal/mol at 498 K.

Figure 3.12. Comparison of the activation states of methane and methyl trifluoroacetate by Rh(DPMS) complexes, showing the product protection afforded. Red denotes the most favored isomer of each type of activation. All free energies are in kcal/mol and relative to the resting state.



Finally, product protection studies were carried out for the  $Rh(bisq^x)$  family of rhodium-ligand complexes. The results are summarized in Figure 3.14. In general the product protection is comparable to the  $Rh(NN^x)$  family at 298 K, but improves significantly by 3.8-4.2 kcal/mol at 498 K. As in the other cases, this is due to the high volatility of Me–TFA.

Since the ease of activation decreases  $CH_3OH > CH_4 > Me-TFA$ , it is important to consider the relative chemical potential of  $CH_3OH$  and Me-TFA in solution. As we have found that the equilibrium  $Me-TFA(g) + H_2O(solv) \Longrightarrow CH_3OH(g) + TFAH(\ell)$  is exergonic by 1.3 kcal/mol at 298 K, it is predicted that these catalysts would be selective for methane oxidation only in the absence of water.

In comparison with previous work, we note that Periana et al. [24] showed that the reason why the Catalytica-Periana bipyrimidine Pt catalyst [25] was able to achieve high selectivity is that the barrier to activate the Me $-OSO_3H$  product is 14 kcal/mol higher than for  $CH_4$  or  $CH_3OH$  and the acidity of the medium drives the protection of methyl products *via* esterification. Although

Figure 3.13. Comparison of the activation states of methane and methyl trifluoroacetate by Rh(DPES) complexes, showing the product protection afforded. Red denotes the most favored isomer of each type of activation. All free energies are in kcal/mol and relative to the resting state.



Figure 3.14. Comparison of the activation states of methane and methyl trifluoroacetate by the Rh(bisq<sup>x</sup>) family of complexes, showing the product protection afforded. Red denotes the most favored isomer of each type of activation. The overall product protection  $\Delta\Delta G^{\ddagger}$  energies are shown in blue. All free energies are in kcal/mol and relative to the resting state.



the Catalytica-Periana system distinguishes between methane and the methyl ester more than the rhodium complexes, we note that a key advantage to our system is the volatility of  $CH_3OH$  and Me-TFA (boiling points at 64.7°C and 43°C, respectively) relative to the nonvolatile  $Me-OSO_3H$ . Increasing selectivity beyond what is provided by the electrophilicity of the metal and esterification is still an important area of research. The addition of nonpolar ligand side-chains may decrease the propensity of methanol coordination to the metal relative to methane coordination.

# 3.5 Discussion

Since our ligands have poor electron-donating ability and  $Rh^{III}$ -centered cycles, we expect the metal center to be electrophilic with reactions proceeding along an electrophilic route [3]h. We can rule out oxidative addition due to the nature of our ligands and the general instability of  $Rh^{V}$  species; hence we expected that the most likely C–H activation pathway is through a base-mediated electrophilic mechanism (Scheme 3.21).



Scheme 3.21. A schematic diagram showing the metal activation of an R-H bond, for example, methane. Activation occurs *via* ligand donation to the electrophilic metal center (a) and basic abstraction of the hydrogen (b).

Because we propose an electrophilic pathway for the methane activation step [3]h, we expect there to be a relationship between the activation transition state energy and some aspect of the metal's electropositivity. To find this relationship, we examined more deeply the calculated constituent energies of rhodium complexes with the  $(NN^x)$ ,  $(ONN^x)$ ,  $(DP\frac{M}{E}S)$ , and (PN) ligands and ligand families. We did not include the  $L_3$  (bisq<sup>x</sup>) family because they require protonation before methane activation can take place; as a result a direct comparison of these ligands with the neutral transition states of our other ligands is not possible.

To estimate the electropositivity, we initially used the calculated energy of the rhodium 4s core orbital in the Rh<sup>III</sup> resting state, which we compared to the corresponding methane activation energies (Figure 3.15). We found that there is approximately a positive correlation between increasing electropositivity (as measured by negative numbers closer to zero) and increase overall transition state barriers. We explain this by noting that decreasing the metal's electropositivity increases its electrophilicity and thus encourages  $\sigma$  donation of the Me–H bond.

Figure 3.15. Graph of the methane activation energy of the various rhodium complexes vs. the 4s orbital energy of the rhodium in their resting states, based on data from Table 3.3. This calculated value is a proxy for the relative overall electropositivity of the specific rhodium-ligand complexes. In all cases the lowest transition state was used; this involves an axial Rh–Me being formed in the cases of the (NN<sup>x</sup>) and (ONN<sup>x</sup>) ligand families, and an equatorial Rh–Me being formed in the (DP $\frac{M}{M}$ S) and (PN) cases.



In the hopes that a more directional aspect of a given rhodium-ligand's electron density might give us a better correlation with the transition state barrier, we then plotted the methane activation energies with the energies of the Rh–C bond in the resultant Rh<sup>III</sup>–Me intermediate (Figure 3.16). These Rh–C bond energies were obtained by performing a Pipek-Mezey orbital localization procedure on the Rh<sup>III</sup>–Me complex's electronic wavefunction [13]. We found that the correlation is much better, with increasingly negative Rh-C bond energies being correlated with decreasing transition state barriers. This may be due to the increasing favorability of forming the rhodium-methyl bond. We give the caveat that again the only outlier is the Rh(NN) ligand complex, but we note that our trend represents only an overestimation, and therefore does not include false positives. In addition, there is a definite positive correlation within a ligand family (i.e. Rh(NN) vs. Rh(NN<sup>F</sup>); Rh(ONN<sup>F</sup>) vs. Rh(ONN) vs. Rh(ONN<sup>NMe2</sup>)). We conclude from this relationship that (a) given a rhodium-ligand complex that already shows some promise, we can further fine-tune its properties with additional modifications on the ligand to further lower the transition state barriers of interest; and (b) given a new rhodium-ligand complex, by calculating the Rh<sup>III</sup>–Me intermediates and extracting the Rh–C bond energy, we can get an estimate of the expected methane activation transition state barrier for that ligand set and thus gauge its worthiness for further investigation.

Ligand	$TS^a$	$\Delta G^b_{\text{precursor}}$	Precursor <sup>c</sup>	-		
(NN)	32.6	1.3	$[{\rm Rh}^{\rm III}({\rm NN})({\rm TFA})_4]^{2-}({\rm H}^+_{\rm ax})({\rm H}^+_{\rm eq})$	-		
$(NN^F)$	27.6	2.2	$[{ m Rh}^{ m III}({ m NN}^{ m F})({ m TFA})_4]^{2-}({ m H}^+_{ m ax})({ m H}^+_{ m eq})^j$			
(ONN)	37.2	3.9	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{ONN})(\mathrm{TFA})_3]^-(\mathrm{H}^+_{\mathrm{ax}})$			
$(ONN^F)$	35.8	$4.0^{k}$	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{ONN}^{\mathrm{F}})(\mathrm{TFA})_{3}]^{-}(\mathrm{H}^{+}_{\mathrm{ax}})^{l}$			
$(ONN^{NMe_2})$	38.7	3.7	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{ONN}^{\mathrm{NMe}_2})(\mathrm{TFA})_3]^-(\mathrm{H}^+_{\mathrm{ax}})$			
(DPMS)	33.9	0.0	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{DPMS})(\mathrm{TFA})_3]^-(\mathrm{H}^+_{\mathrm{eq}})$			
(DPES)	35.6	0.0	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{DPES})(\mathrm{TFA})_{3}]^{-}(\mathrm{H}_{\mathrm{eq}}^{+})$			
(PN)	35.0	$N/A^m$	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{PN})(\mathrm{TFA})_3]^-(\mathrm{H}^+_\mathrm{N})^{\hat{l}}$			
Ligand	Adj. $TS^d$	Rh–C $\sigma^e$	$\mathrm{Rh}\mathrm{-Me}^{f}$	Rh $-$ TFA $4s^g$	Rh–Me $4s^h$	$\Delta 4s^i$
(NN)	31.3	-0.38096	$[{\rm Rh}^{\rm III}({\rm NN})({\rm Me}_{\rm ax})({\rm TFA})_3]^{2-}({\rm H}^+_{\rm ax})({\rm H}^+_{\rm eq})$	-3.1858	-3.13265	0.05315
$(NN^F)$	25.4	-0.39557	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{NN}^{\mathrm{F}})(\mathrm{Me}_{\mathrm{ax}})(\mathrm{TFA})_{3}]^{2-}(\mathrm{H}_{\mathrm{ax}}^{+})(\mathrm{H}_{\mathrm{eq}}^{+})^{j}$	-3.21571	-3.15195	0.06376
(ONN)	33.3	-0.37870	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{ONN})(\mathrm{Me}_{\mathrm{ax}})(\mathrm{TFA})_2]^-(\mathrm{H}^+_{\mathrm{ax}})$	-3.19023	-3.13949	0.05074
$(ONN^{F})$	31.8	-0.38498	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{ONN}^{\mathrm{F}})(\mathrm{Me}_{\mathrm{ax}})(\mathrm{TFA})_{2}]^{-}(\mathrm{H}_{\mathrm{ax}}^{+})$	-3.19724	-3.14661	0.05063
$(ONN^{NMe_2})$	35.0	-0.37739	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{ONN}^{\mathrm{NMe}_2})(\mathrm{Me}_{\mathrm{ax}})(\mathrm{TFA})_2]^-(\mathrm{H}^+_{\mathrm{ax}})$	-3.18448	-3.13750	0.04698
(DPMS)	33.9	-0.38700	$[\mathrm{Rh}^{\mathrm{III}}(\mathrm{DPMS})(\mathrm{Me}_{\mathrm{eq}})(\mathrm{TFA})_2]^{-}(\mathrm{H}_{\mathrm{eq}}^{+})$	-3.20873	-3.15703	0.05170
(DPES)	1		$(\mathbf{p}, \mathbf{H})$ ( $\mathbf{p}, \mathbf{p}, \mathbf{p}, \mathbf{q}$ ) ( $\mathbf{p}, \mathbf{r}$ ) ( $\mathbf{p}, \mathbf{r}$ ) ( $\mathbf{p}, \mathbf{r}$ ) ( $\mathbf{r}, \mathbf{r}$ )	0.00000		0.04505
(D1 L5)	35.6	-0.38539	$[Rh^{m}(DPES)(Me_{eq})(TFA)_{2}]$ $(H_{eq})$	-3.20332	-3.15567	0.04765

Table 3.3. Comparison of the various Rh parameters with the rhodium-ligands complexes' associated transition state barriers. These numbers are plotted in Figures 3.15, 3.16, and 3.17. An "ax" subscript indicates that the moiety is axial with respect to the rhodium-ligand plane; An "eq" subscript indicates that the moiety is equatorial with respect to the rhodium-ligand plane. For  $(DP\frac{M}{E}S)$  the rhodium-ligand plane is defined as the plane spanned by the N-Rh-N moiety. For (PN) complexes, An "N" subscript indicates that the moiety is equatorial with respect to the P-Rh-N plane and trans to the N; A "P" subscript indicates that the moiety is equatorial with respect to the P-Rh-N plane and *trans* to the P. (a) The overall transition state barrier, as reproduced from Table 3.2, in kcal/mol. (b) The free energy of the immediate precursor before the lowest methane activation barrier, in kcal/mol. This typically differs from the resting state only in the geometric placement of TFAH and TFA ligands. (c) The identity of the immediate precursor. (d) The "adjusted" TS barrier, i.e. the free energy change of the actual transition state itself, in kcal/mol. Equal to the overall  $TS - G_{precursor}$ . (e) The energy of the Pipek-Mezey localized Rh-C bond of the Rh<sup>III</sup>-Me species formed as a result of the lowest transition state, in hartrees. (f) The identity of the Rh<sup>III</sup>-Me species formed as a result of the lowest transition state. (g) The 4s orbital energy of the Rh atom in the resting state, in hartrees. (h) The 4s orbital energy of the Rh atom in the Rh<sup>III</sup>–Me species in column f, in hartrees. (i) The change in Rh 4s energies, equal to the difference between the preceding two columns, in hartrees. (j) These species are the lowest neutral species, done for the sake of consistency with the other ligands. The anionic resting states are very similar in energy. (k) An estimated value based on the  $G_{\text{precursor}}$  values of related species Rh(ONN) and Rh(ONN<sup>NMe<sub>2</sub></sup>). (l) Stable conformations of these complexes could not be found due to the ease of isomerization of the TFAH/TFA ligands into axial/equatorial positions. (m) The value is unknown and an estimation was not attempted.

Figure 3.16. Graph of the methane activation energy of the various rhodium complexes vs. the Rh–C bond energy as localized by the Pipek-Mezey method [13] of the lowest-energy Rh–Me complex. This calculated value is a proxy for the relative directional electropositivity of the specific rhodium-ligand complexes towards the methyl bond being formed. Based on data from Table 3.3. In all cases the lowest transition state was used; this involves an axial Rh–Me being formed in the cases of the (NN<sup>x</sup>) and (ONN<sup>x</sup>) ligand families, and an equatorial Rh–Me being formed in the (DP $\frac{M}{E}S$ ) and (PN) cases.



We also wished to see if there was a correlation between the transition state barrier and the rhodium center's hardness as modified by its ligand. Since the hardness of an atom or molecule is defined as the polarizability of its electron cloud [26], we measured the difference in the Rh 4s orbital energy going from the inorganic resting state to the Rh<sup>III</sup>–Me as a proxy for hardness. Although we did not find a correlation with the overall transition state barrier of activation, we did find a negative correlation with the "adjusted" TS barrier, i.e. the free energy change of the actual transition state itself (Figure 3.17). In other words, the activation transition state  $[Rh\cdots CH_4]^{\ddagger}$  is derived from the replacement of a TFAH ligand with  $CH_4$ , but the immediate Rh–TFAH precursor is not the resting state, but differs slightly in its axial/equatorial arrangement of TFAH/TFA ligands and is a few kcal/mol higher in energy. Taking this out gives us our correlation. Hence, we see that increased polarizability or softness, as measured by the amount of energy increase in the rhodium-ligand system when a TFA ligand is exchanged for a methyl, correlates with a lower activation barrier.

The result of our fine tuning has yielded, among those rhodium-ligand complexes with neutral activation transition states, the  $(NN^F)$  ligand set. With a methane activation energy of 27.6 kcal/mol at 298 K, it compares favorably with other homogeneous systems. Indeed, an effective activation barrier of 33.5 kcal/mol is derived from the turnover frequency of the Catalytica-Periana catalyst  $(bpym)PtCl_2$  in  $H_2SO_4$  [27]. Specifically, C–H activation by  $(\eta^3$ -6-phenyl-2,2'-bipyridine)Ir<sup>III</sup>(TFA)- $(C_2H_4)(C_2H_5)$  is shown to catalyze H/D exchange between CH<sub>4</sub> and TFAD with a turnover frequency

Figure 3.17. A graph of the Rh–TFA to Rh–Me change in the 4s orbital energy, a measure of the Rh atom's softness, versus the adjusted TS barrier (see text). Note that the  $(\text{ONN}^{\text{F}})$  data point is an estimated value, which may explain its deviation from the monotonicity (see Table 3.3). In all cases the lowest transition state was used; this involves an axial Rh–Me being formed in the cases of the  $(\text{NN}^x)$  and  $(\text{ONN}^x)$  ligand families, and an equatorial Rh–Me being formed in the  $(\text{DP}\frac{\text{M}}{\text{E}}\text{S})$  and (PN) cases. This graph is based on data from Table 3.3.



of  $2.12 \times 10^{-2} \text{ s}^{-1}$  at 180°C (Scheme 3.18). From the turnover frequency a free energy barrier of 33.5 kcal/mol can be calculated using transition state theory [28].

In the course of these studies we found that it was more difficult to find effective routes of Rh-methyl functionalization than to find low methane activation barriers. We found that the III-II pathway ( $S_R 2$  attack with OVCl<sub>3</sub>) typically gives the lowest barriers, whereas the III-I and III-IV-II pathway ( $S_N 2$  attack on Rh<sup>III</sup> or Rh<sup>IV</sup>, respectively) have some use as well; the I-III pathway (oxidative addition of methane by Rh<sup>I</sup>) was much less likely.

We found that  $Rh(NN^F)$  complexes in water lead to a flatter thermodynamic profile than in TFAH, increased transition state energies for methane activation, and decreased transition state energies for functionalization. We can understand these changes in the thermodynamics by noting that hydroxo ligands' lone pairs stabilize higher oxidation states of rhodium. Overall these changes are favorable for activity, since the functionalization energy is lowered to 31.7 kcal/mol while the methane activation energy of 35.0 kcal/mol remains acceptable. Unfortunately, an aqueous solution is predicted to offer no product protection, a result consistent with the reactivity of platinum diimine catalysts [23].

We can understand the decreased barrier for  $S_N 2$  methane functionalization (III-I, III-IV-II) in terms of several factors: the increased stability of the  $Rh^{IV}$  starting material in water, the greater thermodynamic activity of water in aqueous solution (at 55 M) as opposed to the TFA anion in





TFAH, and the fact that the transition state involves a concerted reaction featuring simultaneous formation of a C–O bond, deprotonation to form neutral methanol, and protonation of a hydroxo ligand on the Rh complex. However, we remain unclear about the reason behind the decreased  $S_R^2$  functionalization barrier for III-II. We speculate that, since some transition states for  $S_N^2$  attack by  $OVCl_3$  (to form Me– $OVCl_3^-$ ) were found and appear to be about 10 kcal/mol higher than their  $S_R^2$  equivalents, there may be nucleophilic character on the oxygen atom in  $OVCl_3 S_R^2$  attack as well.

The most important hurdle that must be cleared experimentally in order for us to have a viable catalytic system is catalyst stability. The trend we have observed, that Rh<sup>III</sup> complexes with less electron-donating ligands tend to have lower activation and functionalization barriers, must be balanced with the consideration that a ligand that is too electron-poor may not have sufficient binding strength for a stable complex with rhodium to be made. The next logical step of our investigation is the experimental synthesis and stability study of the Rh<sup>III</sup>(NN<sup>F</sup>) and Rh<sup>III</sup>(bisq) complexes. However, even if we fail to see good robustness for this particular complex, our more valuable contribution is that we have undertaken the most detailed *ab initio* study of the requirements of a Rh methane activation catalyst to date.

#### 3.6 Conclusions

In our QM virtual screening of potential methane to methanol catalysts, we identified the  $Rh(NN^F)$  and Rh(bisq) complexes as highly promising candidates. Features of the  $Rh(NN^F)$  complex include:

- Transition state barriers for methane activation at 298 K of 27.6 (TFAH) and 35.0 kcal/mol (water), and
- Transition state barriers for functionalization at 298 K of 36.8 (TFAH) or 31.7 kcal/mol (water),

and features of the Rh(bisq) complex include:

- Transition state barriers for methane activation at 298 K of 33.4 (TFAH), and
- Transition state barriers for functionalization at 298 K of 32.0 (TFAH).

These results are better than any other Rh<sup>III</sup> complex we have so far investigated.

Moreover, we provide a rational accounting for the role that ligand design plays in the effectiveness of this promising catalyst. In particular for Rh<sup>III</sup> complexes with neutral methane activation transition states, increased electron-withdrawing ligands leads to lower barriers for both activation and functionalization. We can estimate the overall transition state barrier by simply calculating the Rh<sup>III</sup>-Me species and extracting the Rh-C bond energies. Thus, the only condition opposing even less donating ligands (i.e. lower barriers) is catalyst stability. For the Rh<sup>III</sup>(bisq<sup>x</sup>) family of complexes, requiring one coordination site to be a weak  $\eta^2$ -benzene interaction greatly facilitates functionalization on a methyl group *trans* to it. These results from QM virtual screening are now ready for experimental testing, validation, and improvement. It can also be anticipated that future design of addition ligands may incorporate both concepts, with a weak interaction as well as an anionic or bidentate ligand, so that both activation barriers can be easily prediction and functionalization barriers minimized.

# 3.7 Acknowledgments

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# Chapter 4

# The Reduction-Coupled Oxo Activation mechanistic motif for C–H bond activation and oxidation

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Also includes original work.

#### 4.1 Abstract

The vanadium phosphorus oxide (VPO) catalyst is used commercially for the selective oxidation of n-butane to maleic anhydride. Surprisingly, the mechanism has been shown to initiate with C–H activation by a P=O moiety. In this chapter, we call this phenomenon the *Reduction-Coupled Oxo* Activation (ROA) mechanistic motif, and attribute it to the concomitant formation of a strong oxo-hydrogen bond on the phosphorus atom and a one-electron reduction on the vanadium atom. In addition, we show that the same ROA phenomenon can be extended beyond phosphorus and vanadium to additional main-group elements and transition metals, respectively, and may lead to a new strategy in designing selective catalysts for alkane activation. Finally, we propose the existence of a homogeneous vanadium phosphorus oxo complex that can incorporate the novel ROA mechanistic pathway as a potential propane oxidation catalyst. We considered several oxidation pathways leading to end products such as propylene, isopropanol, and propylene oxide. We support our assertions with density functional theory calculations on potential reaction pathways.

#### 4.2 Introduction

#### 4.2.1 The VPO catalyst for *n*-butane oxidation

Vanadium phosphorus oxide (VPO) is an inorganic complex that catalyzes the oxidation of nbutane to maleic anhydride with a surprisingly high selectivity of 60-70% [1] (Scheme 4.1). Although the overall yield is only *ca.* 50%, its ease of synthesis, use of common elements, and selectivity have allowed this catalyst to be commercialized, producing *ca.* 500 kilotons of maleic anhydride annually [2]. Hence, there was a strong impetus to investigate the mechanism of this reaction in the hopes of rationally designing a modified catalyst with improved yield.

Scheme 4.1. The oxidation of *n*-butane to maleic anhydride using vanadium phosphorus oxide as a catalyst.

A useful parameter for the C–H activating ability of each oxo moiety in the catalyst is the H-atom affinity  $D_{\rm H}$ , which is defined as the enthalpy change when the O–H bond in ·M–O–H is homolytically cleaved to form the M=O oxo. Mechanistic work initially centered on vanadyl pyrophosphate ((V<sup>IV</sup>O)<sub>2</sub>(P<sub>2</sub>O<sub>7</sub>), abbreviated VOPO), the major component of VPO [3]. However, it was quickly found that no vanadium oxo on the VOPO surface has sufficient H-atom affinity to activate *n*-butane (Figure 4.1). The most active V=O in VOPO has a  $D_{\rm H}$  value of 58.2 kcal/mol, whereas the weakest C–H bond in *n*-butane has a dissociation energy of 89.3 kcal/mol, implying an extremely endothermic first step that is categorically inconsistent with the experimentally determined activation energy of 12.9-23.6 kcal/mol [4]. Hence, it was concluded that the reduced vanadyl pyrophosphate (V<sup>IV</sup>O)<sub>2</sub>(P<sub>2</sub>O<sub>7</sub>) alone is unable to initiate the catalytic process.

**Figure 4.1.** O–H bond strength for oxygen atoms on the  $(V^{IV}O)_2(P_2O_7)$  surface. The energy released when an H  $\cdot$  is bound to the V=O (in red) is only 58.2 kcal/mol, not nearly high enough for alkane activation to occur. The energy released when an H  $\cdot$  is bound to the bridging V–O–P oxide (in green) is even lower, at 17.0 kcal/mol. The energy released when an H  $\cdot$  is bound to the P=O was not determined because geometry optimization caused it to be transferred to the V–O–P moiety (in green).



It was then supposed that catalysis requires the presence of adsorbed  $O_2$  on the  $V^{IV}O(P_2O_7)$ 

surface. Adsorption of  $O_2$  may be molecular, in which the O–O bond is retained, two V<sup>IV</sup> centers are oxidized to V<sup>V</sup>, and a vanadium peroxo moiety is formed; or it may be dissociative, in which the O–O bond is broken and four V<sup>IV</sup> centers are oxidized to V<sup>V</sup>. The first case is uphill by 2.8 kcal/mol, whereas the second is downhill by 38.8 kcal/mol. Unfortunately, the  $D_{\rm H}$  values calculated for the resulting vanadium peroxo and vanadium oxo moieties were only 70.0 and 58.9 kcal/mol, respectively. Hence, it was concluded that the reduced VPO complex is not the active catalyst.

**Figure 4.2.** Oxygen adsorption energies on the  $(V^{IV}O)_2(P_2O_7)$  surface and the O–H bond strength  $(D_H)$  to each of these O atoms. Left: molecular  $O_2$  adsorption in which the O–O bond is preserved. Right: dissociative adsorption in which the O–O bond is broken. All energies are in kcal/mol.



Finally, it was proposed that catalysis takes place on a metastable  $V^{V}OPO_{4}$  surface, known as the X1 phase, which has been experimentally determined to be produced in the high oxygen environment of the reaction conditions [5]. However, the largest  $D_{\rm H}$  value found for a vanadium oxo in this phase is only 62.8 kcal/mol (Figure 4.3). Surprisingly though, it was discovered that the phosphorus oxo had a much larger  $D_{\rm H}$  value of 84.3 kcal/mol! This implies a first step that is endothermic by only 5.0 kcal/mol, with an activation energy later calculated to be 13.6 kcal/mol, which is within the experimental range. The stability of the resulting monohydrogenated species was attributed to the fact that spin density appears to be localized on the neighboring vanadium atoms (Figure 4.4).

#### 4.2.2 The ROA mechanistic motif

The surprising discovery of the C-H activation ability of  $P^V = O$  moieties in the  $V^V OPO_4$  catalyst led to the creation a new term, *Reduction-Coupled Oxo Activation* (ROA), to describe this phenomenon. Its usefulness is due to the observation that the basicity of simple transition metal oxos increases with decreasing electron affinity of the metal, due to increasing electron density; whereas for C-H activation it is preferred that both basicity and electron affinity are maximized, since H-atom transfer

**Figure 4.3.** O–H bond strengths for the various oxygen atoms on the  $X1-V^VOPO_4$  surface. The O–H bond strength of 84.3 kcal/mol to the P=O moiety leads to a first step that is endothermic by only 5.0 kcal/mol, with an activation energy later calculated to be 13.6 kcal/mol. Hence, the P=O moiety is the only candidate site whose C–H activation energy is compatible with experimental data.



Figure 4.4. C–H activation by a phosphorus oxo leads to a one electron reduction on the neighboring vanadium. Hence the oxidation state of the phosphorus atom does not change. (a) Vanadium-phosphate archetype: conceptual arrow-pushing scheme for P–V electron transfer with an intervening  $\mu$ -oxo. (b) Vanadium- $\kappa$ –Pphosphinite archetype: conceptual arrow-pushing scheme for P–V electron transfer in which they are directly bound to each other.



involves both proton and electron transfer. The ROA mechanistic motif, by keeping the sites of basicity and reduction on separate moieties, is able to decouple this process and hence allow the best of both worlds with high basicity and high electron affinity [6].

The validity of the ROA mechanistic motif was tested using quantum mechanical calculations on small  $X_4O_{10}$  clusters, where each X is a P or V. The results, shown in Figure 4.5, indicate that a single linkage to V makes the P=O bond 32.3 kcal/mol more active, while coupling to a second V makes it an additional 23.8 kcal/mol more active and coupling to a third V (as in VPO) makes it an additional 4.9 kcal/mol more active. Compared to a pure vanadium (V) oxide case, coupling to one or two P atoms makes it 13.4 and 8.5 kcal/mol more active, respectively.

Figure 4.5. Use of finite cluster models to investigate how the O–H bond strength of P=O moieties varies based on the number of V coupled to it *via* O linkages. Data is summarized from Figure 4.8. All numbers are in kcal/mol.

O <sub>1</sub>	O <sub>1</sub> H			
P	P		Species	$D_{\rm PO(1)-H}$
o   →		a.	$\mathrm{P_4O_{10}}$	28.2
$0 = \frac{x_{3}}{x_{1}} = 0$	$\hat{\mathbf{X}}_{3} = 0  \hat{\mathbf{X}}_{1} = 0$	b.	$\mathrm{P}_{3}\mathrm{VO}_{10}$	60.5
0 / 2 0	0 /2 0	c.	$\mathrm{P}_{2}\mathrm{V}_{2}\mathrm{O}_{10}$	84.3
0 a. X <sub>1</sub> =X <sub>2</sub> =X <sub>3</sub> =	U X <sub>3</sub> =P	d.	$\mathrm{PV}_3\mathrm{O}_{10}$	89.2
b. X <sub>1</sub> =V, X <sub>2</sub> =X	X <sub>3</sub> =P Ka=P	e.	$\mathrm{V_4O_{10}}$	75.8
d $X_1 = X_2 = X_3 = 1$	V			

The data presented in Figure 4.5 shows the validity of the small cluster approach in gauging the activity of the ROA mechanism. In hopes of expanding the chemical space in which this ROA mechanism is available, we have undertaken an investigation of mixed oxos with vanadium and the heavier group 15 (pnictogen) and 16 (chalcogen) elements in the first part of this chapter. (We do not consider group 14 or 17 elements due to the instability of terminal oxos for such elements, against hydration in the group 14 case and explosion in the group 17 case.) For each of these complexes, we have calculated  $D_{\rm H}$ , the oxo-hydrogen bond energy. We use  $D_{\rm H}$  as a proxy for hydrogen-abstraction potential, which is typically the most difficult step in alkane oxidation/functionalization catalysis. We have found that the ROA mechanism is general to group 15 and 16 (pnictogen and chalcogen) vanadium mixed oxos, with phosphorus, selenium, and tellurium being the most active. We have also taken these most active cases, with molybdenum (VI) substituted for vanadium (V), and found similarly promising results. We hence conclude that the reduction-coupled oxo activation mechanistic motif is a viable and interesting new lead for the development of new oxidation catalysts.

#### 4.2.3 Potential homogeneous catalysts utilizing the ROA principle

Although the ROA phenomenon was originally discovered in the VPO system, a heterogeneous catalyst, the principle should hold for homogeneous catalysts as well. Homogeneous catalysts have the advantages of being well-defined, easier to study, and thus more readily able to contribute to basic scientific research. However, homogeneous complexes containing a P(O) - O - V(O) moiety (as shown in figure 4.4a) are very rare in the literature, owing to their difficulty in synthesis [7]. The only known examples are complexes produced by Herron et al. [8] and Cummins et al. [9], both of which were simply precursors to the production of VOPO or related network complexes; and the very recent work by Doyle et al. [7] that features the divanadium pyrophosphate complex  $\{[(V^{IV}O)bipy(H_2O)]_2(\mu - P_2O_7)\} \cdot 3H_2O, which exhibits some catalytic oxidative ability with benzyle and the statement of the stateme$ alcohol. Hence, potential catalysts incorporating an alternative metal core featuring a direct V–P bond (as in figure 4.4b) were explored. Complexes featuring such  $\kappa$ -P phosphinite coordination to metals including Co [10], Ni [11]a, Pd [11], and Pt [12]a have been described. In addition, many other complexes containing a phosphido ligand bonded to metals such as Co [10], Rh [12]b, Pd [12]bc, Ir [13], and Pt [12]abd have also been described. These phosphido complexes are a single monooxygenation step away from the corresponding phosphine oxide complexes, a transformation which is expected to be facile due to the large formation energy of phosphine-oxo bonds and which has in fact been reported for a few of the complexes [10, 12]a. However, since in all these complexes the metal center has been from the late row transition metals, they are not predicted to be effective alkane activation catalysts under the ROA mechanism due to their large number of d electrons.

