New Oxidation Reactions of Palladium and Platinum: Synthetic and Mechanistic Investigations

by

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“For with God nothing shall be impossible.”
-Luke 1:37

To Ruth Muldrow Bruce and Idell Gillum Whitfield

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Table of Contents

Chapter 3

Chapter 4

Chapter 5

Chapter 6

List of Schemes

Chapter 1

Introduction

Chapter 2

Polymer Oxidants in C-H Functionalization

Chapter 3

Synthesis and Reactivity of Chlorinated Palladium(IV) Complexes

Chapter 4

Chlorinated Platinum Complexes – Studies of Oxidative Addition and Mechanistic Proposals

Chapter 5

Synthesis and Reactivity of Platinum(III & IV) Halogen and Carboxylate Complexes

List of Figures

Chapter 1

Introduction

Chapter 2

Polymer Oxidants in C-H Functionalization

Chapter 3

Synthesis and Reactivity of Chlorinated Palladium(IV) Complexes

Chapter 4

Chlorinated Platinum Complexes – Studies of Oxidative Addition and Mechanistic Proposals

Chapter 5

Synthesis and Reactivity of Platinum(III & IV) Halogen and Carboxylate Complexes

Chapter 6

Conclusion

List of Tables

Chapter 2

Polymer Oxidants in C-H Functionalization

Chapter 3

Synthesis and Reactivity of Chlorinated Palladium(IV) Complexes

Chapter 4

Chlorinated Platinum Complexes – Studies of Oxidative Addition and Mechanistic Proposals

Chapter 5

Synthesis and Reactivity of Platinum(III & IV) Halogen and Carboxylate Complexes

Abstract

Organic and inorganic oxidation reactions involving the metals palladium and platinum were developed. Palladium-catalyzed carbon-hydrogen (C-H) functionalization *via* acetoxylation was shown to proceed efficiently using an oxidant immobilized on a solid support. The polymer oxidant has several advantages over a traditional monomer oxidant, including, but not limited to, cost, atom economy, and recyclability. Both sp^2 and sp^3 C-H bonds of small molecules were transformed using this methodology.

Palladium was also employed in stoichiometric oxidation reactions. Oxidation of $Pd^{II}(phpy)_2$ (phpy = 2-phenylpyridine) using the electrophilic chlorinating reagents, $PhICl_2$ and NCS, accessed the elusive high oxidation state of Pd^{IV}. Novel complexes were identified and characterized, incorporating 2 chlorine ligands or 1 chlorine ligand and the succinimide ligand. Both complexes were shown to undergo facile reductive elimination to produce C-Cl, C-C, and even C-N coupled organic products. Other Pd^{IV} complexes were synthesized, examining the outcome of organic reductive elimination from a metal complex with two different ligands, acetate and chlorine. Initial results demonstrate that solvent and ligand position strongly influence the observed organic products.

Platinum complexes were also oxidized by the afore mentioned electrophilic chlorinating reagents. Using conditions from the palladium system, oxidation with $PhICl_2$ afforded similar Pt^{IV} dichloride products, while oxidation with NCS produced a Pt^{III} complex as the major product. The reaction conditions were found to vary the observed ratios of products in the NCS oxidations. These factors were examined in an effort to propose a mechanism to explain formation of all of the species.

Finally, platinum complexes were oxidized by a series of traditional and non-traditional oxidants to access Pt^{III} and Pt^{IV} halogen and carboxylate complexes. Traditional oxidants included Br_2 and I_2, while non-traditional oxidants included XeF_2, $PhI(OAc)_2$ and $PhI(C_2F_3O_2)_2$. All of the compounds formed were stable to ambient conditions. Organic reductive elimination products were not observed in any of the thermolysis experiments. Upon heating the Pt^{IV} complexes either experienced no change or isomerized to an alternate geometry.

Chapter 1

Introduction

Carbon-hydrogen (C-H) bond activation is frequently cited as one of the most important challenges in organic and organometallic chemistry. C-H activation refers to the cleavage of the C-H bond. Strong C-H bonds are replaced with weaker bonds that are functionalized with greater ease.[1] Interest in C-H activation lies in the ability to transform a relatively inert C-H bond with the added challenge of selectivity. Selectivity is vital due to the numerous C-H bonds in the majority of organic molecules and the multiple types of C-H bonds. Since the 1960's, researchers have used transition metals, including nickel, ruthenium, and platinum, to achieve this type of C-H bond transformation.[2-4] The majority of examples of C-H activation employ stoichiometric amounts of a transition metal, which is undesirable for most practical applications.[1, 5] In contrast, catalytic C-H activation and functionalization has proven much more formidable.[6]

Significant strides have been made recently in the area of transition-metal catalyzed C-H activation/functionalization, including contributions from the Sanford laboratory using a ligand-directed approach.[7-12] Ligand-directed C-H activation/functionalization is a powerful tool for regio- and chemoselectively functionalizing C-H bonds of small molecules. Selectivity is promoted by an internal ligand (L) within a small molecule. As shown in Figure 1.1, this ligand directs the transition metal to a specific C-H bond, ultimately allowing for sole functionalization at that particular position. This methodology may be applied to the functionalization of complex, biologically active molecules at late stages in their synthesis. Figure 1.2 displays a series of benzodiazepines. The bolded functionality may be installed *via* ligand-directed functionalization to synthesize molecules **1-7** through **1-9**. Another

alternative would incorporate new functionality into molecule **1-6**, possibly increasing biological activity.

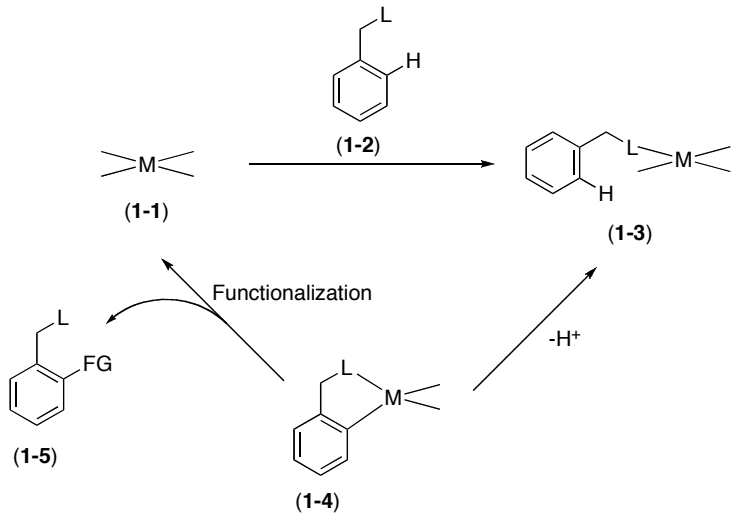
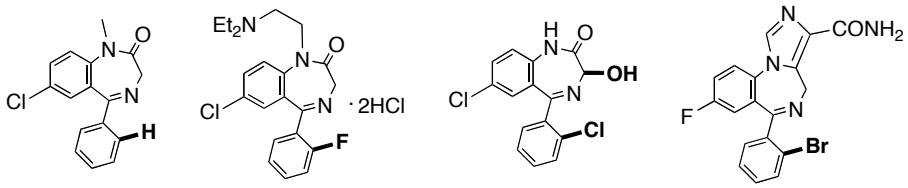


Figure 1.1 – Mechanism for Ligand-Directed C-H Activation/Functionalization



Valium anti anxiety (**1-6**)

Flurazepam hypnotic (**1-7**)

Ativan anti anxiety (**1-8**)

Imidazenil anticonvulsant (**1-9**)

Figure 1.2 –Biologically Active Target Molecules: Benzodiazepines

While Figure 1.1 outlines a general mechanism, the appropriate design of reaction conditions (metal, functionalizing reagent, solvent, temperature) is critical to ensure operation of a given catalytic cycle. In catalytic oxidative functionalization, the combination of oxidant, temperature, reaction time, choice of solvent, and choice of metal will often determine if catalytic turnover is possible. Our methodology has utilized palladium as the metal of choice, and Pd-catalyzed ligand-directed C-H activation/functionalization has been effective in converting C-H bonds (**1-10** in Figure 1.3) to C-FG bonds (**1-12** in Figure 1.3) (FG = functional group and includes OR, F, Cl, Br, I, C).

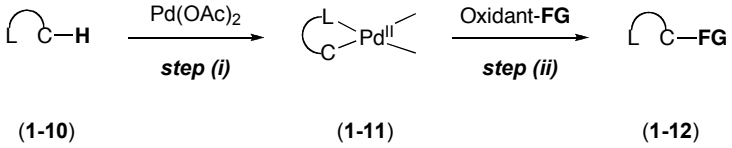
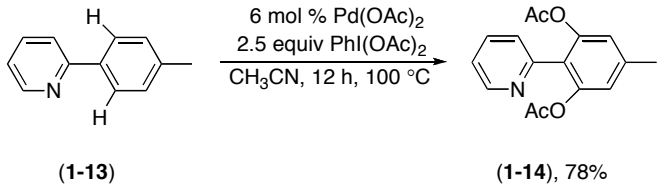


Figure 1.3 – Palladium-Catalyzed Ligand-Directed Oxidative Functionalization

Despite the novelty of these palladium-catalyzed ligand directed C-H activation/functionalization reactions, they do have several key disadvantages that may limit their widespread application. For example, in general, the oxidants required for these oxidative functionalization reactions are costly reagents that have high toxicity and low atom economy. In addition, the oxidants are generally used in stoichiometric amounts, intensifying the disadvantages of toxicity and waste. Temperatures required for ligand-directed functionalization (typically between 80 and 120 ºC) are reasonably high, potentially a disadvantage for more fragile organic systems. Reaction times are fairly long with average durations ranging from 12 hours to multiple days. Finally, solvent selection is truly an empirical choice. Extensive solvent screening must be carried out with each functionalization reaction, sometimes among different substrates within a given reaction. As a result, there are significant areas that can be improved in this important class of catalytic C-H functionalization reactions. The research described in this thesis

seeks to focus on specific areas that may ultimately allow us to address the aforementioned challenges and disadvantages.

As mentioned above, palladium-catalyzed ligand directed C–H functionalization has been developed previously by our laboratory. An example of a C-H bond acetoxylation reaction is shown in Scheme 1.1. This subset of reactions represents a significant advance in arene oxygenation and has been extended to include esterification and etherification of both alkanes and arenes.[7-9] Despite the utility and effectiveness of these reactions, the requirement for $PhI(OAc)_2$ as the oxidant represents a significant disadvantage. In particular, stoichiometric quantities of oxidant are needed for these reactions, generating significant waste.



(**1-13**) (**1-14**), 78%

Scheme 1.1 - Palladium-Catalyzed, Ligand-Directed, C-H Acetoxylation of 2-*p*-Tolylpyridine, **1-13**

The goal of Chapter 2 is to address the inherent disadvantage of by-product generation caused by the choice of oxidant. The solution discussed in Chapter 2 involves utilization of a polymer-immobilized oxidant to functionalize C-H bonds of small molecules. Polymer oxidation provides an environmentally benign alternative for organic synthesis that preserves and/or enhances high standards of yield and selectivity.

Additional points of concerns for constructing effective catalytic cycles include temperature, reaction time, and solvent. In order to gain a full understanding of the influence of each of these parameters, we need to gain an intimate understanding of the reaction mechanism. A general mechanism for Pd-catalyzed ligand-directed functionalization includes the steps shown in Figure 1.4: *i*) C-H activation, *ii*) oxidative

addition, and *iii*) reductive elimination. C-H activation in a palladium catalyzed mechanism results in cyclopalladation (step *i* of Figure 1.4). Cyclopalladation has been extensively studied by several research groups.[13-14] The cyclopalladation of azobenzene was one of the first examples in literature, reported in 1965.[15]

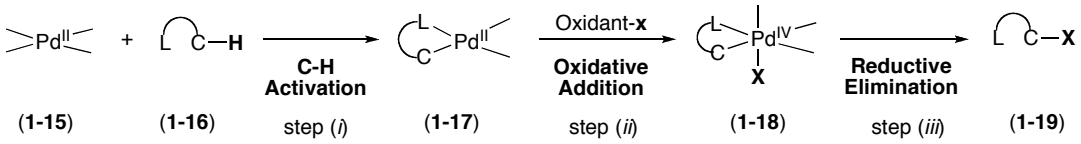
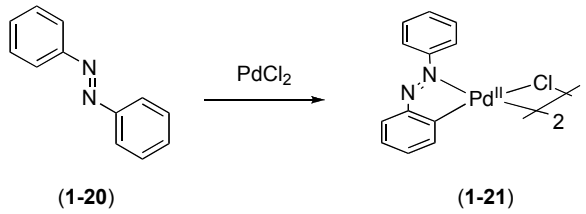


Figure 1.4 – General Mechanism for Palladium-Catalyzed Ligand-Directed Oxidative Functionalization

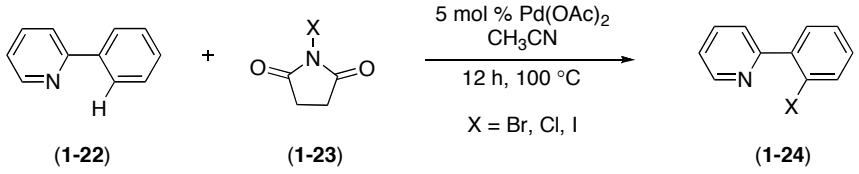


Scheme 1.2 – Cyclopalladation of Azobenzene

While cyclopalladation is fairly established, less is known about oxidative addition at Pd(II) and reductive elimination from the resulting Pd(IV) intermediates. The mechanism proposed for palladium-catalyzed functionalization proposes a palladium(II/IV) cycle (Figure 1.4), whereby a palladium(IV) intermediate, **1-18**, is generated upon oxidative addition and a palladium(II) species is released upon reductive elimination, **1-15**. Palladium(IV) complexes are infrequently reported in literature and have rarely been proposed as key intermediates in C-H activation/functionalization catalytic cycles prior to our work.[16-20]

Chapter 3 explores both steps of oxidative addition and reductive elimination in the context of a different subset of ligand-directed functionalization reactions:

halogenations. Small molecules may be halogenated under palladium-catalyzed conditions as shown in Scheme 1.3.[11-12] Our challenge was to demonstrate the viability of the proposed mechanism for this catalytic halogenation methodology by specifically focusing on the steps of oxidative addition and reductive elimination. The advance in this area of research was to demonstrate both the synthesis of palladium(IV) complexes and the observation of carbon-halogen bond-forming reductive elimination of small molecules from these isolated complexes, thereby supporting the plausibility of the proposed mechanism. Insights from this work related to solvent effects and metal geometry as well as further mechanistic studies, may provide information allowing for further optimization of catalytic halogenations.



Scheme 1.3 – Palladium-Catalyzed Halogenation of 2-Phenylpyridine

The stability of palladium(IV) complexes under ambient conditions, excluding those discussed in Chapter 3, is generally incredibly limited.[16-20] One alternative method for studying high oxidation palladium intermediates involves the use of more stable platinum analogues. The literature has suggested that platinum may serve as a model for palladium for homologous organometallic complexes.[21-25] Chapters 4 and 5 explore this proposal in greater detail. The research described in Chapter 4 reports addition of electrophilic chlorine sources to a platinum complex. Our goal was to evaluate the scope of comparison between analogous palladium and platinum complexes. As shown in Figure 1.5, our studies reveal fundamental differences between the two metal complexes (Figure 1.5). In addition, critical information is gathered to advance mechanistic understanding of several oxidative addition reactions using organic oxidants.

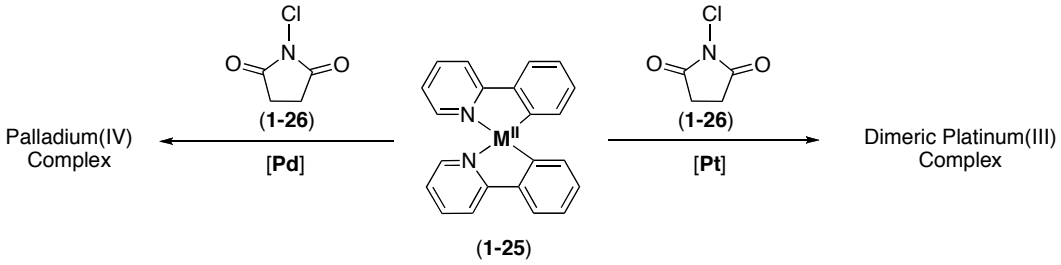


Figure 1.5 – Divergence Between Analogous Palladium and Platinum Complexes

While Chapters 3 and 4 examine a more narrow subset of chlorination reactions, the goal of research in Chapter 5 was to expand the scope of oxidative addition examinations to include all halogens as well as oxygen-containing functional groups (Figure 1.6). Results obtained from these examinations provide further insight into both the advantages and limitations of oxidative addition comparisons between palladium and platinum. The research detailed in Chapter 5 suggests that platinum can be a stable model for palladium in some cases; however, caution should be taken in making generalizations about the similarities between their reactivity.

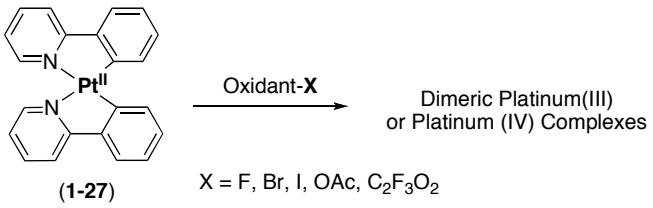


Figure 1.6 – Scope Expansion of Oxidative Addition to Platinum

Each chapter independently aims to address challenges posed by transition-metal catalyzed, ligand-directed C-H activation/functionalization. The research advances

discussed should provide greater understanding that will allow for further expansion within this area of organometallic chemistry.

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Chapter 2

Polymer Oxidants in C-H Functionalization

2.1 Introduction

The oxidative functionalization of organic molecules is an important transformation within organic and organometallic chemistry. Several challenges in this area have been, and continue to be, addressed by the development of mild and efficient transition metal-catalyzed methods.[1-18] One area of particular interest is carbon-hydrogen (C-H) activation/oxidative functionalization. Current methodology for C-H activation employs metals to promote functionalization, as shown in Figure 2.1. C-H activation evokes fascination with researchers due to the unique challenge it represents. While carbon-hydrogen bonds are ubiquitous in nature, they are incredibly strong, with bond-dissociation energies within the range of 105-110 kcal/mol. This strength renders activation, and by definition, cleavage of the carbon-hydrogen bond, a significant challenge.[19] Another challenge presented by the universality of C-H bonds arises when considering regioselectivity. Even when the problem of C-H activation is solved by use of a transition metal, the issue of which C-H bond will be activated remains. For effective applications, one specific C-H bond must undergo activation, rather than multiple, different bonds. C-H activation/functionalization reactions that proceed regioselectively in the context of complex organic substrates could provide important new synthetic approaches to fine chemicals, pharmaceutical intermediates, organic materials, and natural products.[10-18]

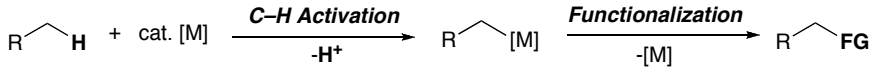


Figure 2.1 – General Methodology for C-H Activation/Functionalization

Research in our laboratory has focused on addressing these issues *via* ligand-directed methods. The organic substrates are designed to contain coordinating functional groups that direct the metal to a specific C-H bond, which allows for functionalization of that bond alone. Figure 2.2 depicts the general mechanism for ligand-directed, C-H activation/functionalization. A small molecule with an internal ligand L, **2-2**, interacts with a metal complex, **2-1**, to generate a new metal complex, **2-3**. The internal ligand on **2-2** then directs the metal to one specific C-H bond based on its proximity to that bond. Formal activation of the C-H bond generates, **2-4**, a new metallocycle complex. Complex **2-4** undergoes functionalization with eventual release of the functionalized small molecule, **2-5**. The metal complex, **2-1**, is regenerated, allowing for re-entry into the catalytic cycle.

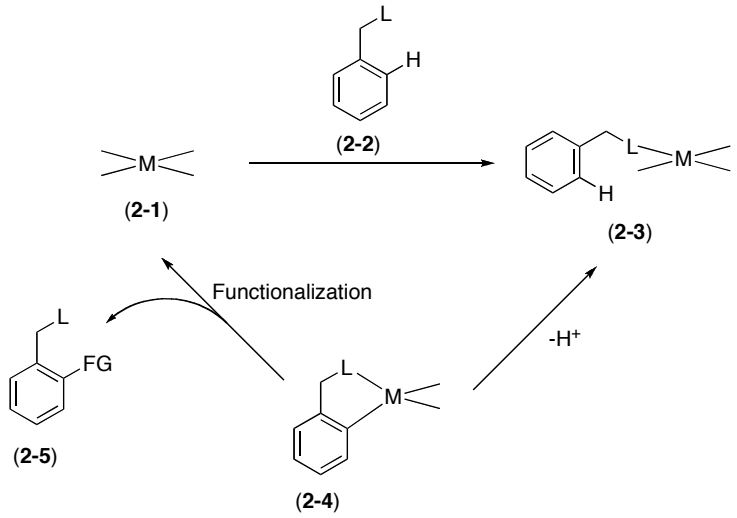
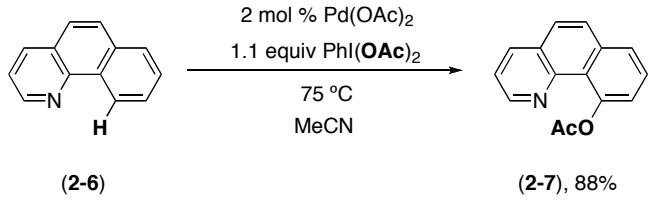
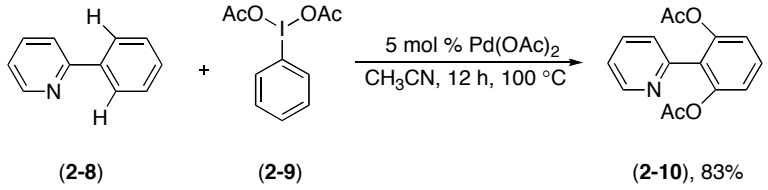


Figure 2.2 – General Mechanism for Ligand-Directed Functionalization

Prior research in our laboratory has shown that this methodology is effective in catalyzing the selective acetoxylation of arene and alkane bonds using iodobenzene diacetate, $PhI(OAc)_2$, as the stoichiometric oxidant.[9-12] These transformations proceed under mild conditions with exceptionally high (typically >99%) levels of regioselectivity. The substrates to be oxidized contain coordinating functional groups, as shown in Figure 2.2. Scheme 2.1 depicts the mono-acetoxylation of an arene, 7,8-benzoquinoline, **2-6**.[10] Research demonstrated that selective acetoxylation is not limited to mono-acetoxylation with arene substrates. Scheme 2.2 displays the di-acetoxylation of 2-phenylpyridine, **2-8**. Selective diacetoxylation was achieved by increasing the equivalents of the oxidant, $PhI(OAc)_2$ to 2.5 equiv.[10, 12]

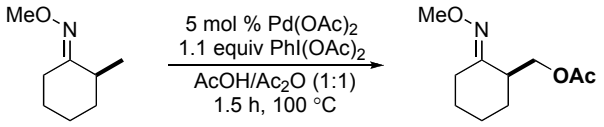


Scheme 2.1 – Palladium-Catalyzed, Ligand-Directed, C-H Acetoxylation of 7,8-Benzoquinoline, **2-6**



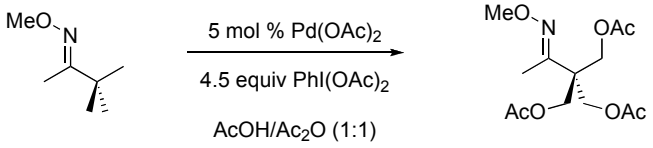
Scheme 2.2 – Palladium-Catalyzed, Ligand-Directed, C-H Acetoxylation of 2-Phenylpyridine, **2-8**

As mentioned, palladium-catalyzed, ligand-directed, C-H acetoxylation could also be applied to alkane substrates. As shown in Scheme 2.3, methyl oxime ether, **2-11**, was mono-acetoxylated in excellent yield.[11] Similar to arene substrates, selective acetoxylation of multiple bonds was demonstrated with several small molecules, including **2-13**, shown in Scheme 2.4.[11]



(**2-11**) (**2-12**), 81%

Scheme 2.3 – Palladium-Catalyzed, Ligand-Directed, C-H Acetoxylation of (*S*,*E*)-2-Methylcyclohexanone *O*-Methyl Oxime, **2-11**



(**2-13**) (**2-14**), 59%

Scheme 2.4 – Palladium-Catalyzed, Ligand-Directed, C-H Acetoxylation of (*E*)-3,3-Dimethylbutan-2-one *O*-Methyl Oxime, **2-13**

Our proposed mechanism for the catalytic C-H activation/acetoxylation of small molecules is depicted in Figure 2.3. The palladium catalyst **2-15**, specifically palladium acetate, begins at an oxidation state of 2+ and reacts with the ligand-containing small molecule, **2-16**, to generate a new palladium(II) complex, **2-17**. Complex **2-17** is oxidized by iodobenzene diacetate, **2-9**, to generate a new palladium(IV) intermediate, **2-18**, where the acetate group from the oxidant is now coordinated to the metal. This palladium(IV)

species, **2-18**, undergoes reductive elimination to release the acetoxylated small molecule, **2-19** and complex **2-15**, which can re-enter the catalytic cycle.

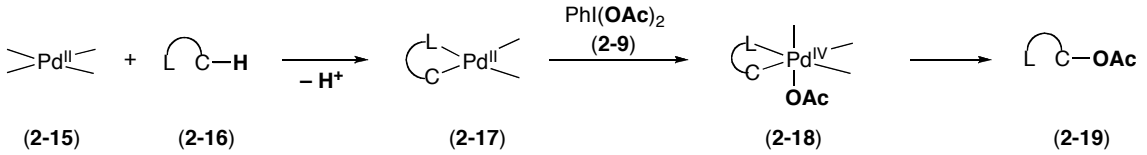


Figure 2.3 – Proposed Mechanism of Palladium-Catalyzed, Ligand-Directed, C-H Acetoxylation

This chapter will discuss the use of poly-4-(diacetoxyiodo)styrene as an alternative to iodobenzene diacetate in palladium-catalyzed, ligand-directed, C-H bond acetoxylation.

2.2 Advantages of Poly-4-(Diacetoxyiodo)Styrene, 2-23

As discussed above, iodobenzene diacetate, **2-9**, is an effective oxidant for the functionalization of small molecules with internal ligands, using the methodology previously developed in the Sanford laboratory. However, as most scientific researchers are aware, there is often room for improvement or further optimization with a given subset of reactions. Optimization could potentially be focused on the catalyst, the reaction medium, temperature, time, or the oxidant. As the first four parameters were carefully screened during the initial development of the methodology, we chose to focus on the latter. Our analysis of iodobenzene diacetate, **2-9**, revealed distinct disadvantages associated with its use.

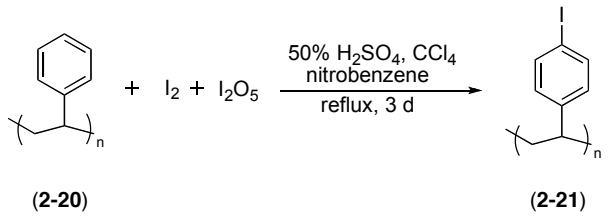
The byproduct from acetoxylation reactions employing **2-9** is iodobenzene, a toxic substance. Generation of one equiv of iodobenzene for every equiv of substrate requires laborious separation from the desired functionalized product. Production of iodobenzene also has a negative impact on the environment. Poor atom economy

increases general waste of substances that must be handled by regulation-approved methods. Iodobenzene diacetate, **2-9**, is also costly, as compared to other reagents - the price is approximately $1 per gram according to Sigma-Aldrich 2008 pricing. While this may not be too expensive for researchers in a laboratory setting, it is certainly not cost-effective for large-scale applications.

Consideration of the drawbacks discussed in the previous paragraph led us to ponder the use of a virtually identical oxidant mounted on a solid support, a polymer-immobilized oxidant. For **2-9**, its polymer analogue would be poly-4-(diacetoxyiodo)styrene. The goal would be to determine if this reagent could be used with the established methodology as an environmentally friendly alternative to the monomeric oxidant. The advantages of poly-4-(diacetoxyiodo)styrene would begin with its recycling potential. The polymer byproduct, poly-4-iodostyrene, could be resubjected to oxidation conditions to regenerate the oxidant, significantly reducing waste from byproducts, and facilitating a safe and environmentally benign process. Recycled oxidant would also reduce costs associated with purchasing oxidant.

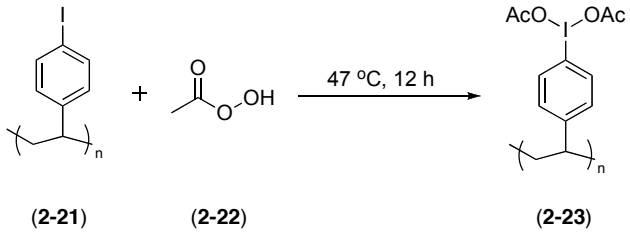
Poly-4-(diacetoxyiodo)styrene is available in two steps from commercial polystyrene.[20-26] Importantly, this reagent has been widely used in organic synthesis for reactions including the iodination of arenes, the α-hydroxylation of ketones, and the oxidation of sulfides, hydroquinones, phenols, and alcohols.[20-26]

Synthesis of poly-4-iodostyrene, **2-21**, involved the treatment of polystyrene, **2-20**, with iodine and iodopentoxide as shown in Scheme 2.5. Poly-4-iodostyrene, **2-21**, was then treated with peracetic acid to afford poly-4-(diacetoxyiodo)styrene, **2-23**, as depicted in Scheme 2.6.



(**2-20**) (**2-21**)

Scheme 2.5 – Synthesis of Poly-4-Iodostyrene, **2-21**



Scheme 2.6 – Synthesis of Poly-4-(Diacetoxyiodo)styrene, **2-23**

2.3 Acetoxylation of 8-Methylquinoline, 2-24

Initial studies focused on the palladium-catalyzed acetoxylation of 8-methylquinoline, **2-24**, using **2-23** as shown in Scheme 2.7.[27] Reaction conditions for functionalization of substrate **2-24** included 1.7 equiv of **2-23** relative to 1 equiv of **2-24**, and 5 mol % of palladium acetate. The reaction was heated in acetic acid at 100 °C for 12 hours, and acetoxylated product **2-25** was isolated in 72% yield. Conveniently, the reaction did not require special handling/purification of solvents or reagents. Commercial acetic acid was used, and the reaction was conducted in the presence of ambient air and moisture.