In order to design a homogeneous oxidation catalyst that utilizes the ROA mechanistic motif, a natural choice for the metal center of a phosphine-oxide-type complex would once again be vanadium (V), due to its activity in the VPO catalyst and its status as an effect  $d^0$  one-electron acceptor. The existing metal  $\kappa$ -P phosphinite and phosphido complexes all feature shared traits such as a late transition metal in a low oxidation state and a phosphorus moiety incorporated as the center of a tricoordinate pincer ligand with flanking phosphines and aryl linkers. Such ligands, which were designed for late transition metals, would likely not form very stable complexes with an early transition metal such as vanadium. However, replacement of the ligand's side phosphines with harder oxygens would be expected to greatly improve stability. Hence, we propose the ligand bis(2-phenoxyl)phosphinite  $\kappa$ -P coordinated on vanadium, abbreviated (OPO)V, as our candidate catalyst, in analogy to the existing Pd complex [11] (Figure 4.6). The robustness of this complex is predicted based on factors such as the chelation effect, the stability of O-V bonds, and the rigidity of the ligand, which guards against insertion of small activating molecules into the V-P bond. We complete the first coordination sphere around V by noting that it prefers to be six-coordinate and to contain a strong vanadium oxo bond [8], and we fill in the last open coordination sites with aqua ligands.

Figure 4.6. Left: known complexes featuring a phosphinite ligand bound  $\kappa$ -P to a transition metal. Right: A proposed vanadium  $\kappa$ -P phosphinite complex (OPO)VOL<sub>2</sub>. In aqueous solution or when water is present in the system, L is H<sub>2</sub>O. Note that both *fac* and *mer* stereoisomers are possible.



We thus propose, in the second part of this chapter, that the hypothetical complex diaqua[bis(2-phenoxy)phosphinite- $\kappa$ -P]oxidovanadium (V) ((OPO)V<sup>V</sup>O(H<sub>2</sub>O)<sub>2</sub>) utilizes the reduction-coupled oxo activation (ROA) mechanistic motif as a catalyst for the oxidation of alkanes in air. In this proposition, we support our assertion with density functional theory (DFT) calculations of the various reaction paths starting from propane, our representative alkane. We describe the most plausible transition state barriers for the conversion of propane and dioxygen to oxidized products such as propylene and isopropanol. Through our theoretical findings we are confident that a realized molecule will hold catalytic ability in a manner heretofore unseen in homogeneous catalysis.

#### 4.3 Materials and methods

All quantum mechanical calculations were carried out using the Jaguar software version 7.9 developed by Schrödinger Inc. [14]. Geometry optimizations were carried out on initial guess structures, and vibrational frequencies were gathered to confirm the optimized geometries as intermediates or transition states and to construct a free energy profile. The temperature was set to be 298.15 K. Solvation energies were calculated in water using the PBF Poisson-Boltzmann implicit continuum solvation model [15] in Jaguar, with a dielectric constant of 80.37 [16] and a probe radius of 1.40 Å [17] for water. Two explicit solvating waters per aqua, hydroxo, or oxo ligand were added for more accurate solvation modeling.

For our proposed molecular catalysts, geometry optimization and vibrational data were calculated using the B3LYP density functional [18] with a smaller basis set, whereas single point gas-phase and solvated energies were calculated using the same functional and a larger basis set. Here the smaller basis set consists of a modified double- $\zeta$  Los Alamos basis set and pseudopotential (LACVP<sup>\*\*</sup>) [19] for transition metals, the uncontracted Los Alamos valence-only basis set and pseudopotential (LAV3P) [20] for heavy main-group elements (e.g., As, Se, Sb, Te, Bi), and the 6-31G<sup>\*\*</sup> basis set [21] for the other atoms; whereas the larger basis set consists of the triple- $\zeta$  Los Alamos basis set and pseudopotential (LACV3P<sup>\*\*</sup>++) for transition metals, the same LAV3P basis set and pseudopotential for heavy main-group elements, and the 6-311G<sup>\*\*</sup>++ basis set [21] for the other atoms. Proposed intermediates and transition states were found to have zero and one negative frequencies, confirming their status as local energy minima and saddle points, respectively.

The pH of the aqueous solution was set at 0 or 7; this corresponds to the free energy of a solvated proton being set as -270.28 or -279.80 kcal/mol, respectively [22].

The free energy for each molecular species in solution was calculated using the formula

$$G = E_{\text{gas}} + \Delta G_{\text{solv}} + \text{ZPE} + H_{\text{vib}} + 6kT - T[S_{\text{vib}} + \gamma(S_{\text{trans}} + S_{\text{rot}} - \alpha) + \beta]$$

where the last term (with  $\alpha = 14.3$  e.u.,  $\beta = 7.98$  e.u., and  $\gamma = 0.54$ ) is an empirical approximation for the change in the translational and rotational entropy of the molecule between the gas phase and the solution phase (due to the finite librational frequencies), derived from Wertz [23].

For gas phase molecules (H<sub>2</sub>, O<sub>2</sub>, propylene, propane, and for our purposes the isopropyl radical), we assumed that equilibration between the dissolved gas and the headspace occurs at a much faster timescale than the reactions in question; leading to  $\Delta G_{\text{gas}\to\text{solv}} = 0$ . Thus, the free energy of such gas molecules can be simply calculated using the formula

$$G = G_{\text{gas}} = E_{\text{gas}} + \text{ZPE} + H_{\text{tot}} - TS_{\text{tot}}.$$

For water, the Gibbs free energy was calculated using the formula

$$G_{\text{liquid}} = E_{\text{gas}} + \text{ZPE} + H_{\text{tot}} - TS_{\text{tot}} + \Delta G_{\text{gas} \rightarrow \text{liquid}}$$

where  $\Delta G_{\text{gas} \to \text{liquid}} = G_{\text{liquid}} - G_{\text{gas}}(1 \text{ atm})$  is the free energy of condensation to liquid from 1 atm gas. We can solve for this by noting that

$$\Delta G_{\text{gas} \to \text{liquid}} = \Delta G_{\text{expansion}} + G_{\text{gas} \to \text{solvation}},$$

where  $\Delta G_{\text{expansion}} = G_{\text{gas}}(P) - G_{\text{gas}}(1 \text{ atm})$  is the expansion of the gas from 1 atm to the vapor pressure P, and  $G_{\text{gas}\to\text{solvation}}$  is the condensation of gas at vapor pressure P to liquid. Since a liquid is by definition at equilibrium with its vapor pressure  $G_{\text{gas}\to\text{solvation}} = 0$ , and we thus have

$$\Delta G_{\text{gas}\to\text{liquid}} = G_{\text{gas}}(P) - G_{\text{gas}}(1 \text{ atm}) = RT \ln\left(\frac{P}{1 \text{ atm}}\right).$$

The vapor pressure of water at 298.15 K is 23.75 mmHg [24].

For a given species X and its monohydrogenated analogue  $XH \cdot$ , the  $D_H$  value is defined as

 $D_{\rm H} = H({\rm X}) + H({\rm H} \cdot) - H({\rm XH} \cdot)$ , and the  $G_{\rm H}$  value is defined analogously.

For our small cluster calculations, only gas phase energies and frequencies were calculated using the smaller basis set.

# 4.4 Validation of ROA on small oxide clusters

We performed our calculations on small oxide clusters (Figure 4.7), which we used as models for large inorganic network systems. Restricting our investigation to small discrete clusters allowed us to perform highly accurate *ab initio* quantum mechanical computations.

Figure 4.7. General models for small oxide clusters. (a) X is a pnictogen in the +V oxidation state; (b) Z is a chalcogen in the +VI oxidation state; (c) Z is a chalcogen in the +IV oxidation state. The oxidation state of each vanadium is +V before hydrogen atom abstraction and either +V or +IV after a hydrogen atom has been adducted.



We begin with X = V, an all-transition metal cluster that will serve as a control. The first column of Figure 4.8 shows the structure of both the non- and monohydrogenated forms. Note that the  $D_{\rm H}$  value of 75.8 kcal/mol is already significantly high, owing to the naturally effective oxidizing potential of vanadium in the +V oxidation state.

Replacing one vanadium atom with phosphorus (Figure 4.8, second column), we find that the  $D_{\rm H}$  energy has strengthened by 13.4 kcal/mol, to 89.2 kcal/mol. This is the canonical example of our reduction-coupled oxo activation mechanism. Replacing a second vanadium with phosphorus (Figure 4.8, third column) gives a slightly reduced, but similar  $D_{\rm H}$  value of -84.3 kcal/mol. Compared to the experimental results in [3], in which the phorphoryl site has a  $D_{\rm H}$  value of 84.3 kcal/mol,

Figure 4.8. Optimized structures of the  $P_x V_{4-x} O_{10}$  species (first row) ( $x \in \{0, 1, 2, 3\}$ ) and their schematic representations (second row); optimized structures of the monohydrogenated  $P_x V_{4-x} O_{10} H$  species (third row) and their schematic representations (fourth row). Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.



D<sub>H</sub> = 75.8

D<sub>H</sub> = 89.2

D<sub>H</sub> = 84.3

D<sub>H</sub> = 60.5

these numbers are a good validation for our cluster model.

We also examined the  $P_2V_2O_{10}H_2$  cluster, i.e. the dehydrogenated version. As the first row of Figure 4.9 indicates, regardless of the location of the hydrogen atoms, it is always the two vanadiums that are reduced to +IV. However, it is preferable by about 12 kcal/mol to attach the hydrogens onto the phosphoryl groups, due to the special stability of the vanadyl unit. The unpaired spins on each V<sup>IV</sup> are essentially independent, as there is almost no difference in energy or geometry between the singlet and triplet in both cases. We found that addition of a third hydrogen to the system always reduces one vanadium atom to +III, leading to either an overall doublet (doublet V<sup>IV</sup> and singlet V<sup>III</sup>) or an overall quartet (doublet V<sup>IV</sup> and triplet V<sup>III</sup>). The phosphorus atoms, in a sign of their resistance to reduction, stay in the +V oxidation state in all cases. The lack of V<sup>V</sup> centers compared to the case in Figure 4.8 accounts for the significant reduction in  $D_{\rm H}$  values.

Figure 4.9. Optimized structures of the dihydrogenated  $P_2V_2O_{10}H_2$  species (first row), their schematic representations, and their energy relative to the lowest isomer; optimized structures of the trihydrogenated  $P_2V_2O_{10}H_3$  species (second row). Only the triplet and quartet structures are shown because the singlet and doublet structures are almost identical to them. Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.



Having established the validity of our model, we now endeavored to survey the span of the group 15 (pnictogen) vanadium (V) oxides. We found that when going down the periodic table, from phosphorus to arsenic to antimony, the  $D_{\rm H}$  energy decreases (Figure 4.10). Bismuth, the last

element in the series, has an  $D_{\rm H}$  that is slightly higher than antimony above it, but it is still not as effective as a pure vanadium-oxygen cluster and furthermore is too susceptible to reduction to the +III state.

Figure 4.10. Optimized structures of the  $XV_3O_{10}$  species (first row) (X  $\in$  {P, As, Sb, Bi} and their monohydrogenated  $XV_3O_{10}H$  counterparts (second row). Schematic structures are as in Figure 4.7a. Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.



We also examined the potential group 16 (chalcogen) vanadium (V) oxides, in clusters as depicted in Figure 4.7bc. We found that for sulfur, selenium, and tellurium in the maximum +VI oxidation state, all structures had  $D_{\rm H}$  values of 90 kcal/mol or greater (Figure 4.11). We view this as a very promising potential direction for new catalysts.

It is well documented that tellurium prefers higher coordination numbers; for example, unlike its lighter cogeners, the hydrated  $H_6 \text{TeO}_6$  is stable whereas the four-coordinate  $H_2 \text{TeO}_4$  is unknown. Examining several potential structures for the hydrated complex  $\text{Te}_2 \text{V}_2 \text{O}_{12} \text{H}_2$ , we found that the lowest energy conformation had a hydration energy of 6.3 kcal/mol downhill. The resultant structure (Figure 4.12) has a bridging  $\mu$ -oxo that renders the two tellurium atoms five coordinate, and a proton on an oxygen atom on each tellurium. The lowest conformation of the corresponding monohydrated complex  $\text{Te}_2 \text{V}_2 \text{O}_{12} \text{H}_3$  gave a  $D_{\text{H}}$  value of 92.0 kcal/mol, very comparable to the dehydrated complex. Upon hydrogen atom abstraction the  $\mu$ -oxo breaks, resulting in only one of the tellurium atoms remaining five-coordinate.

Unfortunately, it appears that there is a strong drive to fully hydrate the complex until both

**Figure 4.11.** Optimized structures of the  $Z_2V_2O_{11}$  species (first row) ( $Z \in \{S, Se, Te\}$ ) and their monohydrogenated  $Z_2V_2O_{11}H$  counterparts (second row). Schematic structures are as in Figure 4.7b. Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.



Figure 4.12. Optimized structures of the hydrated species  $Te_2V_2O_{12}H_2$  and  $Te_2V_2O_{12}H_3$ , along with their schematic representations. Mulliken spin density was used to assign radical character.  $D_H = 92.0$  kcal/mol.



D<sub>H</sub> = 92.0

tellurium atoms are six-coordinate:  $\text{Te}_2 \text{V}_2 \text{O}_{11} + 3 \text{H}_2 \text{O} \longrightarrow \text{Te}_2 \text{V}_2 \text{O}_{14} \text{H}_6$ ,  $\Delta E = -49.2$  kcal/mol. The six-coordinate complex lacks terminal tellurium oxos that can easily abstract hydrogen atoms. Hence, the  $D_{\text{H}}$  values are much less, diminished to about 60 kcal/mol. Attachment of a hydrogen atom onto a tellurium hydroxide results in water loss, and is not energetically more favorable than attachment onto a bridging oxo (Figure 4.13). The implication of this is that any putative catalyst incorporating tellurium in the +VI oxidation state will be poisoned by water and will need to be kept in dry conditions.

Figure 4.13. Optimized structures of the fully hydrated species  $Te_2V_2O_{14}H_6$  and  $Te_2V_2O_{14}H_7$  (first row), along with their schematic representations (second row). Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.



As  $Se^{VI}$  and  $Te^{VI}$  are both easily reduced to the +IV oxidation state, we also investigated whether vanadium oxide clusters incorporating  $Se^{IV}$  and  $Te^{IV}$  might also have good hydrogen abstraction capability. Using the structures in Figure 4.7c to build our model, we found that the complexes  $Se_2V_2O_9$  and  $Te_2V_2O_9$  are also very strong hydrogen atom abstractors (Figure 4.14). In fact,  $Te_2V_2O_9$  has a  $D_H$  value of 100.0 kcal/mol, the strongest value we have seen. We note that abstraction of one hydrogen atom on a tellurium oxo causes the other tellurium oxo to convert to a bridging oxo, rendering the first tellurium five-coordinate. This is not seen in the selenium case.

We also investigated the activity of vanadium oxide clusters with the group 14 elements Si, Ge, Sn, and Pb in the +IV oxidation state (Figure 4.15). Construction of a cluster model analogous to the templates found in Figure 4.7 results in the complexes  $Z_2V_2O_{10}H_2$ , where Z = Si, Ge, Sn, or Pb, which are shown in the first row of Figure 4.7. Note that unlike the group 15 and 16 cases, the base  $Z_2V_2O_{10}H_2$  clusters do not have any terminal oxo functionalities. This is reasonable and consistent

Figure 4.14. Optimized structures of  $Se_2V_2O_9$  and  $Te_2V_2O_9$  and their schematic representations (first row); optimized structures of the monohydrogenated  $Se_2V_2O_9H$  and  $Te_2V_2O_9H$  (second row). Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.


with the common knowledge that group 14 elements other than carbon greatly prefer two single bonds with oxygen over one double bond. Unfortunately, the lack of such terminal oxos results in the inapplicability of the ROA mechanism towards these types of compounds. Hence, the location on each  $Z_2V_2O_{10}H_2$  species that results in the greatest amount of energy released when H  $\cdot$  is bound is a V=O moiety. The  $D_{\rm H}$  are similar to that of  $V_4O_{10}$  (Figure 4.8). Placement of the H  $\cdot$  atom on a Z-OH moiety or bridging oxygen resulted in decomposition of the cluster for the cases of Z = Ge, Sn, and Pb; and led to much smaller  $D_{\rm H}$  values for the case of Z = Si. Hence we conclude that the ROA mechanistic motif does not likely extend to the group 14 elements.

Although our work presented up to now have all involved vanadium as the transition metal that absorbs the spin density, we were also desirous of expanding the breadth of our ROA principle to other transition metals. Hence, we decided to take our best cases, involving phosphorous, selenium, and tellurium, and substitute in  $Mo^{VI}$  for  $V^{V}$ . Unfortunately, we were not able to find a stable structure for monohydrogenated selenium complexes. Our data for phosphorous and tellurium are presented in Figure 4.16.

It can be seen from the data in Figure 4.16 that the activity of phosphorus and tellurium (VI) species are comparable to those with vanadium, but the tellurium (IV) species is ineffectual. This may be due to the two tellurium atoms being too far apart for an oxygen atom to bridge in the same manner as the vanadium case. Nevertheless, we have demonstrated that the ROA pathway which characterizes vanadium (V) chemistry can also be extended to molybdenum (VI).

Whereas calculations on the periodic system appear to show that the spin is delocalized [3], for our cluster calculations, in all cases the spin is not shared, but localized on one atom. This discrepancy may be explained by noting that those prior calculations were made using the PBE density functional, which has been documented to have a bias towards delocalized systems. Regardless, we were able to see the same increased  $D_{\rm H}$  effect without spin delocalization, so that cannot the physical reason behind our ROA mechanism.

Given the observation that main group-vanadium oxide clusters with only certain elements have an increased hydrogen abstraction energy relative to a vanadium oxide cluster alone, it would appear that increases in hydrogen abstraction energy *via* the ROA motif is element-specific and not due to any general chemical principle. For pnictogen vanadium oxide clusters, the only viable candidate was phosphorus, whereas all the chalcogens exhibited similar high activity, especially selenium and tellurium in the +IV oxidation state. These observations cannot be explained by simple periodic trends.

Similar complexes with group 14 elements were not included in this chapter due to the lack of notable positive results. This may be for the same reason as why a fully hydrated tellurium (VI) complex was also poor, due to the lack of an oxo ligand.

**Figure 4.15.** Optimized structures of the group 14-vanadium oxide species  $Z_2V_2O_{10}H_2$ , where  $Z \in \{Si, Ge, Sn, Pb\}$  (first row); along with their schematic representations (second row). Optimized structures of the corresponding monohydrogenated species (third row) and their schematic representations (fourth row). Alternative locations for  $H \cdot$  addition, as well as the corresponding  $D_H$  energies, are shown in the fifth row for Z = Si. Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.



**Figure 4.16.** Optimized structures of the molybdenum-containing species  $P_2Mo_2O_{11}$ ,  $Te_2Mo_2O_{10}$ , and  $Te_2Mo_2O_{12}$  (first row), along with their schematic representations (second row); optimized structures of the corresponding monohydrogenated species (third row) and their schematic representations (fourth row). Mulliken spin density was used to assign radical character. All numbers are in kcal/mol.



### 4.5 Reactions of a homogeneous oxidation catalyst utilizing the ROA mechanistic motif

Potential catalysts incorporating  $\kappa$ -P phosphinite coordination to metal, i.e. a direct V-P bond as in Figure 4.4b, were explored. Although the inspiration for our proposed catalyst structure was heuristic in nature, our confidence in its predicted activity is to a large degree bolstered by comprehensive theoretical investigations in the system using density functional theory. In this section we will discuss our results on various potential reactivity pathways, and suggest additional theoretical pathways that ought to be investigated before experimental work commences.

One potential pitfall in the installation of the bis(2-phenoxyl)phosphinite (OPO) ligand onto V would be the possibility of the P=O moiety on the ligand coordinating via the oxygen atom to the vanadium. However, at no time in our DFT geometry optimizations, aside from some high energy dianionic five-coordinate cases, did we see this sort of isomerization happen, nor did we see negative frequencies in our calculated Hessian matrices. This implies that the homogeneous vanadium complex with a V-P=O unit is a stable coordination isomer that may be realistically synthesized.

#### 4.5.1 Nomenclature

Due to the number of complexes investigated, a systematic shorthand naming convention is desirable. As all of our complexes share the common motif of a vanadium atom bound  $\kappa$ -P to the O-P(=O)-O pincer ligand bis(2-phenoxyl)phosphinite (OPO); we denote this commonality as (OPO)V. If there is an additional R group (such as a hydrogen atom) on the PO moiety of the (OPO), we label it as a subscript: (OPO)<sub>R</sub>V. If the V atom is five-coordinate, then there are two remaining coordination sites; these are labeled with the s or a superscripts depending on whether they are synperiplanar (syn) or antiperiplanar (anti) to the bis(2-phenoxyl)phosphinite's PO moiety, respectively (Figure 4.17, left). If the V atom is six-coordinate, then the (OPO) ligand may be in either a facial (fac) or meridional (mer) configuration (Figure 4.17, center and right, respectively); and there are three remaining coordination sites. In the fac case, the three sites are labeled with the c, s, and t superscripts, depending on whether they are clinal or syn to the PO moiety of the (OPO), or trans to the P, respectively. In the mer case, the three coordination sites are labeled with the s, t, or a superscripts, depending on whether they are syn to the PO, trans to the P, or anti to the PO, respectively. Under this system, the two specific conformational species shown in the right side of Figure 4.6 could be unambiguously expressed as  $(OPO)^f V^V O^s L_2^{ta}$  and  $(OPO)^m V^V O^s L_2^{ta}$ .

Figure 4.17. Template for the nomenclature of investigated complexes. For the (OPO) ligand, an f superscript denotes that the chelation is facial whereas an m superscript denotes that it is meridional. For the V, n is the oxidation state. For the ligands  $L_n$ , the superscript a denotes that the ligand is *anti* to the PO moiety; s denotes that it is *syn* to the PO moiety; c denotes that it is clinal to the PO moiety; and t denotes that it is *trans* to the P atom.



### 4.5.2 The resting $V^V$ state

The first consideration that needs to be investigated is the precise nature of the resting  $V^V$  state: whether it is five or six coordinated, charged or uncharged, with the (OPO) ligand in a *fac* or *mer* conformation, and with what optimal combination of oxo, hydroxo, and aqua ligands. The pH of the environments investigated was set to either 0 or 7. Changing the ambient pH does not affect the relative energetics of isomeric species with the same charge, but does change which charge cohort of species will be most stable.

Table 4.1 is a comprehensive compilation of all  $(OPO)V^{V}=O$  species studied. The most stable species at pH 0 is the neutral  $(OPO)_{H}^{f}V^{V}O^{c}(OH)^{s}(H_{2}O)^{t}$ , in which the P=O moiety on the ligand is already protonated. However, the isomer  $(OPO)^{f}V^{V}O^{c}(H_{2}O)_{2}^{st}$ , which does have a P=O moiety available, is the second-lowest energy species at only 1.6 kcal/mol higher. At pH 7, the most stable species is the doubly deprotonated  $[(OPO)^{f}V^{V}O^{c}(OH)_{2}^{st}]^{2^{-}}$ . The optimized structures of these three species are shown in Figure 4.18. Note that in some *fac* cases, the PO moiety is twisted enough such that the clinal and *syn* positions on the V both become *gauche*. Since this phenomenon was not universal, no relabeling of clinal and *syn* markers was done.

Species	$E_{\rm gas}$	$G_{\mathrm{aq}}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$(OPO)V^V = O$	-1481.9660	-1481.7587	20.9	29.8
$(\mathrm{OPO})\mathrm{V}^{\mathrm{V}}\mathrm{O}^{s}(\mathrm{H_{2}O})^{a}$	-1711.4245	-1711.1621	2.8	11.7
$(\mathrm{OPO})\mathrm{V}^{\mathrm{V}}\mathrm{O}^{a}(\mathrm{H_{2}O})^{s}$	-1711.4238	-1711.1506	10.0	18.9

Species	E <sub>gas</sub>	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$(OPO)V^V(OH)_2$	-1711.4121	-1711.1479	8.6	20.5
$(\mathrm{OPO})_{\mathrm{H}} \mathrm{V}^{\mathrm{V}} \mathrm{O}^{s} (\mathrm{OH})^{a}$	geometry uns	stable		
$(\mathrm{OPO})_{\mathrm{H}} \mathrm{V}^{\mathrm{V}} \mathrm{O}^{a} (\mathrm{OH})^{s}$	geometry uns	stable		
$[\mathrm{(OPO)}_{\mathrm{H}}\mathrm{V}^{\mathrm{V}}\mathrm{O}^{s}(\mathrm{H}_{2}\mathrm{O})^{a}]^{+}$	-1711.8126	-1711.5923	3.1	21.5
$\left[(\mathrm{OPO})_{\mathrm{H}} \mathrm{V}^{\mathrm{V}} \mathrm{O}^{a} (\mathrm{H}_{2} \mathrm{O})^{s}\right]^{+}$	geometry uns	stable		
$[(\mathrm{OPO})\mathrm{V}^{\mathrm{V}}\mathrm{O}^{s}(\mathrm{OH})^{a}]^{-}$	-1710.9247	-1710.7246	7.0	6.4
$[(\mathrm{OPO})\mathrm{V}^{\mathrm{V}}\mathrm{O}^{a}(\mathrm{OH})^{s}]^{-}$	-1710.9181	-1710.7148	13.1	12.5
$\left[(\mathrm{OPO})\mathrm{V}^{\mathrm{V}}\mathrm{O}_{2}\right]^{2-}$	-1710.3205	-1710.2869	11.4	1.2
$(\mathrm{OPO})^{f} \mathrm{V}^{\mathrm{V}} \mathrm{O}^{c} (\mathrm{H}_{2} \mathrm{O})_{2}^{st}$	-1940.8700	-1940.5384	1.6	10.5
$(\mathrm{OPO})^{f} \mathrm{V}^{\mathrm{V}} \mathrm{O}^{s} (\mathrm{H}_{2} \mathrm{O})_{2}^{ct}$	-1940.8658	-1940.5334	4.8	13.7
$(\mathrm{OPO})^{f} \mathrm{\boldsymbol{V}}^{\mathrm{V}} \mathrm{\boldsymbol{O}}^{t} (\mathrm{H}_{2} \mathrm{\boldsymbol{O}})^{cs}_{2}$	-1940.8678	-1940.5327	5.2	14.1
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^c (\mathrm{OH})^s (\mathrm{H_2O})^t$	-1940.8696	-1940.5410	0.0	8.9
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^c (\mathrm{OH})^t (\mathrm{H_2O})^s$	-1940.8648	-1940.5338	4.5	13.4
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^s (\mathrm{OH})^c (\mathrm{H_2O})^t$	-1940.8690	-1940.5363	2.9	11.8
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^s (\mathrm{OH})^t (\mathrm{H_2O})^c$	-1940.8598	-1940.5254	9.8	18.7
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})^c (\mathrm{H_2O})^s$	-1940.8744	-1940.5375	2.2	11.1
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})^s (\mathrm{H_2O})^c$	-1940.8719	-1940.5372	2.4	11.3
$[(\mathrm{OPO})_\mathrm{H}^f \mathrm{V}^\mathrm{V} \mathrm{O}^c (\mathrm{OH})_2^{st}]^-$	-1940.3696	-1940.0919	11.5	10.9
$[(\mathrm{OPO})_\mathrm{H}^f \mathrm{V}^\mathrm{V} \mathrm{O}^s (\mathrm{OH})_2^{ct}]^-$	-1940.3858	-1940.0992	6.9	6.3
$[(\mathrm{OPO})_\mathrm{H}^f \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})_2^{cs}]^-$	-1940.3795	-1940.0966	8.6	8.0
$[(\mathrm{OPO})^{f}\mathrm{V}^{\mathrm{V}}\mathrm{O}^{c}(\mathrm{OH})^{s}(\mathrm{H}_{2}\mathrm{O})^{t}]^{-}$	-1940.3743	-1940.0988	7.2	6.6
$[(\mathrm{OPO})^{f} \mathrm{V}^{\mathrm{V}} \mathrm{O}^{c} (\mathrm{OH})^{t} (\mathrm{H}_{2} \mathrm{O})^{s}]^{-} \ \Bigg  \\$	-1940.3722	-1940.0978	7.8	7.2
$[(\mathrm{OPO})^{f} \mathrm{\boldsymbol{V}}^{\mathrm{V}} \mathrm{\boldsymbol{O}}^{s} (\mathrm{OH})^{c} (\mathrm{H}_{2} \mathrm{O})^{t}]^{-}$	-1940.3677	-1940.0910	12.1	11.5
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Species	$E_{\rm gas}$	$G_{\mathrm{aq}}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$[(\mathrm{OPO})^{f} \mathrm{\boldsymbol{V}}^{\mathrm{V}} \mathrm{\boldsymbol{O}}^{s} (\mathrm{OH})^{t} (\mathrm{H}_{2} \mathrm{O})^{c}]^{-}$	-1940.3600	-1940.0874	14.3	13.7
$[(\mathrm{OPO})^{f} \mathrm{\boldsymbol{V}}^{\mathrm{V}} \mathrm{\boldsymbol{O}}^{t} (\mathrm{OH})^{c} (\mathrm{H}_{2} \mathrm{O})^{s}]^{-}$	-1940.3649	-1940.0887	13.5	12.9
$[(\mathrm{OPO})^{f} \mathrm{\boldsymbol{V}}^{\mathrm{V}} \mathrm{\boldsymbol{O}}^{t} (\mathrm{OH})^{s} (\mathrm{H}_{2} \mathrm{O})^{c}]^{-}$	-1940.3726	-1940.0916	11.8	11.1
$\left[(\text{OPO})^{f} \mathbf{V}^{\mathbf{V}} \mathbf{O}^{c} (\text{OH})_{2}^{st}\right]^{2-}$	-1939.7811	-1939.6634	10.1	0.0
$\left[(\text{OPO})^f \mathbf{V}^{\mathbf{V}} \mathbf{O}^s (\text{OH})_2^{ct}\right]^{2-}$	-1939.7864	-1939.6622	10.9	0.7
$\left[(\mathrm{OPO})^{f} \mathrm{V}^{\mathrm{V}} \mathrm{O}^{t} (\mathrm{OH})_{2}^{cs}\right]^{2-}$	-1939.7640	-1939.6517	17.5	7.3
$[({\rm OPO})^f \textbf{V}^{\textbf{V}}(\textbf{H}_2\textbf{O})^c(\textbf{O})_2^{st}]^{2-}$	-1939.7706	-1939.6550	15.4	5.3
$[({\rm OPO})^f \textbf{V}^{\textbf{V}}(\textbf{H}_2\textbf{O})^s(\textbf{O})_2^{ct}]^{2-}$	-1939.7651	-1939.6465	20.7	10.6
$[({\rm OPO})^f \textbf{V}^{\textbf{V}}(\textbf{H}_2\textbf{O})^t(\textbf{O})_2^{cs}]^{2-}$	-1939.7836	-1939.6595	12.6	2.4
$[(\mathrm{OPO})_{\mathrm{H}}^{f} \mathrm{V}^{\mathrm{V}}(\mathrm{OH})^{c}(\mathrm{O})_{2}^{st}]^{2-}$	-1939.7795	-1939.6556	15.0	4.9
$[(OPO)_{\rm H}^{f} {\rm V}^{\rm V}(O{\rm H})^{s}({\rm O})_{2}^{ct}]^{2-}$	-1939.7662	-1939.6425	23.3	13.1
$[(OPO)_{\rm H}^{f} {\rm V}^{\rm V}(O{\rm H})^{t}({\rm O})_{2}^{cs}]^{2-}$	-1939.7788	-1939.6546	15.7	5.5
$(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^s (\mathrm{H}_2 \mathrm{O})_2^{ta}$	-1940.8672	-1940.5346	4.0	12.9
$(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{H}_2 \mathrm{O})_2^{sa}$	-1940.8513	-1940.5180	14.5	23.4
$(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^a (\mathrm{H}_2 \mathrm{O})_2^{st}$	-1940.8592	-1940.5289	7.6	16.5
$(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^s (\mathrm{OH})^t (\mathrm{H_2O})^a$	geometry uns	stable		
$(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^s (\mathrm{OH})^a (\mathrm{H}_2 \mathrm{O})^t$	geometry uns	stable		
$(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})^s (\mathrm{H_2O})^a$	geometry uns	stable		
$(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})^a (\mathrm{H}_2 \mathrm{O})^s$	-1940.8548	-1940.5201	13.1	22.0
$(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^a (\mathrm{OH})^s (\mathrm{H_2O})^t$	-1940.8449	-1940.5093	19.9	28.8
$(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^a (\mathrm{OH})^t (\mathrm{H_2O})^s$	-1940.8578	-1940.5270	8.8	17.7
$[(\mathrm{OPO})^m \mathrm{V}^{\mathrm{V}} \mathrm{O}^s (\mathrm{OH})^t (\mathrm{H}_2 \mathrm{O})^a]^-$	-1940.3660	-1940.0966	8.6	7.9

Species	$E_{\rm gas}$	$G_{\mathrm{aq}}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$[(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})^s (\mathrm{H}_2 \mathrm{O})^a]^-$	geometry uns	stable		
$[(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})^a (\mathrm{H}_2 \mathrm{O})^s]^-$	-1940.3614	-1940.0845	16.2	15.6
$[(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^a (\mathrm{OH})^s (\mathrm{H_2O})^t]^-$	geometry uns	stable		
$[(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^a (\mathrm{OH})^t (\mathrm{H}_2 \mathrm{O})^s]^-$	-1940.3724	-1940.0932	10.7	10.1
$[(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^s (\mathrm{OH})^{ta}_2]^-$	-1940.3355	-1940.0626	29.9	29.3
$[(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^t (\mathrm{OH})^{sa}_2]^-$	-1940.3573	-1940.0785	20.0	19.3
$[(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V} \mathrm{O}^a (\mathrm{OH})^{st}_2]^-$	-1940.3447	-1940.0654	28.1	27.5
$[(\mathrm{OPO})^m\mathrm{V}^\mathrm{V}\mathrm{O}^s(\mathrm{OH})_2^{ta}]^{2-}$	-1939.7563	-1939.6389	25.5	15.3
$[(\mathrm{OPO})^m \mathrm{V}^{\mathrm{V}} \mathrm{O}^t (\mathrm{OH})_2^{sa}]^{2-}$	-1939.7430	-1939.6271	32.9	22.7
$[(\mathrm{OPO})^m \mathrm{V}^\mathrm{V} \mathrm{O}^a (\mathrm{OH})_2^{st}]^{2-}$	-1939.7472	-1939.6324	29.6	19.4
$[({\rm OPO})^m {\rm V}^{\rm V}({\rm H_2O})^s({\rm O})_2^{ta}]^{2-}$	geometry uns	stable		
${\rm [(OPO)^{\it m}V^V(H_2O)^{\it t}(O)_2^{\it sa}]^{2-}}$	geometry uns	stable		
$[({\rm OPO})^m {\rm V}^{\rm V}({\rm H}_2{\rm O})^a ({\rm O})_2^{st}]^{2-}$	geometry uns	stable		
$\left[(\mathrm{OPO})^m_\mathrm{H}\mathrm{V}^\mathrm{V}(\mathrm{OH})^s(\mathrm{O})^{ta}_2\right]^{2-}$	-1939.7499	-1939.6332	29.1	18.9
$\left[(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V}(\mathrm{OH})^t(\mathrm{O})^{sa}_2\right]^{2-}$	-1939.7799	-1939.6580	13.5	3.4
$\left[(\mathrm{OPO})^m_\mathrm{H} \mathrm{V}^\mathrm{V}(\mathrm{OH})^a(\mathrm{O})^{st}_2\right]^{2-}$	-1939.7503	-1939.6286	32.0	21.8

**Table 4.1.** Comprehensive compilation of all (OPO)V<sup>V</sup> species studied, along with their gas-phase energies  $(E_{\text{gas}})$  and aqueous free energies  $(G_{\text{aq}})$ , both in hartrees. The last two columns show their aqueous free energies relative to each other, in kcal/mol, at pH 0 and 7, respectively. For some entries, geometry optimization led to the formation of a lower-energy isomer. The energies for these entries are not reported.

### 4.5.3 Propane activation transition states

Propane consists of two types of C–H bonds: primary and secondary, and the secondary C–H bond in the middle carbon is more easily activated due to the increased stability of the resulting secondary radical. Those  $(OPO)V^V$  species listed in Table 4.1 which contain unadorned intact P=O moieties were further investigated for their ability to activate the secondary C–H bond of propane. The transition states were located and their free energies at pH 0 and 7 relative to the ground  $(OPO)V^V$ states of  $(OPO)_H^f V^V O^c (OH)^s (H_2O)^t$  and  $[(OPO)^f V^V O^c (OH)_2^{st}]^{2-}$ , respectively, were calculated. The results are shown in Table 4.2.

**Figure 4.18.** The geometry-optimized structures of  $(OPO)_{\rm H}^{f} V^{V} O^{c} (OH)^{s} ({\rm H}_{2}O)^{t}$  and  $(OPO)^{f} V^{V} O^{c} ({\rm H}_{2}O)_{2}^{st}$ , the most stable  $(OPO) V^{V}$  isomers at pH 0; and of the doubly deprotonated  $[(OPO)^{f} V^{V} O^{c} (OH)_{2}^{st}]^{2^{-}}$ , the most stable isomer at pH 7.



Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$[(\mathrm{OPO})_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^{\mathrm{V}}\mathrm{O}^{s}(\mathrm{H}_{2}\mathrm{O})^{a}]^{\ddagger}$	-1830.5749	-1830.2107	39.6	48.5
$[(\mathrm{OPO})_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^{\mathrm{V}}\mathrm{O}^{a}(\mathrm{H}_{2}\mathrm{O})^{s}]^{\ddagger}$	-1830.5628	-1830.1985	47.2	56.1
$[(\mathrm{OPO})_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^{\mathrm{V}}\mathrm{O}^{s}(\mathrm{OH})^{a}]^{-\ddagger}$	geometry uns	stable		
$[(\mathrm{OPO})_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^{\mathrm{V}}\mathrm{O}^{a}(\mathrm{OH})^{s}]^{-\ddagger}$	geometry uns	stable		
$[(\mathrm{OPO})_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^{\mathrm{V}}\mathrm{O}_{2}^{sa}]^{2-\ddagger}$	geometry uns	stable		
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}}\mathbf{V}^\mathbf{V}\mathbf{O}^s(\mathbf{H}_2\mathbf{O})^{ta}_2]^\ddagger$	-2060.0127	-2059.5889	37.2	46.1
$[(\mathrm{OPO})^m_{\mathrm{HiPr}} \mathbf{V}^{\mathrm{V}} \mathbf{O}^t (\mathbf{H}_2 \mathbf{O})^{sa}_2]^{\ddagger}$	-2060.0129	-2059.5909	36.0	44.9
$[(\mathrm{OPO})^m_{\mathrm{HiPr}} \mathbf{V}^{\mathrm{V}} \mathbf{O}^a (\mathbf{H}_2 \mathbf{O})^{st}_2]^{\ddagger}$	-2060.0036	-2059.5752	45.9	54.8
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}}\mathbf{V}^\mathbf{V}\mathbf{O}^s(\mathbf{OH})^t(\mathbf{H}_2\mathbf{O})^a]^{-\ddagger}$	-2059.5055	-2059.1441	46.1	45.5
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}}\mathbf{V}^{\mathrm{V}}\mathbf{O}^s(\mathrm{OH})^a(\mathbf{H}_2\mathbf{O})^t]^{-\ddagger}$	-2059.4829	-2059.1232	59.2	58.6

Species	$E_{\rm gas}$	$G_{\mathrm{aq}}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}} \mathbf{O}^t (\mathrm{OH})^s (\mathbf{H}_2 \mathbf{O})^a]^{-\ddagger}$	-2059.4979	-2059.1286	55.8	55.2
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}} \mathbf{O}^t (\mathrm{OH})^a (\mathbf{H}_2 \mathbf{O})^s]^{-\ddagger}$	-2059.5033	-2059.1384	49.7	49.1
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}} \mathbf{O}^a (\mathrm{OH})^s (\mathbf{H}_2 \mathbf{O})^t]^{-\ddagger}$	-2059.4868	-2059.1247	58.3	57.7
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}} \mathbf{O}^a (\mathrm{OH})^t (\mathbf{H}_2 \mathbf{O})^s]^{-\ddagger}$	-2059.4888	-2059.1282	56.1	55.4
$[(\text{OPO})_{\text{H}i\text{Pr}}^{m}\text{V}^{\text{V}}\text{O}^{s}(\text{OH})_{2}^{ta}]^{2-\ddagger}$	-2058.9071	-2058.6901	60.7	50.6
$[(\text{OPO})_{\text{H}i\text{Pr}}^m \mathbf{V}^{\mathbf{V}} \mathbf{O}^t (\text{OH})_2^{sa}]^{2-\ddagger}$	-2058.8825	-2058.6799	67.1	57.0
$[(\text{OPO})_{\text{H}i\text{Pr}}^m \text{V}^{\text{V}}\text{O}^a(\text{OH})_2^{st}]^{2-\ddagger}$	-2058.8811	-2058.6783	68.1	57.9
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}}(\mathbf{H}_2\mathbf{O})^s \mathbf{O}_2^{ta}]^{2-\ddagger}$	-2058.8702	-2058.6684	74.4	64.2
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}}(\mathbf{H}_2\mathbf{O})^t \mathbf{O}_2^{sa}]^{2-\ddagger}$	geometry uns	stable		
$[(\mathrm{OPO})^m_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}}(\mathbf{H}_2\mathbf{O})^a \mathbf{O}_2^{st}]^{2-\ddagger}$	geometry uns	stable		
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathbf{V}} \mathbf{O}^c (\mathbf{H}_2 \mathbf{O})^{st}_2]^{\ddagger}$	-2060.0212	-2059.6000	30.3	39.2
$[(\mathbf{OPO})^f_{\mathbf{H}i\mathbf{Pr}}\mathbf{V}^{\mathbf{V}}\mathbf{O}^s(\mathbf{H}_2\mathbf{O})^{ct}_2]^\ddagger$	-2060.0208	-2059.5954	33.2	42.1
$[(\mathbf{OPO})_{\mathbf{H}i\mathbf{Pr}}^{f}\mathbf{V}^{\mathbf{V}}\mathbf{O}^{t}(\mathbf{H}_{2}\mathbf{O})_{2}^{cs}]^{\ddagger}$	-2060.0229	-2059.5991	30.8	39.7
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathrm{V}} \mathbf{O}^c (\mathrm{OH})^s (\mathbf{H}_2 \mathbf{O})^t]^{-\ddagger}$	-2059.5101	-2059.1478	43.8	43.1
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathbf{V}} \mathbf{O}^c (\mathrm{OH})^t (\mathbf{H}_2 \mathbf{O})^s]^{-\ddagger}$	-2059.5120	-2059.1514	41.5	40.9
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathbf{V}} \mathbf{O}^s (\mathrm{OH})^c (\mathbf{H}_2 \mathbf{O})^t]^{-\ddagger}$	-2059.5096	-2059.1432	46.7	46.1
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathbf{V}} \mathbf{O}^s (\mathrm{OH})^t (\mathbf{H}_2 \mathbf{O})^c]^{-\ddagger}$	-2059.5118	-2059.1455	45.2	44.6
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathbf{V}} \mathbf{O}^t (\mathrm{OH})^c (\mathbf{H}_2 \mathbf{O})^s]^{-\ddagger}$	-2059.5186	-2059.1506	42.0	41.4
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}} \mathbf{V}^{\mathbf{V}} \mathbf{O}^t (\mathrm{OH})^s (\mathbf{H}_2 \mathbf{O})^c]^{-\ddagger}$	-2059.5170	-2059.1512	41.6	41.0
$[(\text{OPO})_{\text{H}i\text{Pr}}^{f}\text{V}^{\text{V}}\text{O}^{c}(\text{OH})_{2}^{st}]^{2-\ddagger}$	-2058.9002	-2058.6969	56.4	46.3
$[(\text{OPO})_{\text{H}i\text{Pr}}^{f}\text{V}^{\text{V}}\text{O}^{s}(\text{OH})_{2}^{ct}]^{2-\ddagger}$	-2058.9152	-2058.7010	53.9	43.7
$[(\text{OPO})_{\text{H}i\text{Pr}}^{f}\text{V}^{\text{V}}\text{O}^{t}(\text{OH})_{2}^{cs}]^{2-\ddagger}$	-2058.9121	-2058.6971	56.3	46.2
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^\mathrm{V}(\mathrm{H}_2\mathrm{O})^c\mathrm{O}_2^{st}]^{2-\ddagger}$	-2058.8851	-2058.6791	67.6	57.4

Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$\overline{[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^\mathrm{V}(\mathrm{H}_2\mathrm{O})^s\mathrm{O}_2^{ct}]^{2-\ddagger}}$	-2058.8771	-2058.6841	64.5	54.4
$[(\mathrm{OPO})^f_{\mathrm{H}i\mathrm{Pr}}\mathrm{V}^\mathrm{V}(\mathrm{H_2O})^t\mathrm{O}_2^{cs}]^{2-\ddagger}$	-2058.8941	-2058.6763	69.4	59.3

**Table 4.2.** Comprehensive compilation of all the transition states for propane activation by  $(OPO)V^V$ , along with their gas-phase energies  $(E_{\text{gas}})$  and aqueous free energies  $(G_{\text{aq}})$ , both in hartrees. The last two columns show their aqueous free energies, in kcal/mol, relative to the ground states at pH 0 and 7  $((OPO)_{\text{H}}^{f}V^{V}O^{c}(OH)^{s}(\text{H}_{2}O)^{t}$  and  $[(OPO)^{f}V^{V}O^{c}(OH)^{s}]^{2^{-}}$ , respectively). For some entries, geometry optimization led to the formation of a lower-energy isomer. The energies for these entries are not reported.

According to Table 4.2, the most favorable transition state at both pH 0 and 7 is the neutral species  $[(OPO)_{HiPr}^{f}V^{V}O^{c}(H_{2}O)_{2}^{st}]^{\ddagger}$ , whose structure is shown in detail in Figure 4.19. At pH 0, this species is 30.3 kcal/mol above the neutral ground state  $(OPO)_{H}^{f}V^{V}O^{c}(OH)^{s}(H_{2}O)^{t}$ , and with  $\Delta G^{\ddagger} = 28.7$  kcal/mol from its immediate precursor  $(OPO)^{f}V^{V}O^{c}(H_{2}O)_{2}^{st}$ ; we therefore consider it to be accessible for C–H activation. At pH 7, however, the species is 39.2 kcal/mol above the ground state  $[(OPO)^{f}V^{V}O^{c}(OH)_{2}^{st}]^{2-}$ , as this ground state must be the doubly protonated before C–H activation can occur. Doubly protonating the ground state before C–H activation is still preferable to the dianion directly activating propane; this is due to the fact that the negative charge stabilizes the V<sup>V</sup>=O moiety and thus decreases its tendency to be reduced to V<sup>IV</sup>. We conclude from these results that catalysis with the (OPO)V system is much more likely at pH 0. Analysis of the Mulliken spin density supports our assignment of radical character: Whereas the overall spin is 0, the spin density on the vanadium (1.0882), propane's secondary carbon (-0.5389), and the attacking PO oxygen (-0.2084), but not the phosphorus itself (-0.0350), supporting our assertion of attack by the ROA mechanism.

**Figure 4.19.** The geometry-optimized structure of  $[(OPO)_{H_iPr}^f V^V O^c(H_2O)_2^{st}]^{\ddagger}$ , the most stable transition state for C–H activation of propane at either pH 0 or 7.



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### 4.5.4 Monohydrogenated V<sup>IV</sup> states

The result of the C–H activation transition states as described in the previous subsection is an isopropyl radical and a monohydrogenated  $(OPO)_{\rm H}V^{\rm IV}$  complex, which may then isomerize into other  $(OPO)V^{\rm IV}$  species. The various  $(OPO)V^{\rm IV}$  complexes are listed in Table 4.3. Only six-coordinate complexes with *fac*-(OPO) were exhaustively investigated, as Table 4.1 shows that they are lower in energy than their five-coordinate and six-coordinate *mer* counterparts. At pH 0, the lowest energy species is  $(OPO)_{\rm H}^{f}V^{\rm IV}O^{c}({\rm H}_{2}{\rm O})_{2}^{st}$  at 13.4 kcal/mol above the ground state. However, isomerization to  $(OPO)^{f}V^{\rm IV}(OH)^{c}({\rm H}_{2}{\rm O})_{2}^{st}$ , at 13.6 kcal/mol above the ground state, is nearly thermoneutral. At pH 7, the lowest energy species is  $[(OPO)^{f}V^{\rm IV}O^{s}({\rm H}_{2}{\rm O})_{2}^{ct}]^{-}$  at 16.8 kcal/mol above the ground state. These species are shown in detail in Figure 4.20. All species are doublets, and Mulliken spin density analysis reveals that the spins are localized on the vanadium atoms, hence supporting the assignment of V in the +IV oxidation state.

**Figure 4.20.** The geometry-optimized structures of  $(OPO)_{\rm H}^{f} V^{\rm IV} O^{c}({\rm H}_{2}O)_{2}^{st}$  and  $(OPO)^{f} V^{\rm IV} (OH)^{c}({\rm H}_{2}O)_{2}^{st}$ , the most stable  $(OPO) V^{\rm IV}$  isomers at pH 0; and of the deprotonated  $[(OPO)^{f} V^{\rm IV} O^{s}({\rm H}_{2}O)_{2}^{ct}]^{-}$ , the most stable isomer at pH 7.



### 4.5.5 Catalytic cycle involving H-atom abstraction only

The simplest catalytic cycle that can now be envisioned is one that alternates only between the resting state and its corresponding monohydrogenated species, e.g.,  $(\text{OPO})_{\text{H}}^{f} \text{V}^{V} \text{O}^{c} (\text{OH})^{s} (\text{H}_{2} \text{O})^{t}$  and  $(\text{OPO})_{\text{H}}^{f} \text{V}^{\text{IV}} \text{O}^{c} (\text{H}_{2} \text{O})_{2}^{st}$  (We will only consider the pH 0 case since it is kinetically feasible with overall  $\Delta G^{\ddagger} = 30.3$  kcal/mol; see Subsection 4.5.3). After monohydrogenation, the starting  $\text{V}^{\text{V}}$  species is regenerated by sequential removal of H<sup>+</sup> and e<sup>-</sup> (Scheme 4.2). First deprotonating the

Species	$E_{\rm gas}$	$G_{\mathrm{aq}}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$(OPO)_{\rm H} V^{\rm IV}(O)^s ({\rm H_2O})^a$	-1712.0701	-1711.7906	16.2	25.1
$(\mathrm{OPO})_{\mathrm{H}} \mathrm{V}^{\mathrm{IV}}(\mathrm{O})^{a} (\mathrm{H}_{2}\mathrm{O})^{s}$	-1712.0474	-1711.7653	32.1	41.0
$[(OPO)V^{IV}(O)^{s}(H_{2}O)^{a}]^{-}$	-1711.5717	-1711.3486	23.3	22.7
$[(OPO)V^{IV}(O)^{a}(H_{2}O)^{s}]^{-}$	-1711.5440	-1711.3323	33.5	32.9
$(OPO)_{\rm H}^{m} \mathcal{V}^{\rm IV}(O)^{s}(\mathcal{H}_2O)_2^{ta}$	-1941.5038	-1941.1599	19.5	28.4
$(OPO)_{\rm H}^{m} \mathcal{V}^{\rm IV}(O)^{t}({\rm H_2O})_2^{sa}$	-1941.4939	-1941.1627	17.7	26.6
$(OPO)_{\rm H}^m {\rm V}^{\rm IV}(O)^a ({\rm H}_2 O)_2^{st}$	-1941.4894	-1941.1451	28.8	37.7
$[(OPO)^m V^{IV}(O)^s (H_2O)_2^{ta}]^-$	-1940.9974	-1940.7170	27.1	26.5
$[(OPO)^m V^{IV}(O)^t (H_2O)_2^{sa}]^-$	-1940.9955	-1940.7103	31.3	30.7
$[(OPO)^m V^{IV}(O)^a (H_2O)_2^{st}]^-$	-1941.0011	-1940.7064	33.8	33.1
$(OPO)^{f} V^{IV} (OH)^{c} (H_2O)^{st}_2$	-1941.5108	-1941.1692	13.6	22.5
$(OPO)^{f} V^{IV} (OH)^{s} (H_2O)_2^{ct}$	-1941.5065	-1941.1636	17.2	26.1
$(\text{OPO})^f \text{V}^{\text{IV}}(\text{OH})^t (\text{H}_2\text{O})_2^{cs}$	-1941.4999	-1941.1580	20.7	29.6
$(\text{OPO})_{\text{H}}^{f} \text{V}_{\text{UV}}^{^{1}\text{V}} (\text{H}_{2}\text{O})^{c} (\text{OH})_{2}^{st}$	-1941.4953	-1941.1503	25.5	34.4
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^{^{\mathrm{IV}}}(\mathrm{H}_2\mathrm{O})^s (\mathrm{OH})^{ct}_2$	-1941.4931	-1941.1497	25.9	34.7
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{IV} (\mathrm{H_2O})^t (\mathrm{OH})^{cs}_2$	-1941.5068	-1941.1598	19.5	28.4
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{IV}(\mathrm{O})^c(\mathrm{H_2O})^{st}_2$	-1941.5092	-1941.1695	13.4	22.3
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{IV}(\mathrm{O})^s(\mathrm{H_2O})^{ct}_2$	-1941.5180	-1941.1663	15.4	24.3
$(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^{\mathrm{IV}}(\mathrm{O})^t (\mathrm{H}_2 \mathrm{O})^{cs}_2$	-1941.5093	-1941.1667	15.2	24.1
$[({\rm OPO})^f {\rm V}^{\rm IV}({\rm O})^c ({\rm H_2O})_2^{st}]^-$	-1941.0201	-1940.7264	21.2	20.6
$[({\rm OPO})^f {\rm V}^{\rm IV}({\rm O})^s ({\rm H_2O})_2^{ct}]^-$	-1941.0201	-1940.7325	17.4	16.8
$[({\rm OPO})^f {\rm V}^{\rm IV}({\rm O})^t ({\rm H_2O})_2^{cs}]^-$	-1941.0125	-1940.7266	21.1	20.5
$[(\mathrm{OPO})_{\mathrm{H}}^{f} \mathrm{V}_{\mathrm{UV}}^{\mathrm{IV}}(\mathrm{O})^{c} (\mathrm{OH})^{s} (\mathrm{H}_{2}\mathrm{O})^{t}]^{-}$	-1940.9999	-1940.7101	31.4	30.8
$[(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{IV}(\mathrm{O})^c (\mathrm{OH})^t (\mathrm{H_2O})^s]^-$	-1941.0011	-1940.7205	24.9	24.3
$[(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{IV}(\mathrm{O})^s (\mathrm{OH})^c (\mathrm{H_2O})^t]^-$	-1941.0136	-1940.7218	24.1	23.5
$[(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{IV}(\mathrm{O})^s (\mathrm{OH})^t (\mathrm{H_2O})^c]^-$	-1941.0143	-1940.7228	23.5	22.9
$[(\mathrm{OPO})_{\mathrm{H}}^{f} \mathrm{V}_{\mathrm{uv}}^{\mathrm{IV}}(\mathrm{O})^{t} (\mathrm{OH})^{c} (\mathrm{H}_{2}\mathrm{O})^{s}]^{-}$	-1941.0161	-1940.7247	22.3	21.6
$[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{IV}(\mathrm{O})^t(\mathrm{OH})^s(\mathrm{H}_2\mathrm{O})^c]^-$	-1941.0095	-1940.7226	23.6	23.0
$[({\rm OPO})^f {\rm V}^{\rm IV}({\rm O})^c ({\rm OH})^s ({\rm H_2O})^t]^{2-}$	-1940.4101	-1940.2769	33.0	22.8
$[({\rm OPO})^f {\rm V}^{\rm IV}({\rm O})^c ({\rm OH})^t ({\rm H_2O})^s]^{2-}$	-1940.4110	-1940.2804	30.8	20.6
${\rm [(OPO)}^{f}{\rm V}^{\rm IV}({\rm O})^{s}({\rm OH})^{c}({\rm H_2O})^{t}]^{2-}$	-1940.4079	-1940.2745	34.5	24.4
$[(OPO)^{f}V^{IV}(O)^{s}(OH)^{t}(H_{2}O)^{c}]^{2-}$	-1940.4018	-1940.2721	36.0	25.8
$[({\rm OPO})^f \textbf{V}^{\rm IV}(\textbf{O})^t (\textbf{OH})^c (\textbf{H}_2\textbf{O})^s]^{2-}$	-1940.4013	-1940.2790	31.7	21.5
$[({\rm OPO})^f \textbf{V}^{\rm IV}(\textbf{O})^t (\textbf{OH})^s (\textbf{H}_2\textbf{O})^c]^{2-}$	-1940.3952	-1940.2736	35.1	24.9
$[({ m OPO})^f_{ m H}{ m V}^{ m IV}({ m O})^c ({ m OH})^{st}_2]^{2-}$	-1940.3899	-1940.2599	43.6	33.5
$[(OPO)_{\rm H}^{f} {\rm V}_{\rm uv}^{\rm IV} (O)^{s} (OH)_{2}^{st}]^{2-}$	-1940.4093	-1940.2757	33.8	23.6
$[(\mathrm{OPO})^{f}_{\mathrm{H}} \mathrm{V}^{\mathrm{IV}}(\mathrm{O})^{t}(\mathrm{OH})^{st}_{2}]^{2-}$	-1940.4031	-1940.2828	29.3	19.2

**Table 4.3.** Comprehensive compilation of all (OPO)V<sup>IV</sup> species studied, along with their gas-phase energies ( $E_{\text{gas}}$ ) and aqueous free energies ( $G_{\text{aq}}$ ), both in hartrees. The last two columns show their aqueous free energies, in kcal/mol, relative to the ground states at pH 0 and 7 ((OPO)<sup>f</sup><sub>H</sub>V<sup>V</sup>O<sup>c</sup>(OH)<sup>s</sup><sub>2</sub>(H<sub>2</sub>O)<sup>t</sup> and [(OPO)<sup>f</sup>V<sup>V</sup>O<sup>c</sup>(OH)<sup>s</sup><sub>2</sub>)<sup>2<sup>-</sup></sup>, respectively).

monohydrogenated  $(\text{OPO})_{\text{H}}^{f} \text{V}^{\text{IV}} \text{O}^{c}(\text{H}_{2}\text{O})_{2}^{st}$  forms the anionic intermediates  $[(\text{OPO})\text{V}^{\text{IV}}\text{O}(\text{H}_{2}\text{O})_{2}^{c}]^{-}$ , the lowest isomer of which  $([(\text{OPO})^{f} \text{V}^{\text{IV}}(\text{O})^{s}(\text{H}_{2}\text{O})_{2}^{ct}]^{-})$  is 17.4 kcal/mol above the starting complex. The deprotonation energy gain of 4.0 kcal/mol leads to a calculated pK<sub>a</sub> value of 2.9 for the neutral monohydrogenated complex  $(\text{OPO})_{\text{H}}^{f} \text{V}^{\text{IV}} \text{O}^{c}(\text{H}_{2}\text{O})_{2}^{st}$ . However, the reduction potential of the neutral  $(\text{OPO})^{f} \text{V}^{\text{V}} \text{O}^{s}(\text{H}_{2}\text{O})_{2}^{ct}$  is calculated to be 1.07 V versus SHE, whereas that of  $(\text{OPO})^{f} \text{V}^{\text{V}} \text{O}^{c}(\text{H}_{2}\text{O})_{2}^{st}$  is calculated to be 0.77 V versus SHE. Hence, it is difficult to reoxidize the deprotonated  $[(\text{OPO})^{f} \text{V}^{\text{IV}} \text{O}^{c} (\text{H}_{2}\text{O})_{2}^{st}]^{-}$  back to  $\text{V}^{\text{V}}$ , but not impossible; since the standard reduction potential of O<sub>2</sub> is 1.23 V vs. SHE.



Scheme 4.2. Potential catalytic cycle involving H-atom abstraction only: The one-electron oxidation and catalyst regeneration that forms the core of this catalytic cycle. All energies are in kcal/mol. Note that the overall reaction in this cycle is  $C_3H_8 + \frac{1}{2}O_2 \longrightarrow C_3H_6 + H_2O$ , with  $\Delta G = -32.3$  kcal/mol. Hence, whereas the  $(OPO)^f V^V O^c (H_2O)_2^{st}$  and  $(OPO)^f V^V O^s (H_2O)_2^{ct}$  complexes are initially 1.6 and 4.8 kcal/mol above the starting state, after one complete cycle they are -30.7 and -27.4 kcal/mol below the starting state, respectively.

Since this would only be a one-electron oxidative process, two complete cycles are necessary for propane oxidation: first to abstract a hydrogen atom from the starting alkane, and then to abstract a second hydrogen atom from the resulting isopropyl radical. As hydrogen abstraction from an alkyl radical to a closed-shell species is expected to be facile, the rate-limiting step in this case will be the initial propane activation step. From the  $(OPO)^{f}V^{V}O^{c}(H_{2}O)_{2}^{st}$  precursor (1.6 kcal/mol above the ground state), initial H-atom abstraction from propane is uphill by 11.8 kcal/mol. As the weakest C-H bond in propane (i.e. the *i*Pr-H bond) has a dissociation energy of 103 kcal, this implies a very strong hydrogen abstracting power of 91.2 kcal/mol. This number is very close to the hydrogen-abstraction power of the P=O moiety in V<sup>V</sup>OPO<sub>4</sub>, the oxidized surface of the VPO catalyst [3], hence confirming the validity of our ROA mechanism as modified in Figure 4.4b. The overall kinetic

barrier for H-atom abstraction is 30.3 kcal/mol, a value that is low enough to be accessible at elevated reaction temperatures.