Scheme 2.7 – Palladium-Catalyzed Acetoxylation of **2-24** Using **2-23**

The yield obtained using **2-23** was slightly lower than with **2-9** under comparable conditions. The monomeric oxidant (**2-9**), afforded a yield of 88% in the acetoxylation of

2-24, as compared to 72% with **2-23**. Systematic studies revealed that a greater quantity of polymer-immobilized oxidant was required to drive the reactions to completion (1.7 equiv of **2-23** as compared to 1.1 equiv of **2-9**). The fate of the extra oxidizing equivalents has not been definitively determined. Previous literature reports have suggested that some benzylic oxidation of the polymer backbone may take place with polymer-immobilized iodine(III) oxidants.[28] The lower yield with **2-23** may also be due to the moderate solubility of **2-23** in acetic acid and/or the decreased accessibility of the immobilized oxidant, **2-23**, to the active palladium catalyst. Other literature reports have commented on similar reductions in reactivity of **2-23** relative to **2-9** in arene iodination reactions and in the 1,2 aryl migration of alkyl aryl ketones.[20]

2.4 Recycling of Poly-4-(Diacetoxyiodo)Styrene, 2-23

As discussed in section 2.2, one of the primary advantages of using **2-23** as an oxidant is the potential for recycling and regeneration. As shown in Scheme 2.7, **2-21** is the byproduct of any of the catalytic acetoxylation reactions that use **2-23**. Compound **2-21** was easily recovered from the reaction mixture by precipitation with methanol. Complex **2-21**, obtained from precipitation, was found to possess a reasonable level of purity. Immediate re-subjection of **2-21** to peracetic acid, using the conditions depicted in Scheme 2.6, regenerated **2-23** in high (85%) yield.[27]

While the excellent yield of **2-23** verified that recycling was facile, it did not give us information on the reactivity of the regenerated oxidant. Even if high yields of **2-23** were obtained by recycling **2-21**, a key question was whether oxidant **2-23**, obtained by regeneration, would be effective in the C-H acetoxylation reactions. Several trials were conducted to address this question. Results shown in Table 2.1 proved that regenerated oxidant was indeed an effective oxidant; furthermore, it was as effective as newly synthesized oxidant.[27] Across five trials, the yield of the acetoxylated product, **2-25**, ranged from 72 to 82%. The yield of recovered oxidant, **2-23**, ranged from 81 to 86% over these same five trials. These trial runs reveal no loss in activity of the regenerated oxidant, **2-23**, over the course of multiple recycling.

Table 2.1 – Oxidant Regeneration and Reuse in the Palladium-Catalyzed Acetoxylation of **2-24**

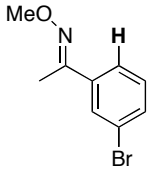
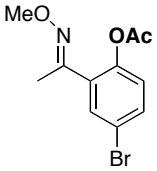
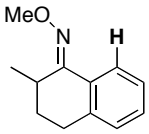
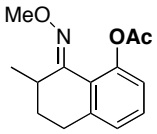
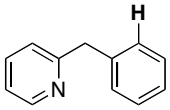
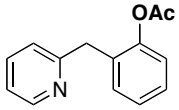
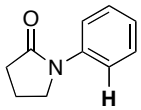
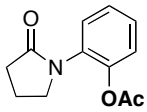
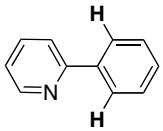
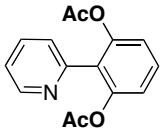
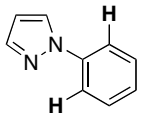
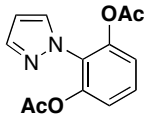
Trial	%Yield of **2-25**	%Yield of **2-23**
1	72	85
2	77	81
3	82	84
4	76	81
5	75	86

2.5 Acetoxylation of sp^2-C-H bonds – Examination of Substrate Scope

Palladium-catalyzed ligand-directed C-H activation/acetoxylation with **2-23** was also demonstrated with arene substrates containing sp^2 C-H bonds.[27] In an effort to investigate the substrate scope of this class of small molecules, oxime ethers, pyrazoles, pyridines, and amides were studied. The aforementioned classes of molecules each have a nitrogen atom within their respective heterocycles. With the exception of the amide, the nitrogen atom directs the functionalization. Oxygen served as the directing group for the amide studied in our reaction.

The reactions for this class of molecules were carried out with 5 mol % $Pd(OAc)_2$, 2.7 equiv of **2-23**, and 1 equiv of the respective substrate in acetic acid or acetic acid/acetic anhydride at concentrations ranging from 0.05 to 0.06 M. Each reaction was allowed to progress for 12 hours at 100 °C. The products and yields are displayed in Table 2.2. Isolated yields resulting from the use of **2-23** are listed in bold, while the isolated yield resulting from use of **2-9** is listed in parenthesis for comparison. Oxime ethers, substrates **2-26** and **2-28**, were efficiently mono-*ortho*-acetoxylated in excellent yields. Substrates **2-26** and **2-28** were isolated in better yield by using **2-23**, rather than **2-9**. Also of note, **2-26** has two different *ortho*-C-H bonds. Acetoxylation took place exclusively at the less sterically hindered *ortho*-position, consistent with previous studies with **2-9**.[12] Isolated samples of **2-27** contained a mixture of oxime E/Z isomers.

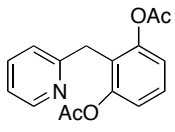
Table 2.2 – Substrate Scope of Chelate-Directed sp^2 C-H Bond Acetoxylation with **2-23**[a]

Substrate	Product	Yield
		**86%** (81%)
(**2-26**)	(**2-27**)	
		**75%** (57%)
(**2-28**)	(**2-29**)	
		**52%** (44%)
(**2-30**)	(**2-31**)	
		**55%** (77%)
(**2-32**)	(**2-33**)	
		**85%** (83%)
(**2-8**)	(**2-34**)	
		**80%**
(**2-35**)	(**2-36**)	

[a]Conditions: 5 mol% $Pd(OAc)_2$, 2.7 equiv **2-23**, 1 equiv substrate (0.05-0.06 M in AcOH or a mixture of AcOH/Ac_2O), 12 h, 100 °C.

2-Benzylpyridine, **2-30**, was mono-acetoxylated in moderate yield. Unreacted starting material, **2-30**, and the bis-*ortho*-acetoxylated product, **2-38**, (Figure 2.4) were observed by GCMS of the crude reaction mixture in yields of 8% and 25%, respectively. While moderate, the yield was again enhanced by the use of **2-23** as an oxidant, rather than **2-9**. The structure of **2-30** dictates that the palladium intermediate formed in the catalytic cycle would be a 6-membered palladacycle. This larger size of the palladacycle, 6-membered versus 5-membered, is believed to account for the observation of mono-acetoxylation as the major product, despite the use of 2.7 equiv of **2-23**. Similar trends are observed in reactions with **2-9**, and likely reflect the rate of C-H activation as a function of palladacycle size and structure.[29] 1-Phenylpyrrolidin-2-one, **2-32**, was also mono-acetoxylated in moderate yield. Use of **2-23**, as compared to acetoxylation with **2-9**, lowered the yield of **2-33**. Unreacted starting material, **2-32**, was observed by GCMS of the crude reaction mixture. It is unknown why **2-23** is a less reactive oxidant for this particular substrate. The observation of mono-acetoxylation in this example is again attributed to the 6-membered palladacycle formed as a catalytic intermediate.

Figure 2.4 - Bis-*Ortho*-Acetoxylated 2-Benzylpyridine, **2-38**



(**2-38**)

2-Phenylpyridine, **2-8**, was diacetoxylated in excellent yield. The yield was slightly enhanced by use of **2-23**. The structure of **2-8** dictates that the palladium intermediate formed in the catalytic cycle would be a 5-membered palladacycle, which is believed to account for the observation of diacetoxylation, rather than mono-

acetoxylation.[29] 1-Phenyl-1*H*-pyrazole, **2-35**, was also diacetoxylated in excellent yield. Again, diacetoxylation is rationalized based on the 5-membered palladacycle intermediate formed.

2.6 Conclusion

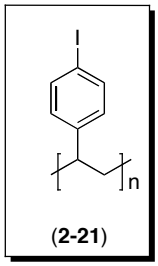
In conclusion, we have demonstrated an alternative, viable method for oxidizing small molecules using the methodology of ligand-directed, palladium-catalyzed C-H activation/functionalization. The use of poly-4-(diacetoxyiodo)styrene, **2-23**, as an oxidant improves upon the use of iodobenzene diacetate, **2-9**, as an oxidant, while maintaining important similarities. Use of a polymer-immobilized oxidant does not compromise the substrate scope and reaction yields; in fact, in several examples, yields of substrates with sp^2 C-H bonds were enhanced. The improvement with this system is due to the simple regeneration of **2-23** with maintained levels of reactivity. As a recyclable alternative, employment of **2-23** is a practical approach to C-H activation/acetoxylation of small molecules.

2.7 Experimental Procedures

General Considerations. NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for ^{1}H; 125.70 MHz for ^{13}C) or a Varian Inova 400 (399.96 MHz for ^{1}H; 100.57 MHz for ^{13}C) spectrometer. ^{1}H NMR chemical shifts are reported in parts per million (ppm) with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet (t), triplet of doublets (td), triplet of triplets (tt), multiplet (m), and broad resonance (br).

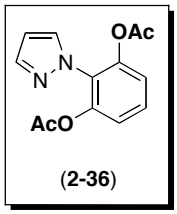
Materials and Methods. Poly-4-iodostyrene, **2-21**, was synthesized according to literature procedures with additional modifications described below.[20] Poly-4-(diacetoxyiodo)styrene, **2-23**, was synthesized according to a literature procedure.[20] The

poly-4-(diacetoxyiodo)styrene, **2-23**, reproducibly contained 88% active oxidant (as measured by iodometry), and all stoichiometries were calculated based on this value. Substrates **2-8**, **2-30**, **2-32**, and **2-35** were purchased from commercial sources (Acros, Lancaster, and Aldrich) and used as received. Substrates **2-26** and **2-28** were synthesized *via* published procedures.[10, 11] Additionally, control reactions were carried out for each substrate in the absence of palladium catalyst. These reactions generally did not exhibit any reaction under our standard conditions.



(**2-21**)

Poly-4-iodostyrene (**2-21**). Polystyrene (8 g, 76.5 mmol), I_2 (9 g, 35.5 mmol, and I_2O_5 (3.5 g, 10.9 mmol) were dissolved in a mixture of CCl_4 (20 mL), 50% aqueous H_2SO_4 (17 mL), and nitrobenzene (100 mL). Notably, we found it essential to use new bottles (or freshly distilled) of CCl_4 and nitrobenzene in this reaction to avoid the formation of an intractable oily black product. The reaction mixture was stirred at 90 °C for 40 h, cooled to 25 °C, and diluted with 50 mL of $CHCl_3$. The light orange product was precipitated by the addition of approximately 700 mL of CH_3OH. **2-21** was purified by three sequential precipitations from $CHCl_3$ with CH_3OH to afford 10.1 g (81% yield) of an off-white solid, **2-21**. Elemental analysis revealed that 88% of the polystyrene phenyl groups were iodinated.



(**2-36**)

2-(1*H*-pyrazol-1-yl)-1,3-phenylene diacetate (**2-36**). Substrate **2-35** (64 mg, 0.44 mmol), complex **2-23** (464 mg, 1.32 mmol), and $Pd(OAc)_2$ (5 mg, 0.022 mmol) were added to a 50 mL round-bottom flask with 1 mL of acetic acid and 9 mL of acetic anhydride. The reaction mixture was stirred at 100 °C for 12 h and cooled to 25 °C. **2-21** was precipitated with CH_3OH, collected on a frit, and washed with CH_3OH. The reaction mixture and washings were combined and evaporated to dryness to afford organic product **2-36** (92 mg, 80%). ^{1}H NMR ($CDCl_3$): δ 7.72 (d, J = 2.4 Hz, 1H), 7.50-7.43 (m, 2H), 7.16 (d, J = 8.4 Hz, 2H), 6.40 (t, J = 2.4 Hz, 1H), 2.08 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 168.36, 146.84, 141.01, 131.78, 129.27, 121.12, 121.09, 106.30, 20.34.

General Procedure for Palladium-Catalyzed Acetoxylation with 2-23 – The organic substrate (1 equiv, 0.05 to 0.1 M), **2-23** (1.7 to 2.7 equiv) and $Pd(OAc)_2$ (5 mol %) were combined in acetic acid or a mixture of acetic acid/acetic anhydride and stirred for 3 to 12 h at 100 °C. The reaction was cooled to 25 °C, and **2-21** was precipitated with CH_3OH, collected on a frit, and washed with CH_3OH. The reaction mixture and washings were combined and evaporated to dryness to afford the organic products. For **2-24**, this procedure afforded analytically pure material. For other substrates produced by acetoxylation, the product was further purified by chromatography on silica gel due to other products corresponding to multiple possible sites for directed oxidation and/or trace amounts of starting materials.[10, 11] These products have been reported previously and were characterized by comparison to literature NMR spectra. [10, 30-31]

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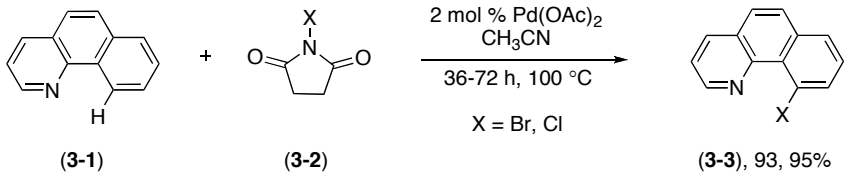
Chapter 3

Synthesis and Reactivity of Chlorinated Palladium(IV) Complexes

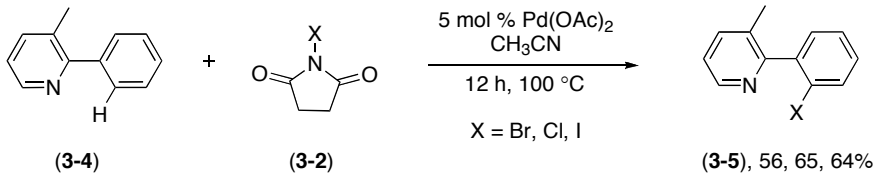
3.1 Introduction

Aryl halides serve as key components of or precursors to a wide variety of natural products, pharmaceuticals, agrochemicals, and materials.[1-7] Common methods for synthesizing aryl halides include halogenation of arenes with iron or aluminum chloride catalysts or addition of a nucleophilic halogen source to an aryl diazonium salt.[8] While these methods are reasonable for simple arenes such as benzene, they are not effective in promoting selective halogenation for more complex aromatic molecules. In order to address this challenge, researchers have employed transition metal catalysts, particularly palladium catalysts, for the selective synthesis of aryl halides.[1-7]

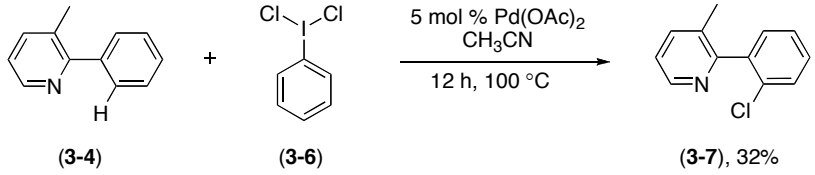
Prior research from our laboratory has shown that palladium(II) catalysts in conjunction with electrophilic halogenating reagents promote the ligand-directed conversion of arene carbon-hydrogen (C–H) bonds into carbon-halogen bonds. As shown in Scheme 3.1, one carbon-hydrogen bond of 7,8-benzoquinoline is functionalized to a carbon-halogen bond when it reacts with an *N*-halosuccinimide in the presence of $Pd(OAc)_2$.[3] Schemes 3.2 and 3.3 depict the halogenation of 2-phenylpyridine using either an *N*-halosuccinimide or dichloroiodobenzene ($PhICl_2$), respectively.[5, 6]



Scheme 3.1 – Palladium-Catalyzed Halogenation of 7,8-Benzoquinoline, **3-1**



Scheme 3.2 – Palladium-Catalyzed Halogenation of 2-Methyl-3-Phenylpyridine, **3-4**, Using *N*-Halosuccinimides



Scheme 3.3 – Palladium-Catalyzed Halogenation of 2-Methyl-3-Phenylpyridine, **3-4**, Using $PhICl_2$

The transformations in Schemes 3.1 through 3.3 were proposed to proceed by a palladium(II)/(IV) catalytic cycle. Figure 3.1 depicts a specific example with 2-methyl-3-phenylpyridine, **3-4**, as the substrate and chlorine as the halogen. The palladium begins at an oxidation state of +2 and reacts with 2-methyl-3-phenylpyridine, **3-4**, to generate a new palladium(II) complex, **3-8**. Complex **3-8** is then oxidized by *N*-chlorosuccinimide (NCS) or dichloroiodobenzene ($PhICl_2$) to generate a new palladium(IV) intermediate, **3-9**, where chlorine is now a ligand on the palladium. Finally, intermediate **3-9** undergoes

reductive elimination to release 2-(2-chlorophenyl)-3-methylpyridine, **3-7**, and a palladium(II) species which can re-enter the catalytic cycle.

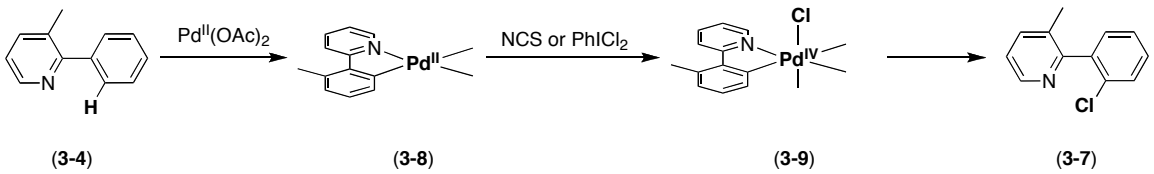
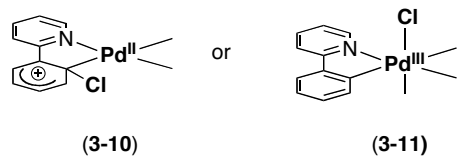


Figure 3.1 – Proposed Mechanism of Palladium-Catalyzed Chlorination

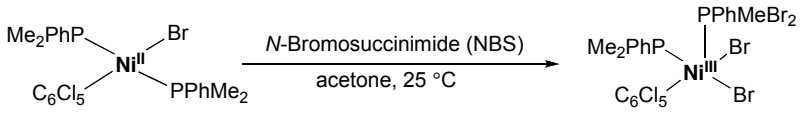
The key intermediate in this cycle is the palladium(IV) intermediate, **3-9**. Chapter 2 introduced the acetoxylation, *via* monomer and polymer forms of $PhI(OAc)_2$, of small molecules, including 2-phenylpyridine, an analogue of 2-methyl-3-phenylpyridine, **3-4**. Mechanistic studies supported the proposal of an acetoxylation mechanism analogous to that proposed in Figure 3.1. Synthesis and characterization of $Pd^{IV}(phpy)_2(OAc)_2$ and other Pd^{IV} carboxylate complexes provide evidence for the feasibility of proposing palladium(IV) intermediates in the halogen system.[9, 10]

While the mechanism in Figure 3.1 is certainly plausible, there are other potential pathways for the halogenation reactions that do not proceed through palladium(IV) intermediates (Figure 3.2). An alternate mechanism would involve direct electrophilic cleavage of the Pd(II)-C bond without a change in oxidation state at palladium (species **3-10**). This type of pathway, which is similar to an organic S_E2 process, has significant precedent at late metal centers.[11-13] Another option would invoke a single electron transfer mechanism, *via* a Pd(III) intermediate of general structure **3-11**. For example, *N*-bromosuccinimide has been shown to react with nickel(II) (another group 10 metal), to afford, **3-13**, a stable analogue of **3-11**, Scheme 3.4.[14]



(**3-10**) (**3-11**)

Figure 3.2 – Alternative Possible Intermediates in Palladium-Catalyzed Chlorination Mechanism



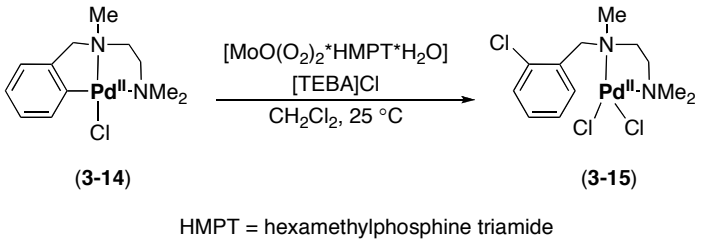
(3-12) **(3-13)**

Scheme 3.4 - Synthesis of $Ni^{III}(PPhMe_2)_2(C_6Cl_5)Br_2$

In order to gain further insight into the mechanism of C–H bond halogenation, we undertook studies of stoichiometric reactions between both $PhICl_2$ and *N*-chlorosuccinimide and the model complex $Pd^{II}(phpy)_2$ (phpy = 2-phenylpyridine). Chlorination was chosen as the halogenation reaction of study in order to investigate the use of two different electrophilic reagents. While both reagents produce the same functionalized organic molecule in their respective catalytic reactions, formation of identical palladium intermediates had not been confirmed. $Pd^{II}(phpy)_2$ was selected for investigation because the cyclometalated phenylpyridine ligands are rigid, electron-donating, and contain nitrogen donors, all features that are expected to stabilize high oxidation states and/or highly electrophilic intermediates, such as **3-9**, **3-10**, and **3-11**.[10, 14-20]

Importantly, several previous reports have described reactions of other Pd^{II} σ-alkyl or aryl complexes with electrophilic halogenating reagents to afford organic halide products.[21-22] For example, van Koten observes chlorination of a cyclopalladated *N*,*N*-dimethylbenzylamine complex, **3-14**, using a molybdenum peroxide and (triethyl) benzyl ammonium chloride ([TEBA]Cl) (Scheme 3.5).[23] Bautista observes iodination of an aryl

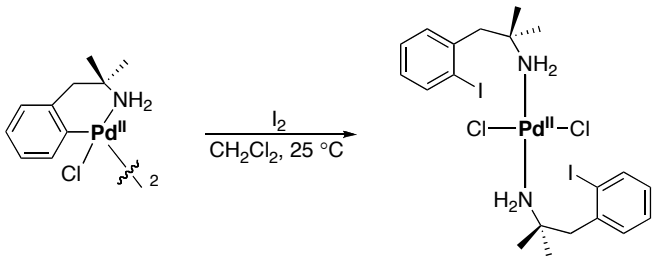
carbon bound to a palladium(II) dimer, **3-17**, as depicted in Scheme 3.6.[24] In both cases palladium(IV) halogen intermediates, with *trans* geometries of the added halogens, are proposed. However these high oxidation-state organometallic intermediates were not observed.



(**3-14**) (**3-15**)

HMPT = hexamethylphosphine triamide

Scheme 3.5 – Chlorination of **3-14** with Molybdenum Peroxide and [TEBA]Cl

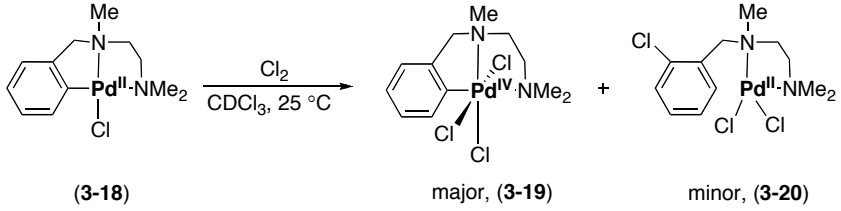


(**3-16**) (**3-17**)

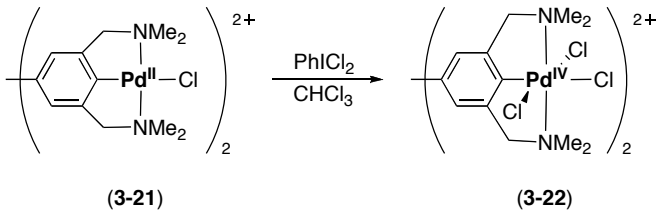
Scheme 3.6 – Iodination of **3-16**

In limited instances, transient Pd^{IV} analogues of **3-9** were identified by ^{1}H or ^{31}P NMR spectroscopy. van Koten was able to observe a palladium(IV) complex, **3-19** (shown in Scheme 3.7) by ^{1}H NMR spectroscopy at room temperature. The observance of **3-19** was attributed to the strongly electron-donating C, N, N' ligand.[17] In another example, van Koten oxidized a different organopalladium complex, using the electrophilic reagent $PhICl_2$. Scheme 3.8 shows the palladium(IV) complex, **3-22**, observed immediately after oxidant addition, by ^{1}H NMR spectroscopy. Immediate

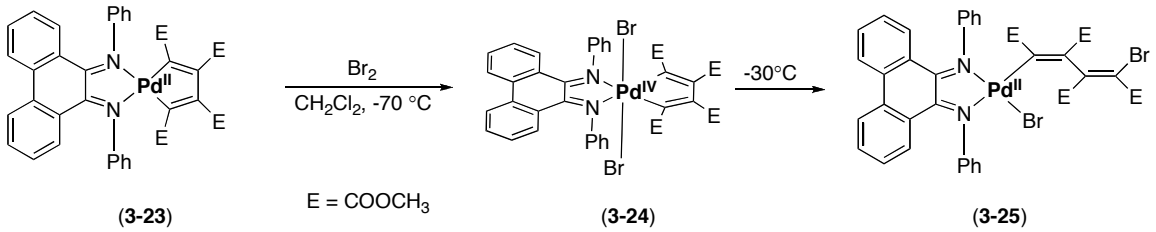
observation of **3-22** was required due to its decomposition within 10 minutes.[18] Elsevier oxidized an organopalladium complex with Br_2 at -70 °C. Transient observation of **3-24** occurred at -40 °C. An additional increase in temperature resulted in the formation of palladium(II) complex, **3-25**.[19] Navarro was able to observe the formation of a palladium(IV) complex, **3-27**, derived from a bis(pentafluorophenyl)palladium(II) complex, **3-26** (Scheme 3.10).[20] Vicente briefly observed a palladium(IV) intermediate, by ^{31}P NMR spectroscopy, from the chlorine oxidation of **3-28** shown in Scheme 3.11.[25]All of the complexes discussed above typically exhibited low stability at ambient temperatures, which precluded further characterization and limited detailed reactivity studies.



Scheme 3.7 – Chlorination of **3-18** with Observance of Pd^{IV} Intermediate

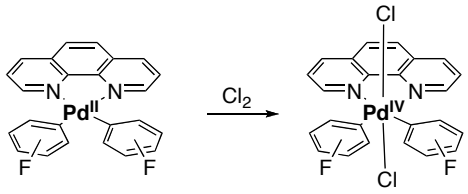


Scheme 3.8 – Oxidation of **3-21** with $PhICl_2$



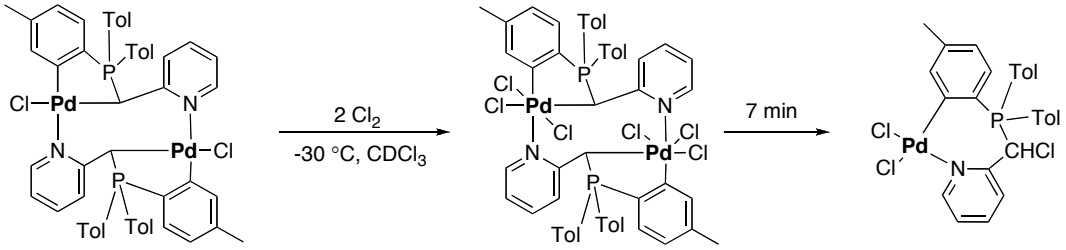
(**3-23**) (**3-24**) (**3-25**)

Scheme 3.9 – Bromine Oxidation of **3-23** with Observance of Pd^{IV} Complex, **3-24**



(**3-26**) (**3-27**)

Scheme 3.10 – Chlorination of **3-26** with Observance of Pd^{IV} Complex, **3-27**



(**3-28**) (**3-29**) (**3-30**)

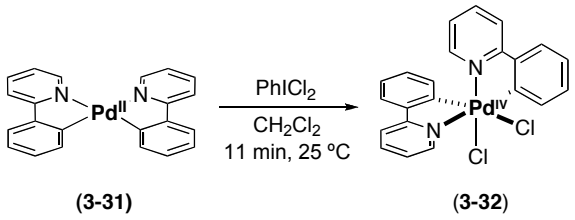
Scheme 3.11 – Chlorination of **3-28** with Observance of Pd^{IV} Intermediate

In contrast to the reactions discussed above, $Pd^{II}(phpy)_2$ reacts with both $PhICl_2$ and N-chlorosuccinimide (NCS) to form stable palladium(IV) products. In this chapter the synthesis of several chlorinated palladium(IV) complexes will be described.

Furthermore, preliminary investigations of the reactivity of these complexes towards reductive elimination will also be described.

3.2 Synthesis and Reactivity of $Pd^{IV}(phpy)_2Cl_2$, 3-32

Initial studies focused on the reaction between $Pd^{II}(phpy)_2$, **3-31**, and $PhICl_2$ in CH_2Cl_2.[26] Careful monitoring showed that a single, major inorganic species was formed after 11 min of stirring at 25 ºC, and this product (**3-32** in Scheme 3.12) was isolated as a yellow solid in 61% yield. The ^1H NMR and ^{13}C NMR spectra of **3-32** are consistent with an octahedral Pd^{IV} complex possessing a *cis* geometry and two inequivalent phpy ligands. In addition, the ^1H NMR spectrum shows diagnostic upfield and downfield signals at 6.49 and 9.90 ppm, respectively, which are characteristic of Pd^{IV} and Pt^{IV} complexes of general structure *cis*-$M^{IV}(phpy)_2X_2$.[10, 27] Notably, **3-32** is stable at room temperature in the solid state for at least 2 weeks and shows <5% decomposition after 10 h in $CDCl_3$ solution.



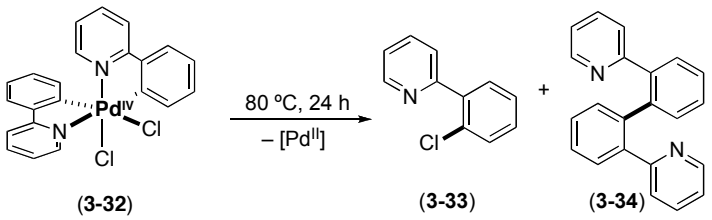
(3-31) (3-32)

Scheme 3.12 – Oxidation of **3-31** with $PhICl_2$

The formation of complex **3-32** demonstrates that palladium(IV) can be accessed with $PhICl_2$ and thereby provides support for the viability of proposed intermediate **3-9** in the catalytic reactions. However, the isolation of **3-32** does not definitively exclude the intermediacy of **3-10** or **3-11** in the catalytic transformations. The isolation of **3-32** does provide a unique opportunity to directly study carbon-halogen bond-forming reductive elimination from Pd^{IV}. Importantly, well-characterized examples of C–X coupling at Pd^{IV}

are extremely rare.[19] Examples of C-X coupling at the more stable Pt^{IV} are even limited.[28-31] Attempts to observe such reactions have been hampered by the low stability of the Pd^{IV} starting materials and/or by the fact that most isolable Pd^{IV} halide complexes contain multiple σ-alkyl/aryl ligands, which undergo fast competing C–C coupling processes.[32-34] However, prior work from our laboratory suggested that C–C reductive elimination from **3-32** might be minimized by the presence of rigid chelating phpy ligands, allowing competing carbon-heteroatom bond-forming processes to be observed.[10]

The structure of **3-32** establishes the possible types of organic reductive elimination products that could be formed. Complex **3-32** could undergo C–C or C–Cl bond-forming reductive elimination to afford 2-(2-chlorophenyl)pyridine, **3-33** or 2,2'-di(pyridin-2-yl)biphenyl, **3-34**, respectively (Scheme 3.13). When **3-32** was heated at 80 ºC for 24 h in pyridine, the C–C coupled product **3-34** was the sole organic species observed by GC and GCMS analysis (Table 3.1, entry 1).[26] Notably, the yields reflected in Table 3.1 are based on an average of four reactions, and a GC calibration of authentic samples of organic products **3-33** and **3-34**. Reductive elimination is expected to generate two different, coordinatively unsaturated Pd^{II} products, which appear to undergo rapid disproportionation/decomposition at 80 ºC. As a result, the inorganic products of these reactions could not be definitively identified/characterized.