As indicated by Scheme 4.2 and its associated discussion, deprotonation of the monohydrogenated  $(OPO)_{\rm H}^{f}V^{\rm IV}O^{c}({\rm H}_{2}O)_{2}^{st}$  precedes oxidation back to a V<sup>V</sup> species. In fact, these steps are both slightly uphill, by 4.0 and 1.6 kcal/mol, respectively, but they are low enough to remain feasible. The second H-atom abstraction, from the isopropyl radical, is quite facile as expected, creating propylene as the oxidation product. The resulting  $(OPO)_{\rm H}^{f}V^{\rm IV}O^{c}({\rm H}_{2}O)_{2}^{st}$  then goes through one more deprotonation, oxidation, and isomerization cycle to regenerate the starting catalyst. Overall, this reaction is quite feasible thermodynamically, and the reaction barriers are not expected to be large, either. Hence we can expect this to be a complete potential catalytic cycle for the dehydrogenation of propane to propylene.

### 4.5.6 Reduced V<sup>III</sup> states

Since reactive isopropyl radicals are generated upon H-atom abstraction, it is necessary to also consider the possibility that they may be trapped by the V<sup>IV</sup> intermediate instead of being converted to propylene by another equivalent of a V<sup>V</sup> species. Once again taking inspiration from Cheng and Goddard [3], in which the produced isopropyl radical is adsorbed onto a V=O moiety, we analogously considered the possibility that the isopropyl radical and monohydrogenated (OPO)V<sup>IV</sup>(O)(H<sub>2</sub>O)<sub>2</sub> species react with each other to form (OPO)V<sup>III</sup>(O*i*Pr) species. The isopropoxy ligand may then be protonated and exchanged with an aqua ligand, resulting in isopropanol being produced.

Table 4.4 is a comprehensive list of  $(OPO)V^{III}$  species with only oxo/hydroxo/aqua ligands, and neutral or -1 charge. As in the case of the  $V^V$  and  $V^{IV}$  species, the  $(OPO)V^{III}$  species are most stable with the (OPO) ligand in the *fac* configuration. Furthermore, the triplet states are universally more stable than their singlet counterparts, supporting the +III assignment for the vanadium atom's oxidation state. Hence, Table 4.5, which lists the  $(OPO)V^{III}(OiPr)$  species, only contains the triplet six coordinate species with the (OPO) ligand in the *fac* configuration.

Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$^{1}\mathrm{(OPO)V^{III}(H_{2}O)_{2}^{sa}}$	-1712.6358	-1712.3473	25.0	33.9
$^{3}(\mathrm{OPO})\mathrm{V}^{\mathrm{III}}(\mathrm{H}_{2}\mathrm{O})_{2}^{sa}$	-1712.6811	-1712.3911	-2.5	6.4
$^{1}\mathrm{(OPO)}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}\mathrm{(OH)}^{s}\mathrm{(H}_{2}\mathrm{O})^{a}$	geometry uns	stable		
$^{3}\mathrm{(OPO)}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}\mathrm{(OH)}^{s}\mathrm{(H}_{2}\mathrm{O})^{a}$	-1712.6895	-1712.3998	-7.9	1.0

Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}(\rm pH=7)$
$^{1}\mathrm{(OPO)}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}\mathrm{(OH)}^{a}\mathrm{(H}_{2}\mathrm{O})^{s}$	-1712.6609	-1712.3705	10.5	19.4
$^{3}\mathrm{(OPO)}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}\mathrm{(OH)}^{a}\mathrm{(H}_{2}\mathrm{O})^{s}$	-1712.6784	-1712.3916	-2.7	6.2
${}^{1}[({\rm OPO}){\rm V}^{\rm III}({\rm OH})^{s}({\rm H_{2}O})^{a}]^{-}$	geometry uns	stable		
${}^{3}[({\rm OPO}){\rm V}^{\rm III}({\rm OH})^{s}({\rm H_{2}O})^{a}]^{-}$	-1712.1787	-1711.9442	7.7	7.1
$^1[(\mathrm{OPO})\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^a(\mathrm{H}_2\mathrm{O})^s]^-$	geometry uns	stable		
${}^{3}[({\rm OPO}){\rm V}^{\rm III}({\rm OH})^{a}({\rm H}_{2}{\rm O})^{s}]^{-}$	-1712.1727	-1711.9391	10.9	10.3
${}^{1}{\rm [(OPO)}_{\rm H}{\rm V}^{\rm III}{\rm (OH)}_{2}^{sa}]^{-}$	geometry uns	stable		
${}^{3}[(OPO)_{H}V^{III}(OH)_{2}^{sa}]^{-}$	geometry uns	stable		
$^{1}(\mathrm{OPO})^{m}\mathrm{V}^{\mathrm{III}}(\mathrm{H}_{2}\mathrm{O})^{sta}_{3}$	-1942.0707	-1941.7179	27.5	36.4
$^{3}(\mathrm{OPO})^{m}\mathrm{V}^{\mathrm{III}}(\mathrm{H}_{2}\mathrm{O})^{sta}_{3}$	-1942.1201	-1941.7641	-1.5	7.4
$^{1}(\mathrm{OPO})^{m}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{s}(\mathrm{H}_{2}\mathrm{O})^{ta}_{2}$	-1942.0625	-1941.7111	31.8	40.7
$^{3}(\mathrm{OPO})^{m}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{s}(\mathrm{H}_{2}\mathrm{O})^{ta}_{2}$	-1942.1196	-1941.7628	-0.7	8.2
$^{1}(\mathrm{OPO})^{m}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{t}(\mathrm{H}_{2}\mathrm{O})^{sa}_{2}$	-1942.0710	-1941.7216	25.2	34.1
$^{3}(\mathrm{OPO})^{m}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{t}(\mathrm{H}_{2}\mathrm{O})^{sa}_{2}$	-1942.1162	-1941.7627	-0.6	8.3
$^{1}(\mathrm{OPO})^{m}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{a}(\mathrm{H}_{2}\mathrm{O})^{st}_{2}$	-1942.0597	-1941.6995	39.1	48.0
$^{3}(\mathrm{OPO})^{m}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{a}(\mathrm{H}_{2}\mathrm{O})^{st}_{2}$	-1942.1097	-1941.7567	3.2	12.0
$^{1}[(\mathrm{OPO})^{m}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{s}(\mathrm{H}_{2}\mathrm{O})^{ta}_{2}]^{-}$	-1941.5661	-1941.2673	40.0	39.3
$^{3}[({\rm OPO})^{m} \mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{s}(\mathrm{H}_{2}\mathrm{O})^{ta}_{2}]^{-}$	-1941.6145	-1941.3211	6.2	$5.\epsilon$
$^{1}[(\mathrm{OPO})^{m}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{t}(\mathrm{H_{2}O})^{sa}_{2}]^{-}$	-1941.5611	-1941.2660	40.8	40.2
$^3[(\mathrm{OPO})^m\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^t(\mathrm{H_2O})_2^{sa}]^-$	-1941.6143	-1941.3217	5.8	5.2
$^{1}[(\mathrm{OPO})^{m}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{a}(\mathrm{H}_{2}\mathrm{O})^{st}_{2}]^{-}$	-1941.5539	-1941.2535	48.6	48.0
$^{3}[(\mathrm{OPO})^{m}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{a}(\mathrm{H}_{2}\mathrm{O})^{st}_{2}]^{-}$	-1941.6047	-1941.3114	12.3	11.7
$^{1}[(\mathrm{OPO})^{m}_{\mathrm{H}}\mathrm{V}^{\mathrm{III}}(\mathrm{H}_{2}\mathrm{O})^{s}(\mathrm{OH})^{ta}_{2}]^{-}$	-1941.5762	-1941.2783	33.1	32.5

Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$^3[(\mathrm{OPO})^m_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{H}_2\mathrm{O})^s(\mathrm{OH})^{ta}_2]^-$	-1941.5886	-1941.3002	19.3	18.7
${}^1[(\mathrm{OPO})^m_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{H}_2\mathrm{O})^t(\mathrm{OH})^{sa}_2]^-$	-1941.5562	-1941.2561	47.0	46.4
${}^3\mathrm{[(OPO)_H^{\mathit{m}}V^{\mathrm{III}}(\mathrm{H_2O})^t(\mathrm{OH})_2^{\mathit{sa}}]^-}$	-1941.6073	-1941.3093	13.6	13.0
${}^1\mathrm{[(OPO)_H^{\mathit{m}}V^{\mathrm{III}}(\mathrm{H_2O})^a(\mathrm{OH})_2^{st}]^-}$	-1941.5988	-1941.3017	18.4	17.7
${}^3\mathrm{[(OPO)_{H}^{\mathit{m}}V^{\mathrm{III}}(\mathrm{H_2O})^a(\mathrm{OH})_2^{st}]^-}$	-1941.6188	-1941.3235	4.7	4.1
$^{1}(\mathrm{OPO})^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{H}_{2}\mathrm{O})^{cst}_{3}$	-1942.0823	-1941.7202	26.0	34.9
$^{3}(\mathrm{OPO})^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{H}_{2}\mathrm{O})_{3}^{cst}$	-1942.1432	-1941.7900	-17.7	-8.8
${}^{1}\mathrm{(OPO)}_{\mathrm{H}}^{f}\mathrm{V}^{\mathrm{III}}\mathrm{(OH)}^{c}\mathrm{(H}_{2}\mathrm{O})_{2}^{st}$	-1942.0873	-1941.7262	22.3	31.2
${}^3(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{OH})^c(\mathrm{H}_2\mathrm{O})^{st}_2$	-1942.1429	-1941.7811	-12.2	-3.3
${}^{1}\mathrm{(OPO)}_{\mathrm{H}}^{f}\mathrm{V}^{\mathrm{III}}\mathrm{(OH)}^{s}\mathrm{(H}_{2}\mathrm{O}\mathrm{)}_{2}^{ct}$	-1942.0885	-1941.7307	19.5	28.4
${}^3(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{OH})^s(\mathrm{H}_2\mathrm{O})^{ct}_2$	-1942.1386	-1941.7818	-12.6	-3.7
${}^{1}(\mathrm{OPO})_{\mathrm{H}}^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{OH})^{t}(\mathrm{H}_{2}\mathrm{O})_{2}^{cs}$	-1942.0732	-1941.7139	30.0	38.9
${}^3(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{OH})^t(\mathrm{H}_2\mathrm{O})^{cs}_2$	-1942.1288	-1941.7765	-9.3	-0.4
${}^1\mathrm{[(OPO)}{}^f\mathrm{V}^\mathrm{III}\mathrm{(OH)}{}^c\mathrm{(H_2O)}{}^{st}\mathrm{]}^-$	-1941.5871	-1941.2738	35.9	35.3
${}^3\mathrm{[(OPO)}{}^f\mathrm{V}^\mathrm{III}\mathrm{(OH)}{}^c\mathrm{(H_2O)}{}_2^{st}\mathrm{]}^-$	-1941.6398	-1941.3377	-4.2	-4.8
${}^1\mathrm{[(OPO)}{}^f\mathrm{V}^\mathrm{III}\mathrm{(OH)}{}^s\mathrm{(H_2O)}{}^{ct}\mathrm{]}^-$	-1941.5861	-1941.2299	63.4	62.8
${}^3\mathrm{[(OPO)}{}^f\mathrm{V}^\mathrm{III}\mathrm{(OH)}{}^s\mathrm{(H_2O)}{}_2^{ct}\mathrm{]}^-$	-1941.6343	-1941.3371	-3.8	-4.5
${}^{1}[({\rm OPO})^{f} {\rm V}^{{\rm III}}({\rm OH})^{t}({\rm H}_{2}{\rm O})^{cs}_{2}]^{-}$	-1941.5637	-1941.2725	36.7	36.1
${}^3\mathrm{[(OPO)}{}^f\mathrm{V}^\mathrm{III}\mathrm{(OH)}{}^t\mathrm{(H_2O)}{}_2^{cs}\mathrm{]}^-$	-1941.6283	-1941.3282	1.8	1.2
${}^1\mathrm{[(OPO)}_\mathrm{H}^f\mathrm{V}^\mathrm{III}(\mathrm{H_2O})^c(\mathrm{OH})_2^{st}]^-$	-1941.6034	-1941.3092	13.7	13.1
${}^3\mathrm{[(OPO)}_\mathrm{H}^f\mathrm{V}^\mathrm{III}(\mathrm{H_2O})^c(\mathrm{OH})_2^{st}]^-$	-1941.6221	-1941.3289	1.3	0.7
${}^1\mathrm{[(OPO)}_\mathrm{H}^f\mathrm{V}^\mathrm{III}(\mathrm{H_2O})^s(\mathrm{OH})_2^{ct}]^-$	-1941.5798	-1941.2804	31.8	31.1
${}^3\mathrm{[(OPO)}_\mathrm{H}^{f}\mathrm{V}^\mathrm{III}\mathrm{(H_2O)}^{s}\mathrm{(OH)}_2^{ct}]^-$	-1941.6323	-1941.3331	-1.3	-2.0
I	1			

Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$\boxed{\ ^1[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{H_2O})^t(\mathrm{OH})^{cs}_2]^-}$	-1941.6015	-1941.3001	19.4	18.8
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{H_2O})^t(\mathrm{OH})^{cs}_2]^-$	-1941.6254	-1941.3234	4.8	4.1

**Table 4.4.** Comprehensive compilation of all (OPO)V<sup>III</sup> species containing only oxo/hydroxo/aqua ligands studied, along with their gas-phase energies ( $E_{\text{gas}}$ ) and aqueous free energies ( $G_{\text{aq}}$ ), both in hartrees. The last two columns show their aqueous free energies, in kcal/mol, relative to the ground states at pH 0 and 7 ((OPO)<sup>f</sup><sub>H</sub>V<sup>V</sup>O<sup>c</sup>(OH)<sup>s</sup>(H<sub>2</sub>O)<sup>t</sup> and [(OPO)<sup>f</sup>V<sup>V</sup>O<sup>c</sup>(OH)<sup>s</sup>2<sup>t</sup>]<sup>2-</sup>, respectively). For some entries, geometry optimization led to the formation of a lower-energy isomer. The energies for these entries are not reported.

Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
$^{3}(\mathrm{OPO})^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^{c}(\mathrm{H}_{2}\mathrm{O})_{2}^{st}$	-1907.1454	-1906.7524	-12.8	-3.9
$^{3}(\mathrm{OPO})^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^{s}(\mathrm{H}_{2}\mathrm{O})_{2}^{ct}$	-1907.1518	-1906.7610	-18.2	-9.3
$^{3}(\mathrm{OPO})^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^{t}(\mathrm{H}_{2}\mathrm{O})_{2}^{cs}$	-1907.1489	-1906.7546	-14.2	-5.3
${}^3(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^c(\mathrm{OH})^s(\mathrm{H_2O})^t$	-1907.1417	-1906.7463	-9.0	-0.1
$^{3}(\mathrm{OPO})_{\mathrm{H}}^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^{c}(\mathrm{OH})^{t}(\mathrm{H}_{2}\mathrm{O})^{s}$	-1907.1398	-1906.7456	-8.6	0.3
${}^3(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^s(\mathrm{OH})^c(\mathrm{H_2O})^t$	-1907.1520	-1906.7574	-16.0	-7.1
${}^3(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^s(\mathrm{OH})^t(\mathrm{H_2O})^c$	-1907.1339	-1906.7422	-6.5	2.4
${}^3(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^t(\mathrm{OH})^c(\mathrm{H}_2\mathrm{O})^s$	-1907.1472	-1906.7494	-10.9	-2.0
${}^3(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^t(\mathrm{OH})^s(\mathrm{H_2O})^c$	-1907.1439	-1906.7503	-11.5	-2.6
${}^3(\mathrm{OPO})^f_\mathrm{H} \mathrm{V}^\mathrm{III}(\mathrm{O}i\mathrm{Pr})^c(\mathrm{H_2O})^{st}_2$	-1907.1448	-1906.7528	-13.1	-4.2
${}^3\mathrm{(OPO)}_\mathrm{H}^{f}\mathrm{V}^\mathrm{III}\mathrm{(OiPr)}^{s}\mathrm{(H_2O)}_2^{ct}$	-1907.1544	-1906.7567	-15.5	-6.6
$^{3}(\mathrm{OPO})_{\mathrm{H}}^{f}\mathrm{V}^{\mathrm{III}}(\mathrm{O}i\mathrm{Pr})^{t}(\mathrm{H}_{2}\mathrm{O})_{2}^{cs}$	-1907.1454	-1906.7458	-8.7	0.2
${}^3[(\mathrm{OPO})^f\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^c(\mathrm{OH})^s(\mathrm{H_2O})^t]^-$	-1906.6425	-1906.3086	-4.6	-5.2
${}^3[(\mathrm{OPO})^f\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^c(\mathrm{OH})^t(\mathrm{H_2O})^s]^-$	-1906.6463	-1906.3113	-6.3	-6.9
${}^3[(\mathrm{OPO})^f\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^s(\mathrm{OH})^c(\mathrm{H_2O})^t]^-$	-1906.6475	-1906.3125	-7.1	-7.7
$^3[(\mathrm{OPO})^f\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^s(\mathrm{OH})^t(\mathrm{H}_2\mathrm{O})^c]^-$	-1906.6369	-1906.3039	-1.7	-2.3
$^3[(\mathrm{OPO})^f\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^t(\mathrm{OH})^c(\mathrm{H_2O})^s]^-$	-1906.6436	-1906.3069	-3.6	-4.2

Species	$E_{\rm gas}$	$G_{ m aq}$	$G_{\rm rel}({\rm pH}=0)$	$G_{\rm rel}({\rm pH}=7)$
${}^3[(\mathrm{OPO})^f\mathrm{V}^{\mathrm{III}}(\mathrm{HO}i\mathrm{Pr})^t(\mathrm{OH})^s(\mathrm{H_2O})^c]^-$	-1906.6461	-1906.3043	-1.9	-2.6
${}^3[({\rm OPO})^f {\rm V}^{\rm III} ({\rm O}i {\rm Pr})^c ({\rm H_2O})_2^{st}]^-$	-1906.6476	-1906.3131	-7.5	-8.1
${}^{3}[({\rm OPO})^{f} \textbf{V}^{\rm III} ({\rm O}i \textbf{Pr})^{s} (\textbf{H}_{2}\textbf{O})^{ct}_{2}]^{-}$	-1906.6425	-1906.3043	-1.9	-2.5
${}^3[({\rm OPO})^f \textbf{V}^{\rm III} ({\rm O}i \textbf{Pr})^t (\textbf{H}_2\textbf{O})_2^{cs}]^-$	-1906.6420	-1906.2957	3.4	2.8
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^c(\mathrm{OH})^{st}_2]^-$	geometry uns	stable		
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^s(\mathrm{OH})^{ct}_2]^-$	-1906.6284	-1906.2897	7.2	6.6
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{HO}i\mathrm{Pr})^t(\mathrm{OH})^{cs}_2]^-$	-1906.6261	-1906.2951	3.8	3.2
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{O}i\mathrm{Pr})^c(\mathrm{OH})^s(\mathrm{H_2O})^t]^-$	-1906.6346	-1906.2971	2.6	1.9
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{O}i\mathrm{Pr})^s(\mathrm{OH})^c(\mathrm{H_2O})^t]^-$	-1906.6346	-1906.3005	0.5	-0.2
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{O}i\mathrm{Pr})^s(\mathrm{OH})^c(\mathrm{H_2O})^t]^-$	-1906.6482	-1906.3055	-2.7	-3.3
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{O}i\mathrm{Pr})^s(\mathrm{OH})^t(\mathrm{H_2O})^c]^-$	-1906.6398	-1906.2991	1.4	0.7
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{O}i\mathrm{Pr})^t(\mathrm{OH})^c(\mathrm{H_2O})^s]^-$	geometry unstable			
${}^3[(\mathrm{OPO})^f_\mathrm{H}\mathrm{V}^\mathrm{III}(\mathrm{O}i\mathrm{Pr})^t(\mathrm{OH})^s(\mathrm{H}_2\mathrm{O})^c]^-$	geometry unstable			

**Table 4.5.** Compilation of all (OPO)V<sup>III</sup>(O*i*Pr) species studied, with only six-coordinate *fac*-(OPO) triplet complexes considered. The second and third columns show the gas-phase energies ( $E_{gas}$ ) and aqueous free energies ( $G_{aq}$ ), both in hartrees. The last two columns show their aqueous free energies, in kcal/mol, relative to the ground states at pH 0 and 7 ((OPO)<sup>f</sup><sub>H</sub>V<sup>V</sup>O<sup>c</sup>(OH)<sup>s</sup>(H<sub>2</sub>O)<sup>t</sup> and [(OPO)<sup>f</sup>V<sup>V</sup>O<sup>c</sup>(OH)<sup>s</sup><sup>t</sup>]<sup>2-</sup>, respectively). For some entries, geometry optimization led to the formation of a lower-energy isomer. The energies for these entries are not reported.

At pH 0, the lowest energy (OPO)V<sup>III</sup>(O*i*Pr) species is  ${}^{3}(OPO)^{f}V^{III}(HO$ *i* $Pr)^{s}(H_{2}O)_{2}^{ct}$  at -18.2 kcal/mol relative to the starting  $(OPO)_{H}^{f}V^{V}O^{c}(OH)^{s}(H_{2}O)^{t}$ , whereas the lowest energy  $(OPO)V^{III}$  species without any isopropoxy groups is  ${}^{3}(OPO)^{f}V^{III}(H_{2}O)_{3}^{cst}$  at -17.7 kcal/mol relative to  $(OPO)_{H}^{f}-V^{V}O^{c}(OH)^{s}(H_{2}O)^{t}$ . Furthermore, the lowest energy five-coordinate  $(OPO)V^{III}$  species without any isopropoxy groups is  ${}^{3}(OPO)_{H}V^{III}(OH)^{s}(H_{2}O)^{a}$  at -7.9 kcal/mol relative to  $(OPO)_{H}^{f}V^{V}O^{c}(OH)^{s}-(H_{2}O)^{t}$ , indicating that it is possible for  ${}^{3}(OPO)^{f}V^{III}(HO$ *i* $Pr)^{s}(H_{2}O)_{2}^{ct}$  and  ${}^{3}(OPO)^{f}V^{III}(H_{2}O)_{3}^{cst}$  to interconvert *via* a labile isopropanol ligand. These three species are shown in detail in Figure 4.21. Note that at pH 7 the same three species are still the most stable, but with energies of -9.3, -8.8, and 1.0 kcal/mol with respect to  $[(OPO)^{f}V^{V}O^{c}(OH)_{2}^{st}]^{2-}$ , respectively.

# 4.5.7 Catalytic cycle involving H-atom abstraction followed by isopropyl addition

By considering the lowest energy configurations of the various  $V^V$ ,  $V^{IV}$ , and  $V^{III}$  intermediates and transition states, we can now construct a catalytic cycle that features both H-atom abstraction

**Figure 4.21.** The geometry-optimized structures of  ${}^{3}(\text{OPO})^{f} \text{V}^{\text{III}}(\text{HO}i\text{Pr})^{s}(\text{H}_{2}\text{O})_{2}^{ct}$ ,  ${}^{3}(\text{OPO})^{f} \text{V}^{\text{III}}(\text{H}_{2}\text{O})_{3}^{cst}$ , and  ${}^{3}(\text{OPO})_{\text{H}} \text{V}^{\text{III}}(\text{OH})^{s}(\text{H}_{2}\text{O})^{a}$ . These are the most stable (OPO) $\text{V}^{\text{III}}(\text{OiPr})$  species, and six and five coordinate (OPO) $\text{V}^{\text{III}}$  species, respectively, at both pH 0 and 7.



from propane and isopropyl radical trapping before reoxidation. This cycle is shown in Scheme 4.3. The first part, involving isomerization of the starting  $(OPO)_{\rm H}^{f}V^{\rm V}O^{c}(OH)^{s}({\rm H}_{2}O)^{t}$  to  $(OPO)^{f}V^{\rm V}O^{c}({\rm H}_{2}O)_{2}^{st}$ , followed by C–H activation to  $(OPO)_{\rm H}^{f}V^{\rm IV}O^{c}({\rm H}_{2}O)_{2}^{st}$ , is identical to that of Scheme 4.2. However, instead of being immediately reoxidized as in Scheme 4.2, the V<sup>IV</sup> species traps the generated isopropyl radical to form a V<sup>III</sup>(OiPr) species. One example of such a pathway is shown in Scheme 4.3, in which the  $(OPO)_{\rm H}^{f}V^{\rm IV}O^{c}({\rm H}_{2}O)_{2}^{st}$  species first isomerizes to the slightly higher (at 15.4 kcal/mol relative to the starting V<sup>V</sup> complex)  $(OPO)_{\rm H}^{f}V^{\rm IV}O^{s}({\rm H}_{2}O)_{2}^{ct}$ , which then combines with the isopropyl radical to form  ${}^{3}(OPO)_{\rm H}^{f}V^{\rm III}(OiPr)^{s}({\rm H}_{2}O)_{2}^{ct}$  at -15.5 kcal/mol, which readily isomerizes to  ${}^{3}(OPO)^{f}V^{\rm III}({\rm HO}^{i}Pr)^{s}({\rm H}_{2}O)_{2}^{t}$ , the lowest energy V<sup>III</sup>(OiPr) species at -18.2 kcal/mol relative to the starting  $(OPO)_{\rm H}^{f}V^{\rm V}O^{c}(OH)^{s}({\rm H}_{2}O)_{2}^{ct}$  at -15.5 kcal/mol, which readily isomerizes to  ${}^{3}(OPO)^{f}V^{\rm III}({\rm HO}^{i}Pr)^{s}({\rm H}_{2}O)_{2}^{t}$ , the lowest energy V<sup>III</sup>(OiPr) species at -18.2 kcal/mol relative to the starting  $(OPO)_{\rm H}^{f}V^{\rm V}O^{c}(OH)^{s}({\rm H}_{2}O)^{t}$ . Loss of the HOiPr product to form the five coordinate species  ${}^{3}(OPO)V^{\rm III}({\rm H}_{2}O)_{2}^{sa}$  (at -1.5 kcal/mol) is uphill but not insurmountably so, and recoordination of an aqua ligand to the sixth coordination site to form  ${}^{3}(OPO)^{f}V^{\rm III}({\rm H}_{2}O)_{2}^{sa}$  recovers (at -17.7 kcal/mol) most of this energy. As the overall reaction  $C_{3}H_{8} + {}^{1}_{2}O_{2} \longrightarrow HOiPr$  has  $\Delta G = -31.2$  kcal/mol, reoxidation of  ${}^{3}(OPO)V^{\rm III}({\rm H}_{2}O)_{2}^{sa}$  to  $(OPO)^{f}V^{\rm V}O^{c}({\rm H}_{2}O)_{2}^{st}$  (assuming that  $O_{2}$  is the terminal oxidation) is downhill by 11

#### 4.5.8 Comparison of the catalytic cycles

The H-atom abstraction-only pathway results in the dehydrogenation of propane to form propylene. However, as this is significantly uphill ( $C_3H_8 \longrightarrow C_3H_6 + H_2$ ,  $\Delta G = 20.3$  kcal/mol), it is unlikely unless some oxidant is coupled to the reaction. Coupling dehydrogenation with dioxygen greatly



Scheme 4.3. A potential catalytic cycle that assumes that the isopropyl radical adds to the vanadium oxo, reducing it to V<sup>III</sup>. This assumption derives from the behavior of the heterogeneous VPO catalyst. All energies are in kcal/mol. Note that the overall reaction in this cycle is  $C_3H_8 + {}^1/{}_2O_2 \longrightarrow HOiPr$ , with  $\Delta G = -31.2$  kcal/mol. Hence, whereas the (OPO) ${}^fV^VO^c(H_2O){}^{st}_2$  complex is initially 1.6 kcal/mol above the starting state, after one complete cycle it is -29.6 kcal/mol below the starting state.

increases its favorability, for a  $\Delta G$  of -32.3 kcal/mol. We have not found any large barriers in the Hatom abstraction-only pathway that might preclude the production of propylene and water as in the overall equation  $C_3H_8 + \frac{1}{2}O_2 \longrightarrow C_3H_6 + H_2O$ ; however, we note that our results do not include the details of how the one-electron oxidation of  $[(OPO)^f V^{IV}(O)^c (H_2O)_2^{st}]^-$  or  $[(OPO)^f V^{IV}(O)^s (H_2O)_2^{ct}]^$ takes place and how the released electron is transferred to dioxygen to ultimately form water. Such a mechanism may involve an inner sphere coordination of dioxygen to form a V<sup>V</sup> superoxo intermediate and may involve further C-H activation by this superoxide. Given the reduction potential of dioxygen versus that of  $[(OPO)^f V^{IV}(O)^c (H_2O)_2^{st}]^-$  or  $[(OPO)^f V^{IV}(O)^s (H_2O)_2^{ct}]^-$  (1.23 V versus 0.77 V or 1.07 V), we believe that the H-atom abstraction-only pathway will be viable and productive in the absence of lower-energy alternative pathways.

Comparing the H-atom abstraction-only versus the H-atom abstraction and isopropyl addition pathways, we note that the branching point is the monohydrogenated complexes  $(OPO)_{\rm H}^{f}V^{\rm IV}(O)$ - $({\rm H}_2{\rm O})_2$ , which may either undergo reoxidation as in the abstraction-only mechanism (Scheme 4.2), or add the isopropyl radical (Scheme 4.3). The former overall is thermodynamically downhill by 0.8 kcal/mol in the lowest isomers; whereas the latter is thermodynamically downhill by 30.9 kcal/mol in one simple elementary step with an intuitively minimal barrier. Hence, the catalytic cycle involving isopropyl addition appears to be more likely to occur than the cycle that only features H-atom abstraction. As in the H-atom abstraction-only case, we have not considered the precise nature of the reoxidation step. However, we anticipate that it may also involve inner sphere coordination of dioxygen, in which case a V<sup>V</sup>  $\eta^2$ -peroxo intermediate is formed. This would be analogous to the heterogeneous VPO system, and we would also need to anticipate C–H activation by these peroxide species as well.

### 4.6 Conclusions

We have identified a new mechanistic motif, which we call the reductive-coupled oxo activation mechanism, in which a normally unreactive main-group oxo becomes a potent hydrogen atom abstractor when coupled to a transition metal (in our case  $V^V$  or  $Mo^{VI}$ ). The new activity of this oxo, which we quantify using the O–H dissociation parameter  $D_{\rm H}$ , is modified from that of the transition metal oxo itself and may be significantly higher for certain elements, specifically phosphorous in the +V oxidation state and selenium and tellurium in the +IV and +VI oxidation states. Our results are consistent with existing experimental and theoretical mechanistic work on the *n*-butane to maleic anhydride VOPO catalyst. We believe that knowledge of this new mechanistic motif will allow for the *de novo* rational design of future oxidation catalysts.