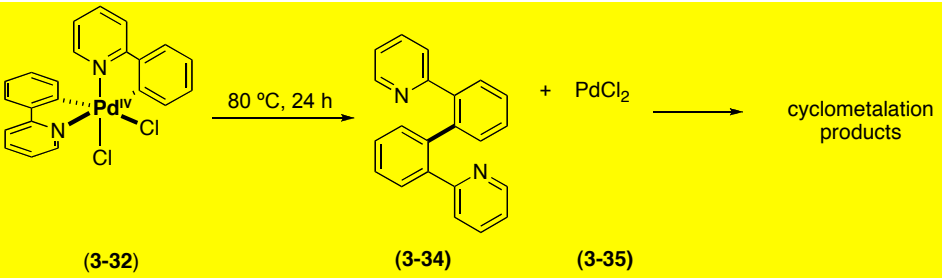
(**3-32**) (**3-33**) (**3-34**)

Scheme 3.13 – Possible Reductive Elimination Reactions of **3-32**

Table 3.1 – Observed Reductive Elimination Products of **3-32**

Entry	Solvent	%**3-33**	%**3-34**	2-phenylpyridine
1	C_5H_5N	<1	60	<1
2	AcOH	49	7	6
3	Acetone	30	8	6
4	CH_3CN	42	10	<1
5	C_6H_6	20	10	1
6	$C_6H_5NO_2$	53	5	7

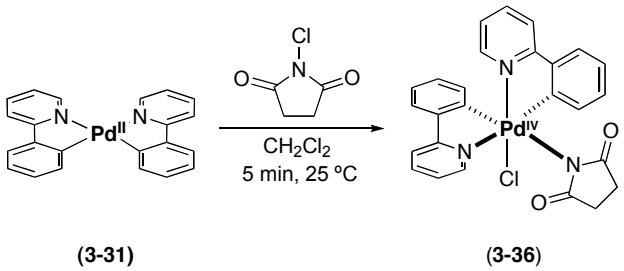
Interestingly, in AcOH (the most effective medium for palladium catalyzed halogenation reactions),[5, 6] thermolysis of **3-32** afforded a 7 : 1 ratio of **3-33** : **3-34** (Table 3.1, entry 2). To our knowledge, this is the first report of carbon-halogen bond-forming reductive elimination occurring in preference to C–C coupling at a Pd^{IV} center. Investigation of other common solvents, including benzene, nitrobenzene, acetone and acetonitrile, led to the formation of mixtures of **3-33** and **3-34** (Table 3.1, entries 3-6). Modest quantities of the free ligand 2-phenylpyridine were also observed in several of the solvents. Acetone and benzene afforded a mass balance of organic products of less than 50% as determined by GC and GCMS. We believe that this may be due to competing cyclometalation of products **3-33** and **3-34** by the Pd^{II} by-products of reductive elimination. This competing cyclometalation most likely occurs in every solvent; however, it may become particularly facile in acetone and benzene.



Scheme 3.14 – Cyclometalation of **3-34** by Palladium(II) Complex, **35**

3.3 Synthesis and Reactivity of $Pd^{IV}(phpy)_2(C_4H_4NO_2)Cl$, 3-36

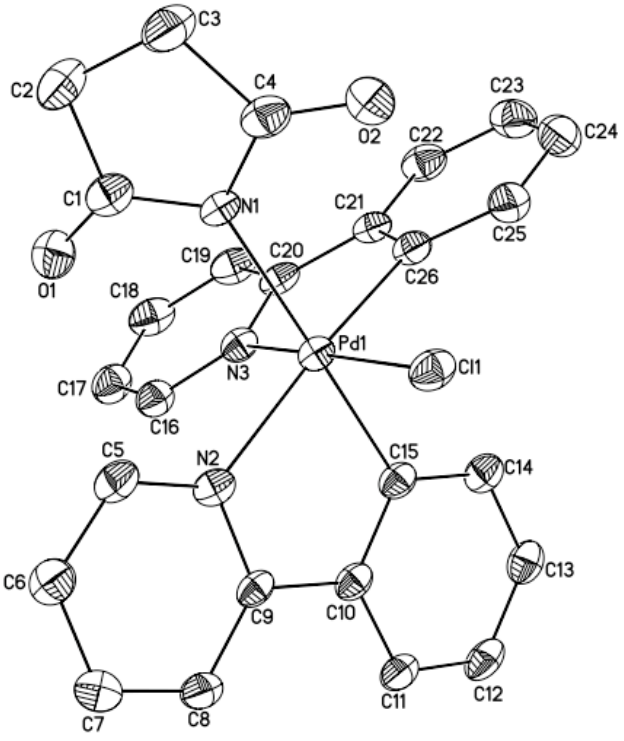
N-Chlorosuccinimide (NCS) also reacted with $Pd^{II}(phpy)_2$ to produce a stable Pd^{IV} oxidative addition product, **3-36**.[26] This reaction was complete within 5 min at 25 ºC, and afforded the novel complex **3-36** in 67% yield as a yellow solid (Scheme 3.15). This is a rare example of direct oxidative addition into the N–X bond of an *N*-halosuccinimide and, to our knowledge, the first reported example of direct oxidative addition at a palladium(II) center.[35, 36] Complex **3-36** was initially characterized by ^1H and ^{13}C NMR spectroscopy, which show signals consistent with *cis* oxidative addition and incorporation of a succinimide ligand.

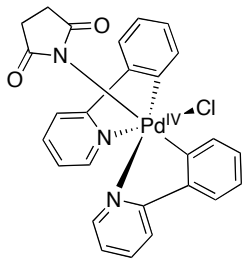


Scheme 3.15 – Oxidation of **3-31** with NCS

X-ray quality crystals were obtained by slow diffusion of pentane into a $CHCl_3$ solution of **3-36**. As shown in Figure 3.3, the X-ray structure confirms the proposed *cis* orientation between the chloride and succinimide ligands. Furthermore, it shows that the succinimide is *trans* to a σ-phenyl ligand, while the chloride is *trans* to a pyridine nitrogen. The selected bond lengths in Table 3.2 offer interesting information regarding the differences between Pd-C bond lengths and Pd-N bond lengths. While the Pd-C bond lengths are virtually identical, there is significant separation between the three Pd-N distances. The nitrogen of the succinimide ligand, trans to the carbon, is the longest at 2.219(3) Å, followed by the nitrogen of 2-phenylpyridine trans to carbon and the nitrogen

of the other 2-phenylpyridine trans to chlorine with distances of 2.145(3)Å and 2.038(3) Å, respectively. The trans influence of carbon is responsible for lengthening the palladium-nitrogen bond, to a greater extent for the nitrogen acting as an X-type ligand rather than the nitrogen forming a dative bond.





(**3-36**)

Figure 3.3 – ORTEP View of $Pd^{IV}(phpy)_2(C_4H_4NO_2)Cl$, **3-36**

Table 3.2 – Selected Bond Lengths (Å) and Angles(°) for $Pd^{IV}(phpy)_2(C_4H_4NO_2)Cl$, **3-36**

Pd(1)-C(15)	2.021(4)	C(15)-Pd(1)-N(3)	88.44(14)
Pd(1)-C(26)	2.027(4)	N(3)-Pd(1)-N(1)	92.15(12)
Pd(1)-N(3)	2.038(3)	C(15)-Pd(1)-Cl(1)	87.16(11)
Pd(1)-N(2)	2.145(3)	C(26)-Pd(1)-N(2)	172.90(13)
Pd(1)-N(1)	2.219(3)	N(3)-Pd(1)-Cl(1)	174.53(10)
Pd(1)-Cl(1)	2.3056(14)	C(15)-Pd(1)-N(1)	178.65(13)
		N(1)-Pd(1)-Cl(1)	92.31(9)

As mentioned above, the clean formation of **3-36** stands in contrast to reactions of other group 10 metal complexes with *N*-halosuccinimides. As shown in Scheme 3.4, $L_2X_2Ni^{II}$ species have been shown to react with NBS to afford the corresponding Ni^{III} bromides,[14] while reactions between $L_2X_2Pt^{II}$, **3-37**, and NCS typically generate either $L_2X_2PtCl_2$, **3-38**,[37] or L_2X_2PtCl(Solvent), **3-39**, adducts.[37, 38]

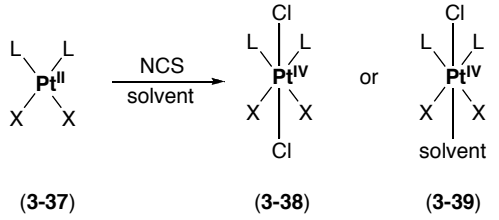
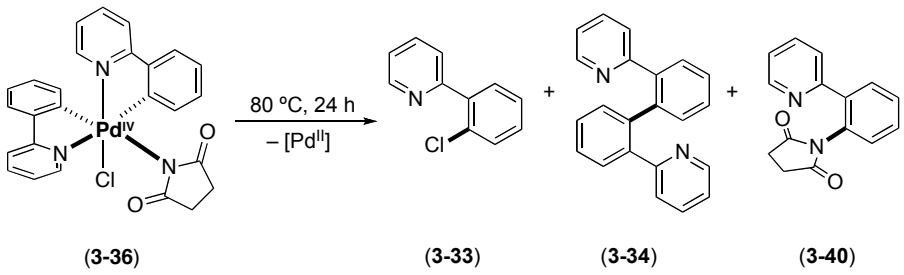


Figure 3.4 – Platinum(IV) Complexes Formed by Oxidation with NCS

The formation of complex **3-36** demonstrates that palladium(IV) can also be accessed with NCS, providing further support for the viability of proposed intermediate **3-9** in the aforementioned catalytic halogenation reactions. Similar to our investigation of the reactivity of **3-32**, we also wanted to examine reductive elimination reactions of **3-36**. Complex **3-36** presents an even more interesting situation where reductive elimination could afford three possible organic products: **3-33**, **3-34**, and/or the C–N coupled product **3-40**, shown in Scheme 3.16.



Scheme 3.16 – Possible Reductive Elimination Reaction of **3-36**

Similar to complex **3-32**, thermolysis of **3-36** in pyridine at 80 °C for 24 h resulted in predominantly C–C reductive elimination to afford **3-34** as the major organic product (Table 3.3, entry 1).[26] However, intriguingly, this reaction also afforded modest (8%) yield of the aminated product **3-40**. This is particularly notable because C–N bond-forming reductive elimination from high oxidation state late metal complexes is extremely rare.[39] Additionally, this result suggests that optimization of reaction medium and catalyst structure might allow for catalytic C–N bond-formation with NCS as the terminal oxidant. However, initial efforts have shown that $Pd(OAc)_2$-catalyzed chlorination (or amination) of 2-phenylpyridine does not proceed in pyridine.

Table 3.3 – Observed Reductive Elimination Products of **3-36**

Entry	Solvent	%**3-33**	%**3-34**	%**3-40**	2-phenylpyridine
1	C_5H_5N	6	81	8	<1
2	AcOH	67	5	<1	7
3	Acetone	10	20	<1	<1
4	CH_3CN	8	20	<1	<1
5	C_6H_6	13	23	6	<1
6	$C_6H_5NO_2$	32	13	<1	<1

In the catalytic reaction solvent AcOH, none of amide **3-40** was observed, and C–Cl bond-forming reductive elimination predominated (Table 3.3, entry 2). Unlike with complex **3-32**, acetic acid was the only solvent where protonated ligand was observed. When the solvent was changed to acetone, acetonitrile, or nitrobenzene, only traces of **3-40** were formed along with mixtures of **3-33** and **3-34**. However, the use of benzene also promoted formation of a modest amount of **3-40**, along with small quantities of **3-33** and **3-34**. As with complex **3-32**, the mass balance in several of the solvents (*e.g.*, acetone, acetonitrile, benzene, nitrobenzene) was quite low, presumably due to subsequent cyclometalation reactions of the products. In contrast to **3-32**, 2-(2-chlorophenyl)pyridine, **3-33**, is the predominant organic product in only two of the entries. The C-C coupled product, **3-34**, is the major product in the majority of reactions examined.

3.4 Consideration of Mixed Isomers of Chlorinated Pd^{IV} Complexes

Oxidation of **3-31** with the electrophilic chlorinating reagents NCS and $PhICl_2$ produced two different palladium(IV) complexes with both comparable and divergent reactivity. While similar reactivity was observed in acetic acid, nitrobenzene and pyridine, with the primary observation of **3-33** and **3-34**, respectively, differing reactivity was observed in other solvents. The major organic product of thermolysis varied from

complex **3-32** to complex **3-36** in the solvents acetone, acetonitrile, and benzene. Although the yields in these solvents were admittedly low, the data they provided was clear. The critical question to address was the origin of these differences.

Attempting to answer this question led us to consider the inherent differences in the palladium(IV) complexes. Compound **3-32** has two chlorine ligands, one *trans* to a carbon, and another *trans* to nitrogen. Compound **3-36** has one chlorine ligand and one succinimide ligand, *trans* to a nitrogen and carbon, respectively. Several possibilities arise when considering the ligands and their absolute location on the metal. For compound **3-36**, the C-Cl reductive elimination product, **3-33**, can only arise from one chlorine ligand. However, with complex **3-32**, the organic product **3-33** may originate from the chlorine that is *trans* to the nitrogen or from the chlorine that is *trans* to the carbon or from both locations. It is unknown if one chlorine is more "preferred" to reductively eliminate based on its geometry.

The *trans* effect dictates that for complex **3-32** the chlorine *trans* to the carbon should be more labile, but it is not certain this is actually the chlorine that is found in the reductive elimination product. It is also unknown whether the lability of the chlorine is a factor, as the mechanism for reductive elimination may not involve dissociation of a chlorine ligand or any ligand. It is entirely possible that the reductive elimination could involve dissociation of an alternate ligand, uninvolved in functionalization or be concerted. Prior work in our laboratory has suggested that the mechanism of reductive elimination from palladium(IV) benzoate complexes, $Pd(phpy)_2(O_2CR)_2$, begins with dissociation of a nitrogen arm of a chelated 2-phenylpyridine ligand.[10] Three mechanisms, shown in Figure 3.5, were considered, including (*i*) initial dissociation of a benzoate ligand, followed by reductive elimination from an ionic, 5-coordinate, Pd^{IV} intermediate, (*ii*) direct reductive elimination from the neutral Pd^{IV} intermediate, and (*iii*) initial dissociation of a nitrogen arm of the chelate ligand, followed by reductive elimination from a neutral, 5-coordinate, Pd^{IV} intermediate.

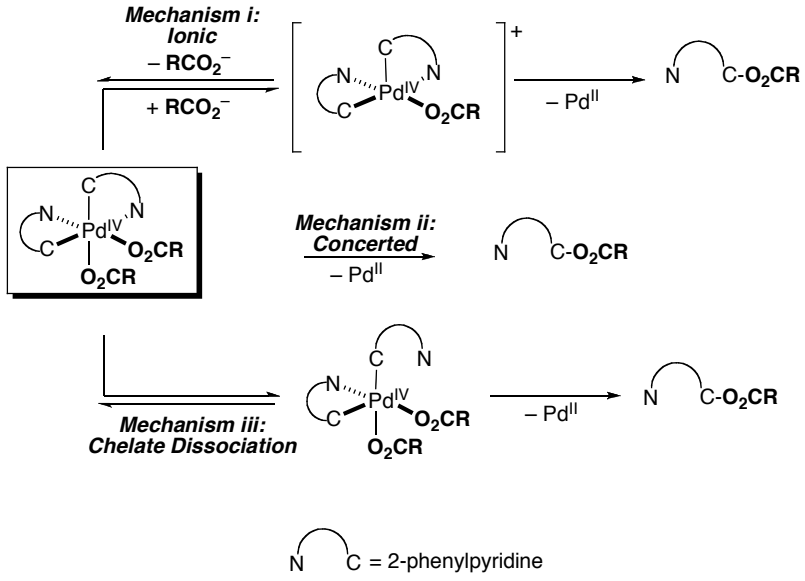
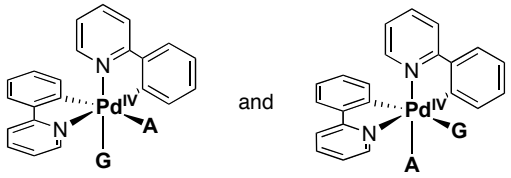


Figure 3.5 – Possible Mechanisms for Reductive Elimination of Pd^{IV} Benzoate Complexes

The inquiry regarding the mechanism of these reactions is interesting, but unnecessary to probe the differences in reactivity of compounds **3-32** and **3-36**. Another difference that must be considered concerns the type and number of ligands. Compound **3-32** has two chlorine ligands, while **3-36** only has one. The fact that **3-36** has different types of ligand also may affect reductive elimination if either ligand preferentially reductively eliminates.

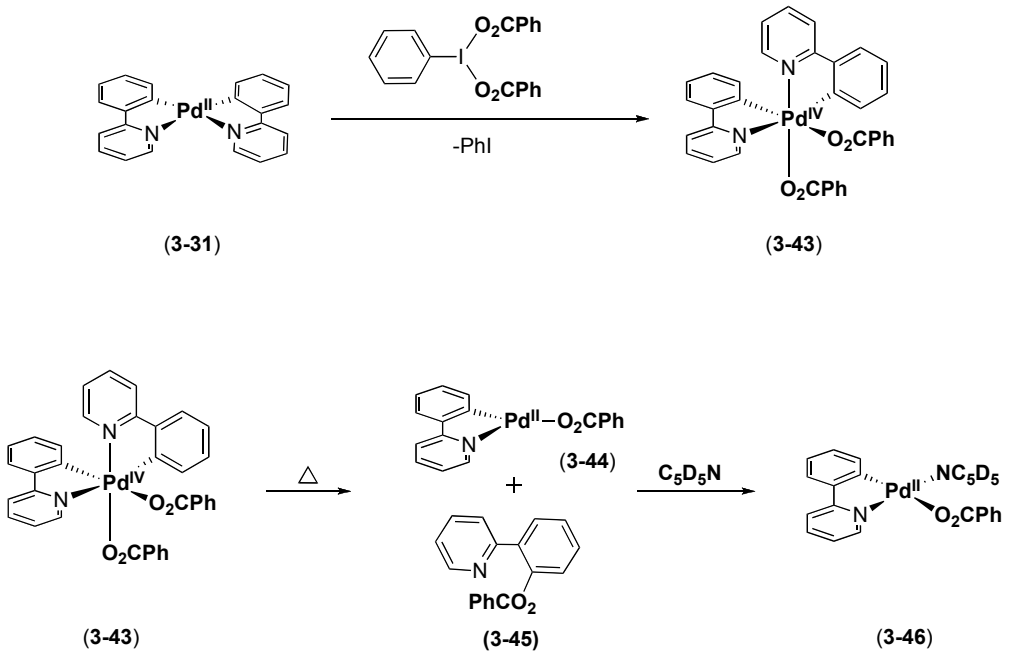
In citing the differences between the chlorinated palladium(IV) compounds, **3-32** and **3-36**, the main considerations were the effect of geometry and the possible preference for reductive elimination of one ligand over another. Our desire was to systematically examine these effects by designing a framework that accounted for both. Our strategy was to synthesize two isomeric palladium(IV) complexes, **3-41** and **3-42**, with two different X-type ligands, represented by A and G in Figure 3.6. The sole difference between the two complexes would be the position of the ligands. Ligand A could be *trans* to carbon or nitrogen. The same would be true for ligand G.



(**3-41**) (**3-42**)

Figure 3.6 – Synthetic Targets for Study of Palladium(IV) Geometry and Ligand Preference

Step two of our strategy required selection of suitable ligands. Chloride and acetate were chosen because of our current and prior investigations of carbon-X reductive elimination of each ligand individually from palladium(IV) centers. This chapter details C-Cl reductive elimination from complex **3-32**. Palladium(IV) benzoates have been previously synthesized and isolated for study of reductive elimination as shown in Scheme 3.17.[10] Clean C-O reductive elimination was observed upon thermolysis of **3-43**.



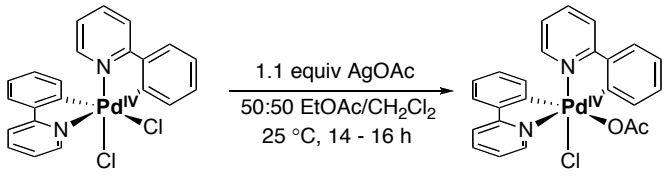
Scheme 3.17 – Synthesis and Reductive Elimination of Pd^{IV} Benzoates

Step three of our strategy required a plan of action for synthesizing the desired isomers with chlorine and acetate ligands. One method that could provide a favorable outcome involved taking advantage of the *trans* effect. In this system, the *trans* effect is expected to render the X-ligand trans to a carbon of 2-phenylpyridine the most labile ligand, and hence the predicted ligand to undergo substitution. The actual synthesis would require beginning with a palladium(IV) complex with one desired X-type ligand in place, *trans* to the nitrogen. Assuming the ligand *trans* to the carbon would exchange, a nucleophilic source of the desired alternate ligand could be used to promote the substitution reaction.

3.5 Synthesis and Reactivity of $Pd^{IV}(phpy)_2(OAc)Cl$ – Isomer 1, 3-47

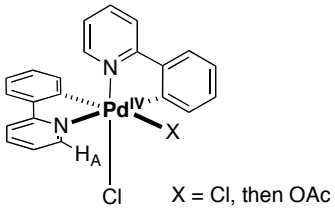
The first isomer of $Pd^{IV}(phpy)_2(OAc)Cl$ was synthesized from $Pd^{IV}(phpy)_2Cl_2$, **3-32**. AgOAc was added to **3-32** in a 50/50 mixture of CH_2Cl_2 and ethyl acetate. The 50/50 solvent mixture was carefully selected to ensure solubility of all reagents. After stirring **3-**

32 and AgOAc at room temperature for approximately 15 h, AgCl precipitated out of the reaction solution leaving the desired complex, **3-47**, in the filtrate (Scheme 3.18). Concentration of the filtrate led to isolation of **3-47** as a bright yellow powder in 63% yield. Initial characterization of **3-47** began with ^{1}H NMR spectroscopy. A comparison of the ^{1}H NMR spectra of **3-32** and **3-47** showed that the diagnostic signal at 9.90 ppm, corresponding to H_A in **3-48** (Figure 3.7), shifted to 9.34 ppm. This upfield shift corresponds to the change in environment experienced by H_A due to the substitution of electronegative chlorine for a less electronegative acetate group.



(**3-32**) (**3-47**)

Scheme 3.18 – Synthesis of $Pd^{IV}(phpy)_2(OAc)Cl$ – Isomer 1, **3-47**

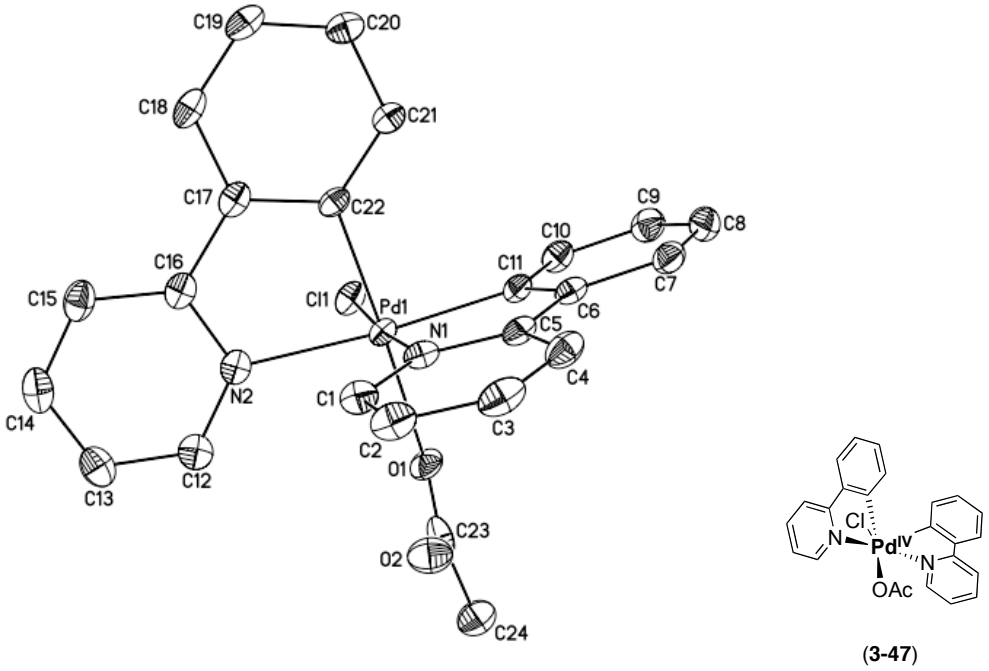


(**3-48**)

Figure 3.7 - H_A in $Pd^{IV}(phpy)_2Cl(X)$

^{1}H NMR spectroscopy provided evidence supporting the proposed structure of **3-47**; however, this assignment of the molecule was not incontrovertible. As this information was critical to our investigations, further confirmation was required. X-ray

quality crystals of **3-47** were obtained that corroborated our initial assignment of the chlorine ligand *trans* to the nitrogen and the acetate ligand *trans* to the carbon (Figure 3.8). Selected bond lengths and angles are reported in Table 3.4. Similar to complex **3-32**, the Pd-C bond lengths are nearly identical and the two Pd-N bond lengths differ substantially. The Pd-O bond length is noticeably shorter than the Pd-Cl bond length even with the trans influence of carbon on oxygen. Analogous platinum complexes reveal that Pt-O bond lengths are typically shorter than Pt-Cl bond lengths (Chapters 4 and 5).



(**3-47**)

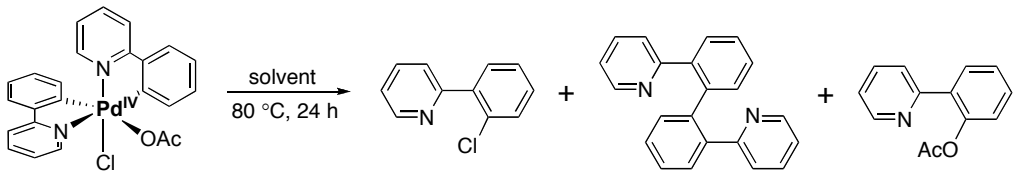
Figure 3.8 – ORTEP view of $Pd^{IV}(phpy)_2(OAc)Cl$, **3-47**

Table 3.4 – Selected Bond Lengths (Å) and Angles(°) for $Pd^{IV}(phpy)_2(OAc)Cl$, **3-47**

Pd(1)-C(22)	2.003(2)	C(22)-Pd(1)-N(1)	87.34(7)
Pd(1)-C(11)	2.007(2)	N(1)-Pd(1)-O(1)	97.74(7)
Pd(1)-N(1)	2.0306(17)	C(22)-Pd(1)-Cl(1)	89.45(6)
Pd(1)-N(2)	2.1381(18)	C(11)-Pd(1)-N(2)	172.66(8)
Pd(1)-O(1)	2.1554(15)	N(3)-Pd(1)-Cl(1)	175.31(5)
Pd(1)-Cl(1)	2.3046(5)	C(22)-Pd(1)-O(1)	174.73(7)
		N(2)-Pd(1)-Cl(1)	89.16(5)

The isolation of **3-47** allowed for an examination of reductive elimination from a new multi-ligand complex of palladium(IV). Four solvents, acetic acid, acetonitrile, benzene, and pyridine, were chosen for initial investigation. With the exception of pyridine, all of the solvents have been shown to promote catalytic C-H functionalization *via* chlorination or acetoxylation.[3, 5-6] Pyridine was included for study because of the intriguing reactivity promoted upon thermolysis of **3-36**. The observance of the C-N coupled product, **3-40**, demonstrated the ability for pyridine to promote alternative functionalization beyond carbon-carbon coupling.

Identical thermolysis conditions for compounds **3-32** and **3-36** were used for complex **3-47**. Upon heating at 80 °C in each solvent, the reductive elimination products shown in Scheme 3.19 were observed in varying amounts as shown in Table 3.5.



(**3-47**) (**3-33**) (**3-34**) (**3-49**)

Scheme 3.19 – Reductive Elimination Reaction of **3-47**

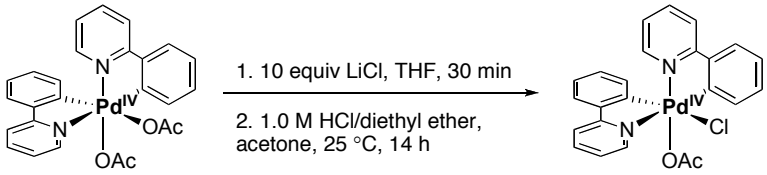
Table 3.5 – Observed Reductive Elimination Products of **3-47**

Entry	Solvent	%**3-33**	%**3-34**	%**3-49**
1	AcOH	40	8	3
2	CH_3CN	13	11	57
3	C_6H_6	11	11	63
4	C_5H_5N	2	13	16

Thermolysis in acetic acid, again primarily produced the C-Cl coupled product as in the case of reductive elimination from **3-32** and **3-36**. In acetonitrile and benzene, the C-OAc reductive elimination predominated significantly over both C-Cl and C-C coupling. In pyridine, the major product also arises from C-OAc reductive elimination, with the added caveat of fairly low yields. It is not unknown as to why the organic mass balance cannot adequately be accounted for in pyridine, given that this is not the case with complexes **3-32** and **3-36**. Repeated attempts to increase the yields in pyridine have been unsuccessful.

3.6 Synthesis and Reactivity of $Pd^{IV}(phpy)_2Cl(OAc)$ – Isomer 2, 3-51

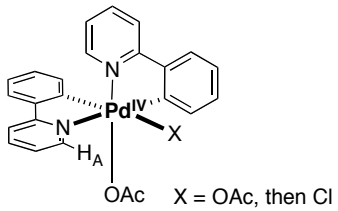
The second isomer of $Pd^{IV}(phpy)_2Cl(OAc)$ was synthesized from $Pd^{IV}(phpy)_2(OAc)_2$, **3-50**. A two-step synthesis was required to ensure that all of the starting material, **3-50**, was converted to the desired isomer (Scheme 3.20). Initially, 10 equiv of LiCl and one equiv of **3-50** were allowed to stir at room temperature for 30 min. This reaction produced a mixture of the desired isomer (**3-51**) along with remaining palladium(IV) starting material, **3-50**. Product collected from the isolation of this Pd^{IV} mixture was subjected to 1.7 equiv (based on desired ligand substitution of approximately 50% of **3-50**) of HCl in diethyl ether using acetone as the solvent. The reaction was stirred at room temperature and proceeded over the course of ~15 h. A pale yellow material precipitated from the reaction mixture and was identified as $Pd^{IV}(phpy)_2Cl(OAc)$ – isomer 2, **3-51**.



(**3-50**) (**3-51**)

Scheme 3.20 – Synthesis of $Pd^{IV}(phpy)_2Cl(OAc)$ – Isomer 2, **3-51**

A comparison of the ^1H NMR spectra of **3-50** and **3-51** showed that the diagnostic signal at 9.24 ppm, corresponding to H_A in Figure 3.9, shifted to 9.62 ppm. This downfield shift is related to the change in environment experienced by H_A, upon substitution of acetate, for a more electronegative chlorine ligand. The ^1H NMR spectra of isomers 1 and 2, **3-47** and **3-51**, respectively, differed significantly in the most downfield signal. Although attempts to grow X-ray quality crystals of **3-51** were unsuccessful, we are highly confident in our assignment of **3-51**. The characterization data support the identification of **3-51** as a palladium(IV) complex that has a chlorine *trans* to a carbon and an acetate ligand *trans* to a nitrogen.

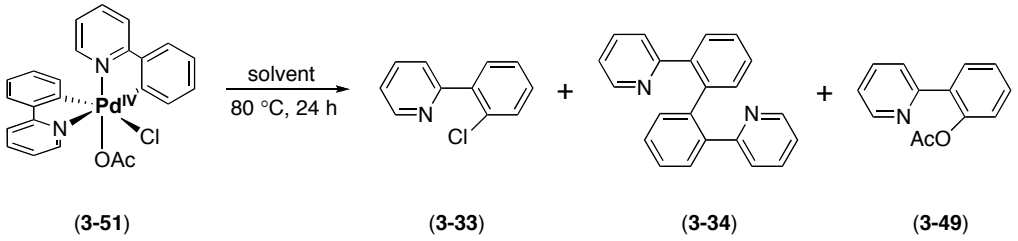


(**3-52**)

Figure 3.9 - H_A in $Pd^{IV}(phpy)_2OAc(X)$

Compound **3-51** was subjected to identical thermolysis conditions of 80 °C for 24 h as shown in Scheme 3.21. We expected to observe the same organic reductive

elimination products, although we anticipated that their relative yields might differ based on the different geometry. However, as shown in Table 3.6, the overall trend of the results did not differ from those obtained from complex **3-47**. In acetic acid, C-Cl reductive elimination was the predominant product. The remaining solvents primarily promoted C-OAc reductive elimination. Thermolysis of **3-51** in pyridine allowed for reasonable accounting of organic mass balance, in contrast to **3-47**.



(**3-51**) (**3-33**) (**3-34**) (**3-49**)

Scheme 3.21 – Reductive Elimination Reaction of **3-51**

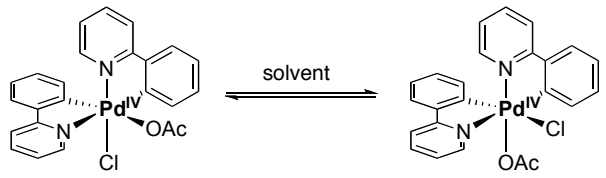
Table 3.6 – Observed Reductive Elimination Products of **3-51**

Entry	Solvent	%**3-33**	%**3-34**	%**3-49**
1	AcOH	36	1	19
2	CH_3CN	3	3	52
3	C_6H_6	2	1	73
4	C_5H_5N	2	2	68

3.7 Discussion of Reductive Elimination Observations from Mixed Isomers 1 and 2

A comparison of the relative yields of organic reductive elimination products for each isomer, **3-47** and **3-51**, revealed that the trends were consistent for both isomers within a given solvent. As our initial hypothesis was that the position of the ligand was a pivotal factor in reductive elimination, these results were unexpected. A new working

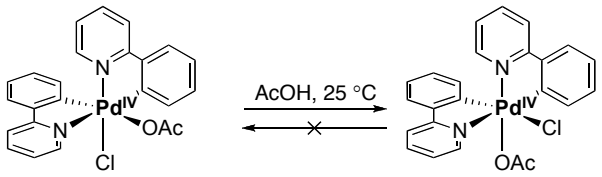
hypothesis would suggest that ligand position is unimportant and solvent dictates the outcome of the reductive elimination process. This hypothesis requires that no interconversion of the isomers takes place under the reaction conditions. Another explanation for the observed yields emerges from the possibility of **3-47** converting to **3-51** or conversely **3-51** converting to **3-47** as shown in Scheme 3.22.



(**3-47**) (**3-51**)

Scheme 3.22 – Interconversion of **3-47** and **3-51**

To investigate the possibility of interconversion, each compound was monitored by ^{1}H NMR spectroscopy at both 25 °C and 80 °C over an extended period of time. First, isomer 1, **3-47**, was monitored at 80 °C for 3 h in d_4-acetic acid. Remarkably, more than 90% of the reductive elimination product was observed within the first 10 min. However, when this same isomer was monitored at 25 ºC over 14 h, initial appearance of isomer 2, **3-51** was observed after 0.05 h (ratio of isomer 2/isomer 1 = 54.6/1), and the ratio of these two compounds steadily decreased over time to 4.7/1 after 13.7 h. When isomer 2, **3-51**, was subjected to the same two sets of conditions, none of isomer 1, **3-47**, was observed by ^{1}H NMR spectroscopy at either 80 °C or 25 °C (Scheme 3.23). At 80 °C, rapid reductive elimination was observed. Observations were also made for both complexes in d_6-benzene at 80 °C. Again reductive elimination was observed within the first hour. Rapid reductive elimination was also observed at 80 °C for isomer 1, **3-47**, in d_5-pyridine.



(**3-47**) (**3-51**)

Scheme 3.23 – Interconversion of Isomer 1, **3-47**, to Isomer 2, **3-51**, at 25 °C

The interconversion of only one isomer, **3-47**, and the relative rate of interconversion lead us to conclude that both ligand position and solvent are essential elements of the reductive elimination mechanism. Ligand position alters the stability of metal complexes. The interconversion of **3-47** to **3-51** signifies that **3-51** is more stable than **3-47**. The more stable complex may have a larger contribution to reductive elimination, depending on the rate of reductive elimination relative to interconversion. Based on the results from the aforementioned NMR spectroscopy experiments at 25 °C, interconversion is most likely faster than reductive elimination. Future work should examine this hypothesis in multiple solvents. The stability of isomer 2, **3-51**, relative to **3-47**, is solely attributed to ligand position.

Solvent effects for both **3-47** and **3-51** demonstrate solvent selection is paramount. Different solvents promote different organic reductive elimination products. It is possible that various solvents promote reductive elimination through contrasting mechanisms. One item of interest includes noting that only the acidic solvent promotes C-Cl reductive elimination, while the other non-acidic solvents promote C-OAc reductive elimination. A possible explanation could involve the requirement of dissociation of one X-type ligand, but not the ligand that will be found in the reductive elimination product. Reductive elimination would take place from the 5-coordinate cationic intermediate. The solvent effects could be explained by suggesting that acetic acid promotes dissociation of the acetate ligand. Goldberg observed acetic acid promotion of C-O coupling from a platinum(IV) complex with an acetate ligand.[40] If the ligand that reductively eliminates is bound to the metal, dissociation of acetate would promote reductive elimination to form a

C-Cl organic product. In general, any of the solvents could allow or promote equilibration to the more stable isomer, **3-51**. In the non-acidic solvents this may be followed by dissociation of the more labile chlorine and reductive elimination of the C-OAc coupled product. Presumably the chlorine ligand is generally more labile in the absence of a substance that would promote an alternate path (*i.e.* - dissociation of acetate or inhibition of chlorine dissociation).

3.8 Conclusion

In conclusion, this chapter has described the reactions of $PhICl_2$ and NCS with $Pd^{II}(phpy)_2$, **3-31**, to afford room temperature stable oxidative addition adducts **3-32** and **3-36**. These novel complexes are shown to undergo competing C–Cl, C–C, and C–N bond-forming reductive elimination reactions to form **3-33**, **3-34**, and **3-40**, respectively. Both the accessibility and the observed reactivity of **3-32** and **3-36** provide support for a $Pd^{II/IV}$ mechanism in palladium-catalyzed halogenation reactions.

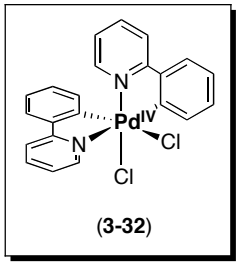
The divergence of the results from reductive elimination in select solvents prompted consideration of a systematic method to examine possible geometry and ligand preferences of metals with respect to reductive elimination. The mixed isomers of $Pd^{IV}(phpy)_2(OAc)Cl$ were chosen in light of independent reductive elimination studies of palladium(IV) complexes with both acetate and chlorine ligands. The mixed isomers, **3-47** and **3-51** were synthesized and shown to undergo competing C-Cl, C-OAc, and C-C bond-forming reductive elimination reactions to form **3-33**, **3-49**, and **3-34**, respectively. Initial results indicate the deciding factors in observed reductive elimination products are both the solvent medium and the ability of isomer 1, **3-47** to convert into isomer 2, **3-51**. The reverse transformation, isomerization of **3-51** to **3-47**, was not observed.

Possible interpretations of the data suggest that high oxidation state palladium complexes have preferences for ligand geometry, which is expected to impact reductive elimination. Yet, in spite of these preferences, solvent is a more critical factor in governing the reductive elimination products and quite possibly the mechanism of reductive elimination itself.

3.9 Experimental Procedures

General Considerations - NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for ^{1}H; 125.70 MHz for ^{13}C) or a Varian Inova 400 (399.96 MHz for ^{1}H; 100.57 MHz for ^{13}C) spectrometer. ^{1}H NMR chemical shifts are reported in parts per million (ppm) with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet (t), triplet of doublets (td), triplet of triplets (tt), multiplet (m), and broad resonance (br). IR spectra were obtained on a Perkin-Elmer "Spectrum BX" FT-IR spectrometer. Mass spectral data were obtained on a Micromass magnetic sector mass spectrometer.

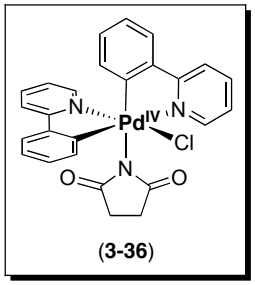
Materials and Methods - Diethylsulfide and 2-phenylpyridine and were purchased from Alfa Aesar, $PhI(OAc)_2$ from Acros, *n*-BuLi from Aldrich, and Na_2PdCl_4 from Pressure Chemical. *trans*-$(Et_2S)_2PdCl_2$ was prepared according to reference 1. Bromination of 2-phenylpyridine to 2'-bromo-2-phenylpyridine was accomplished with NBS and catalytic $Pd(OAc)_2$ according to reference 2. $(Phpy)_2Pd$ was synthesized according to reference 3. Solvents were obtained from Fisher Scientific and used without further purification. All syntheses were carried out under ambient atmosphere unless otherwise stated.



(**3-32**)

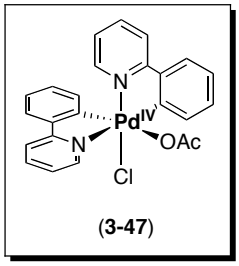
$Pd^{IV}(phpy)_2Cl_2$ (3-32) - $Pd^{II}(phpy)_2$, **3-31**, (97 mg, 0.23 mmol, 1.0 equiv) and $PhICl_2$ (64 mg, 0.23 mmol, 1.0 equiv) were combined in CH_2Cl_2 (19 mL) in a 20 mL vial. The reaction was stirred at room temperature for 11 minutes and then immediately concentrated under reduced pressure. THF (15 mL) was added to the resulting dark yellow solid, and this suspension was sonicated for 3 min. The resulting dark yellow precipitate was collected on top of a one inch layer of Celite on a fritted filter and was washed with THF (30 mL). The yellow solids were then rinsed through the Celite with CH_2Cl_2 (100 mL), and the CH_2Cl_2 was removed under vacuum to afford **3-32** (75 mg,

66%) as a yellow powder. ^{1}H NMR ($CDCl_3$): δ 9.90 (d, *J* = 5.4 Hz, 1H), 8.51 (d, *J* = 8.2 Hz, 1H), 8.09-8.07 (m, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.80 (t, *J* = 7.4 Hz, 1H), 7.73-7.71 (m, 2H), 7.59 (t, *J* = 7.0, 1H), 7.49 (t, *J* = 7.3 Hz, 1H), 7.45 (d, *J* = 5.3 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.98-6.95 (m, 2H), 6.49 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 163.40, 158.84, 156.10, 149.06, 146.33, 146.29, 141.24, 140.52, 139.82, 139.76, 133.38, 133.32, 132.40, 132.31, 26.59, 126.41, 126.12, 125.65, 124.57, 123.84, 121.12, 120.26.



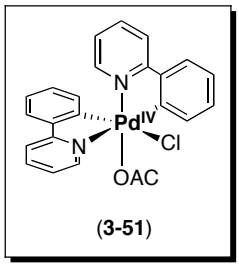
(**3-36**)

$Pd^{IV}(phpy)_2(C_4H_4NO_2)Cl$ (**3-36**) - $Pd^{II}(phpy)_2$, **3-31**, (100 mg, 0.24 mmol, 1.0 equiv) and *N*-chlorosuccinimide (32 mg, 0.24 mmol, 1.0 equiv) were combined in CH_2Cl_2 (18 mL) in a 20 mL vial. The reaction was stirred at room temperature for 5 minutes, and then the solvent was removed under reduced pressure. Acetone (19 mL) was added to the resulting pale yelow solid, and this suspension was sonicated for 3 minutes. The yellow precipitate was collected by vacuum filtration, washed with acetone (50 mL), collected, and dried under vacuum to afford **3-36** (88 mg, 67%) as a pale yellow powder. ^{1}H NMR ($CDCl_3$): δ 9.03 (d, *J* = 5.5 Hz, 1H), 8.75 (d, *J* = 7.3 Hz, 1H), 8.07-8.01 (m, 2H), 7.96 (d, *J* = 5.9 Hz, 1H), 7.75-7.71 (m, 3H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.2, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.94-6.90 (m, 2H), 6.36 (d, *J* = 7.1 Hz, 1H), 2.37 (s, 4H); ^{13}C NMR (DMSO-d_6): δ 169.21, 162.15, 158.82, 155.20, 150.96, 150.57, 141.56, 141.18, 140.68, 135.44, 131.81, 131.46, 131.40, 126.92, 126.64, 126.44, 125.86, 124.44, 123.31, 121.40, 121.13, 31.71, 31.17. (One aromatic peak does not appear due to facile reductive elimination of **3-36** in solution, which precedes the number of scans needed to obtain a complete spectra.) IR (KBr): 1712, 1634 cm^{-1}. HRMS-electrospray (m/z): $[M–(Cl)]^+$ calculated for $C_{22}H_{16}N_2ClPd$, 449.0037; Found 449.0032; Anal. Calc. for $C_{26}H_{20}N_3O_2ClPd$: C, 56.95, H, 3.68, N, 7.66; Found: C, 56.87, H, 4.01, N, 7.65.



(**3-47**)

$Pd^{IV}(phpy)_2(OAc)Cl$ - Isomer 1 (**3-47**) - $Pd^{IV}(phpy)_2Cl_2$, **3-32**, (68 mg, 0.14 mmol, 1.0 equiv) and AgOAc (26 mg, 0.154 mmol, 1.1 equiv) were combined in a 50:50 mixture of CH_2Cl_2/EtOAc (12 mL) in a 20 mL vial. The reaction was stirred at room temperature for 14 - 16 hours. The reaction mixture was poured onto a layer of celite on a fritted filter. The filtrate from the reaction mixture was collected. The precipitate and celite were washed with 30 mL of CH_2Cl_2 to obtain greater quantities of the desired product. The resultant filtrate and washings were completely concentrated. CH_2Cl_2 was removed under vacuum to afford **3-47** (45 mg, 63%) as a bright yellow powder. ^{1}H NMR ($CDCl_3$): δ 9.34 (d, *J* = 5.0 Hz, 1H), 8.53 (d, *J* = 8.0 Hz, 1H), 8.08-8.06 (m, 2H), 7.80-7.78 (m, 2H), 7.71-7.67 (m, 3H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.45-7.41 (m, 2H), 7.10 (t, *J* = 7.2 Hz, 1H), 6.94-6.91 (m, 2H), 6.46 (d, *J* = 8.0 Hz, 1H), 1.90 (s, 3H); FTIR (KBr): 3416, 3050, 1756, 1603, 1568, 1483, 1416, 1313 cm^{-1}.



(**3-51**)

$Pd^{IV}(phpy)_2Cl(OAc)$ - Isomer 2 (**3-51**) - $Pd^{IV}(phpy)_2(OAc)_2$, **3-50**, (53 mg, 0.10 mmol, 1.0 equiv) and LiCl (42 mg, 1.0 mmol, 10 equiv) were combined in THF (8 mL) in a 20 mL vial. The reaction was stirred at room temperature for 30 minutes. The resultant cream-colored precipitate was collected and washed with THF (20 mL). The precipitate was dried under vacuum for 2 – 3 hours. The dry precipitate, a mixture of **3-50** and **3-51**, were combined with acetone (10 mL) and HCl in diethyl ether (84 μL) in a 20 mL vial. The reaction was stirred at room temperature for 14 – 16 hours. The resultant cream-colored precipitate was collected and washed with acetone (20 mL). Any remaining solvent was removed under vacuum to afford **3-51** (16 mg, 31%) as a pale cream powder. ^{1}H NMR (DMSO-d_6): δ 9.62 (d, *J* = 4.0 Hz, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 8.31-8.27 (m, 2H), 8.08-8.04 (m, 2H), 7.97 (d, *J* = 6.5 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.76 (t, *J* = 6.5 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.22-7.21 (m, 2H), 7.12 (t, *J* = 7.0 Hz, 1H), 6.92 (t, *J* = 7.0 Hz, 1H), 6.19 (d, *J* = 8.0 Hz, 1H), 1.72 (s, 3H). FTIR (KBr): 3441, 3052, 1758, 1650, 1603, 1567, 1464, 1421, 1294 cm^{-1}.

General procedure for reductive elimination reactions of 3-32 and 3-36: Complex **3-32** or **3-36** was dissolved in 1 mL of solvent in a 4 mL vial. The vial was fitted with a Teflon-lined cap, and the reaction was stirred at 80 ºC for 24 h. At the end of the reaction, the vial was removed allowed to cool for approximately 2 minutes, and then the solvent was removed completely under reduced pressure. A 1:1 solution of CH_2Cl_2/EtOAc (2 mL) was added to the vial along with poly-4-vinylpyridine (85 mg). The heterogeneous solution was allowed to stir for 1 h and was then filtered through a pipette containing cotton and a 0.5 inch of poly-4-vinylpyridine. The plug was washed with 1:1 CH_2Cl_2/EtOAc (10 mL). The resulting solution was concentrated, and the volatile products were analyzed by GC and GCMS. Yields are typically reported as an average of at least 3 runs, and represent calibrated yields based on nonadecane as an internal standard.

General procedure for reductive elimination reactions of 3-47 and 3-51: Complex **3-47** or **3-51** was dissolved in 1 mL of solvent in a 4 mL vial. The vial was fitted with a Teflon-lined cap, and the reaction was stirred at 80 ºC for 24 h. At the end of the reaction, the vial was removed allowed to cool for approximately 2 minutes, and then the solvent was removed completely under reduced pressure. Benzene (2 mL) was added to the vial along with poly-4-vinylpyridine (85 mg). The heterogeneous solution was allowed to stir for 1 h and was then filtered through a pipette containing cotton with a 0.1 inch layer of celite (diatomaceous earth) and a 0.3 inch layer of alumina. The plug was washed with acetone (10 mL). The resulting solution was concentrated, and the volatile products were analyzed by GC and GCMS. Yields are typically reported as an average of at least 2 runs, and represent calibrated yields based on nonadecane as an internal standard.

X-ray structure determination for $Pd^{IV}(phpy)_2(C_4H_4NO_2)Cl$ (3-36) - Yellow, block-like crystals of **3-36** were grown from a chloroform/pentane solution at -6 °C. A crystal of dimensions 0.28 x 0.28 x 0.20 mm was mounted on a standard Bruker SMART 1K CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV,

40 mA). The X-ray intensities were measured at 108(2) K; the detector was placed at a distance 4.944 cm from the crystal. A total of 4095 frames were collected with a scan width of 0.5° in ω and 0.45°in phi with an exposure time of 30 s/frame. The integration of the data yielded a total of 53162 reflections to a maximum 2θ value of 56.78° of which 8613 were independent and 7034 were greater than 2σ (I). The final cell constants (Table 1) were based on the xyz centroids of 9876 reflections above 10σ (I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P1bar with Z = 2 for the formula $C_{26}H_{20}N_3O_2ClPd•3(CHCl_3)$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0459 and wR2 = 0.1249 [based on I > 2sigma(I)], R1 = 0.0608 and wR2 = 0.1338 for all data.

X-ray structure determination for $Pd^{IV}(phpy)_2(OAc)Cl$ – Isomer 1 (3-47) - Pale yellow needles of **3-47** were grown by slow evaporation of a chloroform/pentane solution at 25°C. A crystal of dimensions 0.26 x 0.11 x 0.09 mm was mounted on a Bruker SMART APEX CCD-based X-ray diffractometer equipped with a low temperature device and fine focus Mo-target X-ray tube (λ = 0.71073 A) operated at 1500 W power (50 kV, 30 mA). The X-ray intensities were measured at 85(1) K; the detector was placed at a distance 5.055 cm from the crystal. A total of 4095 frames were collected with a scan width of 0.5° in ω and 0.45° in phi with an exposure time of 15 s/frame. The integration of the data yielded a total of 52011 reflections to a maximum 2θ value of 56.72° of which 7200 were independent and 6843 were greater than 2σ (I). The final cell constants (Table 1) were based on the xyz centroids of 9743 reflections above 10σ (I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P1bar with Z = 2 for the formula $C_{24}H_{19}N_2O_2PdCl•2(CHCl_3)$. All non-hydrogen

atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0286 and wR2 = 0.0733 [based on I > 2sigma(I)], R1 = 0.0303 and wR2 = 0.0744 for all data.

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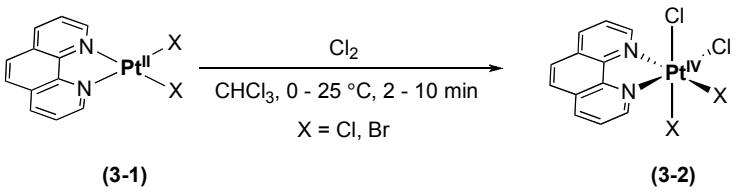
Chapter 4

Chlorinated Platinum Complexes – Studies of Oxidative Addition and Mechanistic Proposals

4.1 Introduction

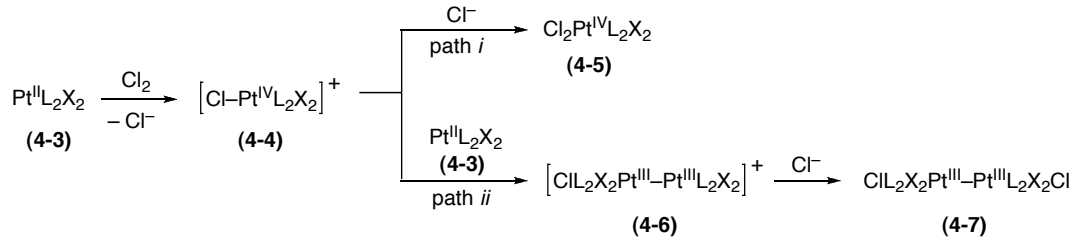
Our isolation of palladium(IV) chloride complexes from *cis*-bis-2-phenylpyridine palladium(II), led us to consider the synthesis of high oxidation state chlorinated platinum products, starting from an analogous platinum(II) complex.[1] The oxidation of Pt^{II} complexes to produce chlorinated platinum products has been explored in detail in the inorganic literature, traditionally using Cl_2 as the oxidant. One of the earliest examples was provided by Rund and Hodges, studying the oxidative addition of chlorine to dihalo(1,10-phenathroline)platinum(II), **3-1**.[2] Chlorine oxidation of this platinum(II) complex produced a new platinum(IV) species, **3-2** with the chorine ligands in a *cis* orientation to one another (Scheme 4.1).



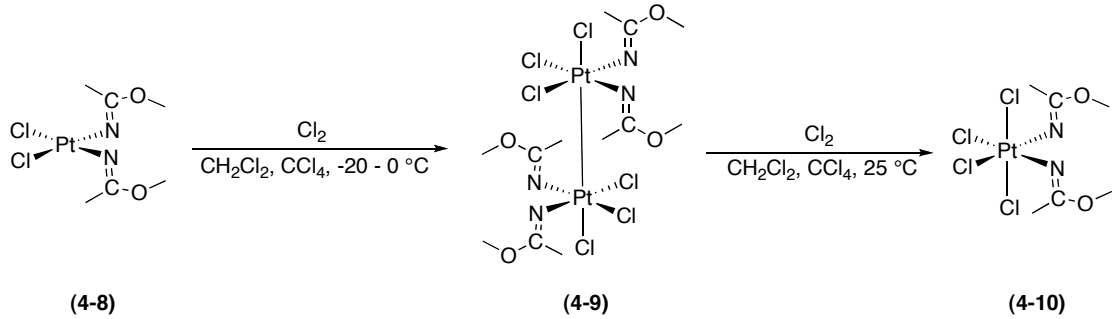
(3-1) (3-2)

Scheme 4.1 – Chlorine Oxidation of Dihalo(1,10-phenanthroline) Platinum(II)

Researchers that have studied oxidations of platinum(II) species with Cl_2 have frequently observed similar results to Rund and Hodges whereby Cl_2 adds to the metal in either a *cis* or *trans* manner to generate a new platinum(IV) product.[3-9] The proposed mechanism for these transformations is an ionic pathway involving nucleophilic attack of Pt^{II} on Cl_2 to generate a cationic five-coordinate Pt^{IV} intermediate (**4-4**) followed by coordination of Cl^- to produce the neutral Pt^{IV} dichloride product **5** (path *i*, Scheme 4.2). However, recent work by Natile and coworkers has shown that another path is also possible with intermediate **4-4** as the starting point. They observed reaction of diimine, dichloro platinum(II) complex **4-8** with Cl_2 generated the new platinum(III) species **4-9**, which could be further oxidized to a platinum(IV) product **4-10** at room temperature in the presence of light. The mechanism for formation of **4-9** is shown in path *ii* in Scheme 4.2, whereby intermediate **4-4** reacts with a second equiv of the Pt^{II} starting material **4-3** to afford the cationic dimeric Pt^{III} species **4-6**. Chloride anion can coordinate with complex **4-6** to produce the neutral Pt^{III} dimer, **4-7**, which has been observed and isolated in some cases.[10, 11] As shown in Scheme 4.3, complex **4-9** may further react with the chlorinating reagents to produce compound **4-10**. This is believed to proceed by an initial reductive elimination of chlorine from **4-9**. The resultant platinum complex, **4-8**, is oxidized by chlorine to directly produce **4-10**. Disproportionation of **4-9** is inhibited by excess chlorine in the absence of light.



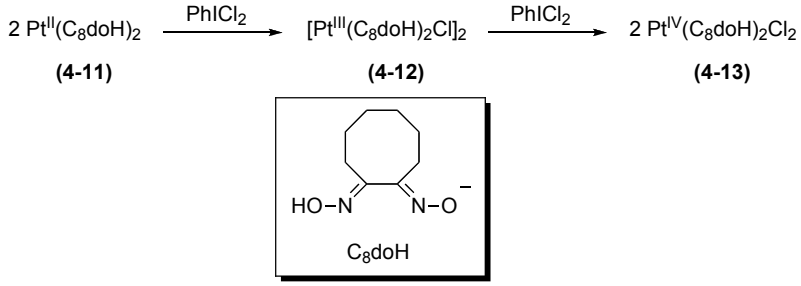
Scheme 4.2 - Formation of Pt^{IV} or Pt^{III} Products in the Oxidation of $Pt^{II}L_2X_2$ with Cl_2



(4-8) **(4-9)** **(4-10)**

Scheme 4.3 - Formation of Pt^{III} and Pt^{IV} Products in the Oxidation of $Pt^{II}[NC(CH_3)(OCH_3)]_2Cl_2$ with Cl_2

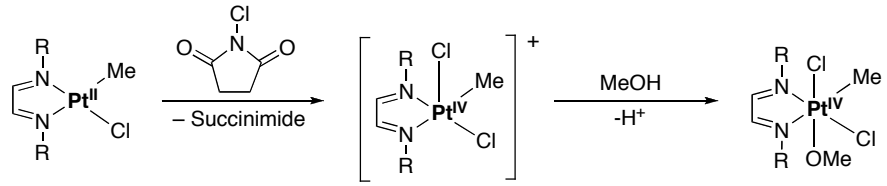
While oxidations with Cl_2 have been studied extensively, significantly less attention has focused on the reactions of Pt^{II} complexes with the electrophilic chlorine oxidants utilized in Chapter 3, $PhICl_2$ $C_8H_{12}(=NO)_2H]_2$ to afford mixtures of Pt^{III} product **4-12** and and Pt^{IV} product **4-13** as shown or *N*-chlorosuccinimide (NCS). Heath has shown that $PhICl_2$ can react with Pt^{II}[in Scheme 4.4.[12] This transformation has been proposed to proceed by a mechanism analogous to that of the Cl_2 reactions (Scheme 4.2).



Scheme 4.4 - Formation of Pt^{III} and Pt^{IV} Products in the Oxidation of $Pt^{II}(C_8doH)_2$ with $PhICl_2$

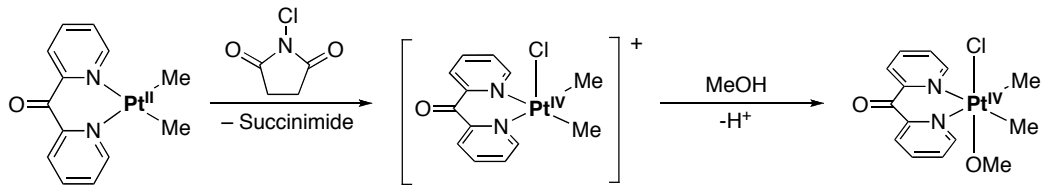
N-Chlorosuccinimide has also been used in limited instances for the oxidation of Pt^{II} species. For example, [$Pt^{II}Me_2$(α-diimine)] (**4-14**) and [$Pt^{II}Me_2$(DPK)] (**4-17**) have

been shown to react with NCS in MeOH to afford Pt^{IV} products that incorporate 1 equiv of chloride and 1 equiv of solvent as an OMe ligand (Scheme 4.5 and 4.6, respectively).[7, 13] As shown in Schemes 4.5 and 4.6, the mechanisms of these transformations are presumed to involve initial, two electron oxidation of Pt^{II} to a cationic Pt^{IV} intermediate followed by trapping of the intermediate with the solvent. Notably, Pt^{III} intermediates have not been previously observed or isolated with NCS as an oxidant.



(4-14) (4-15) (4-16)

Scheme 4.5 - Formation of Pt^{IV} Product in the Oxidation of $Pt^{II}Me_2$(α-diimine) with NCS in MeOH



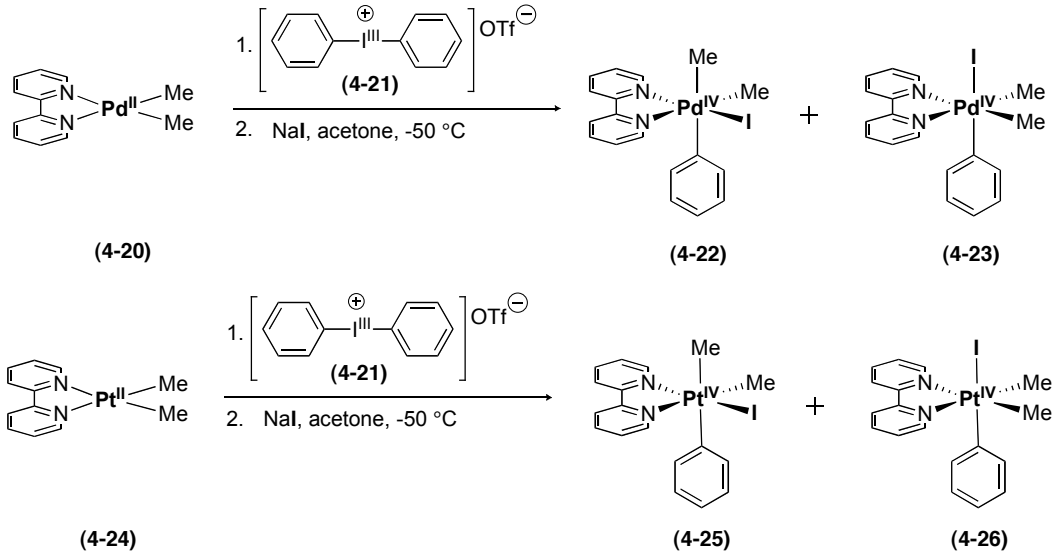
(4-17) (4-18) (4-19)

Scheme 4.6 - Formation of Pt^{IV} Products in the Oxidation of $Pt^{II}Me_2$(DPK) with NCS in MeOH

We anticipated that $Pt^{II}(phpy)_2$ would react with the electrophilic chlorinating reagents $PhICl_2$ and *N*-chlorosuccinimide (NCS) to form similar products to the palladium(IV) products isolated in Chapter 3. This assumption was predicated on several considerations. The first consideration was the literature accounts of platinum(IV)

products resulting from oxidation with $PhICl_2$ and NCS (Schemes 4.4, 4.5 and 4.6).[7, 12, 13] Although a platinum(III) complex (**4-12**) was isolated and characterized when $PhICl_2$ was used, that complex underwent further oxidation to produce a platinum(IV) species.