As a showcase of the power of the ROA mechanistic motif, we have designed a potential inorganic complex  $(OPO)_{H}^{f} V^{V} O^{c} (OH)^{s} (H_{2}O)^{t}$  that may serve as a homogeneous oxidation catalyst for alkanes. We have identified catalytic cycles for the oxidation of propane to propylene or isopropanol. Our likely catalytic cycle involves H-atom abstraction from propane, followed by recombination of the produced isopropyl radical and  $V^{IV}$  species to form a  $V^{III}$  isopropoxy species. Ligand exchange results in the formation of free isopropanol and reoxidation regenerates the starting  $V^{V}$  species. Our theoretical results are encouraging for us to continue our computational work in investigating reoxidation pathways, and to commence experimental work.

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### Chapter 5

## The mechanism of Ni(iPr-pybox)complexes as asymmetric Negishi C-C coupling catalysts

### 5.1 Abstract

The 2,6-bis(4-isopropyl-2-oxazolin-2-yl)pyridine (iPr-pybox) ligand, when combined with a nickel salt in N,N-dimethylacetamide (DMA), generates an *in situ* Ni(iPr-pybox) complex that catalyzes enantioselectively the cross-coupling of secondary  $sp^3$ -C substrates. This system is very notable for its property of stereoconvergence: *both* enantiomers of a racemic substrate may be converted into a single enantiomer of a product. This chapter will computationally explore the mechanism responsible for both the remarkable activity and selectivity of the Ni(iPr-pybox) system; such a mechanism is believed to deviate substantially from the canonical "textbook" mechanism of Negishi coupling. Furthermore, a generalized calculation scheme is presented that allows for the rapid enantioselectivity prediction of many related pybox ligands as well, in order to help predict the next generation of asymmetric Negishi coupling catalysts.

### 5.2 Introduction

The controlled formation of C–C bonds is one of the central challenges of synthetic organic chemistry. Generally, the cross-coupling of two distinct organic moieties R and R' is done by selecting precursors with opposite polarity, for example, an electrophilic R-X (where X is a leaving group) along with a nucleophilic R'-[M'] (where M' is a less electronegative element, often a main-group metal or metalloid). Late transition metals M are typically added as well in order to catalyze activity and encourage the formation of R-R' as opposed to undesired side products. Ligands may also be added in order to further enhance the activity of the transition metal catalyst by the generation of *in situ* complexes.

Scheme 5.1 shows the overall cross-coupling reaction, as well as a general scheme for the mechanism. This mechanism [1] begins with the oxidative addition of R-X by a low-valent M (hence the necessity of using a late transition metal). The X ligand is then exchanged for an R' in the transmetalation step, and finally reductive elimination regenerates the starting M and releases the coupled product R-R'.



Scheme 5.1. Left: the overall C-C bond-forming cross-coupling reaction. Right: the general mechanism for the cross-coupling reaction.

Table 5.1 shows a few examples of cross-coupling reactions. As already mentioned, the electrophile is typically R-X where X is a leaving group such as a halide or sulfonate. Substrates in which the R group is an aryl or alkenyl, or a resonance-stabilized  $sp^3$  radical such as an allyl or propargyl group, tend to be more active. The metal catalyst M is typically Cu, Ni, or Pd, with Pd being the most versatile element but also the rarest and most expensive. The nucleophile is R'-[M'] where M' may well be any element that forms a weaker bond to R' than M, and/or a stronger bond to X.

Coupling	Electrophile	Nucleophile	Catalyst	Reference
Kumada	R-X	$\rm R'-MgBr$	Pd, Ni	[2]
Heck	R-X	alkene	Pd	[3]
Sonogashira	R-X	${\rm R'-C}{\equiv}{\rm CH}$	Pd, Cu	[4]
Negishi	R-X	R'-ZnX	Pd, Ni	[5]
Stille	R-X	$R'-SnR'_3$	Pd	[6]
Suzuki	R-X	$R'-B(OR'')_2$	Pd	[7]
Hiyama	R-X	$R'-SiR'_3$	Pd	[8]

Table 5.1. Examples of various C-C cross-coupling reactions. This list is not exhaustive.

### 5.2.1 The Ni(iPr-pybox) system

Another central challenge of synthetic organic chemistry is the enantioselective synthesis of chiral compounds. For cross-coupling reactions in which C-C bonds are formed, the carbon atoms being bonded are often chiral centers, necessitating techniques for asymmetric synthesis. For cross-coupling reactions, this may be done by adding a chiral ligand to complex the catalyst metal, thus preferentially coupling only one enantiomer of a racemic starting material. Alternatively, one may also simply begin with an enantiopure substrate and chose a coupling reaction that preserves chirality.

The Ni(*i*Pr-pybox) system, developed by Gregory Fu and coworkers, is a Negishi coupling catalyst that utilizes nickel and the 2,6-bis(4-isopropyl-2-oxazolin-2-yl)pyridine ligand, abbreviated as (*i*Pr-pybox), and couples organic halides to organozinc complexes [9]. The (*i*Pr-pybox) ligand contains two chiral centers and can exist in three diastereomers: the  $C_2$  enantiomers (((R, R)-*i*Pr-pybox)) and ((S, S)-*i*Pr-pybox)), and the  $C_s$  meso diastereomer ((R, S)-*i*Pr-pybox). If a chiral  $C_2$  ligand is used, asymmetric catalysis results. The complex and a summary of its catalytic scope is shown in Scheme 5.2 and Table 5.2 [9, 10].



Scheme 5.2. The general reaction of the Ni(iPr-pybox) Negishi coupling catalyst with benzylic secondary alkyl halides.  $\alpha$ -Bromo amides and propargylic halides are also viable substrates that have been studied.

This Ni(iPr-pybox) system is advantageous for several reasons [10]:



**Table 5.2.** Some examples of benzylic secondary alkyl halide substrates coupled by the Ni(iPr-pybox) catalyst. All reactions were performed under conditions as in Scheme 5.2, except for entries 7 and 8 which were performed at room temperature. The data in this table was taken from Arp and Fu [10].

- 1. It is a Negishi coupling catalyst, utilizing organozinc reagents as the nucleophile. Organozinc compounds are relatively tractable and accessible;
- 2. The ligand is known and is not difficult to synthesize from commercially-available starting materials;
- 3. The system is not particularly oxygen or water sensitive, and the reaction may be run under air;
- 4. Coupling reactions with alkyl substrates are typically more difficult than with their aryl counterparts, and unwanted side reactions such as  $\beta$ -hydride elimination may be present. Secondary alkyls are particularly problematic due to their added steric bulk. The pybox system has been demonstrated to work with various secondary alkyl electrophiles such as benzylic halides,  $\alpha$ bromo amides, and propargylic halides [11].

However, one of the Ni(iPr-pybox) system's most interesting properties may be its stereoconvergence. A racemic starting material may be used to generate a nearly enantiopure product with high yield (See Scheme 5.2). This implies that the mechanism requires both the destruction of the starting material's stereochemistry as well as the formation of the product's stereochemistry, and indicates that the mechanism may be more complex than the existing "textbook" mechanism as shown in Scheme 5.1.

### 5.2.2 Existing computational work

The mechanism for the Ni(*i*Pr-pybox) system's remarkable reactivity was computationally investigated by Lin et al., who modeled the coupling of 1-bromoindane (the electrophile in Table 5.2, entry 3) with methylzinc bromide as catalyzed by Ni<sup>I</sup>((S, S)-*i*Pr-pybox)Br to form (R)- and (S)-1methylindane [12]. Their results, which are summarized in 5.1, claim that Ni<sup>I</sup>((S, S)-*i*Pr-pybox)Br is first methylated by methylzinc bromide to form Ni<sup>I</sup>((S, S)-*i*Pr-pybox)Me. Oxidation by 1bromoindane results in Ni<sup>II</sup>((S, S)-*i*Pr-pybox)(Me)Br and the indanyl radical, which then recombine to form Ni<sup>III</sup>((S, S)-*i*Pr-pybox)(Me)(Br)(ind) (ind = 1-indanyl), which undergoes reductive elimination to form the 1-methylindane product and to regenerate the Ni<sup>I</sup>((S, S)-*i*Pr-pybox)Br starting catalyst.

The mechanism put forth by Lin et al. supports the hypothesis of Fu et al. that a Ni<sup>I</sup>-Ni<sup>III</sup> cycle is involved, as opposed to the Ni<sup>0</sup>-Ni<sup>II</sup> cycle of a classical coupling reaction. In addition, their conclusions show a decisive preference for the formation of the (S)-1-methylindane enantiomer, in line with experimental evidence. However, their methodology and analysis have several issues:

1. The density functional theory used, B3LYP, neglects van der Waals interactions, which typically increase in importance for large molecules; Figure 5.1. The computationally studied mechanism by Lin et al. of Ni((S, S)-*i*Pr-pybox) catalysis of methyl-indane coupling. The steps are: methylation and oxidation of Ni<sup>I</sup>((S, S)-*i*Pr-pybox)Br to Ni<sup>II</sup>((S, S)-*i*Pr-pybox)(Me)Br, recombination with indanyl radical to form Ni<sup>III</sup>((S, S)-*i*Pr-pybox)(Me)(Br)(ind), and reductive elimination to form 1-methylindane product. All energies in kcal/mol. Note that for the first two steps (i.e. methylation and oxidation to Ni<sup>II</sup>), the energy differences are only estimates, as the actual calculations were only performed on the parent Ni(pybox) complexes.



- 2. The basis set used, 6-31G<sup>\*</sup> (a Pople-type double- $\zeta$  Gaussian basis set with polarization functions on non-hydrogen atoms) is rather small and limited, and may lead to inaccurate energies [13];
- 3. Whereas the authors claim to investigate the enantioselectivity of the Ni(*i*Pr-pybox) system, in many reactions the simplified pybox ligand (without the isopropyl groups) was used in lieu of (*i*Pr)-pybox to simplify calculations;
- 4. The authors model the methylzinc bromide nucleophile as a simple two-coordinate complex; however, the true nature of the zincate in solution is likely to be much more complex [14];
- 5. Although the reaction conditions and all experimental investigations have used DMA as the solvent, the authors modeled the reaction in DMSO instead;
- 6. Only one radical attack pathway (i.e. that of the indanyl radical approaching axially to the Ni) was considered.

Therefore, it is not surprising that enantioselectivity of the Ni(*i*Pr-pybox) system, which can be measured using the metric  $\Delta\Delta G^{\ddagger} := \Delta G_R^{\ddagger} - \Delta G_S^{\ddagger}$ , was greatly overestimated at 8.7 kcal/mol, whereas the experimentally determined enantiomeric excesses correspond to a  $\Delta\Delta G^{\ddagger}$  value of 2–3 kcal/mol.

Due to these deficiencies, we have undertaken our own computational study of the Ni(*i*Pr-pybox) system's asymmetric catalysis reaction, using larger basis sets, more accurate DFTs and molecular models, and more potential reaction pathways considered. We have found a substantially different mechanism from that of Lin et al., with an overall reaction barrier of 15.9 kcal/mol for the formation of S-methylindane and a  $\Delta\Delta G^{\ddagger}$  value of 2.7 kcal/mol, in line with the experimentally determined values [15]. In addition, we have found a useful protocol for the rapid determination of the  $\Delta\Delta G^{\ddagger}$  enantioselectivity values of other related Ni(pybox) systems. We present some new results

and predictions using this new method.

### 5.3 Materials and methods

For our calculations, the specific reaction we investigated was the coupling of racemic 1-bromoindane with methylzinc iodide to form (S)-1-methylindane, using Ni<sup>I</sup> $((S, S)-i\Pr$ -pybox)Br as a catalyst or precatalyst. The solvent was taken to be DMA and the temperature 258.15 K.

All quantum mechanical calculations were carried out using the Jaguar software version 7.9 developed by Schrödinger Inc. [16]. Geometry optimizations were carried out on initial guess structures, and vibrational frequencies were gathered to confirm the optimized geometries as intermediates or transition states and to construct a free energy profile. Solvation energies were calculated using the PBF Poisson-Boltzmann implicit continuum solvation model [17] in Jaguar, with a dielectric constant of 37.78 [18] and a probe radius of 2.642 Å [19] for DMA.

Geometry optimization and vibrational data were calculated using the B3LYP-D3 density functional [20] with a smaller basis set, whereas single point gas-phase and solvated energies were calculated using the same functional and a larger basis set. The "-D3" suffix refers to the post-SCF correction developed by Grimme et al. that accounts for van der Waals forces [21]. Here the smaller basis set consists of a modified double- $\zeta$  Los Alamos basis set and pseudopotential (LACVP<sup>\*\*</sup>) [22] for transition metals, and the 6-31G<sup>\*\*</sup> basis set [13] for the other atoms; whereas the larger basis set consists of the triple- $\zeta$  Los Alamos basis set and pseudopotential (LACV3P<sup>\*\*</sup>++) for transition metals, the same LAV3P basis set and pseudopotential for heavy main-group elements, and the 6-311G<sup>\*\*</sup>++ basis set [23] for the other atoms. Proposed intermediates and transition states were found to have zero and one negative frequencies, confirming their status as local energy minima and saddle points, respectively.

The free energy for each molecular species in solution was calculated using the formula

$$G = E_{\text{gas}} + \Delta G_{\text{solv}} + \text{ZPE} + H_{\text{vib}} + 6kT - T[S_{\text{vib}} + \gamma(S_{\text{trans}} + S_{\text{rot}} - \alpha) + \beta]$$

where the last term (with  $\alpha = 14.3$  e.u.,  $\beta = 7.98$  e.u., and  $\gamma = 0.54$ ) is an empirical approximation for the change in the translational and rotational entropy of the molecule between the gas phase and the solution phase (due to the finite librational frequencies), derived from Wertz [24].

For the monatomic anions  $Br^-$  and  $I^-$ , the Wertz approximation was not necessary. Hence we used the equation

$$G = E_{\text{gas}} + \Delta G_{\text{solv}} + \frac{5}{2}kT - TS + 1.9$$

to construct the free energy.

For DMA, the Gibbs free energy was calculated using the formula

$$G_{\text{liquid}} = E_{\text{gas}} + \text{ZPE} + H_{\text{tot}} - TS_{\text{tot}} + \Delta G_{\text{gas} \rightarrow \text{liquid}}$$

where  $\Delta G_{\text{gas} \rightarrow \text{liquid}} = G_{\text{liquid}} - G_{\text{gas}}(1 \text{ atm})$  is the free energy of condensation to liquid from 1 atm gas. We can solve for this by noting that

$$\Delta G_{\text{gas} \to \text{liquid}} = \Delta G_{\text{expansion}} + G_{\text{gas} \to \text{solvation}},$$

where  $\Delta G_{\text{expansion}} = G_{\text{gas}}(P) - G_{\text{gas}}(1 \text{ atm})$  is the expansion of the gas from 1 atm to the vapor pressure P, and  $G_{\text{gas}\to\text{solvation}}$  is the condensation of gas at vapor pressure P to liquid. Since a liquid is by definition at equilibrium with its vapor pressure  $G_{\text{gas}\to\text{solvation}} = 0$ , and we thus have

$$\Delta G_{\text{gas} \to \text{liquid}} = G_{\text{gas}}(P) - G_{\text{gas}}(1 \text{ atm}) = RT \ln \left(\frac{P}{1 \text{ atm}}\right).$$

We can find the vapor pressure P at a given temperature using the Antoine Equation:

$$\log_{10} P = A - \frac{B}{C+T},$$

where the empirical parameters A, B, and C vary with the solvent and temperature. For DMA at 258.15 K, A = 6.0888, B = 2725.96, C = 28.209, so the vapor pressure is  $3.71 \times 10^{-4}$  atm [25].

### 5.4 Results

In this section, we present the results of our calculations and the likely mechanism of C-C coupling that the Ni(*i*Pr-pybox) system undergoes. We begin by first outlining the general overarching mechanism, and then examine in depth the details of each step.

### 5.4.1 The overall general mechanism

In the previous work of Lin et al., the authors claimed early in their report that the Ni<sup>0</sup>-Ni<sup>II</sup> cycle that a typical Negishi catalyst might undergo had an overall barrier of 57.3 kcal/mol, and consequently was not feasible [12]. Despite our concerns about their methodology (see Section 5.2.2), we do not believe that addressing these concerns would have any potential to lower the barrier enough to make the Ni<sup>0</sup>-Ni<sup>II</sup> cycle accessible. Hence, we agree with their conclusion that the Ni(*i*Pr-pybox) system most likely goes through a Ni<sup>I</sup>-Ni<sup>III</sup> cycle. We therefore restrict our mechanistic investigations to the Ni<sup>I</sup>-Ni<sup>III</sup> cycle.

Scheme 5.3 shows the Ni<sup>I</sup>-Ni<sup>III</sup> cycle in its most general form. The catalyst alternates between a

Ni<sup>I</sup> and a Ni<sup>III</sup> state (for example, Ni<sup>I</sup>((S, S)-iPr-pybox)Br and Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(Br)-(ind), respectively). Conversion of Ni<sup>I</sup>((S, S)-iPr-pybox)Br to Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(Br)(ind) should proceed *via* methylation and addition of indanyl and bromine radicals, in any order. Conversion of Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(Br)(ind) back to Ni<sup>I</sup>((S, S)-iPr-pybox)Br should proceed *via* reductive elimination of 1-methylindane. The rest of this section will examine the detailed pathways of this generalized scheme.



Scheme 5.3. The generalized mechanism of the Ni(*i*Pr-pybox) Negishi coupling catalyst as it proceeds through a Ni<sup>I</sup>-Ni<sup>III</sup> cycle. The overall equation is  $ind-Br + MeZnI \longrightarrow ind-Me + ZnBrI$ .

### 5.4.2 Nature of the organozinc reagent

In order to address how alkyl transfer of the methylzinc iodide to the Ni(*i*Pr-pybox) complex occurs, it is necessary to first identify the exact nature of the methyl transferring species. Lin et al. depict the complexation of Ni(pybox) with a simple two-coordinate linear MeZnBr species in their calculations; however, it is unclear if such an electron-deficient species is at all present in a strongly polar solvent such as DMA. Indeed, the active methylation species has often been assumed to be a three coordinate MeZn $X_2^-$  [26]. Recent titration work by Organ et al. suggests, however, that the true methylating species is in fact four-coordinate dianionic MeZn $X_3^-$  with a Pd catalyst and a THF or THF/DMI 2:1 solvent (THF = tetrahydrofuran; DMI = N,N'-dimethyl-2-imidazolidinone) [14].

For our mechanistic investigation, we decided to undertake a comprehensive computational investigation of the methylzinc and inorganic zinc species that may be present in the DMA solution under reaction conditions. Scheme 5.4 shows our calculated free energies of complexation of MeZnX and  $ZnX_2$  with one and two equivalents of X<sup>-</sup>, where X may be either bromine or iodine. We found that, contrary to the results of Organ et al., three-coordinate MeZnX<sup>-</sup><sub>2</sub> species are preferred; this discrepancy may be due to our choice of DMA as solvent, which has a much larger dielectric constant of 37.78 compared to the THF as used by Organ et al. ( $\epsilon = 7.2$ ).



Scheme 5.4. Complexation of the various MeZnX (left) and  $ZnX_2$  (right) species with X<sup>-</sup>, where  $X \in \{Br, I\}$ . Numbers next to each arrow are the free energy change for the specific reaction. All numbers in kcal/mol.

We also considered the possibility that the zinc species might form adducts with DMA, or cluster into polynuclear complexes. Given the strong polarity of the DMA solvent, we expected the former possibility to be more likely, but both pathways were explored. Figure 5.2 shows the various adducts and cluster complexes of MeZnX, whereas Figure 5.3 shows the various adducts and cluster complexes of ZnX<sub>2</sub>.

Figure 5.2. The various  $(MeZnI)_m(dma)_n$  species, where *m* may equal 0 (top row, left), 1 (bottom row), or 2 (top row, right); and *n* may equal 0, 1, or 2 as well. All numbers are free energies in kcal/mol and relative to MeZnI. The lowest energy species,  $MeZnI(dma)_2$ , is highlighted in red.



Our results show that the most stable methylzinc species are MeZnBrI<sup>-</sup> and MeZnI(dma)<sub>2</sub>, at -3.1 kcal/mol relative to the base MeZnI; and that the most stable inorganic zinc species is ZnBrI(dma)<sub>2</sub>, at -15.2 kcal/mol relative to the base ZnBrI. For consistency, we have set MeZnI(dma)<sub>2</sub> to be our active methylating agent and ZnBrI(dma)<sub>2</sub> to be our ultimate product. Therefore, the overall reaction that we are investigating can now be written as ind-Br + MeZnI(dma)<sub>2</sub>  $\longrightarrow$  ind-Me + ZnBrI(dma)<sub>2</sub>.

**Figure 5.3.** Left: The various  $(\text{ZnBrI})_m(\text{dma})_n$  species, where *m* may equal 0 (first row) or 1 (second to fifth rows); and *n* may equal 0 (first column), 1 (second column), or 2 (third and fourth columns). Right: The various  $(\text{ZnBrI})_4$  tetrameric clusters. All numbers are free energies in kcal/mol and relative to ZnBrI. The lowest energy species, ZnBrI(dma)<sub>2</sub>, is highlighted in red.


#### 5.4.3 Mechanism for Ni<sup>I</sup> oxidation and methylation

We now address the mechanistic steps that must be taken for the top half of the cycle in Scheme 5.3, i.e. the conversion of Ni<sup>I</sup>((S, S)-iPr-pybox)Br to Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(ind)Br. This conversion is expected to proceed through methylation with MeZnI(dma)<sub>2</sub> and oxidation with ind-Br. Due to the stereoconvergent nature of the catalysis, in which the prior stereochemistry of the starting ind-Br is destroyed, the oxidation is not expected to be a typical one-step oxidative addition reaction. Instead, there is believed to be an initial one-electron oxidation in which Ni<sup>III</sup> and a benzylic-stabilized indanyl radical are produced, followed by recombination to form the Ni<sup>III</sup> species. These assertions are supported by experimental evidence (i.e. the formation of coupling products [15]), and the calculations of Lin et al. [12] support their feasibility.

As a result, we have three possibilities for the conversion of  $Ni^{I}((S, S)-iPr-pybox)Br$  to  $Ni^{III}-((S, S)-iPr-pybox)(Me)(ind)Br$ :

- **The Ni<sup>I</sup> pathway:** Methylation occurs first, converting Ni<sup>I</sup>((S, S)-iPr-pybox)Br to Ni<sup>I</sup>((S, S)-iPr-pybox)Me, and subsequent oxidation by ind-Br produces Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)-(ind)Br;
- **The Ni<sup>II</sup> pathway:** Oxidation by ind-Br to Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub> and free indanyl radical occurs first. Methylation to Ni<sup>II</sup>((S, S)-iPr-pybox)(Me)Br follows, and recombination with ind  $\cdot$  produces Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(ind)Br;
- **The Ni<sup>III</sup> pathway:** Oxidation by ind-Br proceeds to completion with Ni<sup>III</sup>((S, S)-iPr-pybox)-(ind)Br<sub>2</sub> being formed; subsequent methylation produces Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(ind)Br.

These three pathways are shown in Scheme 5.5.

The first branching point is the first step:  $Ni^{I}((S, S)-iPr-pybox)Br$  may either undergo methylation as in the Ni<sup>I</sup> pathway, or one-electron oxidation by ind-Br as in the Ni<sup>II</sup> and Ni<sup>III</sup> pathways. Methylation of Ni<sup>I</sup>((S, S)-iPr-pybox)Br to Ni<sup>I</sup>((S, S)-iPr-pybox)Me is thermodynamically uphill by 15.2 kcal/mol. Unfortunately, we were unable to find any transition states for the concerted transfer of the methyl group from MeZnI(dma)<sub>2</sub> to any Ni<sup>I</sup> species. However, we can consider a dissociative mechanism whereby the bromine on Ni<sup>I</sup>((S, S)-iPr-pybox)Br is exchanged for a methyl group by the successive steps of Br<sup>-</sup> dissociation, MeZnI(dma)<sub>2</sub> association, and ZnI(dma)<sub>2</sub><sup>+</sup> dissociation (Scheme 5.6). Since each ligand association/disassociation step is expected to have minimal barriers if any, we can therefore gain an upper bound for the Ni<sup>I</sup> methylation barrier by simply calculating the relative energies of each intermediate in Scheme 5.6. The results of our analysis shows that the overall barrier for the methylation of Ni<sup>I</sup>((S, S)-iPr-pybox)Br to Ni<sup>I</sup>((S, S)-iPr-pybox)Me is between 15.2 and 20.7 kcal/mol.

The Ni<sup>II</sup> and Ni<sup>III</sup> pathways, by contrast, begin with the oxidation of Ni<sup>I</sup>((S, S)-iPr-pybox)Br



Scheme 5.5. Three potential pathways for the methylation and oxidation of  $Ni^{I}((S, S)-iPr-pybox)Br$  to  $Ni^{III}((S, S)-iPr-pybox)(Me)(ind)Br$ . Red denotes the  $Ni^{I}$  pathway, green the  $Ni^{II}$  pathway, and blue the  $Ni^{III}$  pathway. Open coordination sites may be occupied by dma solvent.



Scheme 5.6. The dissociative pathway for the methylation of  $Ni^{I}((S, S)-iPr-pybox)Br$  to  $Ni^{I}((S, S)-iPr-pybox)Me$ , as part of the  $Ni^{I}$  pathway in Scheme 5.5. The transition state barriers for each associative/dissociative step is expected to be minimal, if existent. Hence, the overall barrier to methylation by this pathway is 20.7 kcal/mol. All numbers are in kcal/mol and relative to  $Ni^{I}((S, S)-iPr-pybox)Br$ .

by ind–Br to Ni<sup>II</sup>((S, S)-iPr–pybox)Br<sub>2</sub> and ind · . This oxidation most likely proceeds through an inner sphere route that begins with coordination of ind–Br to the Ni center. Our results are shown in Scheme 5.7. Initial coordination of (*R*)- and (*S*)-1-bromoindane with Ni<sup>I</sup>((S, S)-iPr–pybox)Br produces an adduct Ni<sup>I</sup>((S, S)-iPr–pybox)(Br)(Br–ind) that is favorable at -4.6 and -5.2 kcal/mol relative to the initial Ni<sup>I</sup> species, respectively. Loss of ind · then results in Ni<sup>II</sup>((S, S)-iPr–pybox)Br<sub>2</sub>, whose triplet energy is -9.3 kcal/mol relative to the initial Ni<sup>I</sup> species. The coordination of a DMA solvent molecule further lowers the triplet energy to -11.9 kcal/mol relative to the initial Ni<sup>I</sup> species. The transition state barriers to ind–Br coordination and ind · dissociation are indeed quite minimal at less than 1.7 kcal/mol, supporting our assumptions about the Ni<sup>I</sup> methylation pathway. Since Ni<sup>I</sup> methylation as *per* the Ni<sup>II</sup> pathway is uphill thermodynamically by 15.2 kcal/mol, and Ni<sup>II</sup> oxidation as *per* the Ni<sup>II</sup> and Ni<sup>III</sup> and Ni<sup>III</sup> pathways for Ni<sup>I</sup>((S, S)-iPr–pybox)Br methylation and oxidation are much more likely than the Ni<sup>I</sup> pathway, which was the only pathway investigated by Lin *et al.* 



Scheme 5.7. The oxidation of Ni<sup>I</sup>((S, S)-iPr-pybox)Br by ind-Br to Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub> and ind  $\cdot$ , as part of the Ni<sup>II</sup> and Ni<sup>III</sup> pathways in Scheme 5.5. The transition state barrier for the coordination of DMA to Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub> is expected to be minimal, if existent. Hence, the overall barrier to oxidation by this pathway is 1.2 kcal/mol for (R)-1-bromoindane and 0.4 kcal/mol for (S)-1-bromoindane. All numbers are in kcal/mol and relative to Ni<sup>II</sup>((S, S)-iPr-pybox)Br.

The second branching point is the subsequent reaction of Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub>(dma), which can either undergo methylation to Ni<sup>II</sup>((S, S)-iPr-pybox)(Me)Br as in the Ni<sup>II</sup> pathway, or recombine with ind  $\cdot$  to form Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>(ind) as in the Ni<sup>III</sup> pathway. Scheme 5.8 shows a comparison of the essential features of the two pathways, whereas Scheme 5.11 is an unabridged diagram of the Ni<sup>II</sup> pathway. Methylation of Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub>(dma) to Ni<sup>II</sup>-((S, S)-iPr-pybox)(Me)Br as in the Ni<sup>II</sup> pathway is uphill by 5.4 kcal/mol. By contrast, recombination with ind  $\cdot$  to form Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>(ind) as in the Ni<sup>III</sup> pathway is downhill by 1.2 or 5.8 kcal/mol, depending on whether the indanyl ligand attaches in an (R) or (S) configuration, respectively. Since the dissociation of DMA from Ni<sup>II</sup> $((S, S)-i\Pr-pybox)Br_2(dma)$  is uphill by 2.6 kcal/mol, and the addition of ind  $\cdot$  is expected to have minimal barrier, we can conclude that the overall barrier of the reaction of Ni<sup>II</sup> $((S, S)-i\Pr-pybox)Br_2(dma)$  and ind  $\cdot$  is likely lower than that of Ni<sup>II</sup> $((S, S)-i\Pr-pybox)Br_2(dma)$  and MeZnI $(dma)_2$ , and hence that the Ni<sup>III</sup> pathway is preferred over the Ni<sup>II</sup> pathway.

The Ni<sup>I</sup>, Ni<sup>II</sup>, and Ni<sup>III</sup> pathways all converge to Ni<sup>III</sup>( $(S, S)-i\Pr-pybox$ )(Me)(ind)Br in the final step. For the Ni<sup>III</sup> pathway, this involves the methylation of the Ni<sup>III</sup>( $(S, S)-i\Pr-pybox$ )Br<sub>2</sub>(ind) formed as described in the previous Scheme 5.8. As in the Ni<sup>I</sup> methylation case, we were unable to find any transition states for the concerted transfer of the methyl group from MeZnI(dma)<sub>2</sub> to any Ni<sup>III</sup> species. Hence we again considered a dissociative mechanism whereby a bromine on Ni<sup>III</sup>( $(S, S)-i\Pr-pybox$ )Br<sub>2</sub>(ind) is exchanged for a methyl group by the successive steps of Br<sup>-</sup> dissociation, MeZnI(dma)<sub>2</sub> association, and ZnI(dma)<sup>+</sup><sub>2</sub> dissociation, assuming that our barriers are minimal and thus estimating our overall methylation barriers using thermodynamic energies only. A comprehensive accounting of all species studied for this Ni<sup>III</sup> methylation reaction is given in Scheme 5.12 in Section 5.7.