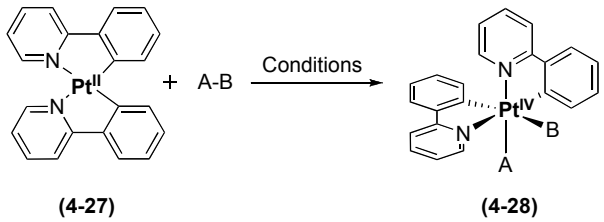
Another consideration was the numerous literature reports showing that Pt^{II} and Pd^{II} complexes with identical ligand environments display similar reactivity towards oxidants. For example, Canty has shown that (bpy)M$(Me)_2$ complexes (bpy = bipyridine, M = Pd and Pt) undergo very analogous oxidation reactions with $[Ph_2I]OTf$.[26] As shown in Scheme 4.7, both reactions provide *cis* and *trans* isomers of the M^{IV} product. However, although the Pt^{IV} product was stable at room temperature, the Pd^{IV} product decomposed above –50 ºC.



Scheme 4.7 - Oxidative Addition to Palladium(II) and Platinum(II) Complexes

Our final considerations involved examining known oxidation reactions of $Pt^{II}(phpy)_2$. While the reaction of $Pt^{II}(phpy)_2$ with NCS or $PhICl_2$ had not been previously reported, related transformations with other oxidants have been well documented. For example, von Zelewsky has demonstrated that $Pt^{II}(phpy)_2$ (**4-27**) reacts with diverse electrophiles A–B (A–B = Br_2, I_2, CH_3I, CH_2Cl_2) to afford the Pt^{IV} oxidative addition

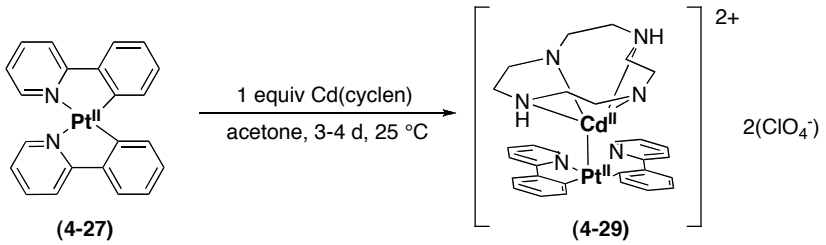
products $Pt^{IV}(phpy)_2(A)(B)$ (Scheme 4.8). For the elemental halogens, A and B are the individual atoms.[14-16] For CH_3I and CH_2Cl_2, A is defined as CH_3 and CH_2Cl, respectively, while B is I or Cl.[17-19] Mechanistic studies have shown that these transformations can proceed via thermal or photochemical pathways, depending on the reaction conditions and the oxidant. A thermal pathway has been demonstrated for the elemental halogens and methyl iodide at room temperature in the absence of light, while halogenated solvents, such as CH_2Cl_2 oxidatively add to $Pt^{II}(phpy)_2$ in a photochemical manner.



(4-27) (4-28)

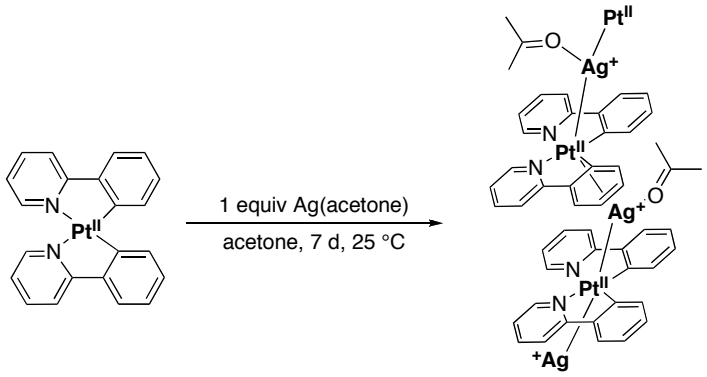
Scheme 4.8 - Oxidation of **4-27** with General Electrophiles A-B

In addition, Ito and coworkers have carried out studies of the interaction of $Pt^{II}(phpy)_2$ with d^{10} metal salts (metal = Cd^{II}, Ag^{I}, Au^{I}). These reactions were shown to result in the formation of dative M –> Pt^{II} bonds when the metal was Cd^{II} or Ag^{I}. The use of Cd^{II} produced a single dative bond between the metal atoms in **4-27** and $Cd^{II}(cyclen)^{2+}$ (Scheme 4.9).[20] In a slight variation, when M was Ag^{I}, a helical chain complex formed between **4-27** and $Ag(ClO_4)$ in a solution of acetone that consisted of alternating platinum(II) atoms and cationic silver ions (Scheme 4.10). The presence of acetone allowed for its incorporation into the structure, with one molecule of acetone coordinating to each Ag atom.[21] In contrast, reaction of **4-27** with $AuCl(SMe_2)$ led to oxidation of the Pt^{II} starting material to the Pt^{III} dimer **4-31** (Scheme 4.11).[22]



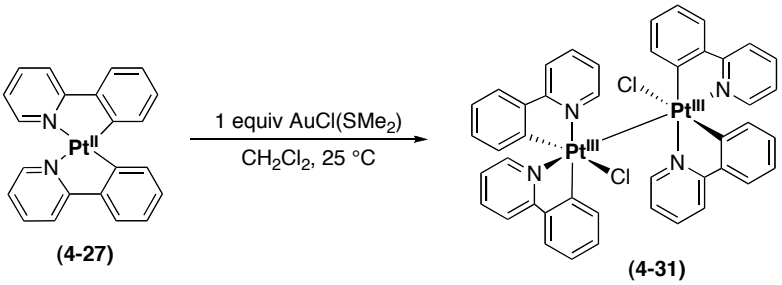
(4-27) (4-29)

Scheme 4.9 – Formation of Dative Bond Between **4-27** and $Cd(cyclen)(ClO_4)_2$



(4-27) (4-30)

Scheme 4.10 – Formation of Dative Bond Between **4-27** and $Ag(ClO_4)$ in Acetone



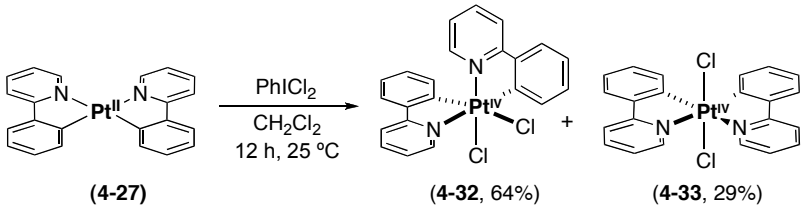
(4-27) (4-31)

Scheme 4.11 - Oxidation of **4-27** with $AuCl(SMe_2)$

As predicted, we have found that $Pt^{II}(phpy)_2$ reacts with $PhICl_2$ to provide the Pt^{IV} analogue of **4-32** in Chapter 3, $Pt^{IV}Cl_2(phpy)_2$, as a mixture of symmetrical and unsymmetrical isomers. However, in contrast, the reaction of $Pt^{II}(phpy)_2$ with NCS proceeds very differently from the analogous palladium system, affording a mixture of the Pt^{III} dimer $[(phpy)_2(Cl)Pt^{III}]_2$ and $Pt^{IV}Cl_2(phpy)_2$, whose ratio varies as a function of reaction time, concentration, and the presence/absence of ambient light. This chapter will discuss the synthesis of these high oxidation state platinum compounds. The effect of varying reaction conditions will be discussed as well as the implications of these results for the mechanisms of the platinum oxidation reactions.

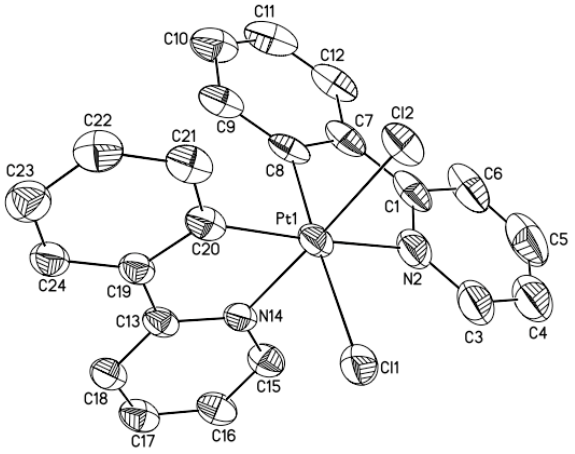
4.2 Reaction of $Pt^{II}(phpy)_2$, 4-27, with $PhICl_2$

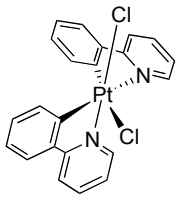
The treatment of $Pt^{II}(phpy)_2$, **4-27**, with $PhICl_2$ under identical conditions to the palladium reaction in Scheme 4.12 afforded $Pt^{IV}Cl_2(phpy)_2$ as a 1.8 : 1 mixture of two isomers (**4-32** and **4-33**). Complexes **4-32** and **4-33** were readily separated when the reaction time was increased to 12 h, as **4-33** precipitated from the CH_2Cl_2 solution. Under these conditions, **4-32** and **4-33** were isolated as pale yellow solids in 64% and 29% yield, respectively (Scheme 4.12). The major isomer (**4-32**), which is a direct analogue of **3-32** from the palladium reaction, is the unsymmetrical product of *cis* oxidative addition. The ^1H NMR spectrum of **4-32** exhibits 12 sets of peaks due to overlapping signals associated with the 16 inequivalent protons of this complex, while the ^{13}C NMR spectrum shows the expected 22 resonances.



Scheme 4.12 - Oxidation of **4-27** with $PhICl_2$

Complex **4-32** was also characterized by X-ray crystallography. The solid-state structure of this octahedral complex is shown in Figure 4.1 while selected bond lengths and angles are listed in Table 4.1. The coordination sphere of **4-32** is octahedral, although slightly distorted. The greatest distinction within the metrical parameters occurs for the varying Pt-Cl bond lengths. The two Pt-Cl bond distances, 2.3313(16) Å and 2.4173(17) Å, differ considerably, presumably due to the *trans* influence exerted by the σ-aryl ligand, effectively lengthening the Pt-Cl bond.





(4-32)

Figure 4.1 – ORTEP View of *cis*-$Pt^{IV}(phpy)_2Cl_2$, **4-32**

Table 4.1 – Selected Bond Lengths (Å) and Angles(°) for *cis*-$Pt^{IV}(phpy)_2Cl_2$, **4-32**

Pt(1)-C(20)	2.026(6)	C(20)-Pt(1)-N(2)	173.4(2)
Pt(1)-C(8)	2.029(6)	N(14)-Pt(1)-Cl(2)	176.33(15)
Pt(1)-N(14)	2.045(5)	C(8)-Pt(1)-Cl(1)	175.85(18)
Pt(1)-N(2)	2.121(6)	C(8)-Pt(1)-N(14)	91.23(19)
Pt(1)-Cl(2)	2.3313(16)	C(20)-Pt(1)-Cl(2)	95.33(15)
Pt(1)-Cl(1)	2.4173(17)	C(8)-Pt(1)-Cl(2)	176.33(15)
		Cl(2)-Pt(1)-Cl(1)	90.84(6)

The ^{1}H NMR spectrum of the second isomer **4-33** shows 8 resonances between 7.2 and 9.3 ppm, indicative of a symmetrical oxidative addition product. Notably, no analogous symmetrical product was observed in the Pd reaction. As shown in Figure 4.2, there are four potential symmetrical isomers of $Pt^{IV}(phpy)_2Cl_2$ (complexes **4-34** through **4-37**). Although none of these possibilities can be definitively ruled out, we believe that isomers **4-35** and **4-37** are unlikely because they require a *trans* orientation between the two strongly σ-donating aryl ligands. Additionally, structure **4-36** can be discounted based on spectroscopic comparison to recently reported *cis*-$Pt^{IV}(p\text{-F-phpy})_2Cl_2$ (which was confirmed to assume geometry **4-36** by X-ray crystallography).[23] The ^{1}H NMR spectrum of $Pt^{IV}(p\text{-F-phpy})_2Cl_2$ exhibits a characteristic upfield resonance at 5.71 ppm for H_A, indicative of shielding due to the proximity of this proton to the ring current of the adjacent aromatic ring.[24] The lack of such an upfield signal in the ^{1}H NMR spectrum of **4-33** is inconsistent with geometry **4-36**; furthermore, an upfield signal for H_A would not be expected in **4-34**. As such, we propose that isomer **4-34** is the most likely structure of product **4-33**.

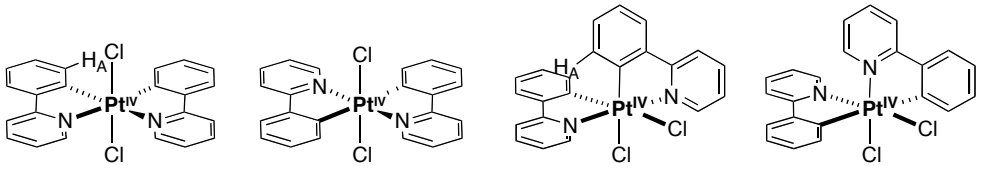
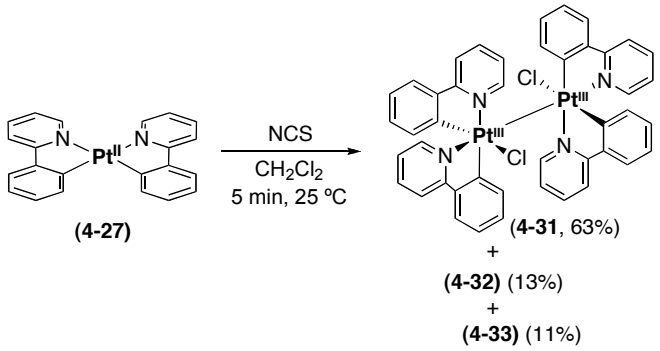


Figure 4.2 - Possible Symmetrical Oxidative Addition Products for **4-33**

Notably, comparable yields and isomer ratios were obtained when the reaction of $Pt^{II}(phpy)_2$ (**4-27**) with $PhICl_2$ was conducted in the presence or absence of ambient light (*i.e.*, in clear vials versus amber vials covered in foil). This is indicative of a thermal oxidative addition pathway, similar to that found for reaction of **4-27** with Br_2 or I_2. In addition, the yield and ratio of **4-32**:**4-33** was independent of the reaction time (within the range of 0.1–96 h) and reaction concentration (within the range of 1.25–10 mM).

4.3 Reaction of $Pt^{II}(phpy)_2$, 4-27, with *N*-chlorosuccinimide in CH_2Cl_2

The reaction of $Pt^{II}(phpy)_2$ (**4-27**) with *N*-chlorosuccinimide was also explored under otherwise identical conditions to the palladium reaction in Scheme 4.13 (1.1 equiv NCS, 5 min in CH_2Cl_2). Intriguingly, this transformation afforded <5% yield of the N–Cl oxidative addition complex $Pt^{IV}(phpy)_2Cl(C_4H_4NO_2)$. The <5% yield was determined based on comparison of the crude ^1H NMR spectrum of this reaction to the ^1H NMR spectrum of **3-36** (the major product of the analogous palladium reaction in chapter 3).[1, 25-28] Instead, ^1H NMR analysis of the crude mixture showed that Pt^{III} dimer, $Pt_2Cl_2(phpy)_4$ (**4-31**), was the major product (63%), along with substantial quantities of Pt^{IV} species **4-32** (13%) and **4-33** (11%) (Scheme 4.13). Isolation of **4-31** resulted in 55% yield. Notably, dimer **4-31** is the same complex reported previously by Ito from the reaction of $Pt^{II}(phpy)_2$ with $AuCl(SMe_2)$ in CH_2Cl_2. As such, we identified and characterized **4-31** based on data from this prior report. Notably, Ito reported that the Au oxidant provided 37% isolated yield of **4-31**.



Scheme 4.13 - Oxidation of **4-27** with NCS in CH_2Cl_2

To gain further insights into this surprising reaction of $Pt^{II}(phpy)_2$ with NCS, we studied the effect of the reaction conditions on the ratio of oxidized products (Pt^{III} complex **4-31** relative to Pt^{IV} complexes **4-32**/**4-33**). We found that this transformation was sensitive to a number of variables, including reaction time, concentration, and the presence/absence of light. Representative data that summarizes these observations is shown in Tables 4.2 and 4.3. Reactions were carried out in CH_2Cl_2 at 25 ºC, evaporated to dryness, and analyzed by ^{1}H NMR spectroscopy in DMSO-d_6. Yields for the following reactions were determined by integration of the ^{1}H NMR signals associated with each product relative to an internal standard and represent an average of two runs. In cases where the yield does not add up to 100%, small quantities of unidentified minor side products were noted. Observed trends for the collected data are discussed below.

In general, increasing the reaction time (from 5 min to 96 h) led to increased yields of Pt^{IV} complexes **4-32/4-33** relative to the Pt^{III} product **4-31** (Table 4.2, entries 1-4). Reaction concentration had a significant effect on the products obtained from this transformation. Under otherwise identical conditions, higher concentrations led to preferential formation of the Pt^{III} dimer, **4-31**, (entry 3), while approximately 10-fold dilution of the reaction mixture resulted in predominance of the Pt^{IV} compounds **4-32** and **4-33** (entry 6).

Table 4.2 - Oxidation of **4-27** with NCS as a Function of Time and Concentration

Entry	Time (h)	Concentration (mM)	Yield of **4-31**	Yield of (**4-32** + **4-33**)
1	5 min	10	63%	24%
2	12	10	59%	31%
3	24	10	56%	35%
4	96	10	46%	41%
5	24	5	36%	43%
6	24	1.25	11%	79%

We also examined the effect of ambient light on this transformation, since both Pt^{II} and Pt^{III} complexes are well-known to undergo photochemically-induced oxidation reactions.[10, 11, 29] Interestingly, when the reaction of $Pt^{II}(phpy)_2$ with NCS was carried out under standard conditions (25 ºC, 24 h, 10 mM) in the dark (amber vial covered in foil), the yields of Pt^{III} product **4-31** and of Pt^{IV} products **4-32** and **4-33** were essentially identical to those observed in ambient light (Table 4.3, entry 1). However, lowering the reaction concentration had a very different effect on the dark reactions relative to those conducted in the presence of ambient light. In the dark, Pt^{III} complex **4-31** was the major product at all concentrations examined (1.25-10 mM), while in the light, Pt^{IV} products **4-32** and **4-33** predominated as the reaction was diluted (Table 4.3, entries 2 and 3).

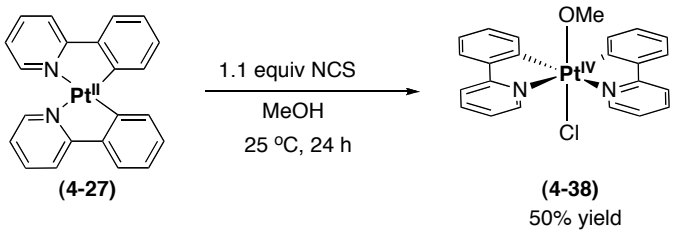
Table 4.3 - Oxidation of $Pt^{II}(phpy)_2$, **4-27**, with NCS in Presence and Absence of Light

Entry	Concentration (mM)	Light: Yield of **4-31**	Light: Yield of (**4-32** + **4-33**)	Dark: Yield of **4-31**	Dark: Yield of (**4-32** + **4-33**)
1	10	56%	35%	54%	28%
2	5	36%	43%	61%	29%
3	1.25	11%	79%	56%	35%
4	10	65%	29%	61%	24%

Finally, we examined the effect of excess chloride ion on the product distribution of these transformations. These studies revealed that the addition of up to 10 equiv of Cl^- (added as NBu_4Cl) had no discernible effect on the ratio and/or yields of **4-31** to **4-32**/**4-33** under both light and dark reaction conditions (Table 4.3, entry 4).

4.4 Reaction of $Pt^{II}(phpy)_2$, 4-27, with *N*-chlorosuccinimide in MeOH

We also examined the reactivity of **4-27** with NCS in MeOH. Although this was not a solvent used to synthesize palladium(IV) products, literature reports have identified it as a favored solvent for the synthesis of platinum(IV) complexes.[7, 13] For example, most reactions of *N*-chlorosuccinimide with Pt^{II} starting materials have been reported to cleanly afford chloro/methoxy Pt^{IV} products (**4-16** and **4-19**, Scheme 4.5 and 4.6) when conducted in MeOH. The initial transformation in MeOH was conducted under otherwise identical conditions to the NCS reactions above. This reaction afforded the Pt^{IV} complex $[Pt^{IV}(phpy)_2(Cl)(OMe)]$ (**4-38)** as the major product in 50% yield (as determined by ^1H NMR analysis of the crude reaction mixture). Analytically pure samples of **4-38** were obtained in only 10% isolated yield by concentration of the reaction mixture, which led to slow precipitation of the desired product. Yields comparable to the ^1H NMR yield could be obtained by separating the filtrate and adding hexanes to precipitate the product. However, small amounts of impurities were still present in these samples.



Scheme 4.14 - Oxidation of **4-27** with NCS in MeOH

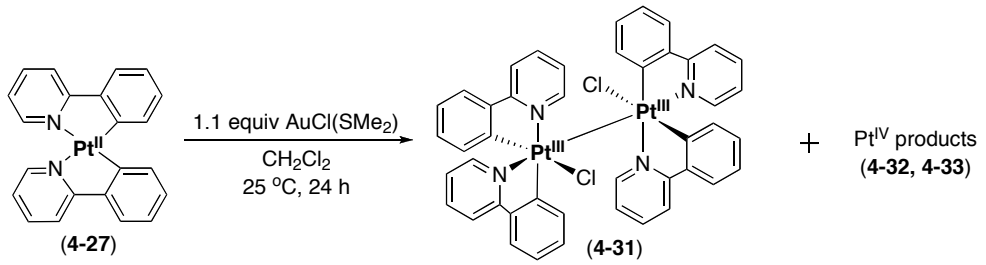
The ^{1}H and ^{13}C NMR spectra of complex **4-38** showed resonances associated with two equivalent phenylpyridine ligands, indicative of a *trans* orientation of the chloro and methoxy ligands. The similarity between the ^{1}H NMR spectra of **4-33** and **4-38**, led us to propose the structure shown in Scheme 4.14. The resonance associated with the methoxy ligand (appearing at 2.41 ppm) exhibited distinct platinum satellites whose coupling constant (J = 32 Hz) is within the range of previously reported Pt^{IV}-OMe ligands (where J values ranging from 14-61 Hz have been observed).[7, 13] Furthermore, ^{195}Pt NMR spectroscopy showed a resonance at –883 ppm (versus Na_2PtCl_6) indicative of a Pt^{IV} complex.

The modest (50%) yield of **4-38** was due, in part, to the formation of traces of several side products, including the Pt^{IV} complex **4-32** (10%) and the dimeric Pt^{III} compound **4-31** (16%). The remaining 24% of material in the crude reaction is attributed to other unidentified products. The relative ratio of products **4-38**, **4-31**, and **4-32** in this reaction was not affected by the reaction time or the presence/absence of light. However, dilution of the reaction mixture (from 10 mM to 1.25 mM) resulted in increased yield of **4-38** (70%) and decreased formation of both **4-31** (7%) and **4-32** (2%).

4.5 Reaction of $Pt^{II}(phpy)_2$, 4-27, with $AuCl(SMe_2)$

As discussed above, Pt^{III} complex **4-31** was synthesized previously *via* the reaction of **4-27** with $AuCl(SMe_2)$ in CH_2Cl_2.[22] The formation of Pt^{IV} byproducts was not discussed in this work; however, the isolated yield of **4-31** was only 37% and the remainder of the material was not accounted for. As a result, we wondered whether Pt^{IV} complexes **4-32** and/or **4-33** were also formed in reactions with the Au^{I} oxidant. Indeed, when the reaction of **4-27** with $AuCl(SMe_2)$ was carried out under our standard conditions (25 ºC, 24 h, 10 mM in CH_2Cl_2 in the light), a mixture of **4-31** (63%) and the *cis* Pt^{IV} product **4-32** (32%) was formed (Scheme 4.15, Table 4.4, entry 1). (Interestingly, only traces (<1%) of the corresponding *trans* Pt^{IV} complex **4-33** were formed under these conditions.) As summarized in Table 4.4, when the time was increased to 96 h or the concentration was lowered to 1.25 mM, the yield of Pt^{IV} complex **4-32** increased dramatically with concomitant decreases in Pt^{III} adduct **4-31** (entries 2-3). For entry 3 the

remaining 15% of the material was unreacted starting material. The observed trends are analogous to those seen in the corresponding reactions with *N*-chlorosuccinimide.



(**4-27**) (**4-31**)

Scheme 4.15 - Oxidation of **4-27** with $AuCl(SMe_2)$

Table 4.4 - Oxidation of **4-27** with $AuCl(SMe_2)$ Under Various Reaction Conditions

Entry	Time (h)	Temperature (ºC)	Concentration (mM)	Yield of **4-31**	Yield of **4-32** + **4-33**
1	24	25	10	63%	32%
2	96	24	10	49%	51%
3	24	25	1.25	12%	73%

We next examined the reaction of **4-27** with $AuCl(SMe_2)$ in MeOH rather than CH_2Cl_2 under our standard conditions (25 ºC, 24 h, 10 mM in the light). Interestingly, despite the change of medium, this transformation afforded Pt^{III} complex **4-31** in a slightly higher yield (75%) than the analogous reactions in CH_2Cl_2. The Pt^{IV} complexes **4-32**/**4-33** accounted for the remainder of the products. In sharp contrast to the reactions with NCS, none of the chloro/methoxy product **4-38** was observed in this system.

4.6 Oxidation reactions of Pt^{III} complex 4-31

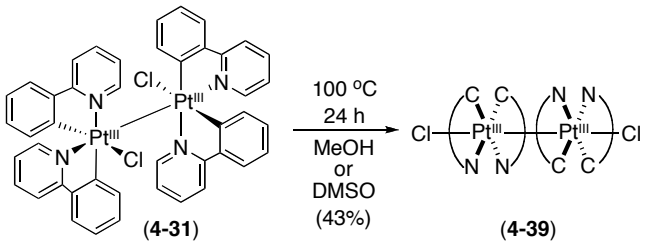
We next sought to investigate whether Pt^{III} complex **4-31** served as an intermediate to the formation of **4-32/4-33** in reactions with NCS. Our initial studies showed that isolated samples of **4-31** do indeed react with NCS in CH_2Cl_2 to form appreciable quantities (15% yield) of **4-32/4-33** under standard conditions (25 ºC, 24 h, 10 mM, Table 4.5, entry 1). However, interestingly, a comparable yield of $Pt^{IV}(phpy)_2Cl_2$, **4-32/4-33**, was obtained when this reaction was conducted in CH_2Cl_2 in the absence of NCS (Table 4.5, entry 2). In the NCS-free reactions, the yield of Pt^{IV} products increased with reaction time (Table 4.5, entry 3) and with lower reaction concentration (Table 4.5, entry 4). These trends are analogous to those observed in the reactions between $Pt^{II}(phpy)_2$, **4-27**, and *N*-chlorosuccinimide. However, notably, low conversion of **4-31** to **4-32/4-33** was observed in the dark, even under dilute conditions (Table 4.5, entry 5).

Table 4.5 - Conversion of **4-31** to Pt^{IV} Products

Entry	Time (h)	Added Oxidant (1.1 equiv)	Concentration (mM)	Amount of **4-31** remaining	Yield of **4-32** + **4-33**
1	24	NCS	10	80%	15%
2	24	None	10	83%	10%
3	96	None	10	66%	24%
4	24	None	1.25	51%	20%
5	24	None	1.25	76%	12%

The reactivity of isolated samples of Pt^{III} complex **4-31** was also examined in the non-halogenated solvents DMSO and MeOH. Only small quantities (<20%) of the Pt^{IV} dichloride products **4-32** or **4-33** were observed under the conditions examined (25-100 ºC, 12-24 h, 1.25-10 mM). While no appreciable reaction was observed at room temperature, at elevated temperatures, complex **4-31** underwent isomerization to afford a

new product (**4-39**), which was isolated in 43% yield as a dark yellow solid (Scheme 4.16). Complex **4-39** was assigned as a symmetrical isomer of the unsymmetrical Pt^{III} dimer, $Pt^{III}_2Cl_2(phpy)_4$, **4-31**, based on ^1H, ^{13}C, and ^{195}Pt NMR spectroscopy. The ^1H NMR spectrum of **4-39** showed 8 resonances between 6.5 and 8.5 ppm and the ^{13}C NMR spectrum exhibited signals associated with 11 distinct aromatic carbons. In addition, ^{195}Pt NMR spectroscopy of **4-39** showed a resonance at –2293 ppm vs. Na_2PtCl_6. This signal is very close to that of Pt^{III} dimer **4-31** (which appears at –2355 ppm) and differs substantially from that of the Pt^{II} starting material **4-27** (–3542 ppm) and the Pt^{IV} product **4-32** (–1725 ppm). HRMS analysis of this product showed $[(Cl)(phpy)_2Pt]^+$ as the major signal. Collectively, this data is consistent with the symmetrical Pt^{III} complex **4-39**, in which all of the cyclometalated phenylpyridine ligands are in identical environments. While we have chosen the structure of **4-39** as depicted in Scheme 4.16, another possible structure of complex **4-39** would have each of the four 2-phenylpyridine ligands bridging the two Pt^{III} centers. Preliminary molecular modeling suggests that this structure would be substantially higher in energy than the unbridged symmetrical structure proposed.

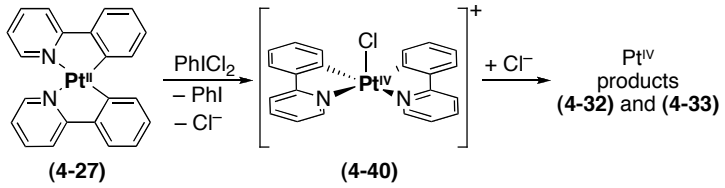


Scheme 4.16 – Thermally Induced Isomerization of **4-31** in Non-Halogenated Solvents

4.7 Discussion of Reactions Involving Conversion of Pt^{II} to Pt^{IV}

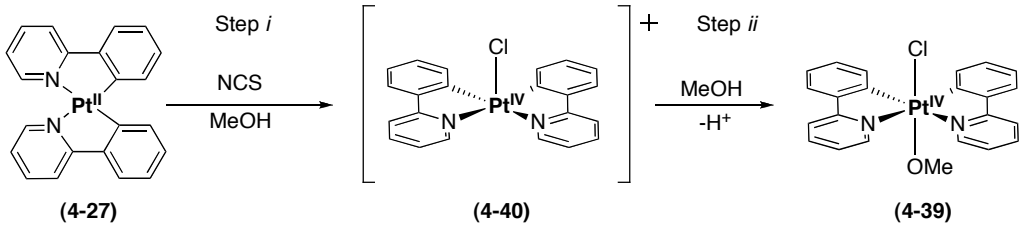
The reaction of $Pt^{II}(phpy)_2$, **4-27**, with $PhICl_2$ afforded two isomers of $Pt^{IV}Cl_2(phpy)_2$ (**4-32** and **4-33**) under all conditions examined. Based on extensive literature precedent for closely analogous reactions between Pt^{II} complexes and Cl_2 or $PhICl_2$, we propose that the current transformation proceeds via $PhICl_2$-promoted two-

electron oxidation of $Pt^{II}(phpy)_2$, **4-27**, to form cationic Pt^{IV} intermediate **4-40** followed by reaction of **4-40** with Cl^- to yield **4-32** and **4-33** (Scheme 4.17). It is unclear why two different isomers are formed here while a single isomer is observed in the analogous Pd reaction; however, several other reports have described differences in *cis*/*trans* isomer ratios in oxidative addition as a function of metal (M = Pd versus Pt).[26-28]



Scheme 4.17 Proposed Mechanism of Oxidation of $Pt^{II}(phpy)_2$ with $PhICl_2$

The reaction between **4-27** and *N*-chlorosuccinimide in methanol afforded mixed Pt^{IV} chloro methoxy complex **4-38** as the major product. This reaction is also believed to proceed via an ionic two-electron pathway that involves the oxidation of Pt^{II} to Pt^{IV} intermediate **4-40** followed by solvation of the cation with MeOH (Scheme 4.18). Importantly, an analogous mechanism has been proposed previously for closely related reactions between Pt^{II} and *N*-chlorosuccinimide in MeOH.[7, 13] In addition, the fact that the Pt^{IV} product **4-38** was *not* observed in reactions of $AuCl(SMe)_2$ with **4-27** provides further evidence in support of the above proposed mechanism. $AuCl(SMe)_2$ is a one-electron rather than a two-electron oxidant, and should therefore not be capable of effecting step *i* of this transformation (Scheme 4.18). Notably, $AuCl(SMe)_2$ did produce an alternative product (Pt^{III} complex **4-39**) and significant amounts of **4-32** were also observed in reactions with NCS in CH_2Cl_2.

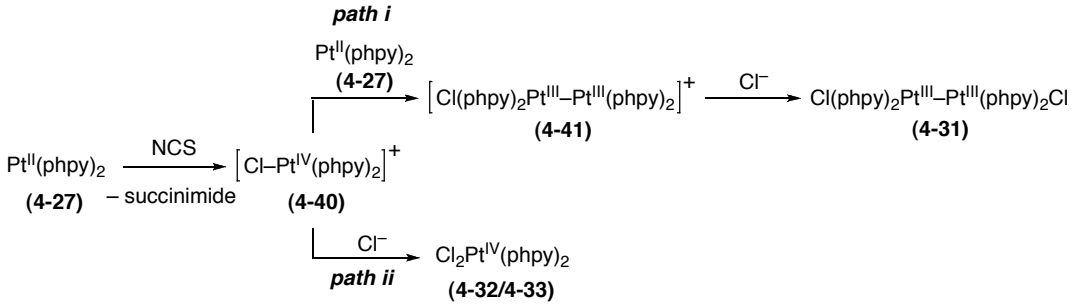


Scheme 4.18 - Proposed Mechanism for the Oxidation of **4-27** with NCS in MeOH

4.8 Discussion of Reactions Involving Conversion of Pt^{II} to Pt^{III}

The reaction of $Pt^{II}(phpy)_2$, **4-27**, with NCS in CH_2Cl_2 produced Pt^{III} complex **4-31** as the major product along with a mixture of **4-32** and **4-33**. When attempting to assess the mechanism of this transformation, it is important to recall that Pt^{III} product **4-31** undergoes subsequent reaction with the CH_2Cl_2 solvent to afford **4-32/4-33** (refer to section 4.9 for a full discussion of this process). As such, the observed product distributions reflect contributions from both: (1) the ratio of Pt^{III} and Pt^{IV} products produced in the initial reaction between $Pt^{II}(phpy)_2$, **4-27**, and NCS and (2) depletion of the initially formed Pt^{III} product **4-31** to generate **4-32/4-33**. In order to gain insights into just the initial reaction between $Pt^{II}(phpy)_2$ and NCS, we examined the product distributions obtained in the absence of light, since the background conversion of **4-31** to **4-32/4-33** occurs to a significantly lesser degree under these conditions.

A first possible pathway for the formation of Pt^{III} product **4-31** could be an ionic S_N2-type mechanism involving (*a*) nucleophilic attack of **4-27** on NCS to generate cationic five-coordinate Pt^{IV} intermediate (**4-40**), (*b*) reaction of **4-40** with a second equiv of $Pt^{II}(phpy)_2$, **4-27**, to generate dimer **4-41**, followed by (*c*) attack by free Cl^- in solution to afford **4-31** (Scheme 4.19, path *i*). This mechanism would also account for the generation of Pt^{IV} products **4-32** and **4-33**, which could be formed by trapping of intermediate **4-40** with Cl^- prior to the dimerization step (Scheme 4.19, path *ii*). Importantly, this type of mechanism has been proposed in the literature for the formation of Pt^{III} products closely related to **4-31** in reactions of $L_2X_2Pt^{II}$ with Cl_2 and $PhICl_2$. [10-12, 30]



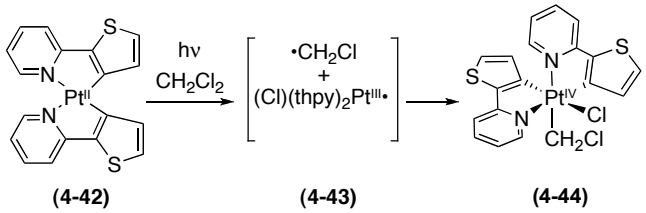
Scheme 4.19 - Ionic Mechanism for Reaction of **4-27** with *N*-Chlorosuccinimide

However, we discount the mechanism in Scheme 4.19 based on several pieces of evidence. First, there is no obvious source of Cl^- (which is required for formation of **4-31**, **4-32**, and **4-33** in this cationic mechanism) in this system. While it is possible that the oxidant might be contaminated with traces of chloride salts, this seems unlikely in the context of the other available data. A second result that suggests strongly against an ionic mechanism is that the addition of an excess of free Cl^- to these reactions had a negligible effect on the yield of **4-31** or on the distribution of Pt^{III} versus Pt^{IV} products. In an ionic, two-electron oxidation, a high concentration of Cl^- would be expected to efficiently compete for the cationic 5-coordinate Pt^{IV} intermediate **4-40**, resulting in substantially increased yields of Pt^{IV} dichloride products **4-32/4-33** relative to **4-31**. Third, the same Pt^{III} complex **4-31** was the major product in reactions with NCS, which can potentially act as either a one or a two-electron oxidant, [31-34] and with $AuCl(SMe_2)$ (which should only be capable of acting as a one electron oxidant).[22]

Finally, the reaction of **4-27** with $PhICl_2$, which is believed to proceed by an ionic mechanism (*vide supra*, Scheme 4.17), did not afford any of Pt^{III} complex **4-31**. Notably, we have independently confirmed that **4-31** is reasonably stable in the presence of $PhICl_2$. Greater than 50% of **4-31** remained after 24 hours at 25 ºC in the presence of 2.2 equiv of $PhICl_2$. As such, the inability to observe **4-31** in these systems does not appear to be due to its instability under the $PhICl_2$ oxidation conditions. If **4-31** were a kinetically

accessible intermediate along this pathway, we would expect to observe it in this transformation as well.

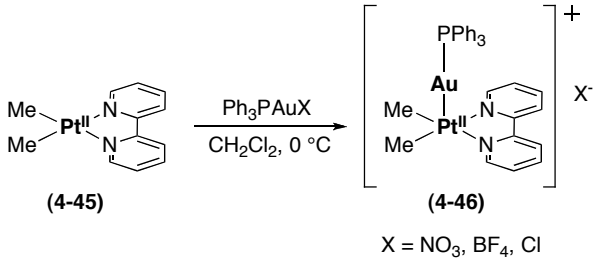
Based on the evidence collected above, we hypothesize that the reactions of **4-27** with NCS proceed via a radical rather than an ionic pathway. The viability of one-electron oxidation processes of Pt^{II} arylpyridine complexes has been demonstrated previously. For example, **4-27** and *cis*-bis[2-(2'-thienyl)pyridine]platinum(II), $Pt^{II}(thpy)_2$, have been shown to undergo irreversible one-electron electrochemical oxidation in MeCN at +0.26 and +0.33 V, respectively, versus SCE.[16, 19] In addition, oxidative addition reactions that proceed through Pt^{III} radical intermediates is well-precedented for $Pt^{II}(thpy)_2$ a closely-related complex to $Pt^{II}(phpy)_2$, **4-27**. As summarized in Scheme 4.20, $Pt^{II}(thpy)_2$, **4-42**, undergoes photochemically-induced oxidative addition of CH_2Cl_2 via initial photoexcitation of the Pt^{II} starting material followed by Cl• abstraction from solvent to form Pt^{III} radical **4-43** and finally radical cage recombination to afford Pt^{IV} product **4-44**.[18] It is presumed that **4-27** undergoes a similar mechanism upon oxidation to the analogous $Pt^{IV}(phpy)_2(CH_2Cl)Cl$ since they have identical reactivity under photochemical conditions.[17]



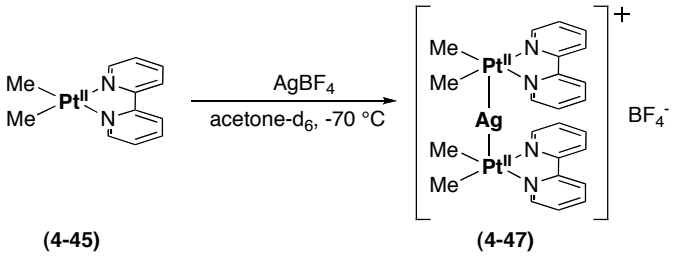
Scheme 4.20 - Proposed Mechanism for Photochemical Oxidative Addition of CH_2Cl_2 to $Pt^{II}(thpy)_2$

In light of this precedent, we propose that the current reactions could begin with a dative interaction between the electrophilic oxidant *N*-chlorosuccinimide and the Pt d_z^2 orbital. Such an interaction could be considered analogous to the Pt^{II}–Ag^+ and Pt^{II}–Cd^{II} complexes recently described by Yamaguchi and Ito, or the Pt-I_2 complexes described by

van Koten.[20, 21, 35, 36] Other similar interactions are described by Puddephatt with both Au and Ag complexes. Puddephatt demonstrates dative interactions between bis(2,2'-bipyridine)(di-methyl)platinum(II) [$PtMe_2$(2,2'-bpy)] and electrophilic gold or silver complexes (Schemes 4.21 and 4.22).[37] Notably, a similar interaction was proposed by Ito and coworkers in their initial communication on the synthesis of **4-31** with $AuCl(SMe_2)$.[22]



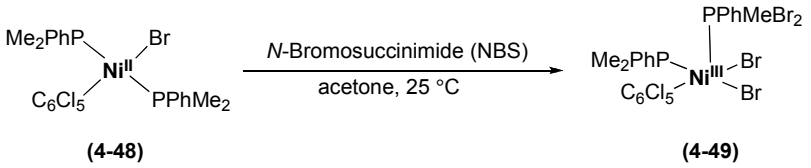
Scheme 4.21 – Formation of Dative Bond Between $PtMe_2$(2,2'-bpy) and $AuX(PPh_3)$



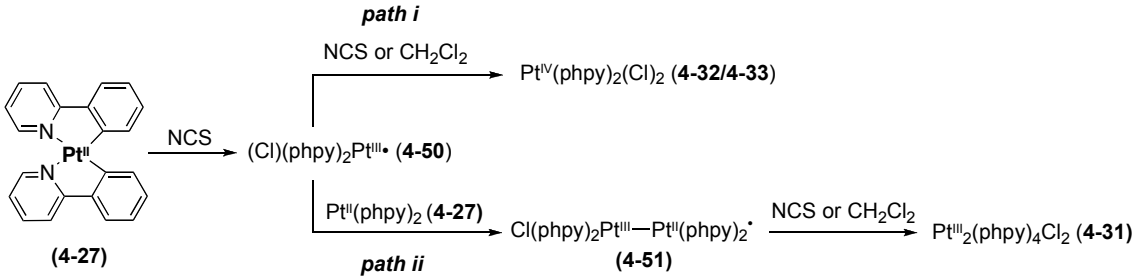
Scheme 4.22 – Formation of Dative Bond Between $PtMe_2$(2,2'-bpy) and $AgBF_4$

This coordination of the oxidant and the Pt d_z^2 orbital would be followed by electron transfer from $Pt^{II}(phpy)_2$ to the oxidant and transfer of a Cl ligand to afford the Pt^{III} radical $(Cl)(phpy)_2Pt^{III}\bullet$ (**4-50**), quite similar to Pt^{III}-based radical $(Cl)(thpy)_2Pt^{III}\bullet$ (**4-43**) in Scheme 4.20.[18] Importantly, a related one-electron oxidation of

$Ni^{II}(PPhMe_2)_2(C_6Cl_5)(Br)$, **4-48**, by *N*-bromosuccinimide (Scheme 4.23) has been reported to afford the isolated and characterized Ni^{III} product $(PPhMe_2)_2(C_6Cl_5)(Br)_2Ni^{III}\bullet$, **4-49**, which is analogous to the proposed intermediate **4-50**.[38]



Scheme 4.23 - Oxidation of $Ni^{II}(PPhMe_2)_2(C_6Cl_5)Br$ with NBS



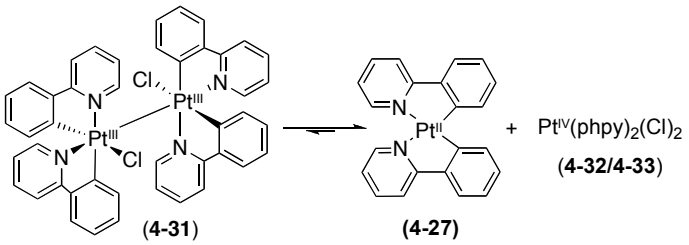
Scheme 4.24 - Proposed Mechanism for Oxidation of $Pt^{II}(phpy)_2$ with NCS

The Pt^{III} radical species **4-50** could potentially then undergo several competing reactions. First, it could react with a chlorine atom source (likely either a second equiv of NCS or the CH_2Cl_2 solvent) to afford Pt^{IV} products **4-32** and **4-33** (Scheme 4.24, path *i*). Alternatively, it could react with the Pt^{II} starting complex, **4-27**, to afford a new dimeric radical that could then react with a chlorine atom source to afford **4-31** (Scheme 4.24, path *ii*). Finally, it could react with a second equiv of itself to directly generate complex

4-31. Notably, the latter reaction is expected to be negligible, due to the very low relative concentrations of **4-50** in solution at a given time.[18]

4.9 Discussion of Reactions Involving Conversion of Pt^{III} to Pt^{IV}

The Pt^{III} complex **4-31** was found to convert to **4-32/4-33** on its own in CH_2Cl_2, in the absence of an oxidant like $PhICl_2$ or NCS. A first possible mechanism for this transformation would involve disproportionation of **4-31** to Pt^{IV} product **4-32/4-33** and $Pt^{II}(phpy)_2$, **4-27** (Scheme 4.25). Importantly, other unsupported Pt^{III} dimers, including $Pt^{III}_2Cl_2(acac)_2$, $Pt^{III}_2Cl_6[HN{=}C(OH)C(CH_3)_3]_4$, and $Pt^{III}_2Cl_4[(E)\text{-}HN{=}C(OMe)Me]_2$, have been shown to undergo facile disproportionation reactions of this type. [10-12, 30]

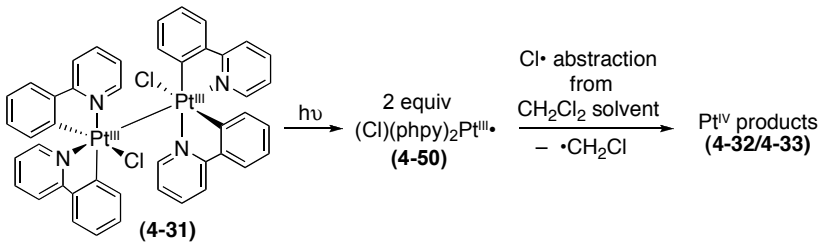


Scheme 4.25 - Possible Disproportionation Mechanism for the Formation of **4-32/4-33** from **4-31**

However, several key pieces of data suggest against a disproportionation mechanism for the formation of **4-32/4-33** from **4-31**. Most importantly, the stoichiometry of this transformation requires the formation of equimolar quantities of **4-27** and Pt^{IV} complexes **4-32/4-33**. However, $Pt^{II}(phpy)_2$, **4-27**, was never observed by ^1H NMR spectroscopy in these systems. In addition, negligible conversion of **4-31** to form **4-32/4-33** was observed in non-halogenated solvents (*e.g.*, DMSO, MeOH), suggesting that

an external source of Cl is required to provide the chlorine atoms required for the generation of **4-32/4-33**.

An alternative mechanism for the formation of **4-32/4-33** from **4-31** in CH_2Cl_2 would involve initial homolysis of the Pt–Pt bond to afford the monomeric Pt-based radical **4-50** (Scheme 4.26). This radical species could then abstract Cl• from the solvent to afford the observed Pt^{IV} product. Importantly, there is some literature precedent for the photochemically induced homolysis of Pt–Pt bonds. Roundhill suggests that the platinum-platinum bond of diplatinum(III) complex $K_4[Pt_2(\mu\text{-}P_2O_5H_2)_4X_2]$, with X identified as Cl, Br, or I, is homolytically cleaved by the absorption of light.[39] In addition, the Pt^{III} radical **4-43** has been proposed by von Zelewsky as an intermediate in the photochemical oxidative addition of CH_2Cl_2 to $Pt^{II}(thpy)_2$.[18] As shown in Scheme 4.20, this intermediate was proposed to undergo radical cage recombination with $\bullet CH_2Cl$ to afford the Pt^{IV} oxidative addition product **4-44**. In the current system, reaction between **4-50** and the diffusing $\bullet CH_2Cl$ radical is unlikely due to both the low concentrations of the two radical species (**4-50** and $\bullet CH_2Cl$) in solution and the presence of O_2, which can readily quench carbon-based radicals. However, interestingly, when the reaction of **4-31** in CH_2Cl_2 (10 mM, 100 ºC, 24 h, ambient light) was conducted in the absence of air, a trace (~2% as determined by ^1H NMR analysis of the crude reaction mixture) of oxidative addition product $Pt^{IV}(phpy)_2(CH_2Cl)Cl$ was detected, which is further consistent with the proposed mechanism.



Scheme 4.26 - Proposed Mechanism for Reaction of **4-31** to Form Pt^{IV} Products

Several additional pieces of data support the mechanism proposed in Scheme 4.26. Most importantly, the reaction of **4-31** with CH_2Cl_2 to form **4-32/4-33** is promoted by light (Table 4.5, entry 4 versus entry 5). In addition, the observed effect of reaction concentration on the reactivity of **4-31** appears consistent with this mechanism. The proposed effect of concentration is not caused by the increase in the number of solvent molecules as the reaction is diluted. Optical limiting is a preferable theory for explaining the effects of concentration. As the reaction is diluted, greater amounts of light can diffuse into the reaction, promoting the initial homolysis. When the reaction is concentrated, light is less likely to diffuse through. Finally, the fact that **4-31** did not undergo significant oxidation to Pt^{IV} products in solvents that do not possess weak C–Cl bonds (*e.g.,* MeOH, DMSO) offers further evidence in support of this mechanism.

The proposed mechanism suggests that the quantity of Pt^{IV} products formed should be dependent on the relative rate of recombination of the Pt^{III} radicals to produce **4-31** versus that of Cl• abstraction from solvent. We anticipated that the latter process would be affected by changing the Cl atom source. As such, we compared the product ratio from the reaction of **4-31** in pure CH_2Cl_2 (C–Cl bond strength of CH_2Cl_2 = 84 kcal/mol) to that from the reaction of **4-31** in either a 1:3 mixture of $CHCl_3$: CH_2Cl_2 (C–Cl bond of $CHCl_3$ = 81 kcal/mol) or a 1:3 mixture of CCl_4: CH_2Cl_2 (C–Cl bond of CCl_4 = 73 kcal/mol).[40, 41] Notably, the 75% of remaining CH_2Cl_2 in these reactions was used to maintain an approximately constant dielectric medium as well as to ensure the solubility of **4-31**. The reactions were carried out in the respective chlorinated solvents under dilute conditions (1.25 mM, 25 ºC, 24 h) in the presence of light.

As summarized in Table 4.6, these reactions showed a clear trend in which the amount of Pt^{IV} products obtained increased as the homolytic bond strength of the co-solvent decreased, providing further evidence in support of the proposed mechanism in Scheme 4.26.

Table 4.6 - Oxidation of **4-31** with Various Chlorinated Co-Solvents

Entry	Solvent	Ratio of **4-31** to Pt^{IV} products **4-32/4-33**
1	CH_2Cl_2	2.50
2	1 : 3 $CHCl_3$: CH_2Cl_2	0.34
3	1 : 3 CCl_4 : CH_2Cl_2	0.17

4.10 Conclusion

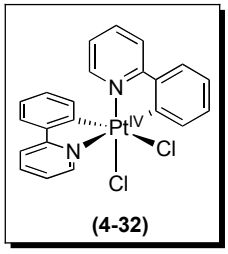
In conclusion, this chapter describes studies of reactions between $Pt^{II}(phpy)_2$ and two different electrophilic chlorinating reagents – $PhICl_2$ and *N*-chlorosuccinimide. Under a variety of different conditions, $PhICl_2$ reacted to afford isomers of $Pt^{IV}Cl_2(phpy)_2$ (**4-32** and **4-33**) as the exclusive products. In contrast, *N*-chlorosucccinimide (NCS) provided mixtures of Pt^{III} and Pt^{IV} oxidation products, whose ratios varied as a function of solvent, time, concentration, and the presence/absence of light. The observed results can be rationalized based on a series of competing one and two electron oxidation reactions (often involving participation from the solvent) to afford both Pt^{III} and Pt^{IV} products. Importantly, while the reaction of $Pt^{II}(phpy)_2$ with $PhICl_2$ afforded similar products to that of its Pd^{II} analogue, the reaction with NCS proceeded very differently. As such, this work demonstrates that analogies between Pt^{II} and Pd^{II} oxidation reactions should be made with caution, even when considering complexes with identical ligand environments under identical reaction conditions.

4.11 Experimental Procedures

General Considerations. NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for ^1H; 125.70 MHz for ^{13}C) or a Varian Inova 400 (399.96 MHz for ^1H; 100.57 MHz for ^{13}C) spectrometer. ^1H NMR chemical shifts are reported in parts per million (ppm) with the residual solvent peak used as an internal reference. ^{195}Pt NMR spectra

were obtained on a Varian Inova 500 (107.25 MHz for ^{195}Pt). ^{195}Pt chemical shifts are reported in parts per million (ppm) and were referenced using the frequency of the lock signal and the estimated chemical shift of the solvent, DMF-d_7, according to IUPAC recommendations (Ξ = 21.496784).[42] Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet (t), triplet of doublets (td), triplet of triplets (tt), multiplet (m), and broad resonance (br). IR spectra were obtained on a Perkin-Elmer "Spectrum BX" FT-IR spectrometer. Mass spectral data were obtained on a Micromass magnetic sector mass spectrometer.

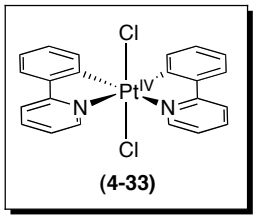
Materials and Methods. K_2PtCl_4 was purchased from Pressure Chemical and *N*-chlorosuccinimide from Acros, and both were used as received. $PhICl_2$ was prepared from iodobenzene and Cl_2 according to a literature procedure.[43] $Pt^{II}(phpy)_2$, **27**, was synthesized from 2-(*o*-bromophenyl)pyridine [44] and $PtCl_2(SEt_2)_2$ [45] according to a published procedure.[14] Solvents were obtained from Fisher Scientific and used without further purification. Unless otherwise noted, all reactions were carried out on the bench top in the presence of ambient air and moisture.



(4-32)

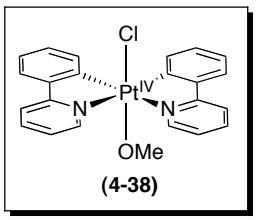
unsymmetrical *cis*-$PtCl_2(phpy)_2$ (4-32) - $Pt^{II}(phpy)_2$, **4-27**, (100 mg, 0.20 mmol, 1.0 equiv) and $PhICl_2$ (60 mg, 0.22 mmol, 1.1 equiv) were combined in CH_2Cl_2 (10 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 12 h, during which time a pale yellow solid precipitated from solution. This solid (**4-33**) was removed by filtration, the filtrate was concentrated, and hexanes (20 mL) was added to precipitate product **4-32**. The pale yellow precipitate was collected by vacuum filtration, washed with hexanes (100 mL) and dried under vacuum to afford **4-32** (73 mg, 64%). ^{1}H NMR (DMSO-d_6): δ 9.61 (d, J = 6 Hz, 1H), 8.50 (d, J = 8 Hz, 1H), 8.36-8.32 (m, 2H), 8.07-7.98 (m, 4H), 7.88 (m, 1H), 7.56 (d, J = 6 Hz, 1H), 7.48-7.41 (m, 2H), 7.22 (m, 1H), 7.09 (m, 1H), 6.92 (m, 1H), 6.19 (d, J = 8 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 164.10, 160.79, 147.73, 147.06, 143.71,

141.91, 141.72, 141.46, 136.22, 132.03, 131.86, 131.62, 131.29, 131.26, 126.59, 126.47, 126.25, 126.10, 125.70, 125.55, 121.88, 121.77. ^{195}Pt NMR (DMF-d_7): δ –1725.62. FTIR (KBr, cm^{-1}) 3051, 1606, 1582, 1483, 1441, 1023. HRMS-electrospray (*m/z*): $[M - Cl_2]^+$ calcd for $C_{22}H_{16}N_2{}^{194}Pt$, 502.0940; Found, 502.0920. LRMS-electrospray (*m/z*): $[M]^+$ calcd for $C_{22}H_{16}N_2PtCl_2$, 572.03; Found, 572.0.



(4-33)

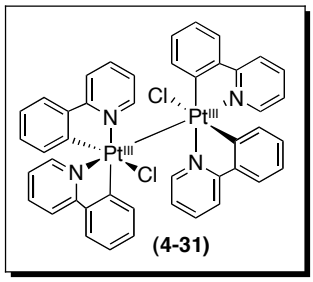
symmetrical $PtCl_2(phpy)_2$ (4-33) - $Pt^{II}(phpy)_2$, **4-27**, (100 mg, 0.20 mmol, 1.0 equiv) and $PhICl_2$ (60 mg, 0.22 mmol, 1.1 equiv) were combined in CH_2Cl_2 (10 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 12 h during which time a pale yellow solid precipitated from solution. This precipitate was collected by filtration, washed with CH_2Cl_2 (50 mL) and hexanes (100 mL), and dried under vacuum to afford **4-33** (33 mg, 29%) as a pale yellow powder. ^{1}H NMR (DMSO-d_6): δ 9.21 (d, *J* = 6 Hz, 2H), 8.45 (d, *J* = 8 Hz, 2H), 8.23 (m, 2H), 8.00 (d, *J* = 6 Hz, 2H), 7.76 (d, *J* = 8 Hz, 2H), 7.70 (m, 2H) 7.37 (m, 2H), 7.30 (m, 2H). Complex **4-33** was not sufficiently soluble to obtain a ^{13}C NMR spectrum. FTIR (KBr, cm^{-1}) 3054, 1605, 1582, 1480, 1313, 1019. HRMS-electrospray (*m/z*): $[M - Cl_2]^+$ calcd for $C_{22}H_{16}N_2{}^{194}Pt$, 502.0918; Found, 502.0940. LRMS-electrospray (*m/z*): $[M]^+$ calcd for $C_{22}H_{16}N_2PtCl_2$, 572.03; Found, 572.0.



(4-38)

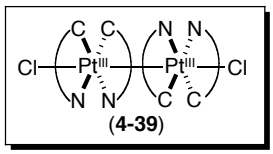
symmetrical-$PtClOMe(phpy)_2$ (4-38) - $Pt^{II}(phpy)_2$, **4-27**, (60 mg, 0.12 mmol, 1.0 equiv) and NCS (18 mg, 0.13 mmol, 1.1 equiv) were combined in MeOH (12 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 24 h, during which time a yellow solid precipitated from solution. The solids (*unsymmetrical*-$PtCl_2(phpy)_2$ (**4-32**) and *unsymmetricali*-$Pt_2Cl_2(phpy)_4$ (**4-31**)) were removed by filtration. The filtrate was concentrated to approximately 2 mL at which point product **4-38** precipitated from solution. The precipitate was collected by filtration, washed with hexanes (50 mL), and dried under vacuum to afford **4-38** (7 mg, 10%) as a cream-colored powder. The filtrate also contained significant quantities of **4-38**; however ^{1}H NMR spectroscopy revealed the presence of trace impurities. Notably, ^{1}H NMR

spectroscopy of the crude reaction mixture in DMSO-d_6 revealed that the crude yield was 50%. ^{1}H NMR ($CDCl_3$): δ 9.03 (d, J = 5.2 Hz, 2H), 8.11 (t, J = 8.0 Hz, 4H), 8.09 (t, J = 7.4 Hz, 2H), 7.75 (d, J = 7.4 Hz, 2H), 7.48 (t, J = 6.1 Hz, 2H), 7.38 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.3 Hz, 2H), 2.41 (s, J_{Pt-H} = 32 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 163.25, 146.54, 142.77, 139.50, 139.34, 133.61, 130.30, 125.68, 124.98, 122.31, 120.61, 60.26. ^{195}Pt NMR (DMF-d_7): δ –883.46. FTIR (KBr, cm^{-1}) 2782, 1706, 1604, 1582, 1480, 1441, 1422, 1065, 1021.



(4-31)

unsymmetrical $Pt^{III}_2Cl_2(phpy)_4$ (4-31) - $Pt^{II}(phpy)_2$, **4-27**, (100 mg, 0.20 mmol, 1.0 equiv) and *N*-chlorosuccinimide (30 mg, 0.22 mmol, 1.1 equiv) were combined in CH_2Cl_2 (20 mL) in a 50 mL round-bottom flask. The flask was sealed with a septum, and the reaction was stirred at room temperature for 24 h, during which time a yellow solid precipitated from solution. This precipitate was collected by filtration, washed with CH_2Cl_2 (25 mL) and hexanes (100 mL), and dried under vacuum to afford **4-31** (59 mg, 55%) as a bright yellow powder. The ^{1}H, ^{13}C, and ^{195}Pt NMR spectral data for **4-31** was in agreement with literature values. [22]



(4-39)

symmetrical $Pt^{III}_2Cl_2(phpy)_4$ (4-39) - Complex **4-31** (30 mg, 0.028 mmol) was dissolved in MeOH (6 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 100 ºC for 24 h. The reaction mixture was concentrated to approximately 1 mL and then diethyl ether (20 mL) was added to precipitate the product. The precipitate was collected by vacuum filtration, washed with hexanes (50 mL), and dried under vacuum to afford **4-39** (13 mg, 43%) as a dark yellow powder. ^{1}H NMR (DMSO-d_6): δ 8.52 (d, J = 8.5 Hz, 4H), 8.23 (t, J = 8.5 Hz, 4H), 8.11 (d, J = 8 Hz, 4H), 7.72 (d, J = 5.5 Hz, 4H), 7.49 (m, 4H), 7.29 (m, 4H), 7.10 (m, 4H), 6.47 (d, J = 8 Hz, J_{Pt-H} = 22 Hz, 4H). ^{13}C NMR (DMSO-d_6): δ 162.09, 147.57, 142.46, 142.06, 133.01, 131.77, 127.22, 126.67, 125.24, 122.64, 120.43. ^{195}Pt NMR (DMF-d_7): δ –2293.50. FTIR (KBr, cm^{-1}) 2348, 1658, 1606,

1550, 1529, 1483, 1441. HRMS-electrospray (*m/z*): $[(Cl)(phpy)_2Pt]^+$ calcd for $C_{22}H_{16}N_2{}^{194}PtCl$, 538.0649; Found, 538.0628.