Scheme 5.9 shows the essential features of the mechanism of Ni<sup>III</sup> methylation. The initial  $Ni^{III}((S,S)-iPr-pybox)Br_2(ind)$  may lose a bromo ligand, resulting in a five-coordinate cationic species  $[Ni^{III}((S, S) - iPr - pybox)Br(ind)]^+$  that may exist in three separate but interchangeable geometric conformations. Each conformation may then trap an equivalent of MeZnI(dma)<sub>2</sub>, with the species  $[Ni^{III}((S,S)-iPr-pybox)Br^{eq}((S)-ind)^{ax}-Me^{ax}-ZnI(dma)_2]^+$  the most favorable at -3.1 kcal/mol relative to the starting Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>((S)-ind). However, it is the isomer  $[Ni^{III}((S,S)-iPr-pybox)Br^{ax}(ind)^{ax}-Me^{eq}-ZnI(dma)_2]^+$  that eventually leads to the lowest  $Ni^{III}(Me)(ind)Br$  species,  $Ni^{III}((S,S)-iPr-pybox)Br^{ax}(ind)^{ax}Me^{eq}$ . Dissociation of ZnBrI(dma) from  $Ni^{III}((S,S)-iPr-pybox)Br^{ax}(ind)^{ax}-Me^{eq}-ZnBrI(dma)$  leads to  $[Ni^{III}((S,S)-iPr-pybox)-iPr-pybox)-iPr-pybox]$  $Br^{ax}(ind)^{ax}Me^{eq}$  and is 6.8 or 4.5 kcal/mol uphill from the starting Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>-((S)-ind), but coordination of ZnBrI(dma) with solvent back to ZnBrI(dma)<sub>2</sub> drives this reaction forward. As we have assumed that association and dissociation barriers are minimal for these reactions, the overall barrier for the methylation of  $Ni^{III}((S,S)-iPr-pybox)Br_2((S)-ind)$  is approximately the difference between the highest point  $([Ni^{III}((S,S)-iPr-pybox)Br^{ax}(ind)^{ax}Me^{eq} +$  $\operatorname{ZnBrI}(\operatorname{dma})$  and the lowest point ([Ni<sup>III</sup>((S, S) - iPr-pybox)Br<sup>eq</sup>((S) - ind)<sup>ax</sup> - Me<sup>ax</sup> - ZnI(dma)<sub>2</sub>]<sup>+</sup>), equal to 9.9 and 7.6 kcal/mol for the formation of  $Ni^{III}((S,S)-iPr-pybox)Br^{ax}((R)-ind)^{ax}Me^{eq}$ and  $Ni^{III}((S, S) - iPr - pybox)Br^{ax}((S) - ind)^{ax}Me^{eq}$ , respectively.



Scheme 5.8. Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub> and its subsequent methylation as part of the Ni<sup>II</sup> pathway, or recombination with ind  $\cdot$  as part of the Ni<sup>III</sup> pathway. The lowest energy Ni<sup>II</sup>((S, S)-iPr-pybox)MeBr complex is 5.4 kcal/mol higher than the starting Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub>, so the overall barrier for methylation is at least this much. By contrast, the transition state barrier for the coordination of ind  $\cdot$  to Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub> is expected to be minimal, if existent. Hence, the overall barrier to ind  $\cdot$  recombination is 2.6 kcal/mol, and the Ni<sup>III</sup> pathway is thus more likely to occur. All numbers are in kcal/mol and relative to Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub>. Red denotes the starting Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub>(dma) complex, green the Ni<sup>III</sup> pathway, and blue the Ni<sup>IIII</sup> pathway. Note that indanyl recombination is reversible, so that Ni<sup>III</sup>((R)-iPr-pybox)Br<sub>2</sub>((S)-ind) and Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>((S)-ind) can interconvert.



Scheme 5.9. The methylation of Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>((S)-ind) to produce Ni<sup>III</sup>-((S, S)-iPr-pybox)(Br)(ind)Me. The reaction initially proceeds to [Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sup>eq</sup>-((S)-ind)<sup>ax</sup>-Me<sup>ax</sup>-ZnI(dma)<sub>2</sub>]<sup>+</sup>, a thermodynamic sink, and must increase in energy in order to reach the Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sup>ax</sup>(ind)<sup>ax</sup>Me<sup>eq</sup> product. All numbers are in kcal/mol and relative to Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>((S)-ind). Red denotes the lowest point and thermodynamic sink, [Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sup>eq</sup>((S)-ind)<sup>ax</sup>-Me<sup>ax</sup>-ZnI(dma)<sub>2</sub>]<sup>+</sup>; and green the highest point, Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sup>ax</sup>(ind)<sup>ax</sup>Me<sup>eq</sup> + ZnBrI(dma).

#### 5.4.4 Mechanism for reductive elimination

After the formation of Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(ind)Br, the final step to closing the catalytic cycle is the reductive elimination of ind-Me and the reformation of Ni<sup>I</sup>((S, S)-iPr-pybox)Br (Scheme 5.3, bottom half of cycle). In the computational work of Lin et al., only the reductive elimination of ind-Me from Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)<sup>eq</sup>(ind)<sup>ax</sup>Br<sup>ax</sup> was considered. However, we believe that this is not the only possible pathway for the reductive elimination of ind-Me. Specifically:

- Reductive elimination may proceed from either Ni<sup>III</sup>((S,S)-iPr-pybox)(Me)<sup>ax</sup>(ind)<sup>eq</sup>Br<sup>ax</sup> or Ni<sup>III</sup>((S,S)-iPr-pybox)(Me)<sup>eq</sup>(ind)<sup>ax</sup>Br<sup>ax</sup>;
- 2. It is possible for the bromo ligand to be lost, resulting in five-coordinate cationic  $[Ni^{III}-((S,S)-iPr-pybox)(Me)(ind)]^+$  species that may also reductively eliminate;
- 3. It is possible for the five coordinate cationic species to be stabilized by a solvent ligand, resulting in the six-coordinate cationic  $[Ni^{III}((S,S)-iPr-pybox)(Me)(ind)dma]^+$  species that may also reductively eliminate;
- 4. It is also possible for the five coordinate cationic species to coordinate to zinc, forming an adduct Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(ind)-Br-[Zn] that may also reductively eliminate.

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For the last possibility, the only transition states found that contained the Ni–Br–Zn moiety were the geometric isomers of  $[Ni^{III}((S,S)-iPr-pybox)(Me)(ind)-Br–ZnBr_2I]^-$ . In all other cases, the Br–[Zn] moiety dissociated from the Ni during geometry optimization.

Figure 5.4 shows all the transition states that have been found, and their energies relative to  $[Ni^{III}((S,S)-iPr-pybox)Br^{eq}((S)-ind)^{ax}-Me^{ax}-ZnI(dma)_2]^+$ , the lowest energy state of the catalyst. A reaction scheme showing the pathways to all transition states is given in Section 5.7 as Scheme 5.13. The lowest energy transition state that produces (R)-1-methylindane is  $[Ni^{III}-((S,S)-iPr-pybox)(Me)^{ax}((R)-ind)^{eq}-Br^{ax}-ZnBr_2I]^-$ , with an overall barrier of 18.6 kcal/mol, and the lowest energy transition state that produces (S)-1-methylindane is  $[Ni^{III}((S,S)-iPr-pybox)-(Me)^{ax}((S)-ind)^{eq}]^+$ , with an overall barrier of 15.9 kcal/mol. Hence, the preference for (S)-1methylindane is  $\Delta\Delta G^{\ddagger} = 2.7$  kcal/mol, in line with experimentally determined enantiomeric excesses [15].

#### 5.5 Discussion

#### 5.5.1 Overall catalytic cycle

Figure 5.5 is a reaction coordinate diagram that summarizes our results for the investigation of the oxidation and methylation of Ni<sup>I</sup>((S, S)-iPr-pybox)Br to Ni<sup>III</sup>((S, S)-iPr-pybox)(Me)(ind)Br, and the subsequent reductive elimination of ind-Me and reformation of Ni<sup>I</sup>((S, S)-iPr-pybox)Br. All three pathways are shown and the Ni<sup>III</sup> pathway is clearly the easiest. The lowest point and thermodynamic sink, [Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sup>eq</sup>((S)-ind)<sup>ax</sup>-Me<sup>ax</sup>-ZnI(dma)<sub>2</sub>]<sup>+</sup>, is now considered the resting state, and all other free energies given are relative to it. The overall barrier is 18.6 and 15.9 kcal/mol for the formation of (R)-1-methylindane and (S)-1-methylindane, respectively.

#### 5.5.2 Predictions for new ligands

Now that the mechanism of Ni((S, S)-*i*Pr-pybox) asymmetric Negishi coupling catalysis has been ascertained, it is useful to consider how modification of the ((S, S)-*i*Pr-pybox) ligand may affect enantioselectivity. The most obvious point of modification is the R groups on the oxazoline moieties. However, the synthesis and mechanistic analysis of a multitude of R-pybox ligands would be expected to be costly and time-consuming. Hence, it is better to computationally examine a generalized mechanism of R-pybox catalysis that may be systematically and rapidly adapted for different R groups, for high-throughput screening of new R-pybox catalysts for asymmetric Negishi coupling.

A generalized catalytic mechanism for the Ni(R-pybox) complexes is given in Scheme 5.10. The starting complex  $Ni^{I}(R-pybox)Br$ , **G**, is oxidized and methylated to  $Ni^{III}(R-pybox)(Me)(ind)Br$  (not shown). The  $Ni^{III}(R-pybox)(Me)(ind)Br$  species, which can exist in three geometric isomers

**Figure 5.4.** Transition states for the reductive elimination of 1-methylindane from various Ni<sup>III</sup>- $((S, S)-i\Pr$ -pybox)(Me)ind species. All numbers are in kcal/mol and relative to  $[Ni^{III}((S, S)-i\Pr$ -pybox)- $Br^{eq}((S)-ind)^{ax}-Me^{ax}-ZnI(dma)_2]^+$ . The lowest transition states for the formation of (R)- and (S)-1-methylindane are highlighted in green and blue, respectively.

-Me

1. Neutral



Figure 5.5. Reaction coordinate diagram of the entire catalytic cycle for the coupling of ind-Br and MeZnI to form ind-Me. All numbers are in kcal/mol and relative to  $[Ni^{III}((S,S)-iPr-pybox)Br^{eq}-((S)-ind)^{ax}-Me^{ax}-ZnI(dma)_2]^+$ .



A1, A2, and A3, may lose  $Br^-$  to form the five coordinate cationic  $[Ni^{III}(R-pybox)(Me)ind]^+$ species B1, B2, and B3, respectively. A DMA solvent molecule may then coordinate to the open coordination site to form cationic  $[Ni^{III}(R-pybox)(Me)(ind)dma]^+$  species C1, C2, and C3, respectively. Neutral A1 and A2 (but not A3) may also undergo reductive elimination through the transition states D1 and D2, respectively, to release methylindane and reform the starting complex G. Likewise, B1, B2, and B3 may undergo reductive elimination through E1, E2, and E3, respectively, to release methylindane and form cationic  $[Ni^{I}(R-pybox)]^+$ , H, which can regain the bromide to reform the starting complex G. Finally, cationic C1 and C2 (but not C3) may undergo reductive elimination through the transition states F1 and F2, respectively, to release methylindane and cationic  $[Ni^{I}(R-pybox)dma]^+$ , J, which can replace its dma ligand with a bromide to reform the starting complex G.

In order to rapidly calculate the enantioselectivity of Ni(R-pybox) catalysts containing different R groups, we simply need to find the transition states **D**, **E**, and **F**. (In our future analyses, we will also consider Zn adducts as well, but that is not included in this study.) For our demonstration, we have selected potential R groups to be adamantyl (Ad), cyclohexyl (Cy), methyl (Me), phenyl (Ph), (R)-sec-butyl ((R)-sBu), (S)-sec-butyl ((S)-sBu), tert-butyl (tBu), and 2-phenylethyl  $(C_2H_4Ph)$ . In addition, we also considered the a variant pyridine bis(indenoxazoline) ligand with fused indane rings, which we term pybindox. These are shown in Figure 5.6.

Our results are given in Table 5.3. A complete collection of all calculated intermediate and transition state energies is given in Tables 5.4 through 5.6 in Section 5.7.

Despite the variety of different R groups investigated, several universal characteristics may be observed from the data in Tables 5.3 through 5.6. In every case, the lowest energy intermediate was a neutral **A** species, usually the **A2** isomer. However, the lowest transition states are of type **E**,



Scheme 5.10. A generalized catalytic mechanism that Ni(R-pybox) complexes undergo in Negishi coupling. This scheme is used to rapidly calculate the predicted enantioselectivity of a variety of complexes related to the original Ni(*i*Pr-pybox) system.

Figure 5.6. Modified ligands studied which, when complexed to Ni, may allow for different enantioselective properties as compared to the original (iPr-pybox) ligand.



	[Ni <sup>III</sup> (	L)(Mein	d)Br] $^{\ddagger}$ (D)	[Ni <sup>III</sup> (	L)(Mein	$d)]^{+\ddagger} (E)$	$[Ni^{III}(L)(Me-ind)dma]^{+\ddagger}(\mathbf{F})$			
R	minim	um $\Delta G^{\ddagger}$	$\Delta \Lambda C^{\ddagger}$	minim	um $\Delta G^{\ddagger}$	$\Delta \Delta C^{\ddagger}$	minimum $\Delta G^{\ddagger}$		$\Delta \Delta G^{\ddagger}$	
	(R)	(S)		(R)	(S)		(R)	(S)		
$i \Pr$	18.4	17.3	1.1	15.7	12.4	3.3	16.4	15.3	1.1	
Ad	19.1	19.6	-0.5	14.9	16.4	-1.5	19.3	17.2	2.1	
Су	28.5	28.9	-0.3	20.3	18.8	1.5	N/A	30.9	N/A	
Me	20.3	18.9	1.4	15.2	13.8	1.4	N/A	19.2	N/A	
Ph	17.7	16.2	1.6	14.9	12.6	2.3	17.1	15.8	1.3	
$(R)-s\mathrm{Bu}$	18.3	15.7	2.6	12.5	12.1	0.5	N/A	N/A	N/A	
$(S)-s\mathrm{Bu}$	18.1	17.0	1.2	15.4	13.5	1.9	N/A	16.5	N/A	
t Bu	18.9	18.9	0.0	16.1	16.7	-0.6	19.5	18.3	1.2	
$\mathrm{C_2H_4Ph}$	17.5	19.4	-1.9	12.8	10.7	2.1	N/A	14.7	N/A	
pybindox	20.5	18.9	1.7	13.7	13.3	0.3	17.3	15.0	2.3	

Table 5.3. Comparison of activation energies for transition states of type **D**, **E**, and **F** for various Ni(R-pybox) catalysts. The Ni(*i*Pr-pybox) data is also given here for comparison. For each transition state type, only the energy of the lowest geometric isomer is reported. For all R groups, cationic five-coordinate transition states (**E**) were most favored. The (R)- $(S) \Delta\Delta G^{\ddagger}$  value is also calculated for each transition state type and (R-pybox) ligand. All numbers are in kcal/mol. Energies given are relative to the lowest calculated type **A** neutral Ni<sup>III</sup>(R-pybox)(Me)(ind)Br complex. Numbers in blue are the lowest energy transition states for the production of (R)-1-methylindane, whereas numbers in red are the lowest energy transition states for the production of (S)-1-methylindane. Numbers in green are the final  $\Delta\Delta G^{\ddagger}$  values for each R. (L) is ((S, S)-R-pybox).

although the particular isomer (i.e. **E1**, **E2**, or **E3**) may vary. The enantioselectivity as measured by  $\Delta\Delta G^{\ddagger}$  varies from -1.5 to 2.3 kcal/mol, in all cases inferior to the original Ni(*i*Pr-pybox)'s  $\Delta\Delta G^{\ddagger}$  value of 2.7 kcal/mol. In our future studies, we will seek to gain more accurate  $\Delta\Delta G^{\ddagger}$  values for our existing R groups by also considering Zn adduct formation, as we have done for Ni(*i*Pr-pybox); and broaden our search to examine more R groups.

### 5.6 Conclusions

In this chapter, we have computationally studied the mechanism of the Ni(*i*Pr-pybox) system, which is a enantioselective and stereoconvergent Negishi C–C coupling catalyst. Our results support existing experimental and theoretical evidence that the mechanism proceeds through a Ni<sup>I</sup>-Ni<sup>III</sup> cycle, with the stereochemistry of the initial ind–Br destroyed by homolytic cleavage of the C–Br bond. We found that Ni<sup>I</sup>((S, S)-*i*Pr-pybox)Br is initially oxidized by ind–Br, and then methylated to form Ni<sup>III</sup>((S, S)-*i*Pr-pybox)(Me)(ind)Br, which can form an adduct with Zn to result in the resting state [Ni<sup>III</sup>((S, S)-*i*Pr-pybox)Br<sup>eq</sup>((S)-*i*Mr-pybox)(Me)<sup>ax</sup>-Me<sup>ax</sup>-ZnI(dma)<sub>2</sub>]<sup>+</sup>. Reductive elimination then proceeds through either [Ni<sup>III</sup>((S, S)-*i*Pr-pybox)(Me)<sup>ax</sup>((R)-ind)<sup>eq</sup>-Br<sup>ax</sup>-ZnBr<sub>2</sub>I]<sup>-</sup> at an overall barrier of 18.6 kcal/mol to form (R)-1-methylindane), or [Ni<sup>III</sup>((S, S)-*i*Pr-pybox)-(Me)<sup>ax</sup>((S)-*i*Mr)<sup>eq</sup>]<sup>+</sup> at an overall barrier of 15.9 kcal/mol to form (S)-1-methylindane, with an enantioselectivity of  $\Delta\Delta G^{\ddagger} = 2.7$  kcal/mol preference for forming the (S) enantiomer. These results are also in line with experimental evidence.

In addition, we formulated a systematic approach that allows us to rapidly study related Ni-(R-pybox) systems, where R is Ad, Cy, Me, Ph, (R)-sBu, (S)-sBu, tBu, or  $C_2H_4Ph$ , or the ligand is pybindox. For these cases, we have found  $[Ni^{III}(R-pybox)(Me)(ind)]^+$  (E) to be universally the lowest energy transition states for the production of either (R)- or (S)-1-methylindane. Our  $\Delta\Delta G^{\dagger}$  values measured range from -1.5 to 2.3 kcal/mol, which are not as good as the original Ni(iPr-pybox). We are continuing to improve our screening system and broadening our scope to find new catalysts for efficient asymmetric and stereoconvergent catalysis for C-C coupling.

### 5.7 Supporting figures

Scheme 5.11 is an expanded diagram of the Ni<sup>II</sup> pathway, whose essential features were presented in Scheme 5.8. Although methylation of Ni<sup>II</sup>((S, S)-iPr-pybox)Br<sub>2</sub> to Ni<sup>II</sup>((S, S)-iPr-pybox)(Me)Br is uphill by 5.4 kcal/mol, further methylation to Ni<sup>II</sup>((S, S)-iPr-pybox)Me<sub>2</sub> is uphill by an additional 16.7 kcal/mol. Reductive elimination of ethane is thermodynamically favorable, but the loss of methyl radical from either Ni<sup>II</sup>((S, S)-iPr-pybox)(Me)Br or Ni<sup>II</sup>((S, S)-iPr-pybox)Me<sub>2</sub> is very uphill. Hence, the overall barrier to ethane production is at least 22.1 kcal/mol, the energy of the lowest Ni<sup>II</sup>((S, S)-iPr-pybox)Me<sub>2</sub> species.

Scheme 5.12 is an expanded version of Scheme 5.9, showing the methylation of Ni<sup>III</sup>((S, S)-iPr-pybox)Br<sub>2</sub>((S)-ind) to [Ni<sup>III</sup>((S, S)-iPr-pybox)Br(ind)Me, as well as all side reactions and isomers investigated.

Scheme 5.13 shows the reactions of Ni<sup>III</sup>((S, S) - iPr-pybox)(Br)(ind)Me that lead to ind-Me reductive elimination. (*R*)- and (*S*)-1-methylindane are produced in separate pathways, highlighted in red and blue, respectively. The overall barriers are 18.6 kcal/mol for the production of (*R*)-1-methylindane and 15.9 kcal/mol for production of (*S*)-1-methylindane, leading to a  $\Delta\Delta G^{\ddagger}$  preference of 2.7 kcal/mol for the (*S*) isomer.

Tables 5.4 through 5.6 show the calculated energies of all transition states and intermediates **A** through **J** for the high-throughput screening of Ni(R-pybox) catalysts, where R is Ad, Cy, Me, Ph, (R)-sBu, (S)-sBu, tBu, or  $C_2H_4Ph$ , or the ligand is pybindox. Specifically, Table 5.4 shows the neutral sequence  $\mathbf{A} \longrightarrow \mathbf{D} \longrightarrow \mathbf{G}$ ; Table 5.5 shows the cationic sequence  $\mathbf{B} \longrightarrow \mathbf{E} \longrightarrow \mathbf{H}$ ; and Table 5.6 shows the cationic sequence  $\mathbf{C} \longrightarrow \mathbf{F} \longrightarrow \mathbf{J}$  (see Scheme 5.10). A future study will also include Ni-Br-Zn adducts as well.



Scheme 5.11. Expanded diagram of Ni<sup>II</sup>((S, S) - iPr-pybox)Br<sub>2</sub> methylation as part of the Ni<sup>II</sup> pathway. The lowest energy Ni<sup>II</sup>((S, S) - iPr-pybox)MeBr complex is 5.4 kcal/mol higher than the starting Ni<sup>II</sup>((S, S) - iPr-pybox)Br<sub>2</sub>, and the lowest energy Ni<sup>II</sup>((S, S) - iPr-pybox)Me<sub>2</sub> complex is 22.1 kcal/mol higher than the starting Ni<sup>II</sup>((S, S) - iPr-pybox)Br<sub>2</sub>. All numbers are in kcal/mol and relative to Ni<sup>II</sup>((S, S) - iPr-pybox)Br<sub>2</sub>. The lowest Ni<sup>II</sup>((S, S) - iPr-pybox)Br<sub>2</sub>, Ni<sup>II</sup>((S, S) - iPr-pybox)(Me)Br, and Ni<sup>II</sup>((S, S) - iPr-pybox)Me<sub>2</sub> species are highlighted in red.



Scheme 5.12. Expanded diagram of Ni<sup>III</sup>((S, S) - iPr-pybox)Br<sub>2</sub>((S)-ind) methylation as part of the Ni<sup>III</sup> pathway. All numbers are in kcal/mol and relative to Ni<sup>III</sup>((S, S) - iPr-pybox)Br<sub>2</sub>((S)-ind). Red denotes the lowest point and thermodynamic sink, [Ni<sup>III</sup>((S, S) - iPr-pybox)Br<sup>eq</sup>((S)-ind)<sup>ax</sup>-Me<sup>ax</sup>-ZnI(dma)<sub>2</sub>]<sup>+</sup>, as well as an alternative thermodynamic sink Ni<sup>III</sup>((S, S) - iPr-pybox)Br<sup>ax</sup>((S)-ind)<sup>eq</sup>-Br<sup>ax</sup>-Zn<sup>R</sup>MeI(dma); and green the highest point, Ni<sup>III</sup>((S, S) - iPr-pybox)Br<sup>ax</sup>(ind)<sup>ax</sup>Me<sup>eq</sup> + ZnBrI(dma), in the production of [Ni<sup>III</sup>((S, S) - iPr-pybox)(Br)(ind)Me.



Scheme 5.13. The reactions of the various  $Ni^{III}((S,S)-iPr-pybox)(Me)$  ind species that lead to the reductive elimination of ind-Me. All numbers are in kcal/mol and relative to  $[Ni^{III}((S,S)-iPr-pybox)Br^{eq}((S)-ind)^{ax}-Me^{ax}-ZnI(dma)_2]^+$ . The starting point is  $Ni^{III}((S,S)-iPr-pybox)(Br)^{ax}(ind)^{ax}Me^{eq}$ , which was produced at the end of Schemes 5.9 or 5.12; the end point is  $Ni^{I}((S,S)-iPr-pybox)Br$ . Both the starting and end points are highlighted in red. The lowest energy pathways leading to the formation of (R)- and (S)-1-methylindane are highlighted in green and blue, respectively, when separate and in purple when concurrent.

	Ni <sup>III</sup>	((S,S)	-R-p	ybox)	(Me)(ii	nd)Br	[Ni <sup>II</sup>	$^{II}(L)(Me)$	eind)l	Br]‡	Ni <sup>I</sup> (L)Br	
R	Α	.1	A2		A	.3	L	01	D2		G	
	(R)	(S)	(R)	(S)	(R)	(S)	(R)	(S)	(R)	(S)	U	
Ad	4.9	2.8	2.1	0.0	$5.0^{a}$	10.3	$19.1^{b}$	$19.6^{b}$	21.3	20.0	-23.9	
Су	$9.8^{b}$	8.1	2.1	0.0	$6.7^{a}$	11.3	$28.5^{b}$	$28.9^{b}$	32.5	32.5	-24.1	
Me	5.8	2.1	1.4	0.0	7.7	6.6	20.3	18.9	21.0	19.9	-27.2	
Ph	0.0	1.7	1.2	1.2	9.4	8.4	17.7	16.2	19.0	19.0	-21.7	
$(R)-s\mathrm{Bu}$	3.8	0.7	2.7	0.0	$3.7^{a}$	6.8	18.3	15.7	20.5	19.8	-32.1	
(S)-sBu	3.0	1.0	2.3	0.0	8.2	6.1	18.1	17.0	21.3	22.1	-27.5	
$t\mathrm{Bu}$	5.0	3.1	2.1	0.0	$4.8^{a}$	9.8	$18.9^{b}$	$18.9^{b}$	21.3	19.9	-25.3	
$\mathrm{C_2H_4Ph}$	2.5	0.9	2.6	0.0	9.5	6.2	17.6	19.4	17.5	20.0	-27.3	
pybindox	5.5	2.5	1.3	0.0	5.8	5.0	20.5	18.9	21.0	20.5	-28.0	

**Table 5.4.** Relative energies of the neutral **A**, **D**, and **G** species for various Ni(R-pybox) complexes. All numbers are in kcal/mol. Energies given are relative to the lowest calculated type **A** neutral Ni<sup>III</sup>(R-pybox)(Me)(ind)Br complex. Numbers in blue are the lowest energy (R)-ind geometric isomers for **A** and **D**, whereas numbers in red are the lowest energy (S)-ind geometric isomer for **A** and **D**. (L) is ((S,S)-R-pybox). a) The Ni-ind bond is very long and likely to be very labile. b) An oxazoline ligand is dissociated from the Ni center in the geometry optimized structure.

	[N	$i^{III}((S,$	S)-R	-pybe	ox)(Me)(ir	nd)] <sup>+</sup>		[Ni <sup>I</sup>	$^{II}(L)(N$	feind	)] <sup>+‡</sup>		$[Ni^{I}(L)]^{+}$
R	B	1	B	<b>2</b>	В	3	E	1	E2		E	3	н
	(R)	(S)	(R)	(S)	(R)	(S)	(R)	(S)	(R)	(S)	(R)	(S)	11
Ad	13.6	9.5	6.6	5.3	$16.3^{a}$	$N/A^ac$	21.2	19.1	14.9	16.4	$N/A^{c}$	$N/A^c$	-13.0
Су	8.8	7.5	5.6	5.0	$11.7^{a}$	$10.6^{a}$	$N/A^c$	$N/A^c$	20.3	19.4	26.6	18.8	-15.1
Me	11.1	6.5	3.3	2.9	$14.9^{a}$	13.2	$N/A^d$	$N/A^d$	15.2	14.9	17.1	13.8	-5.4
Ph	10.4	6.5	4.3	2.5	$15.2^{a}$	13.6	14.9	12.6	15.1	14.8	$N/A^{c}$	$N/A^c$	-9.7
(R)-sBu	7.9	5.1	2.7	0.9	$16.1^{a}$	$12.4^{a}$	12.5	12.1	13.8	14.0	$N/A^{c}$	$N/A^b$	-18.4
(S)-sBu	9.4	6.7	4.6	3.3	$16.0^{a}$	13.1	15.4	13.5	15.8	16.0	$N/A^{c}$	$N/A^b$	-13.4
tBu	5.8	10.1	5.9	4.9	$N/A^ac$	$12.4^{a}$	16.1	19.7	16.9	16.7	$N/A^{c}$	20.7	-16.2
$C_2H_4Ph$	8.1	0.6	2.6	1.9	$15.7^{a}$	12.7	14.6	7.0	9.1	9.6	12.1	10.3	-16.3
pybindox	10.8	6.2	2.5	1.5	$N/A^ac$	12.6	17.3	16.2	13.7	13.3	$N/A^{c}$	15.2	-11.6

**Table 5.5.** Relative energies of the cationic **B**, **E**, and **H** species for various Ni(R-pybox) complexes. All numbers are in kcal/mol. Energies given are relative to the lowest calculated type **A** neutral Ni<sup>III</sup>(R-pybox)(Me)(ind)Br complex. Numbers in blue are the lowest energy (R)-ind geometric isomer for **B** and **E**, whereas numbers in red are the lowest energy (S)-ind geometric isomer for **B** and **E**. (L) is ((S, S)-R-pybox). a) The Ni-ind bond is very long and likely to be very labile. b) Geometry optimized to a Me<sup>ax</sup>ind<sup>eq</sup> (**B1/E1**) configuration. c) Geometry optimized to a Me<sup>eq</sup>ind<sup>ax</sup> (**B2/E2**) configuration. d) Geometry optimized to a Me<sup>ax</sup>ind<sup>ex</sup> (**B3/E3**) configuration.

	[Ni <sup>III</sup>	((S,S))	-R-py	pox)(Me	e)(ind)	$dma]^+$	[Ni <sup>II</sup>	<sup>I</sup> (L)(Me	ind)dm	ıa] <sup>+</sup> ‡	$[Ni^{I}(L)dma]^{+}$
R	0	C1	C2		0	C <b>3</b>	F	<b>`1</b>	F	2	т
	(R)	(S)	(R)	(S)	(R)	(S)	(R)	(S)	(R)	(S)	J
Ad	4.1	1.5	0.9	-0.3	$4.9^{a}$	$2.6^{a}$	19.3	17.2	$N/A^b$	$N/A^b$	-25.9
Су	7.4	6.9	1.3	0.6	$4.8^{a}$	$5.4^a$	$N/A^b$	30.9	$N/A^b$	$N/A^b$	-27.2
Me	3.8	3.5	3.1	2.5	$7.0^{a}$	$6.4^a$	$N/A^b$	19.2	$N/A^b$	$N/A^b$	-24.6
$\mathbf{Ph}$	0.4	2.3	2.6	1.7	$3.9^a$	$2.8^{a}$	17.1	15.8	$N/A^b$	$N/A^b$	-25.7
$(R)-s\mathrm{Bu}$	1.7	-0.2	3.8	1.6	$7.9^{a}$	$3.2^a$	$N/A^b$	$N/A^b$	$N/A^b$	$N/A^b$	-30.0
$(S)-s\mathrm{Bu}$	1.8	1.9	3.3	1.4	$7.1^{a}$	$4.3^a$	$N/A^b$	16.5	$N/A^b$	$N/A^b$	-27.3
t Bu	5.8	3.1	2.8	0.8	$5.1^{a}$	$5.6^{a}$	19.5	18.3	$N/A^b$	$N/A^b$	-26.5
$\mathrm{C_2H_4Ph}$	4.3	2.7	1.2	-0.6	$4.5^{a}$	$4.5^{a}$	$N/A^b$	14.7	$N/A^b$	$N/A^b$	-28.2
pybindox	3.7	-0.1	-0.7	-2.6	$4.4^{a}$	$3.5^a$	17.3	15.0	$N/A^b$	$N/A^b$	-25.2

**Table 5.6.** Relative energies of the cationic **C**, **F**, and **J** species for various Ni(R-pybox) complexes. All numbers are in kcal/mol. Energies given are relative to the lowest calculated type **A** neutral Ni<sup>III</sup>(R-pybox)(Me)(ind)Br complex. Numbers in blue are the lowest energy (R)-ind geometric isomer for **C**, whereas numbers in red are the lowest energy (S)-ind geometric isomer for **C**. (L) is ((S, S)-R-pybox). a) The Ni-ind bond is very long and likely to be very labile. b) A species containing a Ni-dma bond could not be found.

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## Appendix A

## C–H activation using Rh<sup>1</sup> complexes supported by bis-nitrogen chelating ligands

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#### A.1 Abstract

Rhodium (I) complexes  $(DAB^F)Rh(COE)(TFA)$  **1** and (BOZO)Rh(COE)(TFA) **2**  $((DAB^F) = N, N$ bis(pentafluorophenyl)-2,3-dimethyl-1,4-diaza-1,3-butadiene, (COE) = cyclooctene, (TFA) = trifluoroacetate, <math>(BOZO) = bis(2-oxazolin-2-yl) have been synthesized. Complexes **1** and **2** are catalyst precursors for the efficient C–H bond activation of arenes with TFA–D. DFT calculations determined that H/D exchange is possible through reversible oxidative addition of benzene onto the Rh<sup>I</sup> complex. Catalyst **1** is reported to have a TOF of 227.5 h<sup>-1</sup> and is the most active H/D exchange catalyst reported to date.

#### A.2 Introduction

In the search for a rhodium analogue to the Shilov cycle catalyst, putative rhodium complexes are often first experimentally tested for their C–H activation ability by investigating their ability to catalyze the exchange of hydrogen and deuterium atoms on various aliphatic and aromatic substrates. towards this end, Kloek, Heinekey, and Goldberg have reported an example of a rhodium complex containing a (PNP) pincer ligand that catalyzes the H/D exchange of benzene with D<sub>2</sub>O with a turnover frequency (TOF) of 0.1 h<sup>-1</sup> [1]. Goldberg and Jones et al. have also reported H/D exchange with deuterated trifluoroacetic acid (TFA–D) and benzene with a pendant acetate rhodium complex, which had a TOF of 1.6 h<sup>-1</sup> [2]. Despite the success of these rhodium catalysts for the C–H activation of arenes, the rates of reaction as determined by turnover frequency have been significantly slower, e.g., by an order of magnitude, than comparable results for Pd and Pt based catalysts [3]. Bidentate nitrogen chelating ligands have been used successfully for H/D exchange with these Pd and Pt systems. In this chapter we report the reactivity and computational study of two new rhodium complexes with bidentate nitrogen chelating ligands which have rates of arene H/D exchange comparable to platinum/palladium systems.

#### A.3 Materials and methods

Experimentally, complexes  $(DAB^{F})Rh(COE)(TFA)$  **1** and (BOZO)Rh(COE)(TFA) **2**  $((DAB^{F}) = N, N$ -bis(pentafluorophenyl)-2,3-dimethyl-1,4-diaza-1,3-butadiene, (COE) = cyclooctene, (TFA) = trifluoroacetate, (BOZO) = bis(2-oxazolin-2-yl)) (Scheme A.1) were synthesized by reaction of  $[(COE)_{2}Rh(TFA)]_{2}$  dimer with 1 equivalent of ligand in THF at room temperature for 1 hour to afford **1** and **2** as purple solids in 58% and 73% yield, respectively. Both of these complexes were characterized by <sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F NMR spectroscopy, and elemental analysis.

Computational investigations were made as described in Section 3.3.

#### A.4 Results and discussion

#### A.4.1 Experimental results

We screened these rhodium complexes for C–H activation by monitoring H/D exchange between  $d_1$ -trifluoroacetic acid and benzene. Under our conditions (1.6 mol % Rh, 1 equiv. C<sub>6</sub>H<sub>6</sub> in 17.5 equiv. of  $d_1$ -trifluoroacetic acid, 2 hours, 800 psi Ar, at 130°C), both complexes **1** and **2** showed rapid H/D exchange with turnover numbers of  $89 \pm 13$  and  $90 \pm 11$ , respectively, resulting in turnover frequencies (TOFs) of 0.01 s<sup>-1</sup> over the 2 hour period for both catalysts, as determined by GC-MS. Minimal turnovers were detected for the reaction of just [(COE)<sub>2</sub>Rh(TFA)]<sub>2</sub> in trifluoroacetic acid



Scheme A.1. Synthesis of rhodium H/D exchange catalysts  $(DAB^F)Rh(COE)(TFA)$  1 and (BOZO)Rh(COE)(TFA) 2.

under our conditions.

Measuring the effect of temperature on catalysis (Figure A.1) shows that highest turnovers at 2 hours occur at 150°C. TON decreases at temperatures above 150°C, most likely due to catalyst decomposition. Complex **2** has the highest TON when the temperature is 130°C, with a decrease in turnovers at higher temperatures.

Figure A.1. Temperature dependence vs. turnover numbers for complexes 1 and 2. Reactions were performed using 1.6 mol % Rh, 1 equiv.  $C_6H_6$  in 17.5 equiv.  $d_1$ -trifluoroacetic acid, for 2 hours, under 800 psi Ar.



To determine the optimal solvent for catalysis, H/D exchange of benzene was then examined with other deuterated solvents at the optimized temperature. However, no significant measurable H/D exchange of benzene above the background reactions was observed for  $D_2O$ ,  $CD_3OD$ ,  $D_3PO_4$ ,  $D_2SO_4$ , or  $CD_3COOD$  for either 1 or 2.

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We then sought to determine the dependence on catalyst concentration. By lowering the catalyst loading to 0.4% relative to benzene, a large increase in TON was observed (Figure A.2). After 2 hours at 150°C, complex 1 showed 456 TON to give a TOF of 228  $h^{-1}$ .





The selectivity of the reaction mechanism was determined by examining the H/D exchange of toluene in trifluoroacetic acid at each catalyst's respective optimal temperature. The *ortho:meta:para* selectivity is 6.87 : 1 : 6.39 and 5.68 : 1 : 5.24 for **1** and **2**, respectively. No clear deuteration of the methyl fragment of toluene was seen.

A crucial aspect of catalysis is the recyclability of the catalyst. To study this, each complex was run and sampled, and then the contents of the reaction were evaporated off, leaving behind the catalyst. Fresh trifluoroacetic acid and benzene were added to the reaction vessel and the experiment was run again. For complex 1, this was successfully done over four times for a period of over 72 hours, with H/D exchange observed each time.

An interesting question is the role of cyclooctene in the mechanism. The addition of cyclooctene to the experiment showed a clear decrease in turnover number for complex **2**. We hypothesized that this is due to COE binding to the rhodium metal competitively to slow down catalysis. However, upon careful consideration of the <sup>1</sup>H and <sup>13</sup>C NMR spectra, clear peaks for the trifluoroacetate adduct of cyclooctene can be seen. Indeed, a report from Nordlander indicates that cyclooctene in trifluoroacetic acid funnels to a cyclooctyl trifluoroacetate complex [4]. Attempts to synthesize either complex with a trifluoroacetic acid ligand instead of cyclooctene were unsuccessful.

Attempts to extend this reactivity to substrates other than aromatics were investigated. H/D exchange was attempted with methane under a variety of pressures and temperatures; however, no

deuterated methane species was observed by GC-MS. In addition, H/D exchange of benzene  $sp^2$  C-H bonds with cyclohexane was also attempted, but no deuteration was observed after 2 hours at the optimal conditions for each catalyst.

#### A.4.2 Computational results

We have also undertaken a computational investigation for the mechanism of H/D exchange by complexes 1 and 2. We set our reference complex to (L)Rh(TFA)(TFAH) (3 and 4 for  $L = (DAB^F)$  or (BOZO), respectively); these being the presumed species after the (COE) ligand is hydrotrifluoroacetylated off from the base (L)Rh(TFA)(COE) species. We hypothesized that C-H activation of benzene could proceed through one of two routes. The first route is by direct oxidative addition to (L)Rh<sup>I</sup>(TFA)(TFAH) to form (L)Rh<sup>III</sup>(TFA)(TFAH)(Ph)(H). H/D exchange could then occur because the Rh<sup>III</sup>(H) bond can be reversibly reductively deprotonated: Rh<sup>III</sup>(TFA)(H)  $\rightleftharpoons$  Rh<sup>I</sup>(TFAH). The second is by an internal protonation (L)Rh<sup>I</sup>(TFA)(TFAH)  $\longrightarrow$  (L)Rh<sup>III</sup>(TFA)<sub>2</sub>(H), followed by either benzene coordination and deprotonation by TFA *via* a six-membered ring transition state, or direct hydrogen exchange with the Rh<sup>III</sup>(H) hydride. We found that, in both the (DAB<sup>F</sup>) and (BOZO) ligands, the first scenario (direct oxidative addition) was more likely, with lower transition states.

Direct oxidative addition of benzene by **3** or **4** is shown in Scheme A.2. The lowest barrier found for **3** is 22.2 kcal/mol at 298 K and 23.7 kcal/mol at 498 K. In contrast, the lowest barrier found for **4** is 18.5 kcal/mol at 298 K and 19.5 kcal/mol at 498 K. All of these values imply accessible benzene oxidative addition at the reaction temperatures investigated. The increased activity of **3** compared to **4** is most likely simply due to the increased temperature that H/D exchange with catalyst **1** can be run without decomposition. A comparison of direct oxidative addition and benzene coordination/deprotonation is shown in Scheme A.3 for complex **3** and Scheme A.4 for complex **4**.



Scheme A.2. Oxidative addition of benzene by  $Rh(DAB^F)$  and Rh(BOZO) complexes 3 and 4. H/D exchange most likely proceeds through these transition states. All free energies in kcal/mol.

Methane activation by complex 3, in a manner analogous to benzene activation, was also in-



Scheme A.3. The  $Rh(DAB^F)$  complex 3 activates benzene with a barrier of 22.2 kcal/mol at 298 K and 23.7 kcal/mol at 498 K. Top row: direct oxidative addition of benzene by  $Rh^I$ . Elsewhere: internal oxidative addition of 3 followed by benzene coordination. All free energies in kcal/mol.



**Scheme A.4.** The Rh(BOZO) complex **4** activates benzene with a barrier of 18.5 kcal/mol at 298 K and 19.5 kcal/mol at 498 K. Bottom row, first and second TSs: Direct oxidative addition of benzene by Rh<sup>I</sup>. Elsewhere: internal oxidative addition followed by benzene coordination. All free energies in kcal/mol.

vestigated, with the results shown in Scheme A.5. The Rh(Me) intermediates and transition states were approximately 7-19 kcal/mol higher in energy than their Rh(Ph) counterparts. In particular, the direct oxidative addition of methane has in its lowest transition state a barrier of 32.4 kcal/mol at 298 K and 37.6 kcal/mol at 498 K, which is prohibitively high under reaction conditions. This is consistent with the lack of experimentally observed methane activation by complex **1**.



Scheme A.5. Activation of methane by the  $Rh(DAB^F)$  complex 3 in a manner analogous to the oxidative addition of benzene (see Scheme A.3). The lowest transition state found has a barrier of 32.4 kcal/mol at 298 K and 37.6 kcal/mol at 498 K, rendering methane activation inaccessible. All free energies in kcal/mol.

### A.5 Conclusions

This work has demonstrated two efficient rhodium catalysts for H/D exchange between benzene and TFAD. To the best of our knowledge, catalyst 1 is the most active rhodium catalyst yet discovered for benzene H/D exchange. These results demonstrate TOFs similar to platinum and palladium systems. In addition, these rhodium complexes were studied under catalytically relevant conditions for industrial C-H activation and functionalization.

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## Appendix B

## Energy levels of group 10 transition metal atoms and ions

### B.1 Abstract

The energies of the group 10 transition metals (Ni, Pd, and Pt) in different configurations  $(d^8s^2, d^9s^1, \text{ and } d^{10})$  are calculated using various DFT methods. Furthermore, energies of the corresponding 1+ and 2+ ions are also calculated. The results of the various DFT methods are compared with the experimental energies [1] and previous calculations [2], with the purpose of determining the best DFT method for each atom. Finally, inconsistent energies in supposedly degenerate orbitals of the ionic states are observed and a potential solution is proposed.

Atom	Config.	Hartree Fock	Relativistic HF	Experimental
	$d^8s^2$	0.00	0.00	0.00
Nickel	$d^9s^1$	1.27	1.63	-0.03
	$d^{10}$	5.47	6.04	1.71
	$d^8s^2$	0.00	0.00	0.00
Palladium	$d^9s^1$	-3.01	-2.09	-2.43
	$d^{10}$	-3.76	-2.19	-3.38
	$d^8s^2$	0.00	0.00	0.00
Platinum	$d^9s^1$	-3.28	-0.40	-0.64
	$d^{10}$	-4.69	0.50	-0.16

Table B.1. Relativistic vs. nonrelativistic Hartree-Fock excitation energies, taken from Martin and Hay [2].

Relative energies in eV. The experimental energies are averages over spin-orbit components [1].

## **B.2** Introduction

Density function theory has found widespread application in computational chemistry as a fast alternative to *ab initio* calculations with correlation. However, the accuracy of DFT calculations is sometimes called into question in many transition metal-containing systems, due to the fact that transition metals often have several closely-spaced low-lying energy levels and that DFT is not always able to predict the correct ground state. In this report we present the results of calculations of the levels of Ni, Pd, and Pt with the following DFTs: B3LYP, M06, M06-2X, M06-HF, M06-L, PBE, PBE0, and XYGJ-OS (Ni only); and we contrast these with a few electron-correlation calculations, including HF, MP2, and CCSD, and with previous calculations done by Martin and Hay [2].

#### B.3 The neutral atom

The group 10 transition metals are notable in that each atom in the column has a different ground state electron configuration, viz.  $d^8s^2$  for Ni,  $d^{10}$  for Pd, and  $d^9s^1$  for Pt. While Ni conforms to the Aufbau principle, Pd and Pt do not. This is due to a complex interplay of electron correlation and relativistic effects. The ordering of the ground and excited states of Pd and Pt have long been known (Table B.1), but the identity of the ground state of Ni has been somewhat more contentious [3].

There are a few observations to note in Table B.1. First, the experimentally determined ground state of Ni is  $d^8s^2 {}^3F_4$ , but the energies in Table B.1 are averages over all J = 2, 3, 4, which in the case of Ni results in an energy that is slightly higher than the  ${}^3P$  average. Secondly, we find that relativistic corrections, though unnecessary for Ni, become important for Pd and absolutely vital for Pt. Finally, we find that the Hartree-Fock calculations do a poor job of ordering the configurations

Atom	Config.	Hartree Fock	Relativistic HF	Experimental
Nickel	$d^8s^2$	0.00	0.00	0.00
N;+	$d^9$	7.61	8.12	7.59
111	$d^8s^1$	6.98	7.09	8.67
Palladium	$d^8s^2$	0.00	0.00	0.00
$\mathbf{Pd}^+$	$d^9$	2.91	4.25	5.13
Iu	$d^8s^1$	6.36	6.66	8.32
Platinum	$d^8s^2$	0.00	0.00	0.00
$Pt^+$	$d^9$	2.68	7.26	8.46
ΙU	$d^8s^1$	6.26	7.51	9.22

Table B.2. Relativistic vs. nonrelativistic Hartree-Fock excitation energies for the M<sup>+</sup> ions [2].

Relative energies in eV.

Table B.3. Excitation energies of Pt atom as calculated by various DFTs.

Config.	Exp.	HF	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0
$d^9s^1$		-118.23	-119.08	-119.03	-118.95	-118.91	-119.08	-119.07	-119.04
$d^{10}$	11.07	25.41	14.67	0.40	11.72	24.95	14.01	14.39	15.03
$d^8s^2$	14.76	5.95	6.84	19.17	15.24	21.07	0.86	-0.05	9.08

The  $d^9s^1$  row contains the absolute energies in hartrees. The other rows contain the energies relative to the  $d^9s^1$  ground state, in kcal/mol. Experimental energies derived from Moore [1]. Color coding represents deviation from experimental value. Gray: within 1 kcal/mol; blue: within 5 kcal/mol; green: within 10 kcal/mol; yellow: within 15 kcal/mol.

for the Pt atom. Hence, the first part of this report shall many focus on DFT calculations of the Pt atom, with additional data for Ni and Pd for purposes of comparison.

We also examine the previously-calculated excitation energies for the singly-charged cations Ni<sup>+</sup>, Pd<sup>+</sup>, and Pt<sup>+</sup>. These numbers are taken from the same reference [2] and are reproduced in Table B.2.

Looking at the values in Table B.2, two things are apparent: First, the numbers for Ni<sup>+</sup>, while close, are in the wrong order, putting the  $d^8s^1$  configuration below the  $d^9$  configuration in energy. And secondly, while the HF calculations for Pd<sup>+</sup> and Pt<sup>+</sup> give the correct ground state configuration, the relative energies are significantly off. This report will also give updated excitation energy calculations for the singly-charged cations.

#### B.3.1 Platinum (0)

Calculations with Pt were performed on Jaguar version 7.5 [4]. The basis set used was a variant of  $LACV3P^{**}++$ , modified to include f functions [5]. The results are presented in Table B.3.

Table B.4.	Excitation	energies	of Pt	$\operatorname{atom}$	calculated	without	f functions.
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Config.	Exp.	HF	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0
$d^9s^1$		-118.23	-119.08	-119.03	-118.95	-118.91	-119.08	-119.07	-119.04
$d^{10}$	11.07	27.96	14.67	0.40	11.72	24.95	14.01	14.43	15.03
$d^{8}s^{2}$	14.76	1.41	5.10	12.22	15.04	21.11	6.99	0.02	8.24
$\delta\delta$ (a)		30.24	28.38	26.43	31.96	39.30	32.84	29.52	30.94
$\pi\pi$ (b)		8.50	12.77	19.62	19.46	30.11	16.22	15.22	15.26
$\sigma\delta$ (c)	14.76	1.25	7.57	17.36	15.30	27.04	10.68	10.50	10.03

The  $d^9s^1$  row contains the absolute energies in hartrees. The other rows contain the energies relative to the  $d^9s^1$  ground state, in kcal/mol. Experimental energies derived from Moore [1]. Color coding represents deviation from experimental value. Gray: within 1 kcal/mol; blue: within 5 kcal/mol; green: within 10 kcal/mol; yellow: within 15 kcal/mol.

(a) Energy of the  $d^8s^2$  configuration with singly occupied  $d_{xy}$  and  $d_{x^2-y^2}$  orbitals. (b) Energy of the  $d^8s^2$  configuration with singly occupied  $d_{xz}$  and  $d_{yz}$  orbitals. (c) Extrapolated energy of the ground  $d^8s^2$  configuration according to the formula  $E_{\sigma\delta} = \frac{4}{3}E_{\pi\pi} - \frac{1}{3}E_{\delta\delta}$ .

An examination of the data presented in Table B.3 shows that while most DFT methods are very good at predicting the  $d^9s^1 - d^{10}$  separation, they are considerably poorer at correctly ordering the  $d^8s^2$  state, often putting it near the  $d^9s^1$  state instead of above the  $d^{10}$  state. An examination of the molecular orbitals in the  $d^8s^2$  output files in Molden revealed considerable mixing of the d and s orbitals in some of the cases. Hence, the true configuration,  $d^9s^1$  or  $d^8s^2$ , could not be ascertained, and hence the values could not be trusted.

In order to prevent this catastrophic mixing of orbitals, the input files for the  $d^8s^2$  cases were rerun with the symmetry turned on (Table B.4, row 3). This prevented the basis set from using the added f functions. Fortunately, an examination of the rerun numbers for the  $d^9s^1$  and  $d^{10}$  cases (Table B.4, rows 1-2) showed that the f functions play a very minor role in the total energy and hence can be safely ignored.

Unfortunately, examination of the molecular orbitals in the  $d^8s^2$  output files in Molden revealed that there was still some mixing between the filled s orbital and the empty  $d_{z^2}$  orbital among the  $\beta$  electrons. This is due to both orbitals being totally symmetric in the point group used for the calculations ( $D_{4h}$  or its largest Abelian subgroup  $D_{2h}$ ). Hence, instead of calculating the lowest  $d^8s^2$ state directly, it may be more accurate to calculate higher  $d^8s^2$  states and extrapolate the ground  $d^8s^2$  (see Section B.6). The revised energies are given in Table B.4, rows 4-6.

Electron-correlation calculations were also performed on the Pt atom, on Q-Chem version 4.0 using the MP2 and CCSD methods on the LACVP basis set with ECP. A guess wavefunction with the correct orbital population was first generated by DFT methods, and then the electron-correlation values were calculated with the orbital overlap maximized. The results, given in Table B.5, are in decent agreement with the experimental values, but are not an improvement over DFT methods.

Table B.5. Excitation energies of Pt atom calculated using electron-correlation methods.

Config.	Exp.	MP2	CCSD
$d^9s^1$		-118.284	-118.289
$d^{10}$	11.07	13.41	16.83
$d^8s^2$	14.76	5.43	0.92
$\delta\delta$ (a)		30.16	12.41
$\pi\pi$ (b)		11.37	3.29
$\sigma\delta$ (c)	14.76	5.10	0.24

The  $d^9s^1$  row contains the absolute energies in hartrees. The other rows contain the energies relative to the  $d^9s^1$  ground state, in kcal/mol. Experimental energies derived from Moore [1]. Color coding represents deviation from experimental value. Blue: within 5 kcal/mol; green: within 10 kcal/mol; yellow: within 15 kcal/mol.

(a) Energy of the  $d^8s^2$  configuration with singly occupied  $d_{xy}$  and  $d_{x^2-y^2}$  orbitals.

(b) Energy of the  $d^8s^2$  configuration with singly occupied  $d_{xz}$  and  $d_{yz}$  orbitals.

(c) Extrapolated energy of the ground  $d^8s^2$  configuration according to the formula  $E_{\sigma\delta} = \frac{4}{3}E_{\pi\pi} - \frac{1}{3}E_{\delta\delta}$ .

Unfortunately, neither method gave the correct ordering of states; both methods put the singlet state at the highest energy. Furthermore, CCSD performed more poorly than MP2. This observation is probably due to the fact that CCSD is designed for calculating ground state energies.

We can draw several conclusions from the data presented for the Pt atom. First, DFT values are closer to the relativistic HF calculations than to the nonrelativistic calculations (see Table B.1). This is due to the effective core potential taking relativistic effects into account. Secondly, for the  $d^9s^1 - d^{10}$  transition, most DFTs gave values that were a little high, while the HF calculation gave a value that was much too high. Thirdly, most DFTs ordered the relative energy levels of the different configurations in the same way as Martin and Hay's relativistic HF values, differently from the experimental result. And finally, M06-2X gave the best values.

#### B.3.2 Palladium (0)

Calculations with Pd were performed on Jaguar version 7.5 using the basis set LACV3P<sup>\*\*</sup>++ [4], and on Q-Chem version 4.0 using the basis set LACVP [6]. The results from Jaguar are presented in Table B.6; however, it was difficult to calculate the  $d^8s^2$  configuration properly due to the wide separation from  $d^9s^1$  and the aforementioned symmetry issues. Hence, all DFT values were recalculated in Q-Chem; the results are presented in Table B.7. The  $d^{10} - d^9s^1$  energy gap is very similar to the numbers in Jaguar; hence we can expect reasonably accurate values for the  $d^8s^2$  configuration as well. In addition, the use of Q-Chem allows us to take advantage of the electron-correlation MP2 and CCSD methods.

It can be concluded from the tables for palladium that the best overall method was MP2, whereas

**Table B.6.**  $d^{10} - d^9 s^1$  Excitation energies of Pd atom as calculated by Jaguar.

Config.	Exp.	HF	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0
$d^{10}$		-125.87	-126.72	-126.72	-126.61	-126.52	-126.75	-126.68	-126.67
$d^9s^1$	21.91	1.97	20.79	38.15	27.53	10.89	28.16	22.28	20.72

The  $d^{10}$  row contains the absolute energies in hartrees. The  $d^9s^1$  row contains the energies relative to the  $d^{10}$  ground state, in kcal/mol. Experimental energy derived from Moore [1]. Color coding represents deviation from experimental value. Gray: within 2 kcal/mol; blue: within 5 kcal/mol; green: within 10 kcal/mol; yellow: within 15 kcal/mol.

Table B.7. Excitation energies of Pd atom as calculated by Q-Chem.

Config.	Exp.	HF	MP2	CCSD	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0
$d^{10}$		-125.87	-125.97	-125.96	-126.71	-126.71	-126.61	-126.51	-126.74	-125.90	-126.67
$d^9s^1$	21.91	1.72	22.42	15.95	19.98	38.63	26.07	10.09	30.66	9.43	19.99
$d^8s^2$	77.94	55.17	80.54	67.28	84.79	114.45	97.61	89.50	97.18	67.17	88.40

The  $d^{10}$  row contains the absolute energies in hartrees. The other rows contain the energies relative to the  $d^{10}$  ground state, in kcal/mol. Experimental energy derived from Moore [1]. Color coding represents deviation from experimental value. Gray: within 2 kcal/mol; blue: within 5 kcal/mol; green: within 10 kcal/mol; yellow: within 15 kcal/mol.

the best DFT calculation was B3LYP.

#### B.3.3 Nickel (0)

Unlike the cases for Pt and Pd, calculations with Ni were performed without any effective core potential, using the basis set G3LARGE with the program Q-Chem version 4.0. The results are summarized in Table B.8 for the electron-correlation methods and Table B.9 for the DFT methods.

It can be concluded from the tables for nickel that the best overall method was CCSD, whereas

Table B.8. Excitation energies of Ni atom as calculated by Q-Chem; electron-correlation methods.

Config.	Exp.	HF	MP2	CCSD
$d^{8}s^{2}$		-1506.83	-1507.83	-1507.78
$d^9s^1$	$-0.69^{*}$	1.72	-30.92	0.49
$d^{10}$	39.43	55.17	-44.60	47.07

The  $d^{10}$  row contains the absolute energies in hartrees. The other rows contain the energies relative to the  $d^{10}$  ground state, in kcal/mol. Experimental energy derived from Moore [1]. Color coding represents deviation from experimental value. Gray: within 2 kcal/mol; blue: within 5 kcal/mol; green: within 10 kcal/mol; red: within 25 kcal/mol.

\* See the discussion for Table B.1.

Table B.9. Excitation energies of Ni atom as calculated by Q-Chem; DFT methods.

Config.	Exp.	XYGJ-OS	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0
$d^{8}s^{2}$		-1507.36	-1508.31	-1508.19	-1508.24	-1508.35	-1508.03	-1506.75	-1508.02
$d^9s^1$	$-0.69^{*}$	-5.66	-9.11	-10.33	-3.59	-14.01	5.26	-12.30	-9.18
$d^{10}$	39.43	19.57	22.65	19.43	48.36	49.11	50.00	29.37	85.06

The  $d^{10}$  row contains the absolute energies in hartrees. The other rows contain the energies relative to the  $d^{10}$  ground state, in kcal/mol. Experimental energy derived from Moore [1]. Color coding represents deviation from experimental value. Blue: within 5 kcal/mol; green: within 10 kcal/mol; yellow: within 15 kcal/mol; red: within 25 kcal/mol.

\* See the discussion for Table B.1.

Table B.10. Excitation energies of the group 10 atoms from  $d^9$  to  $d^8s^1$ , as calculated using various DFTs.

	Exp.	XYGJ-OS	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0
$Ni^+ d^9$	175.03	390.57	173.62	166.76	167.85	156.59	75.48	164.53	167.67
$d^8s^1$	199.93	392.65	201.51	209.30	199.48	187.66	105.56	183.01	193.56
$\Delta E$	24.90	2.08	27.89	42.54	31.63	31.07	30.08	18.48	25.90
$Pd^+ d^9$	197.30	N/A	198.16	209.32	196.01	182.01	196.53	177.85	
$d^8s^1$	271.61	N/A	287.29	323.64	298.99	280.43	297.30	250.10	282.91
$\Delta E$	74.31	N/A	89.14	114.33	102.98	98.42	100.77	72.25	89.14
$Pt^+ d^9$	195.09	N/A	217.38	207.69	206.89	212.36	203.26	208.54	211.33
$d^8s^1$	212.62	N/A	242.80	253.62	242.30	238.70	237.12	233.96	235.47
$\Delta E$	17.53	N/A	25.42	45.92	35.41	26.34	33.86	25.42	24.14

All numbers are given in kcal/mol relative to  $d^8s^2$  for Ni,  $d^{10}$  for Pd, and  $d^9s^1$  for Pt. Experimental energy derived from Moore [1]. Color coding represents deviation from experimental value. Gray: within 2 kcal/mol; blue: within 5 kcal/mol; green: within 10 kcal/mol; yellow: within 15 kcal/mol; red: within 25 kcal/mol. XYGJ-OS not implemented for ECP; hence only Ni was calculated.

the best DFT calculation was M06-2X.

#### B.4 The singly-charged cation

Whereas the neutral group 10 metals each have different ground state configurations, the singlycharged cations Ni<sup>+</sup>, Pd<sup>+</sup>, and Pt<sup>+</sup> are uniformly  $d^9$  in the ground state. The excitation energy from  $d^9$  to  $d^8s^1$  for each metal has been calculated by various DFTs and electron-correlation methods. A summary of the results, along with the experimental values [1], is given in tables B.10 and B.11. All calculations were done on Q-Chem version 4.0. The G3LARGE basis set was used for Ni<sup>+</sup> while the LACVP basis set with ECP was used for Pd<sup>+</sup> and Pt<sup>+</sup>.

An examination of the data presented in tables B.10 and B.11 shows that CCSD is unequivocally the best method for  $Ni^+$ , while B3LYP is the best DFT method. M06-2X and PBE0 also gave good

	Exp.	HF	MP2	CCSD
$Ni^+ d^9$	175.03	252.85	140.27	167.93
$d^8s^1$	199.93	162.26	192.18	192.82
$\Delta E$	24.90	-90.59	51.91	24.90
$Pd^+ d^9$	197.30	147.93	176.65	171.10
$d^8s^1$	271.61	217.87	283.37	251.33
$\Delta E$	74.31	69.94	106.72	80.22
$Pt^+ d^9$	195.09	178.87	188.91	188.25
$d^8s^1$	212.62	188.39	205.44	205.81
$\Delta E$	17.53	9.52	16.54	17.57

**Table B.11.** Excitation energies of the group 10 atoms from  $d^9$  to  $d^8s^1$ , as calculated using various electroncorrelation methods.

All numbers are given in kcal/mol relative to  $d^8s^2$  for Ni,  $d^{10}$  for Pd, and  $d^9s^1$  for Pt. Experimental energy derived from Moore [1]. Color coding represents deviation from experimental value. Gray: within 2 kcal/mol; blue: within 5 kcal/mol; green: within 10 kcal/mol; red: within 25 kcal/mol.

results. As for  $Pt^+$ , both CCSD and MP2 gave excellent results. Unfortunately, there was no single method for  $Pd^+$  that gave good results for all energies: most methods were good at estimating the  $d^9$  state; only M06-HF and PBE0 came close to estimating the  $d^8s^1$  state; and HF, CCSD, and PBE were able to approximate the energy difference between the ion states well. Overall, however, these numbers are all nonetheless in better agreement with experimental data than the previous calculations as presented in Table B.2.