General procedure for reactions in Tables 4.1–4.5 (light). $Pt^{II}(phpy)_2$, **4-27**, (5 mg, 0.01 mmol, 1.0 equiv) and the oxidant (1.5 mg, 0.011 mmol, 1.1 equiv) were combined in CH_2Cl_2 (1 mL) in a 4 mL clear vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature. The solvent was removed under vacuum, and the resulting crude solids were redissolved in DMSO-d_6 (1 mL) and analyzed by ^{1}H NMR spectroscopy. The yields of each product were calculated by integration of characteristic ^{1}H NMR resonances relative to an internal standard.

General procedure for reactions in Tables 4.2 and 4.4 (dark). $Pt^{II}(phpy)_2$, **4-27**, (5 mg, 0.01 mmol, 1.0 equiv) and oxidant (1.5 mg, 0.011 mmol, 1.1 equiv) were combined in a 4 mL amber vial, which was subsequently covered with aluminum foil. All lights in the immediate vicinity were turned off and CH_2Cl_2 (1 mL) added. The vial was rapidly sealed with a Teflon-lined cap, and the reaction was stirred at room temperature. The solvent was removed under vacuum, and the resulting crude solids were redissolved in DMSO-d_6 (1 mL) and analyzed by ^{1}H NMR spectroscopy. The yields of each product were calculated by integration of characteristic ^{1}H NMR resonances relative to an internal standard.

X-ray structure determination for *unsymmetrical*-$PtCl_2(phpy)_2$ (4-32) - Fine colorless needles of **4-32** were crystallized from a chloroform/diethyl ether solution at 23 °C. A crystal of dimensions 0.60 x 0.08 x 0.08 mm was mounted on a standard Bruker SMART 1K CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 123(2) K; the detector was placed at a distance 4.969 cm from the crystal. A total of 4095 frames were collected with a scan width of 0.5° in ω and phi with an exposure time of 20 s/frame. The integration of the data yielded a total of 32571 reflections to a maximum 2θ value of 56.62° of which 5944

were independent and 4910 were greater than $2\sigma(I)$. The final cell constants were based on the xyz centroids of 6565 reflections above $10\sigma(I)$. Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P1bar with Z = 2 for the formula $C_{22}H_{16}N_2Cl_2Pt\bullet(CHCl_3)$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0367 and wR2 = 0.0898 [based on I > 2sigma(I)], R1 = 0.0546 and wR2 = 0.0987 for all data.

4.12 References

(1) Reproduced in part with permission from Whitfield, S. R.; Sanford, M. S. " Reactions of Platinum(II) Complexes with Chloride-Based Oxidants: Routes to Pt(III) and Pt(IV) Products" *Organometallics* **2008***, 27*, 1683-1689. Copyright 2008 American Chemical Society.

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Chapter 5

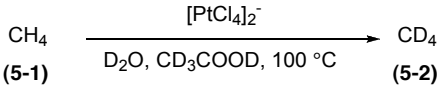
Synthesis and Reactivity of Platinum(III & IV) Halogen and Carboxylate Complexes

5.1 Introduction

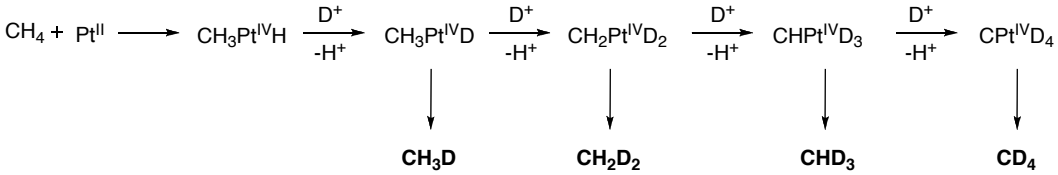
Our research on the oxidative addition of electrophilic chlorinating oxidants to group 10 metals has highlighted key differences between palladium and platinum. Further examination of platinum complexes may increase our understanding of the scope of these differences. This chapter will focus on the synthesis and reactivity of platinum(IV) complexes with either halogens (bromine, iodine, or fluorine) or carboxylate functional groups (CH_3COO^- or CF_3COO^-) as ligands. The synthesis of these complexes will accentuate the importance of oxidative addition, emphasize the variability of high oxidation state platinum complexes formed, and provide a comparison for reductive elimination between palladium and platinum. This chapter will also consider the role of oxidant, as it dictates both the geometry and oxidation state of the resultant platinum complex.

Understanding oxidative addition is critical to identifying and understanding key intermediates within Pd and Pt catalytic cycles. For example, one important class of Pt-catalyzed reactions involves the incorporation of deuterium into methane and other alkanes using catalytic potassium tetrachloroplatinate in D_2O/CD_3CO_2D (Scheme 5.1).[1] The mechanism of deuterium incorporation hinges on the C–H activation of methane, proposed as the rate determining step in this reaction. This step is believed to proceed by oxidation of platinum(II) to a platinum(IV) alkyl hydride (Scheme 5.2). Electrophilic substitution of a deuterium ion for a proton is then followed by carbon-deuterium

reductive elimination to release both an alkane molecule and a platinum(II) compound. This cycle is presumably to be iterative to achieve a fully deuterated molecule.

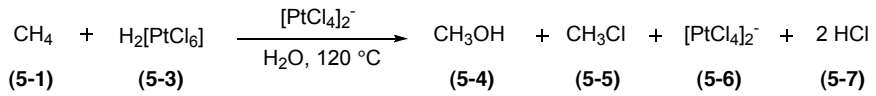


Scheme 5.1 – Tetrachloroplatinate Activation of Methane

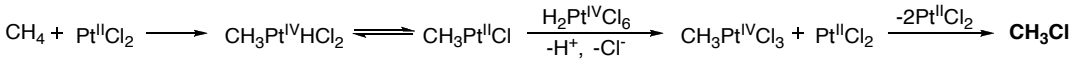


Scheme 5.2 – Platinum Catalyzed H-D Exchange of Methane

In addition, the heating of an aqueous solution of hexachloroplatinic acid with methane in the presence of sodium tetrachloroplatinate has been shown to lead to a mixture of products with incorporation of either hydroxyl or chlorine ligands (Scheme 5.3).[2] The key mechanistic steps here are C–H activation and oxidation of a platinum(II) species to platinum(IV). Specifically, the hexachloroplatinic acid is the pivotal component of this reaction as it oxidizes the alkyl platinum(II) intermediate, allowing for subsequent release of either a chlorinated or hydroxylated alkane from the platinum(IV) intermediate (Scheme 5.4). As demonstrated by both of these examples, the functionalized molecule is generated from a platinum(IV) intermediate, highlighting the importance of high oxidation state platinum(IV) complexes.

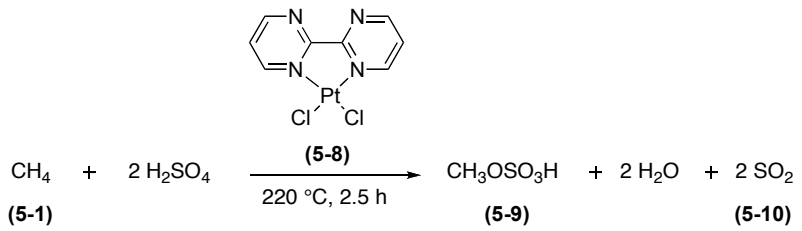


Scheme 5.3 – Hexachloroplatinic Acid Activation of Methane

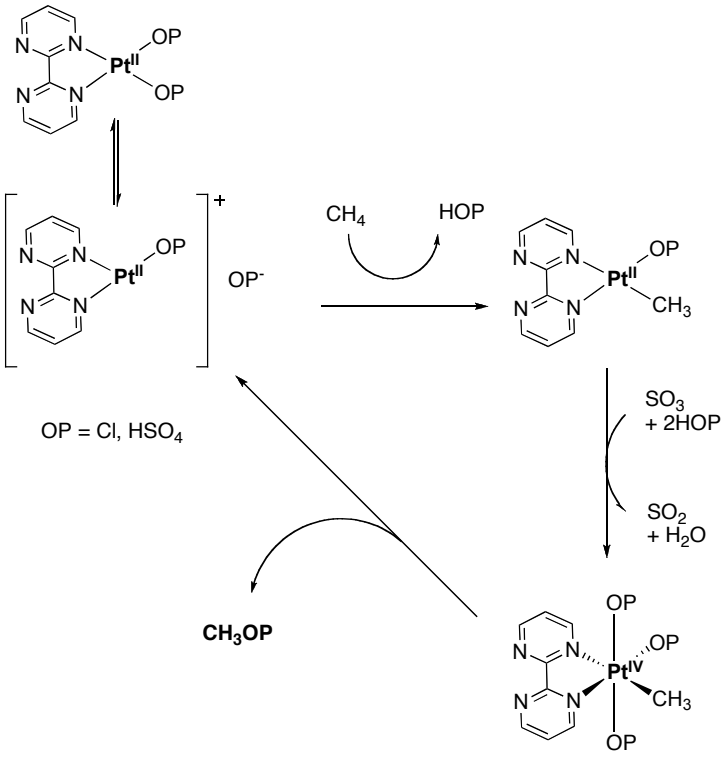


Scheme 5.4 – Mechanism of Chlorine Oxidation for Hexachloroplatinic Acid Activation of Methane

Periana reported another example of catalysis with platinum and methane that is believed to involve a high oxidation state platinum complex formed as a result of oxidative addition.[3] As shown in Scheme 5.5, this reaction converts methane into methyl bisulfate with ~90% conversion of CH_4 and turnover numbers greater than 500. Similar to the reactions described above, the first step is C-H activation, presumably from a 14-electron complex (Scheme 5.6). However, in contrast, this does not result in oxidation of the platinum intermediate. Sulfur trioxide then oxidizes the alkylplatinum(II) intermediate to platinum(IV). This step, proposed as the rate-determining step, is critical because of the shift in polarity (less electron density at metal center) experienced by the newly generated alkylplatinum(IV) species. Functionalization is facilitated by this polarity shift, allowing for release of methyl bisulfate.



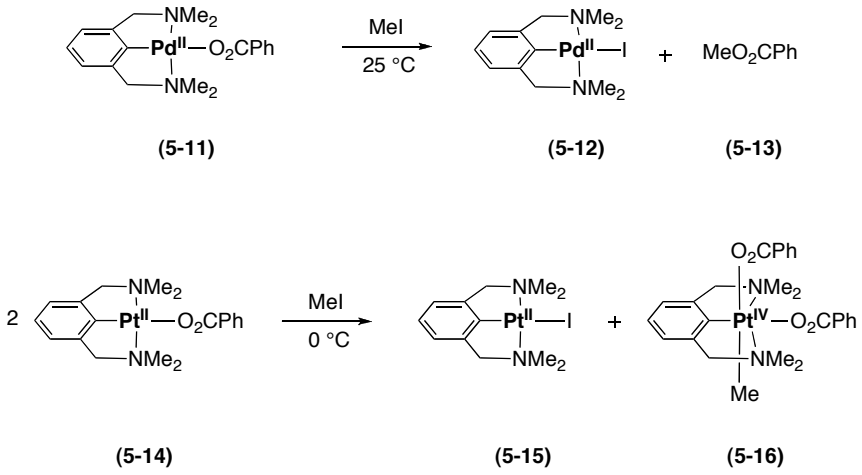
Scheme 5.5 – Catalytic Platinum Oxidation of Methane



Scheme 5.6 – Proposed Mechanism of Platinum Oxidation of Methane

Platinum(IV) complexes are also important and valuable as models for intermediates in palladium(II) oxidation reactions.[4-8] Research by Canty has frequently encompassed both palladium and platinum complexes. In addition to the example cited in Chapter 4, with identical bipyridine and alkyl ligand environments for both palladium and platinum[9], Canty has also studied both metals using [2,6-

(dimethylaminomethyl)phenyl-*N*,*C*,*N*]$^-$, a pincer ligand.[4] Canty examined the MeI oxidation of palladium and platinum benzoate complexes **5-11** and **5-14** (Scheme 5.7).[4] The palladium(II) complex, **5-11**, upon oxidation, released a new palladium(II) species, **5-12**, and methyl benzoate, **5-13**. Presumably the intermediate in this reaction is a Pd^{IV} species, but this was not observed. However, the corresponding platinum reaction did produce a Pt^{IV} species, **5-16**, in addition to the Pt^{II} complex analogous to its palladium counterpart, **5-15**. As platinum complexes are known to have greater stability than palladium complexes, it is not surprising that the desired high oxidation state intermediates are observed with platinum and not with palladium. The isolated platinum complex is believed to be a model of the transient palladium(IV) intermediate.



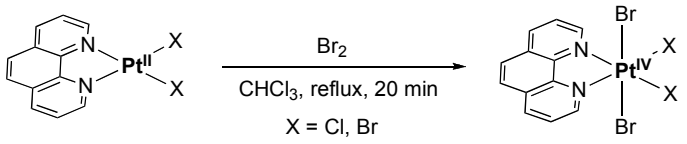
Scheme 5.7 – Reactivity of MeI with Pd^{II} and Pt^{II} Complexes

An expanded examination of oxidative addition and reductive elimination is the basis for our synthesis of high oxidation state platinum complexes. Results obtained from these analyses may provide further insights into the preparation and reactivity of high oxidation state platinum complexes. Results may also provide additional insight into the viability of oxidative addition comparisons between palladium and platinum.

5.2 Oxidation with Bromine

Early investigations of oxidative addition to platinum complexes began with simple oxidants, particularly the elemental form of the halogens.[10] Halogens were chosen because of their availability, simplicity, and the predictability of the resultant complexes (*i.e.* – addition of two bromine ligands to the metal). Bromine in particular was frequently employed as an oxidant because it is a liquid that may be handled either neat or diluted by solvent.

Oxidative addition with bromine was historically studied with respect to oxidation of platinum(II) to platinum(IV). An early example of this type of oxidation was provided by Rund and Hodges, studying the oxidative addition of bromine to dihalo(1,10-phenathroline)platinum(II) (Scheme 5.8).[11] The addition of bromine to the platinum(II) complex produced a new platinum(IV) species with the bromine ligands in the axial positions, in a *trans* orientation to one another. The literature suggests that this *trans* orientation of X_2 ligands from oxidative addition is normally observed, with the occasional isomerization of the platinum(IV) product to one with ligands in a *cis* orientation, one X ligand is in an axial position, the other is equatorial.[12] In the example provided by Hodges, there is limited characterization data (infrared spectra only) that definitively identifies the platinum complex as a *trans* adduct.

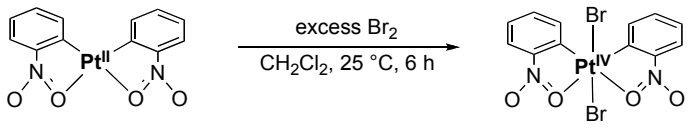


(5-17) **(5-18)**

Scheme 5.8 – Bromine Oxidation of Dihalo(1,10-Phenanthroline)Platinum(II)

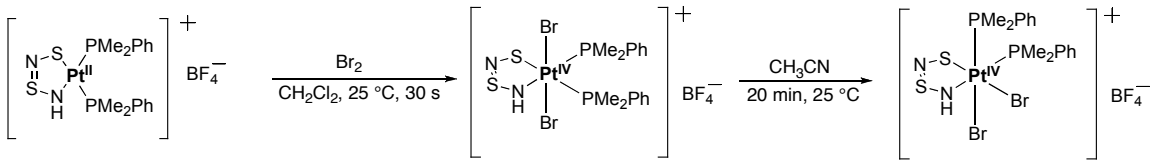
Vicente also presents a platinum(IV) complex resulting from the oxidative addition of bromine to a platinum(II) starting material (Scheme 5.9). This report also describes a *trans* platinum(IV) product, **5-20**, again based on infrared spectral data, as

well as comparison to an analogous dichloride complex that was identified by X-ray crystallography.[13] Woolins has identified multiple oxidative addition complexes of platinum(II) and bromine (Scheme 5.10).[14] The *trans* platinum(IV) complex, **5-22**, was characterized by ^{31}P NMR; however, it isomerized to the *cis* complex, **5-23**, within 20 min and could then be isolated and identified by X-ray crystallography. Fornies, in contrast, only observed a *cis* platinum(IV) complex, **5-25** in Scheme 5.11, from oxidation with bromine.[15] Mechanistic experiments failed to find evidence of the initial formation of a *trans* complex that isomerizes to a *cis* orientation. Fornies proposed a rearrangement of the likely five-coordinate intermediate that allowed for the final bromine ligand to add in an equatorial position, resulting in a *cis* product.



(5-19) **(5-20)**

Scheme 5.9 – Bromine Oxidation of *o*-Nitrophenyl Complex of Platinum(II)



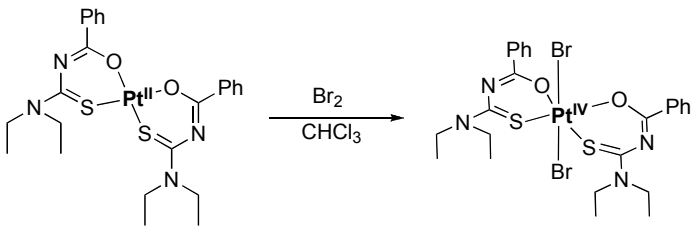
(5-21) **(5-22)** **(5-23)**

Scheme 5.10 – Bromine Oxidation of $[Pt(S_2N_2H)(PR_3)_2]BF_4$

(5-24) (5-25)

Scheme 5.11 – Bromine Oxidation of $[NBu_4][Pt(C_6F_5)_2(C_5H_4NS)]$

Koch offered an example of an isolated *trans* platinum(IV) complex (Scheme 5.12). Using a *cis*-bisplatinum(II) complex, **5-26**, with benzoylthiourea ligands, he demonstrated the formation of the *trans* oxidative addition product, **5-27**. The mechanism proposed by Koch invokes a cationic five-coordinate intermediate, which does not rearrange and is subsequently attacked by the anionic bromide ligand to generate the neutral platinum(IV) product.[16] One observation illustrated by the prior examples of bromine oxidation calls attention to the relationship between the formal charge of the platinum(II) complexes to be oxidized and the resultant geometry of the platinum(IV) product. Literature examples with cationic platinum(II) complexes, demonstrated by Woolins and Fornies, produced *cis* orientations in the platinum(IV) products, through one or two-step processes. This may be differentiated from literature examples with neutral platinum(II) complexes, demonstrated by Rund, Vicente, and Koch, with the sole observation of *trans* platinum(IV) products. These general observations have not been discussed in the literature and their importance is unknown at this time.



(5-26) **(5-28)**

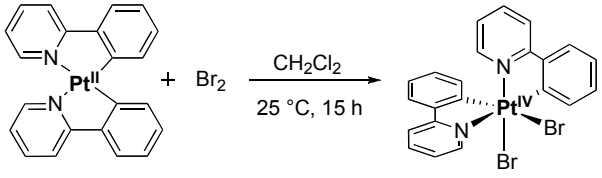
Scheme 5.12 – Bromine Oxidation of Platinum(II) Complex with *N*,*N*-Dialkyl-*N*'-Benzoylthiourea Ligands

The preceding literature examples employed a wide variety of ligands bonded to the platinum(II) metal including carbon, nitrogen, oxygen, phosphorus, and sulfur donor atoms. Our interests in comparing oxidation of platinum(II) with bromine to the previously discussed oxidations of palladium and platinum(II) led us to 2-phenylpyridine as our ligand set. The oxidation of *cis*-bis(2-phenylpyridine)platinum(II), complex **27** introduced in Chapter III, would allow for direct comparison of the resultant platinum complexes to complexes **4-31**, **4-32**, and **4-33** in Chapter 4, as well as with any future analogous palladium(IV) species.

Our investigations began with the oxidation of complex **4-27**, $Pt^{II}(phpy)_2$, with elemental bromine, Br_2. Complex **4-27** was combined with Br_2 in a solution of CH_2Cl_2, and this mixture was allowed to stir at 25 ºC for approximately 15 h. The platinum(IV) product was isolated from the reaction mixture in 71% yield through precipitation with hexanes. A complex identified as $Pt^{IV}(phpy)_2Br_2$ had been previously synthesized by von Zelewsky, using the same starting materials and a similar synthetic method.[17, 18] Although this platinum(IV) complex was identified previously by elemental analysis, its absolute geometry was not determined.

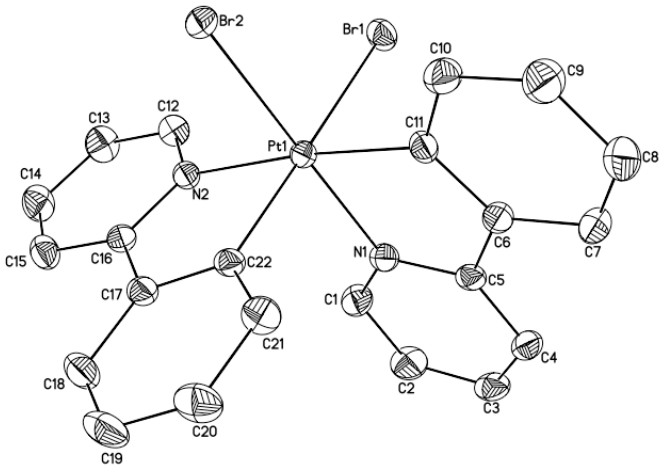
$Pt^{IV}(phpy)_2Br_2$ complex **5-29**, was identified as having a *cis* geometry based on both ^{1}H NMR spectroscopy and X-ray crystallography. ^{1}H NMR spectroscopy showed 12 sets of protons, indicating an asymmetrical complex that included overlapping peaks. Integration of the peaks in the ^{1}H NMR spectrum accounted for the 16 protons on both 2-phenylpyridine ligands. X-ray crystallography supported this assessment, revealing that

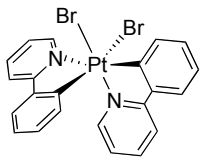
the bromine ligands are trans to the nitrogen and carbon atoms of differing 2-phenylpyridine chelates, (Figure 5.1). Selected bond lengths and bond angles are listed in Table 5.1. The different *trans* environment of each nitrogen accounts for the variation in Pt–Br bond lengths. The Pt–Br bond length for the bromine *trans* to the nitrogen is 2.44 Å, while the bond length for the Pt–Br *trans* to the carbon is 2.57 Å. The greater *trans* influence of carbon relative to nitrogen provides a rationale for the differences in length.



(4-27) **(5-29)**

Scheme 5.13 - Oxidation of **4-27** with Bromine





(**5-29**)

Figure 5.1 - ORTEP View of *cis*-$Pt^{IV}(phpy)_2Br_2$, **5-29**

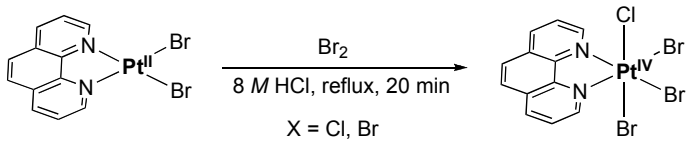
Table 5.1 – Selected Bond Lengths (Å) and Angles (°) for *cis*-$Pt^{IV}(phpy)_2Br_2$, **5-29**

Pt(1)-C(11)	2.019(3)	C(11)-Pt(1)-N(2)	174.16(10)
Pt(1)-C(22)	2.026(3)	N(1)-Pt(1)-Br(2)	176.73(7)
Pt(1)-N(1)	2.039(2)	C(11)-Pt(1)-Br(2)	96.32(8)
Pt(1)-N(2)	2.138(2)	C(22)-Pt(1)-N(2)	80.26(10)
Pt(1)-Br(1)	2.5734(7)	C(11)-Pt(1)-Br(1)	89.26(8)
Pt(1)-Br(2)	2.4408(6)	C(22)-Pt(1)-Br(1)	175.92(8)
		Br(2)-Pt(1)-Br(1)	91.50(2)

Our observance of the *cis* complex of **5-29** is comparable to Fornies sole observance of *cis* compound **5-25**. A mechanism similar to that proposed by Fornies may explain the observance of the *cis* geometry; however, the five-coordinate intermediate would be cationic rather than neutral, as in Koch's system. As mentioned previously, Fornies research involved the use of cationic platinum(II) complexes, resulting in the observation of the *cis* geometry. Based on the general observations cited earlier, we would have expected the formation of a *trans* adduct from the oxidation of our neutral platinum(II) complex. While we are unable to determine the origin of this discrepancy, it is clear that our examinations in this area have defined the prior literature observations as a broad trend, with areas of exceptions, rather than an absolute requirement. The difference in geometrical outcome of the platinum(IV) complexes is also not immediately clear based on the oxidant, bromine. Bromine has demonstrated an ability to oxidize platinum(II) complexes to produce both geometries, perhaps suggesting differences may be traced back to ligand sets. This assumption discourages a generalization on predicting the geometry of the platinum(IV) complexes based on the platinum(II) starting material or the use of molecular bromine as an oxidant.

Interestingly, despite the fact that this reaction was carried out in a chlorinated solvent (CH_2Cl_2), no incorporation of chloride into the platinum(IV) product was observed. This is especially notable in light of the role of solvent in the formation of

complexes **4-31**, **4-32**, and **4-33**, and it implies that the significance of these solvent effects may not extend past that particular system. Of note, the literature cited earlier also does not report mixed platinum(IV) complexes of bromine and chlorine being formed at room temperature in CH_2Cl_2, $CHCl_3$ or CCl_4. However, Hodges and Rund did isolate a mixed platinum(IV) complex of bromine and chlorine by oxidizing the dibromo(1,10-phenathroline) platinum(II) complex with bromine in boiling 8 M HCl. This suggests that harsh conditions are required to incorporate a ligand that is not donated by the oxidant.



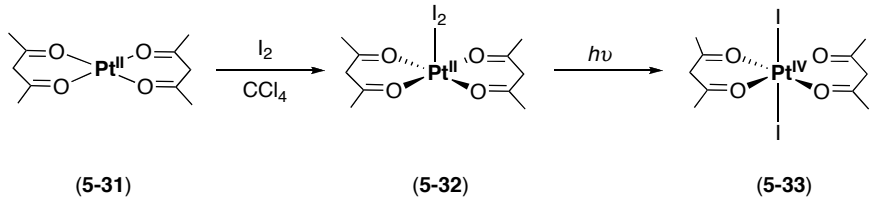
(**5-17**) (**5-30**)

Scheme 5.14 – Incorporation of Chlorine in Br_2 Oxidation of Dihalo(1,10-Phenanthroline)Platinum(II)

Complex **5-29** was found to be stable under ambient conditions at room temperature both in the solid state and in solution. It was also showed minimal reactivity upon thermolysis in dimethyl sulfoxide at 150 ºC overnight. Examination of the crude reaction mixture by ^{1}H NMR spectroscopy revealed that complex **5-29** was virtually unperturbed and remained the major species in solution. Smaller signals were present; however, these did not correspond with 2-(2-bromophenyl)pyridine, the expected C–Br bond-forming reductive elimination product or with 2,2'-di(pyridin-2-yl)biphenyl, another possible product that could be formed by C–C bond-forming reductive elimination. As the smaller peaks were not indicative of a symmetrical compound, *cis-trans* isomerism may also be eliminated as an explanation. The identity of the smaller peaks remains unknown at this time, although one possibility could involve the incorporation of dimethyl sulfoxide as a ligand that replaced a bromine ligand on the platinum.

5.3 Oxidation with Iodine

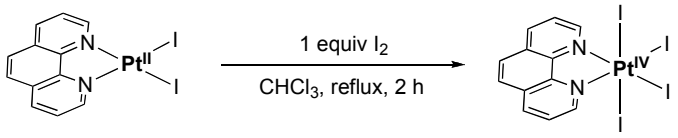
The oxidative addition of iodine at platinum(II) complexes has also been investigated in the literature. One of the earliest examples was provided by Hopgood and Jenkins with their study of the oxidative addition of iodine to platinum acetylacetonate.[19] Based on X-ray diffraction and other spectroscopic techniques they were able to observe a *trans* platinum(IV) adduct, **5-33**, which was preceded by a platinum(II) Lewis acid-base adduct intermediate, **5-32** (Scheme 5.15). They also observed that the oxidation of **5-32** to **5-33** was promoted by light. The mechanistic explanation for the observance of the platinum(II) Lewis acid-base adduct is that the d_z^2 orbital of the platinum donates electron density to the empty σ^* orbital of an iodine molecule.[19] Platinum as a donor, forms a donor-acceptor complex with iodine, in part because iodine is the best electron acceptor of the halogens and the mildest oxidizing agent.[25] The photochemical pathway of the platinum oxidation is postulated to be radical in nature.



Scheme 5.15 – Oxidative Addition of Iodine to Platinum Acetylacetonate, **5-31**

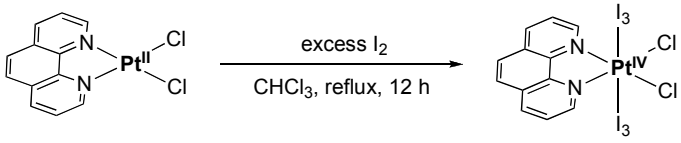
The observance of *trans* platinum(IV) complexes generated by oxidation of platinum(II) with iodine is prevalent throughout the literature. Rund and Hodges provided other early examples of iodine oxidation with the examination of dihalo(1,10-phenathroline)platinum(II), previously cited for oxidation with bromine.[11] Interestingly, two different products were observed when the halogens trans to the nitrogen atoms of the 1,10-phenathroline ligand differed. When the halogens were iodine atoms, $Pt^{IV}(phen)I_4$ was observed, however when the halogens were chlorine atoms, the new

ligands were identified as triiodide ligands (Schemes 5.16 and 5.17, respectively). The stoichiometry of the added iodine is likely the major contributor to this difference in reactivity. For oxidation of **5-34**, one equiv of iodine was added, allowing for sole formation of iodine atoms as ligands. In contrast, complex **5-36** was allowed to interact with an excess amount of iodine for a significantly longer reaction period, leading to the formation of the triiodide product. Of note, both complexes have the iodine atoms or ions in the axial positions, rather than equatorial.



(**5-34**) (**5-35**)

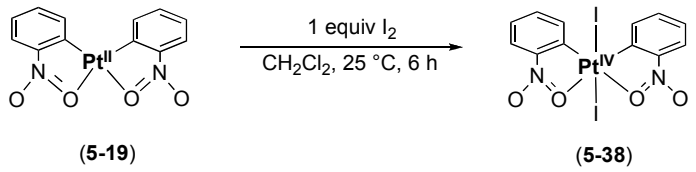
Scheme 5.16 – Iodine Oxidation of Diiodide(1,10-Phenanthroline)Platinum(II)



(**5-36**) (**5-37**)

Scheme 5.17 – Iodine Oxidation of Dichloride(1,10-Phenanthroline)Platinum(II)

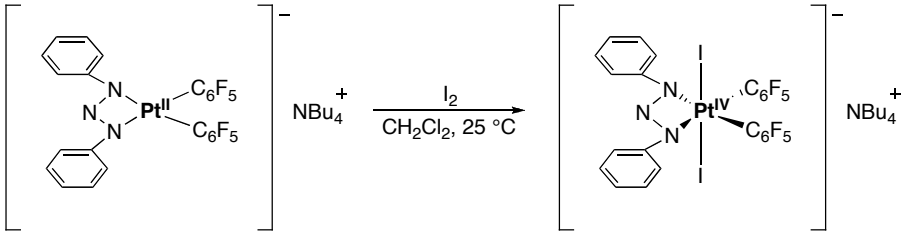
Vicente also reports a platinum(IV) product resulting from the oxidative addition of iodine to a platinum(II) complex, **5-19** (Scheme 5.18). A *trans* platinum(IV) iodine structure is proposed, based on infrared spectra data and comparison to the analogous dichloride complex.[13] Notably, while the analogous oxidation with Br_2 required 20 equiv of oxidant, oxidation with iodine proceded efficiently with only one equiv of I_2.