## B.5 Angular momentum-dependent artifacts in

## **DFT** calculations

During the course of calculating these energies it became apparent that certain artifacts were being introduced in the calculations of the cations. These errors have been documented before [7] and the reason is innate to the nature of the exchange functional of DFT [8]. Potential solutions have been proposed [9] [10] but not yet widely implemented.

# **B.5.1** Angular momentum of the electron/hole in the $d^1/d^9$ configuration of the cation

The various microstates of a  $d^1$  or  $d^9$  configuration give rise to only one permissible spin state: <sup>2</sup>D. Hence, it should not matter which real d orbital contains the electron or hole, respectively. However, we find that for DFT methods the calculated energy does vary: For example, according to B3LYP the
$d^9$ hole	LACV3I	P**++	LACY	V3P	LAV1S	
	Energy	$E_{rel}$	Energy	$E_{rel}$	Energy	$E_{rel}$
$z^2$	-118.739	0.000	-118.738	0.000	-26.961	0.000
xy	-118.741	-1.123	-118.740	-1.157	-26.960	0.791
$x^2 - y^2$	-118.741	-1.123	-118.740	-1.154	-26.960	0.870
xz	-118.737	1.141	-118.736	1.079	-26.958	1.591
yz	-118.737	1.141	-118.736	1.078	-26.958	1.591

**Table B.12.** "Degenerate" energies of the  $Pt^+$   $d^9$  ground state.

Calculations done in Jaguar. The "Energy" columns contain values in hartrees, whereas the " $E_{rel}$ " columns contain values in kcal/mol.

**Table B.13.** "Degenerate" energies of the  $Pt^{9+} d^1$  ground state.

$d^1$	Energy	$E_{rel}$
$z^2$	-98.151343	0.000
xy	-98.151819	-0.299
$x^2 - y^2$	-98.151822	-0.301
$xz^*$	-98.151822	-0.301
$yz^*$	-98.151822	-0.301

M06-2X/LACV3P\*\*++ done in Jaguar. The "Energy" column contains values in hartrees, whereas the " $E_{rel}$ " column contains values in kcal/mol.

\* Jaguar could only run these calculations using Abelian  $(D_{2h})$  symmetry. Therefore, when the electron was localized in a  $\pi$  symmetry orbital, the  $d_{x^2-y^2}$  and  $d_{z^2}$  orbitals mixed and thus the  $d_{xz}$  or  $d_{yz}$  orbital was reanalyzed into a  $\delta$  symmetry orbital. Hence the energy is not expected to differ from the energy of the  $d_{xy}$  or  $d_{x^2-y^2}$  hole.

energy of the ion Pt<sup>+</sup> is different whether the hole is of  $\sigma$  symmetry  $(d_{z^2}, L = 0)$ ,  $\pi$  symmetry  $(d_{xz}, L = 1)$ , or  $\delta$  symmetry  $(d_{x^2-y^2}$  or  $d_{xy}, L = 2)$ . The specific numbers are given in Table B.12. Similarly, the energy of Pt<sup>9+</sup> as calculated by M06-2X depends (completely unphysically) on which orbital the lone d electron is placed (Table B.13).

A more extensive study was done on the Ni<sup>+</sup> ion, using Q-Chem version 4.0. The results of calculations using DFT methods are given in Table B.14 and the results of calculations using electron-correlation methods are given in Table B.15. It is clear that, whereas the electron-correlation methods correctly predict the degeneracy of the five d holes in  $^{2}D$  Ni<sup>+</sup>, the DFT methods mostly do not. The only exception among the DFTs is XYGJ-OS, a double-hybrid DFT.

$d^9$	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0	XYGJ-OS
$z^2$	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
xy	0.293	0.407	-0.589	-1.681	-0.285	-0.111	0.372	0.000
$x^2 - y^2$	0.289	0.414	-0.560	-1.603	-0.329	-0.109	0.369	-0.001
$xz^*$	0.290	0.416	-0.583	-1.675	-0.276	-0.111	0.358	0.018
$yz^*$	0.290	0.430	-0.568	-1.647	-0.287	-0.109	0.359	0.016

Table B.14. "Degenerate" energies of the Ni<sup>+</sup>  $d^9$  ground state as calculated by DFT methods.

Energies are relative to the  $d_{z^2}$  hole and in kcal/mol.

\* Because Q-Chem runs the calculations using Abelian  $(D_{2h})$  symmetry, when the electron was localized in a  $\pi$  symmetry orbital, the  $d_{x^2-y^2}$  and  $d_{z^2}$  orbitals mixed and thus the  $d_{xz}$  or  $d_{yz}$  orbital was reanalyzed into a  $\delta$  symmetry orbital. Hence the energy is not expected to differ from the energy of the  $d_{xy}$  or  $d_{x^2-y^2}$  hole.

Table B.15. Degenerate energies of the  $Ni^+ d^9$  ground state as calculated by electron-correlation methods.

$d^9$	HF	MP2	CCSD
$z^2$	0.000	0.000	0.000
xy	-0.012	0.007	-0.002
$x^2 - y^2$	-0.008	0.007	-0.002
$xz^*$	0.000	0.023	-0.002
$yz^*$	-0.001	0.009	-0.002

Energies are relative to the  $d_{z^2}$  hole and in kcal/mol.

\* Because Q-Chem runs the calculations using Abelian  $(D_{2h})$  symmetry, when the electron was localized in a  $\pi$  symmetry orbital, the  $d_{x^2-y^2}$  and  $d_{z^2}$  orbitals mixed and thus the  $d_{xz}$  or  $d_{yz}$  orbital was reanalyzed into a  $\delta$  symmetry orbital. Hence the energy is not expected to differ from the energy of the  $d_{xy}$  or  $d_{x^2-y^2}$  hole.

Hole typ	e	Energy	$E_{rel}$
$z^2, x^2 - y^2$	$\sigma\delta$	-118.0461	0.00
$xy, z^2$	$\sigma\delta$	-118.0461	0.02
xz, yz	$\pi\pi$	-118.0372	5.59
$xz, x^2 - y^2$	$\pi\delta$	-118.0366	6.00
$yz, x^2 - y^2$	$\pi\delta$	-118.0366	6.00
xz,xy	$\pi\delta$	-118.0359	6.43
yz,xy	$\pi\delta$	-118.0359	6.43
$xz, z^2$	$\sigma\pi$	-118.0201	16.33
$yz, z^2$	$\sigma\pi$	-118.0201	16.33
$xy, x^2 - y^2$	δδ	-118.0145	19.84

**Table B.16.** Energies of the  $Pt^{2+} d^8$  configuration, calculated by B3LYP/LACV3P\*\*++.

Energies are in hartrees;  $E_{rel}$  values are in kcal/mol.

# **B.5.2** Angular momentum of the holes in the $d^8$ configuration of the dication

When there are two holes, there are two triplet states:  ${}^{3}F$  and  ${}^{3}P$ . In terms of the real orbital holes, there are several intermediate energy levels: the  $\sigma\delta$  holes are at  ${}^{3}F$ ; the  $\pi\pi$  and  $\pi\delta$  holes are at  $\frac{4}{5}{}^{3}F + \frac{1}{5}{}^{3}P$ , the  $\sigma\pi$  holes are at  $\frac{2}{5}{}^{3}F + \frac{3}{5}{}^{3}P$ , and the  $\delta\delta$  holes are at  $\frac{1}{5}{}^{3}F + \frac{4}{5}{}^{3}P$ . These values are derived in the Section B.6.

Table B.16 has the values for  $Pt^{2+}$  calculated in B3LYP with the LACV3P\*\*++ basis set in Jaguar. While the numbers are close to the theoretically predicted values, the  $\pi\pi$  and  $\pi\delta$  holes are split into three different sets of closely spaced energy levels. As in the case of the  $d^9$  M<sup>+</sup> ions, this is an artifact of the DFT calculation and is not physical.

Similar calculations were also performed for  $Pd^{2+}$ . The results are shown in Table B.17. However, due to difficulties with Jaguar, Q-Chem was used instead. The reduction of the atom to an Abelian subgroup prevented the calculation of  $\pi\delta$  and  $\sigma\pi$  holes, however. Fortunately, the calculated  $\sigma\delta$ ,  $\pi\pi$ , and  $\delta\delta$  holes are in good agreement with experiment.

The most extensive calculations were done on nickel. Values calculated with Jaguar are given in Table B.18 while values calculated with Q-Chem and experimental values are given in Table B.19. Again, note that it was not possible to get  $\pi\delta$  and  $\sigma\pi$  hole energies with Q-Chem.

# **B.6** Energies of $d^2$ and $d^8$ triplet states

Given a  $d^2$  or  $d^8$  atomic configuration, we can easily derive that the various microstates give rise to the  ${}^3F$  and  ${}^3P$  triplet states and the  ${}^1G$ ,  ${}^1D$ , and  ${}^1S$  singlet states. Furthermore, we know from

Hole type		Energy	$E_{rel}$	Exp/J (a)	Exp/avg (b)
$z^2, x^2 - y^2$	$\sigma\delta$	-125.663	0.00	0.00	0.00
$xy, z^2$	$\sigma\delta$	-125.663	0.01	0.00	0.00
xz, yz	$\pi\pi$	-125.651	7.45	7.83	6.46
$xz, x^2 - y^2$	$\pi\delta$	-125.663	0.01 (c)	7.83	6.46
$yz, x^2 - y^2$	$\pi\delta$	-125.663	0.01 (c)	7.83	6.46
xz, xy	$\pi\delta$	-125.651	7.45 (d)	7.83	6.46
yz,xy	$\pi\delta$	-125.651	7.45 (d)	7.83	6.46
$xz, z^2$	$\sigma\pi$	-125.663	0.01 (c)	23.50	19.38
$yz, z^2$	$\sigma\pi$	-125.663	0.01 (c)	23.50	19.38
$xy, x^2 - y^2$	$\delta\delta$	-125.619	27.93	31.33	25.84

**Table B.17.** Energies of the  $Pd^{2+} d^8$  configuration, calculated by B3LYP/LACVP.

Energies are in hartrees;  $E_{rel}$  and experimental values are in kcal/mol. Experimental values from [1]. (a) Experimental value using the lowest J energy.

(b) Experimental value derived from the average of spin-orbit coupling.

(c) Collapsed to  $\sigma\delta$ .

(d) Collapsed to  $\pi\pi$ .

**Table B.18.** Energies of the Ni<sup>2+</sup>  $d^8$  configuration, calculated on Jaguar using the 6-31G(tm)\*\*++ basis.

Hole type		HF	B3LYP	M06	M06-2X	M06-HF	M06-L	PBE	PBE0
$z^2, x^2 - y^2$	$\sigma\delta$	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
$xy, z^2$	$\sigma\delta$	0.00	0.05	-0.27	-0.83	-0.53	-0.42	0.08	0.06
xz, yz	$\pi\pi$	11.29	10.25	10.35	4.13	-7.93	16.22	10.23	10.37
$xz, x^2 - y^2$	$\pi\delta$	11.62	9.80	7.50	6.05	0.52	13.17	9.39	9.79
$yz, x^2 - y^2$	$\pi\delta$	11.62	9.80	7.50	6.05	0.52	13.17	9.39	9.79
xz, xy	$\pi\delta$	11.62	10.42	10.49	4.29	-7.70	16.38	10.38	10.53
yz,xy	$\pi\delta$	11.62	10.42	10.49	4.29	-7.70	16.38	10.38	10.53
$xz, z^2$	$\sigma\pi$	34.34	28.33	18.12	19.90	10.28	35.85	26.60	28.15
$yz, z^2$	$\sigma\pi$	34.34	28.33	18.12	19.90	10.28	35.85	26.60	28.15
$xy, x^2 - y^2$	$\delta\delta$	45.42	38.44	23.84	26.92	14.84	48.36	36.66	38.33

Energies are in kcal/mol.

(a) Experimental value using the lowest J energy.

(b) Experimental value derived from the average of spin-orbit coupling.

(c) Collapsed to  $\sigma\delta.$ 

(d) Collapsed to  $\pi\pi$ .

Hole type		Exp/J (a)	Exp/avg (b)	XYGJ-OS	MP2	CCSD
$z^2, x^2 - y^2$	$\sigma\delta$	0.00	0.00	0.00	0.00	0.00
$xy, z^2$	$\sigma\delta$	0.00	0.00	-0.03	0.00	0.00
xz, yz	$\pi\pi$	9.53	9.00	9.39	8.54	7.58
$xz, x^2 - y^2$	$\pi\delta$	9.53	9.00	0.00~(c)	-0.01 (c)	0.00~(c)
$yz, x^2 - y^2$	$\pi\delta$	9.53	9.00	0.00~(c)	0.00~(c)	0.00~(c)
xz, xy	$\pi\delta$	9.53	9.00	9.39 (d)	8.54 (d)	7.58 (d)
yz, xy	$\pi\delta$	9.53	9.00	9.39 (d)	8.54 (d)	7.58 (d)
$xz, z^2$	$\sigma\pi$	28.58	27.01	0.00~(c)	35.08~(e)	35.09~(e)
$yz, z^2$	$\sigma\pi$	28.58	27.01	0.00~(c)	0.00 (c)	0.00 (c)
$xy, x^2 - y^2$	$\delta\delta$	38.11	36.02	37.82	35.08	35.09

Table B.19. Energies of the  $Ni^{2+} d^8$  configuration, experimental and calculated on Q-Chem using the G3LARGE basis.

Energies are in kcal/mol.

(a) Experimental value using the lowest J energy.

(b) Experimental value derived from the average of spin-orbit coupling.

(c) Collapsed to  $\sigma\delta$ .

(d) Collapsed to  $\pi\pi$ .

(e) Collapsed to  $\delta\delta$ .

Hund's rules that the  ${}^{3}F$  state is the ground state. However, sometimes it is useful to know the energy given the two electrons or holes in specific, real orbitals (e.g.,  $d_{z^2}$  or  $d_{xy}$ ). In this case we must calculate the energies of intermediate states, i.e. between that of  ${}^{3}F$  and  ${}^{3}P$ .

#### B.6.1 Background

The *d* orbital electrons, which have  $\ell = 2$ , can be represented by either the complex spherical harmonics  $Y_{2m}$  or the real spherical harmonics  $Z_{2m}$ . Below is a list of the complex spherical harmonics:

$$\begin{split} r^2 Y_{2\overline{2}} &= \sqrt{\frac{15}{32\pi}} (x - iy)^2 \\ r^2 Y_{2\overline{1}} &= \sqrt{\frac{15}{8\pi}} z (x - iy) \\ r^2 Y_{20} &= \sqrt{\frac{5}{16\pi}} (2z^2 - x^2 - y^2) \\ r^2 Y_{21} &= \sqrt{\frac{15}{8\pi}} z (x + iy) \\ r^2 Y_{22} &= \sqrt{\frac{15}{32\pi}} (x + iy)^2 \end{split}$$

And of the real spherical harmonics:

$$\begin{split} r^2 Z_{2\overline{2}} &= \sqrt{\frac{15}{4\pi}} xy \\ r^2 Z_{2\overline{1}} &= \sqrt{\frac{15}{4\pi}} yz \\ r^2 Z_{20} &= \sqrt{\frac{5}{16\pi}} (2z^2 - x^2 - y^2) \\ r^2 Z_{21} &= \sqrt{\frac{15}{4\pi}} xz \\ r^2 Z_{22} &= \sqrt{\frac{15}{16\pi}} (x^2 - y^2) \end{split}$$

It is easy to see that the complex and the real spherical harmonics are closely related:

$$\begin{split} Y_{2\overline{2}} &= \frac{1}{\sqrt{2}} (Z_{22} - iZ_{2\overline{2}}) \\ Y_{2\overline{1}} &= \frac{1}{\sqrt{2}} (Z_{21} - iZ_{2\overline{1}}) \\ Y_{21} &= \frac{1}{\sqrt{2}} (Z_{21} + iZ_{2\overline{1}}) \\ Y_{22} &= \frac{1}{\sqrt{2}} (Z_{22} + iZ_{2\overline{2}}) \end{split}$$

 $Y_{20} = Z_{20}$ 

$$Z_{2\overline{2}} = \frac{1}{\sqrt{2}i}(Y_{22} - Y_{2\overline{2}})$$
$$Z_{2\overline{1}} = \frac{1}{\sqrt{2}i}(Y_{21} - Y_{2\overline{1}})$$
$$Z_{21} = \frac{1}{\sqrt{2}}(Y_{21} + Y_{2\overline{1}})$$
$$Z_{22} = \frac{1}{\sqrt{2}}(Y_{22} + Y_{2\overline{2}})$$

# **B.6.2** The $d^2$ and $d^8$ triplet states

The triplet states are  ${}^{3}F$  and  ${}^{3}P$ . We shall now examine the complex spherical harmonic wavefunctions associated with the  $M_{L}$  values of each state. To do so we will start with the highest possible  $M_{L}$  value and successively apply the lowering operator  $\hat{L}_{-}$ :

$$\hat{L}_{-}|\ell m\rangle = \sqrt{(\ell+m)(\ell-m+1)}|\ell m-1\rangle.$$

Also, we will use  $\mathcal{A}$  to represent antisymmetric functions, e.g.,  $\mathcal{A}[UV] = UV - VU$ .

## **B.6.2.1** The ${}^{3}F$ state

The  ${}^{3}F$  state has  $M_{L}$  values that range from -3 to 3. For  $M_{L} = 3$  the only possible configuration is  $\mathcal{A}[Y_{22}Y_{21}]$ . Similarly, for  $M_{L} = 2$  the only possible configuration is  $\mathcal{A}[Y_{22}Y_{20}]$ .

For  $M_L = 1$ , however, we note that  $\hat{L}_-$  can act on either  $Y_{22}$  or  $Y_{20}$ ; consequently we get a mix:

$$\mathcal{A}[2Y_{21}Y_{20} + \sqrt{6}Y_{22}Y_{2\overline{1}}];$$

which is normalized to

$$\mathcal{A}[\sqrt{\frac{2}{5}}Y_{21}Y_{20} + \sqrt{\frac{3}{5}}Y_{22}Y_{2\overline{1}}].$$

For  $M_L = 0$ , applying  $\hat{L}_-$  once again yields

$$\mathcal{A}[\sqrt{\frac{2}{5}}(\sqrt{6}Y_{21}Y_{2\overline{1}}) + \sqrt{\frac{3}{5}}(2Y_{21}Y_{2\overline{1}} + 2Y_{22}Y_{2\overline{2}})],$$

which simplifies and normalizes to

$$\mathcal{A}[\frac{2}{\sqrt{5}}Y_{21}Y_{2\overline{1}} + \frac{1}{\sqrt{5}}Y_{22}Y_{2\overline{2}}].$$

By symmetry arguments we can see that  $M_L = -1$  corresponds to

$$\mathcal{A}[\sqrt{\frac{2}{5}}Y_{20}Y_{2\overline{1}} + \sqrt{\frac{3}{5}}Y_{21}Y_{2\overline{2}}];$$

We also see that  $M_L = -2$  corresponds to  $\mathcal{A}[Y_{20}Y_{2\overline{2}}]$  and  $M_L = -3$  corresponds to  $\mathcal{A}[Y_{2\overline{2}}Y_{2\overline{2}}]$ .

#### **B.6.2.2** The ${}^{3}P$ state

The  ${}^{3}P$  state has  $M_{L}$  values that range from -1 to 1. For  $M_{L} = 1$  the wavefunction must be orthogonal to the  ${}^{3}F$   $M_{L} = 1$  case; it is easy to see that the wavefunction

$$\mathcal{A}[\sqrt{\frac{3}{5}}Y_{21}Y_{20} - \sqrt{\frac{2}{5}}Y_{22}Y_{2\overline{1}}]$$

fulfills this condition. Likewise, for  $M_L = 0$  it is easy to see that

$$\mathcal{A}[\frac{1}{\sqrt{5}}Y_{21}Y_{2\overline{1}} - \frac{2}{\sqrt{5}}Y_{22}Y_{2\overline{2}}]$$

is orthogonal to the  ${}^{3}F M_{L} = 0$  configuration.

By symmetry we can add that

$$\mathcal{A}[\sqrt{\frac{3}{5}}Y_{20}Y_{2\overline{1}} - \sqrt{\frac{2}{5}}Y_{21}Y_{2\overline{2}}]$$

corresponds to the  ${}^{3}P M_{L} = -1$  case.

# B.6.3 Pure and mixed complex orbital configurations

In the previous section, we saw that the complex orbital configurations  $\mathcal{A}[Y_{22}Y_{21}]$ ,  $\mathcal{A}[Y_{22}Y_{20}]$ ,  $\mathcal{A}[Y_{20}Y_{2\overline{2}}]$ , and  $\mathcal{A}[Y_{2\overline{1}}Y_{2\overline{2}}]$  are pure <sup>3</sup>F states, while the other combinations are mixed. In this section we shall deconvolute the mixed states.

## **B.6.3.1** $M_L = 1$

We have

$$\Psi_1^{^3F} = \mathcal{A}[\sqrt{\frac{2}{5}}Y_{21}Y_{20} + \sqrt{\frac{3}{5}}Y_{22}Y_{2\overline{1}}]$$

and

$$\Psi_1^{^{3}P} = \mathcal{A}[\sqrt{\frac{3}{5}}Y_{21}Y_{20} - \sqrt{\frac{2}{5}}Y_{22}Y_{2\overline{1}}];$$

Hence

$$\mathcal{A}[Y_{21}Y_{20}] = \sqrt{\frac{2}{5}}\Psi_1^{^3F} + \sqrt{\frac{3}{5}}\Psi_1^{^3P}$$

 $\quad \text{and} \quad$ 

$$\mathcal{A}[Y_{22}Y_{2\overline{1}}] = \sqrt{\frac{3}{5}}\Psi_1^{^3F} - \sqrt{\frac{2}{5}}\Psi_1^{^3P}.$$

**B.6.3.2**  $M_L = 0$ 

We have

$$\Psi_0^{{}^3F} = \mathcal{A}[\frac{2}{\sqrt{5}}Y_{21}Y_{2\overline{1}} + \frac{1}{\sqrt{5}}Y_{22}Y_{2\overline{2}}]$$

and

$$\Psi_0^{^{3}P} = \mathcal{A}[\frac{1}{\sqrt{5}}Y_{21}Y_{2\overline{1}} - \frac{2}{\sqrt{5}}Y_{22}Y_{2\overline{2}}];$$

Hence

$$\mathcal{A}[Y_{21}Y_{2\overline{1}}] = \frac{2}{\sqrt{5}}\Psi_0^{3F} + \frac{1}{\sqrt{5}}\Psi_0^{3P}$$

 $\quad \text{and} \quad$ 

$$\mathcal{A}[Y_{22}Y_{2\overline{2}}] = \frac{1}{\sqrt{5}}\Psi_0^{^3F} - \frac{2}{\sqrt{5}}\Psi_0^{^3P}.$$

### **B.6.3.3** $M_L = -1$

From symmetry with the  $M_L = 1$  case we have

$$\mathcal{A}[Y_{20}Y_{2\overline{1}}] = \sqrt{\frac{2}{5}}\Psi_{-1}^{^{3}F} + \sqrt{\frac{3}{5}}\Psi_{-1}^{^{3}P}$$

and

$$\mathcal{A}[Y_{21}Y_{2\overline{2}}] = \sqrt{\frac{3}{5}}\Psi_{-1}^{^{3}F} - \sqrt{\frac{2}{5}}\Psi_{-1}^{^{3}P}.$$

## B.6.4 Real orbital configuration energies

We are now ready to calculate the energies of the configuration of electrons or holes in real orbitals. We should first note that the  $d_{z^2}$  orbital  $(Z_{20})$  has  $\sigma$  symmetry, the  $d_{xz}$  and  $d_{yz}$  orbitals  $(Z_{21}$  and  $Z_{2\overline{1}})$  have  $\pi$  symmetry, and the  $d_{x^2-y^2}$  and  $d_{xy}$  orbitals  $(Z_{22} \text{ and } Z_{2\overline{2}})$  have  $\delta$  symmetry. Also, let us define  $\epsilon = E({}^{3}P) - E({}^{3}F)$  as the excitation energy to  ${}^{3}P$ .

## **B.6.4.1** Energy of $\sigma\pi$ and $\sigma\overline{\pi}$

$$\sigma\pi \equiv \mathcal{A}[Z_{21}Z_{20}] = \mathcal{A}[\frac{Y_{20}}{\sqrt{2}}(Y_{21} + Y_{2\overline{1}})]$$

$$E(Z_{21}Z_{20}) = \frac{1}{2}(E(Y_{21}Y_{20}) + E(Y_{2\overline{1}}Y_{20}))$$
  
=  $\frac{1}{2}[(\frac{2}{5}E(^{3}F) + \frac{3}{5}E(^{3}P)) + (\frac{2}{5}E(^{3}F) + \frac{3}{5}E(^{3}P))]$   
=  $\frac{2}{5}E(^{3}F) + \frac{3}{5}E(^{3}P) = E(^{3}F) + \frac{3}{5}\epsilon$ 

A very similar calculation for the  $\sigma \overline{\pi}$  case yields the same energy,  $\frac{3}{5}\epsilon$  above the ground state.

#### **B.6.4.2** Energy of $\sigma\delta$ and $\sigma\overline{\delta}$

$$\sigma \delta \equiv \mathcal{A}[Z_{22}Z_{20}] = \mathcal{A}[\frac{Y_{20}}{\sqrt{2}}(Y_{22} + Y_{2\overline{2}})]$$
$$E(Z_{22}Z_{20}) = \frac{1}{2}(E(Y_{22}Y_{20}) + E(Y_{2\overline{2}}Y_{20})) = \frac{1}{2}[E(^{3}F) + E(^{3}F)] = E(^{3}F)$$

A very similar calculation for the  $\sigma \overline{\delta}$  case yields the same energy, i.e. the energy of the ground state.

#### **B.6.4.3** Energy of $\pi \overline{\pi}$

$$\pi \overline{\pi} \equiv \mathcal{A}[Z_{21}Z_{2\overline{1}}] = \mathcal{A}[\frac{1}{2i}(Y_{21} + Y_{2\overline{1}})(Y_{21} - Y_{2\overline{1}})] = \frac{1}{\sqrt{2i}}(Y_{21}Y_{2\overline{1}} - Y_{2\overline{1}}Y_{21})$$
$$E(Z_{21}Z_{2\overline{1}}) = \frac{1}{2}(E(Y_{21}Y_{2\overline{1}}) + E(Y_{2\overline{1}}Y_{21})) = E(Y_{21}Y_{2\overline{1}}) = \frac{4}{5}E(^{3}F) + \frac{1}{5}E(^{3}P) = E(^{3}F) + \frac{1}{5}\epsilon$$

**B.6.4.4** Energy of  $\pi\delta$ ,  $\pi\overline{\delta}$ ,  $\overline{\pi}\delta$ , and  $\overline{\pi}\overline{\delta}$ 

$$\pi\delta \equiv \mathcal{A}[Z_{22}Z_{21}] = \mathcal{A}[\frac{1}{2}(Y_{22} + Y_{2\overline{2}})(Y_{21} + Y_{2\overline{1}})] = \mathcal{A}[\frac{1}{2}(Y_{22}Y_{21} + Y_{22}Y_{2\overline{1}} + Y_{2\overline{2}}Y_{21} + Y_{2\overline{2}}Y_{2\overline{1}})]$$

$$\begin{split} E(Z_{22}Z_{21}) &= \frac{1}{4} [E(Y_{22}Y_{21}) + E(Y_{22}Y_{2\overline{1}}) + E(Y_{2\overline{2}}Y_{21}) + E(Y_{2\overline{2}}Y_{2\overline{1}})] \\ &= \frac{1}{4} [E(^{3}F) + (\frac{3}{5}E(^{3}F) + \frac{2}{5}E(^{3}P)) + (\frac{3}{5}E(^{3}F) + \frac{2}{5}E(^{3}P)) + E(^{3}F)] \\ &= \frac{4}{5}E(^{3}F) + \frac{1}{5}E(^{3}P) = E(^{3}F) + \frac{1}{5}\epsilon \end{split}$$

Very similar calculations for the  $\pi \overline{\delta}$ ,  $\overline{\pi} \delta$ , and  $\overline{\pi} \overline{\delta}$  cases yield the same energy, i.e.  $\frac{1}{5}\epsilon$  above the ground state.

#### **B.6.4.5** Energy of $\delta \overline{\delta}$

$$\delta\overline{\delta} \equiv \mathcal{A}[Z_{22}Z_{2\overline{2}}] = \mathcal{A}[\frac{1}{2i}(Y_{22} + Y_{2\overline{2}})(Y_{22} - Y_{2\overline{2}})] = \frac{1}{\sqrt{2}i}(Y_{22}Y_{2\overline{2}} - Y_{2\overline{2}}Y_{22})$$
$$E(Z_{22}Z_{2\overline{2}}) = \frac{1}{2}(E(Y_{22}Y_{2\overline{2}}) + E(Y_{2\overline{2}}Y_{22})) = E(Y_{22}Y_{2\overline{2}}) = \frac{1}{5}E(^{3}F) + \frac{4}{5}E(^{3}P) = E(^{3}F) + \frac{4}{5}E(^{3}F) + \frac{4}{5}E(^{3}F) + \frac{4}{5}E(^{3}F) + \frac{4}{5}E(^{3}F) + \frac{4}{5}E(^{3}F) + \frac{4}{5}E(^{3}F) + \frac{4}{5$$

#### B.6.5 Summary

A triplet  $d^2$  or  $d^8$  atomic configuration gives rise to a mix of  ${}^3F$  and  ${}^3P$  states. The  $\sigma\delta$  configurations are pure  ${}^3F$ , the  $\pi\pi$  and  $\pi\delta$  configurations are one-fifth of the way towards  ${}^3P$ , the  $\sigma\pi$  configurations are three-fifths of the way towards  ${}^3P$ , and the  $\delta\delta$  configuration is four-fifths of the way towards the  ${}^3P$  energy level. Hence we see that the energy is the lowest when the electrons or holes are allowed to freely roam about the atom (the  $\sigma\delta$  case) and the highest when they are restricted to one plane (the  $\delta\delta$  case).

# **B.7** Conclusions

For the neutral atoms, M06-2X gave the best DFT results for Pt and Ni, while B3LYP gave the best DFT results for Pd. This may be due to the contraction of the *d* functions of the basis set in Pd. Considering only electron-correlation methods, MP2 gave the best results for Pt and Pd, while CCSD gave the best results for Ni. This may be due to the use of an ECP on Pt and Pd. In comparing DFT versus electron-correlation methods, the electron-correlation method (CCSD or MP2) was better for Pd and Ni, whereas the DFT M06-2X was better than any electron-correlation method for Pt. For the singly-charged cation, B3LYP gave the best results for Pt and Ni whereas there was no method found that gave good results for Pd.

The singly-charged cation in the  $d^9$  configuration should have a hole in one of five degenerate orbitals; this is not borne out by DFT calculations and the discrepancy is not physical. The use of electron-correlation calculations removes this artifact. Similar issues are observed with the doublycharged cation in the  $d^8$  configuration. This problem is innate to DFT and its resolution is still an active area of research.

# **B.8** References

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