(**5-19**) (**5-38**)

Scheme 5.18 – Iodine Oxidation of *o*-Nitrophenyl Complex of Platinum(II)

Perez also proposes *trans* addition of I_2 to the platinum(II) complex **5-39** (Scheme 5.19).[20] While the anionic triazenide ligand of **5-39** is quite different from neutral 2-phenylpyridine (phpy), this complex is similar to $Pt^{II}(phpy)_2$ (**5-27**) in the identity of atoms bonded to the platinum atom. The presence of only one type of C_6F_5 group in the ^{19}F NMR spectra led Perez to the conclusion that the product is a symmetrical complex. Multiple symmetrical isomers are possible, but the isomer with a trans orientation of the iodine atoms was proposed based on X-ray crystallography of an analogous platinum(IV) chloride structure and on the orbital symmetry theory cited by Hopgood and Jenkins for iodine molecules.

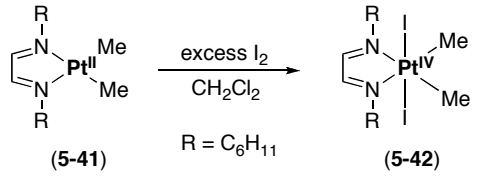


(**5-39**) (**5-40**)

Scheme 5.19 – Oxidative Addition of Iodine to $[NBu_4][Pt(C_6F_5)_2(\eta^2\text{-PhNNNPh})]$

Importantly, the stoichiometry of I_2 is not the sole factor in determining the structures of the products. For example, Bercaw has shown that the use of excess iodine

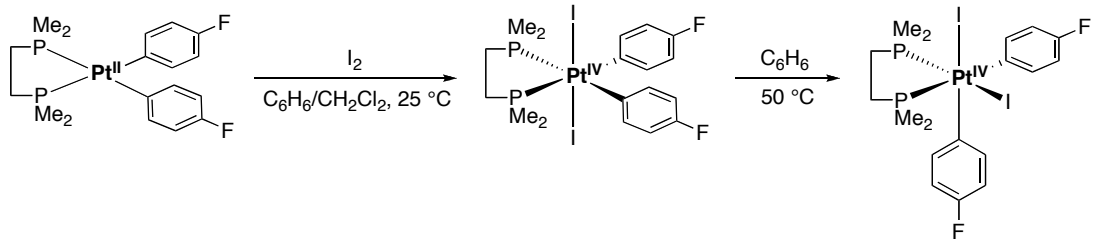
in the oxidation of **5-41** affords product **5-42**, containing iodine rather than triodide ligands (Scheme 5.20).[21] While the quantitative amount of excess is not identified in this work, it seems likely that triiodide ligand formation was plausible but did not occur under these conditions.



(**5-41**) (**5-42**)

Scheme 5.20 - Oxidation of $Pt^{II}Me_2(\alpha\text{-diimine})$ with I_2

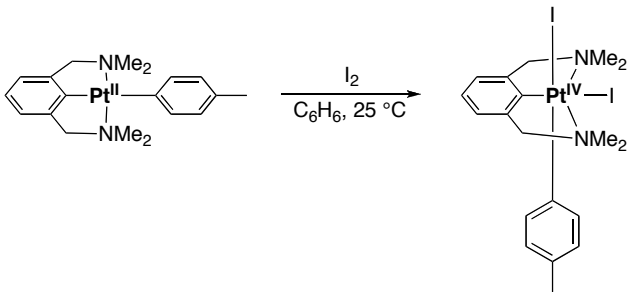
Vigalok observed the *trans* addition of I_2 to an aryl-phosphorous platinum(II) complex, with a unique result. [22, 23] Upon isolation of this *trans* complex, thermolysis in benzene promoted isomerization to the *cis* compound (Scheme 5.21), where one of the iodine atoms has shifted from the axial to the equatorial position. Vigalok postulated that the observance of *trans/cis* isomerization confirmed literature suggestions of *trans* adducts forming as kinetic products of oxidative addition versus *cis* adducts forming as thermodynamic products.[12]



(**5-43**) (**5-44**) (**5-45**)

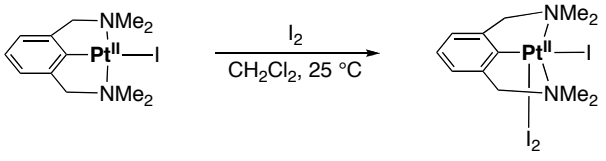
Scheme 5.21 – Formation & Isomerization of $Pt^{IV}(dmpe)(C_6H_4F)_2I_2$

Although *trans*-platinum(IV) complexes with iodine ligands are frequently observed as kinetic products of oxidative addition, there is also some literature precedence for the direct formation of *cis*-platinum(IV) diiodide compounds. For example, van Koten has demonstrated that Pt^{II}(p-tolyl)(NCN) (NCN = ($C_6H_3\{CH_2NMe_2\}_2$-2,6)) reacts with molecular iodine to form Pt^{IV}(p-tolyl)-(NCN)I_2 with one iodine atom in an axial position and the other in an equatorial position (Scheme 5.22).[24, 25] van Koten has also provided further support for the orbital symmetry theory by isolating a Lewis acid-base adduct with an I_2 ligand and identifying it definitively through X-ray crystallography (Scheme 5.23). Similar to the compound observed by Hopgood and Jenkins, this complex has the I_2 ligand in the axial position.[24, 25]



(**5-46**) (**5-47**)

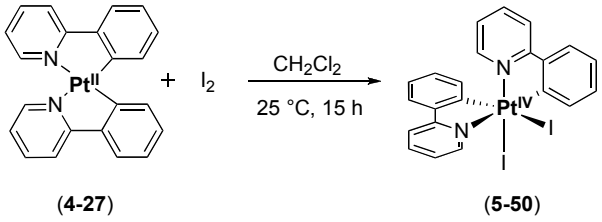
Scheme 5.22 – Formation of Pt^{IV}(NCN)(*p*-tolyl)I_2



(**5-48**) (**5-49**)

Scheme 5.23 – Formation of Pt^{II}(NCN)I(I_2)

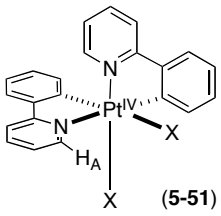
With significant literature precedent for the formation of *trans* adducts of iodine with platinum, our investigations continued with the oxidation of complex **4-27**, $Pt^{II}(phpy)_2$, using elemental iodine, I_2. Complex **4-27** was combined with one equiv of I_2 in a solution of CH_2Cl_2, and this mixture was allowed to stir at 25 ºC for approximately 15 h. Two products, major and minor, could be observed in the crude reaction mixture. The major platinum(IV) product was isolated in 74% yield from the reaction mixture through precipitation with hexanes. The complex was initially identified as *cis*-$Pt^{IV}(phpy)_2I_2$, **5-50**, based upon its ^{1}H NMR spectrum. A *trans* compound is expected to show a maximum of 8 aromatic resonances in the ^{1}H NMR spectrum due to the symmetry of the ligands. However, 11 sets of peaks were clearly visible, with several peaks accounting for only one proton, indicating the inequivalence of the protons and an absence of the required symmetry for a *trans* compound.



(**4-27**) (**5-50**)

Scheme 5.24 - Oxidation of **4-27** with Iodine

The ^{1}H NMR spectrum of **5-50**, is quite comparable to that of *cis*-$Pt^{IV}(phpy)_2Br_2$, **5-29**. The proton α to the nitrogen of the 2-phenylpyridine ring that is in proximity to an iodide ligand is shifted significantly downfield at 10.06 ppm. Comparison of the family of *cis*-$Pt^{IV}(phpy)_2X_2$ complexes, with X equal to Cl, Br, and I shows that the previously mentioned proton, H_A in Figure 5.2, shifts further downfield as the size of the halogen increases (Table 5.2). This clear trend provides support for the identification of **5-50** as a platinum(IV) complex with iodine atoms, rather than a platinum(II) compound with I_2 ligands.



(**5-51**)

Figure 5.2 - H_A in $Pt^{IV}(phpy)_2X_2$ Complexes

Table 5.2 - Chemical Shift of H_A in $Pt^{IV}(phpy)_2X_2$ Complexes

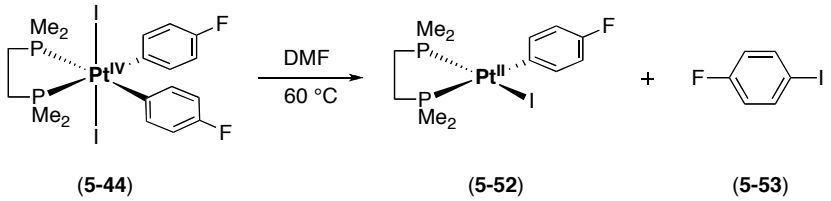
Complex	**Chemical Shift of H_A in DMSO-d_6 (ppm)**
cis-$Pt^{IV}(phpy)_2Cl_2$ (**4-32**)	9.61
cis-$Pt^{IV}(phpy)_2Br_2$ (**5-29**)	9.81
cis-$Pt^{IV}(phpy)_2I_2$ (**5-50**)	10.06

High resolution mass spectrometry also allowed us to confirm the identity of **5-50** based upon comparison to complex **5-29**. The spectra for both **5-29** and **5-50** reveal a lack of fragmentation during the analysis process. In compound **5-29**, two bromine atoms could be accounted for, while in compound **5-50**, only two iodine atoms could be accounted for, suggesting against a platinum(IV) complex with triiodide ligands.

An oxidative addition complex had been previously synthesized by von Zelewsky, with either **4-27** or **4-42** and I_2.[18] The report of this oxidative addition does not identify or characterize the products produced with complex **4-27**, although the presumption is that platinum(IV) complexes are formed. von Zelewsky identifies the oxidative addition product $Pt^{IV}(thpy)_2I_2$ as having 2 or 3 isomers visible in the ^1H NMR spectrum, though he does not offer quantitative data regarding the relative amounts or ratios of the different isomers. The presence of multiple isomers is consistent with our observations in the crude reaction mixture.

Complex **5-50** is stable to air and ambient moisture in the solid state for several months at a time. In addition, it does not decompose in most common solvents within a

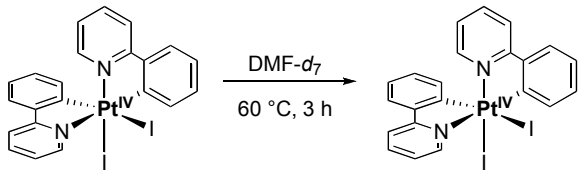
48 h period at ambient temperature. In an effort to induce reductive elimination, we subjected **5-50** to thermolysis conditions. Importantly, Vigalok demonstrated that platinum(IV) iodine species, **5-44**, reacted to produce the aryl-iodide reductive elimination product **5-53** after 25 minutes at 60 ºC in DMF (Scheme 5.25).[23] Notably, the ancillary ligands used in his system were phosphines, rather than nitrogen donors.



(**5-44**) (**5-52**) (**5-53**)

Scheme 5.25 – C-I Reductive Elimination of Complex **5-44**

Even with the ligand differences, Vigalok's reaction conditions warranted investigation. Complex **5-50** was heated in deuterated DMF at 60 °C over the course of 3 hours (Scheme 5.26). No reaction was observed. Next, we attempted facilitating a reaction using harsher conditions. Complex **5-50** was heated in dimethyl sulfoxide at 120 ºC overnight to probe for C–I bond-forming reductive elimination. Examination of the crude reaction mixture by ^{1}H NMR spectroscopy revealed that complex **5-50** remained the major species in solution. Smaller signals were present that did not correspond with 2-(2-iodophenyl)pyridine, the C–I bond-forming reductive elimination product, or with 2,2'-di(pyridin-2-yl)biphenyl. Interestingly, these peaks were also present in the crude reaction mixture as one component of the filtrate. The unidentified peaks are not indicative of a symmetrical compound; therefore, *cis-trans* isomerism may also be eliminated as an explanation. Upon heating of **5-50** at 120 ºC for one week, the new peaks previously mentioned were approximately 50% of the reaction mixture. Again, reductive elimination products or peaks corresponding to *trans* isomerism were not observed. The identity of these peaks remains unknown at this time, though it is believed they represent another type of platinum-iodide complex.



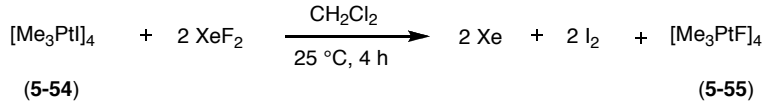
Scheme 5.26 – Attempted C-I Reductive Elimination of Complex **5-50**

5.4 Oxidation with Xenon Difluoride

While Br_2 and I_2 can be readily used for oxidation of platinum complexes, molecular fluorine could not. As a result, researchers needed to find other reagents that can be used to achieve fluorine addition/metal oxidation. One reagent employed in the preparation of late transition metal fluorides is XeF_2.[26] XeF_2, the simplest, neutral, xenon-containing molecule, was discovered in 1962.[26-27] XeF_2 is generally considered to be a highly reactive source of F^+ as it typically reacts with platinum(II) complexes at low temperatures (room temperature and below).

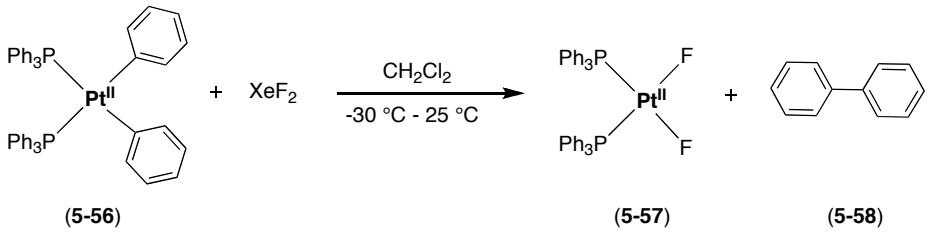
XeF_2 is a molecule that has only recently been employed as an oxidant. A small amount of literature precedent exists for XeF_2 oxidation platinum complexes. There are significant challenges in attempting to generate platinum fluoride complexes. The "soft" nature of platinum suggests limited interactions with a "hard" anion such as fluoride. Indeed, well-defined metal-fluoride complexes are rare for late transition metals. Another challenge is the minimal number and type of ligands to support "push-pull" interactions between metals and ligands.[28] The "push-pull" theory states that a metal-fluoride complex is stabilized by the presence of a π-acceptor ligand trans to the fluorine, which is a π-donor. Although the fluorine increases the energy of the metal π orbitals, backbonding between the metal orbitals and the π-acceptor orbitals is increased, creating greater stabilization. These types of ligands are typically carbonyl, nitrosyl, or phenyl. Finally, other orbital interactions may be unfavorable in metal-fluorides, specifically pπ-dπ four electron repulsions.[29-30] These challenges mainly account for the sparse literature precedent for the synthesis of platinum fluorides.

One of the first examples of a platinum fluoride complex was the formation of a cubane cluster complex, $[PtMe_3F]_4$.[31] The analogous complexes with other halogens in place of the fluoride were fairly straightforward to synthesize. After numerous attempts to synthesize the fluoride complex using AgF, HgF_2, KF, HF, MeF, and an *N*-fluoropyridinium salt, Lorberth and co-workers were able to prepare the elusive complex using XeF_2. As shown in Scheme 5.27, the iodine cubane complex, **5-54**, was the starting point, and the conditions for the synthesis of **5-55** (treatment with XeF_2 at room temperature in CH_2Cl_2) were quite similar to the synthesis of other platinum organometallic halides.



Scheme 5.27 – Synthesis of $[PtMe_3F]_4$ Using XeF_2

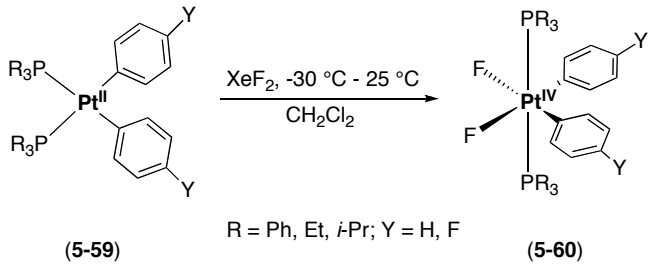
Vigalok has reported several other examples of both platinum(II) and (IV) fluorides. His synthesis of PtF_2L_2, where L is an alkyl or aryl phosphine ligand, begins with the aryl platinum(II) species **5-56** (Scheme 5.28).[32] While no mechanism was proposed for this transformation, one hypothesis would be that complex **5-56** is oxidized to an intermediate Pt^{IV} species that then undergoes reductive elimination to produce biphenyl, **5-58**, along with the desired metal complex, **5-57**.



(**5-56**) (**5-57**) (**5-58**)

Scheme 5.28 – Synthesis of $Pt^{II}(PPh_3)_2F_2$ with Reductive Elimination of Biphenyl

In the example in Scheme 5.28, there is no net change in oxidation state at the platinum(II) center; furthermore, the intermediates in the transformation were neither isolated nor observed. However, Vigalok's subsequent publication detailed the synthesis and characterization of Pt^{IV}-fluoride complexes.[33] A platinum(II) diaryl complex with phosphine ligands was oxidized using XeF_2 to produce a Pt^{IV} fluorine complex, **5-60**, with two fluorines in equatorial positions, *cis* to one another. The identity of **5-60** was confirmed by NMR spectroscopy and single crystal X-ray analysis.

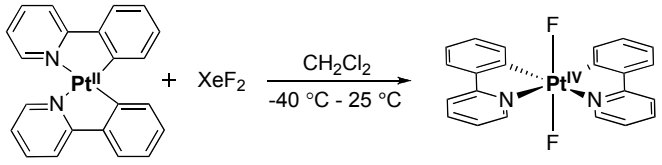


(**5-59**) (**5-60**)

Scheme 5.29 – Synthesis of $Pt^{IV}(Ar)_2(PR_3)_2F_2$

The limited literature precedent for the formation of platinum-fluoride complexes is actually quite exciting. Unlike the cases with iodine and bromine, precedent had not been set with $Pt^{II}(phpy)_2$ or any related complexes with carbon-nitrogen ligand donors. Our investigations continued with the oxidation of complex **4-27**, $Pt^{II}(phpy)_2$, using XeF_2. A methylene chloride solution of complex **4-27** was combined with a CH_2Cl_2 solution of

XeF_2 under an inert atmosphere. The reaction was initially allowed to stir at –40 °C over the course of 4 hours. After this time, the reaction mixture was allowed to gradually warm to room temperature. The reaction mixture was concentrated to approximately 1 mL of volume. The addition of hexanes precipitated the platinum-fluorine species.



(**4-27**) (**5-61**)

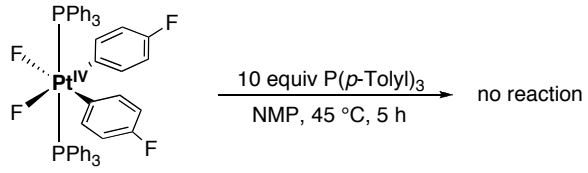
Scheme 5.30 - Oxidation of **4-27** with XeF_2

The platinum complex obtained was identified as *trans*-$Pt^{IV}(phpy)_2F_2$ (Scheme 5.30), based upon the ^1H and ^{19}F NMR spectra of the isolated complex. The ^1H NMR spectrum displayed seven sets of peaks. Six of the seven accounted for 2 protons, while the last peak accounted for 4 protons, indicative of a symmetrical complex. Further support was provided by one signal in the ^{19}F NMR spectrum. The chemical shift obtained in DMSO-d_6 was -315.18 ppm. This value is similar to that obtained for other platinum(IV) fluoride complexes, as shown in Table 5.3.[34] It is also within an acceptable range of the values given for Vigalok's symmetrical Pt^{IV} fluorides, shown in entries 6 and 7.

Table 5.3 - ^{19}F NMR Spectrum Values for Various Pt^{IV} Complexes

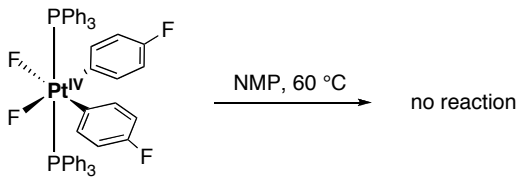
Entry	Complex	$\delta^{19}F$ (ppm)
1	$[PtF_2(OH)_2(CF_3)_2]^{2-}$	-376.8
2	$[PtClF(OH)_2(CF_3)_2]^{2-}$	-287.7
3	*cis*-$[PtF_2(CF_3)_4]^{2-}$	-278.2
4	$[NBu_4]_2[PtF(CF_3)_5]$	-311.0
5	$K_2[PtF(CF_3)_5]$	-302.7
6	$PtF_2(PPh_3)_2(C_6H_4F)_2$	-255.2
7	$PtF_2(PEt_3)_2(C_6H_4F)_2$	-270.9

Reactivity of platinum-fluoride complexes has been even less frequently studied than their synthesis. Vigalok attempted to observe reductive elimination from complex **5-60**. However, he found that complex **5-60** was unreactive at 45 ºC in NMP in the presence of 10 equiv of P(*o*-tolyl)$_3$ and at 60 °C in NMP. It is unclear if more forcing conditions were examined.



(**5-60**)

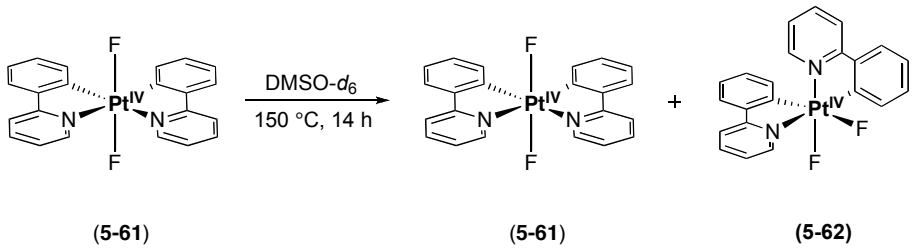
Scheme 5.31 – Attempted Reductive Elimination/Ligand Substitution of $Pt^{IV}(PPh_3)_2(C_6H_4F)_2F_2$



(**5-60**)

Scheme 5.32 – Attempted Reductive Elimination of $Pt^{IV}(PPh_3)_2(C_6H_4F)_2F_2$

$Pt^{IV}(phpy)_2F_2$, **5-61**, is stable to air and ambient moisture in the solid state for several weeks at a time. Decomposition in most common solvents has not been observed within a 48 h period at ambient temperature, though this may be largely attributed to a lack of solubility. We subjected **5-61** to thermolysis at 150 ºC in DMSO overnight to probe for C–F bond-forming reductive elimination. Examination of the crude reaction mixture by ^{1}H NMR spectroscopy showed that **5-61** was the major component of the reaction mixture. However an additional species was observed that exhibited one resonance at 9.61 ppm and one at 6.17 ppm. Such signals are diagnostic of the unsymmetrical *cis*-$Pt^{IV}(phpy)X_2$ complexes discussed in this chapter as well as in Chapter 4. As a result, we propose that *trans*-*cis* isomerization took place. The literature has established that the *cis* isomer of a metal complex is the thermodynamically more stable isomer.[12] The *cis* designation refers to the oxidative addition ligands, in our case halogens, being adjacent to one another, both equatorial or equatorial and axial rather than both axial.[35, 36]



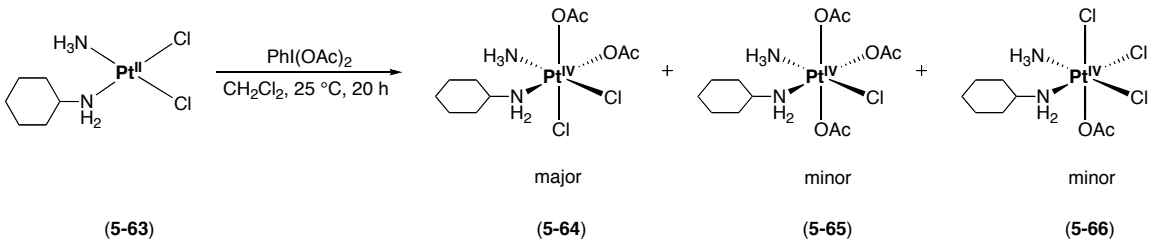
(**5-61**) (**5-61**) (**5-62**)

Scheme 5.33 – Attempted Reductive Elimination of **5-61**

5.5 Oxidation with Iodobenzene Diacetate

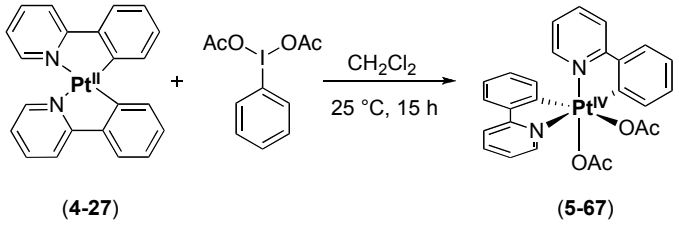
Iodobenzene diacetate has gained acceptance as an effective oxidant for the oxidation of transition metals. In several cases, $PhI(OAc)_2$ oxidizes a metal intermediate, promoting a critical step in the catalytic cycle. While $PhI(OAc)_2$ has been frequently employed in organic reactions, it has been used significantly less frequently in stroichiometric inorganic reactions. To our knowledge, only one example of platinum oxidation exists with this reagent.

Barnard demonstrated that an amine platinum(II) complex, **5-63**, could be oxidized with $PhI(OAc)_2$ to generate three different isomers, the predominant isomer having acetate ligands *cis* to one another in both axial and equatorial positions (Scheme 5.34).[37] As with the previous oxidizing reagents discussed, a chlorinated solvent was used in order to prevent solvent coordination to the metal. Interestingly, although CH_2Cl_2 was not found to bind to the metal under these conditions, it most likely accounts for the presence of minor isomer **5-66**, where an additional chlorine ligand has been incorporated into the Pt^{IV} product.



Scheme 5.34 – Oxidation of *cis*-$Pt^{II}Cl_2(NH_3)(c\text{-}C_6H_{11}NH_2)$ with $PhI(OAc)_2$

Having synthesized the palladium analogue, **3-50**, of our desired product $Pt^{IV}(phpy)_2(OAc)_2$,[38] we were interested in determining whether the oxidation would proceed in a similar manner with complex **4-27** to afford the analogous unsymmetrical oxidative addition product. Complex **4-27** was combined with approximately one equiv of $PhI(OAc)_2$ in a solution of CH_2Cl_2. After 15 hours of stirring at 25 ºC, the volume was concentrated, and hexanes added to precipitate product. Isolation of the platinum species afforded the unsymmetrical *cis*-$Pt^{IV}(phpy)_2(OAc)_2$.



Scheme 5.35 - Oxidation of **4-27** with $PhI(OAc)_2$ in CH_2Cl_2

^1H NMR spectroscopy of the resulting product in $CDCl_3$ showed nine sets of peaks with several peaks representing multiplets of overlapping peaks. The integration accounted for 16 aromatic protons. Even more diagnostic for identifying **5-67** as an unsymmetrical *cis* isomer was the presence of two different signals associated with the two acetate ligands of the complex, indicating that they are inequivalent. Further

conformation was provided by a comparison of the ^{1}H NMR spectrum of **5-67** to that of $Pd^{IV}(phpy)_2(OAc)_2$ (**3-50**) in DMSO-d_6. Platinum and palladium complexes with identical ligand environments typically have very similar ^{1}H NMR spectra.[4, 8-9, 39-40] As summarized in Table 5.4, these species indeed show nearly identical spectra.

Table 5.4 - Comparison of ^{1}H NMR Spectrum Signals for $Pt^{IV}(phpy)_2(OAc)_2$, **5-67**, and $Pd^{IV}(phpy)_2(OAc)_2$, **3-50**, in DMSO-d_6

$Pt^{IV}(phpy)_2(OAc)_2$ (ppm)	$Pd^{IV}(phpy)_2(OAc)_2$ (ppm)
9.20	9.22
8.38	8.37
8.25	8.24
8.14	8.18
7.92	7.92
7.85	7.90
7.73	7.70
7.41	7.48
7.10	7.14
7.00	7.09
6.79	6.87
6.06	6.15

Our final confirmation of the structure of **5-67** was provided by X-ray crystallography. As shown in Figure 5.3, one acetate ligand is *trans* to a nitrogen of 2-phenylpyridine, while the other acetate is *trans* to a carbon of a different 2-phenylpyridine. Selected bond lengths and angles are displayed in Table 5.5. As with $Pt^{IV}(phpy)_2Br_2$ (**5-29**), we observed that the *trans* influence of σ-aryl ligands results in a difference of 0.142 Å between the Pt–O(3) and Pt–O(1) bonds.

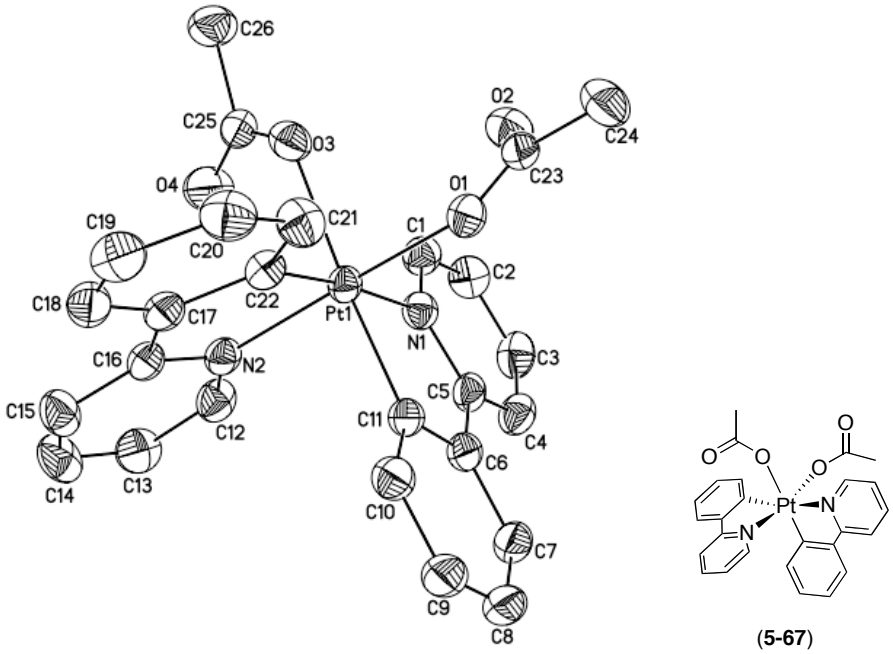


Figure 5.3 - ORTEP View of *cis*-$Pt^{IV}(phpy)_2(OAc)_2$, **5-67**

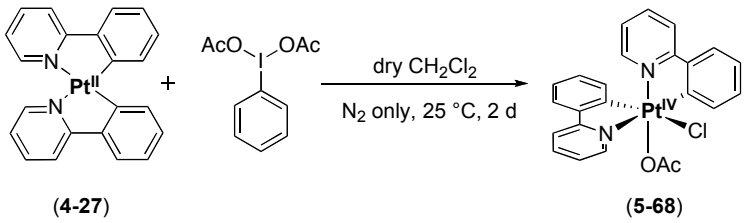
Table 5.5 – Selected Bond Lengths (Å) and Angles (°) for *cis*-$Pt^{IV}(phpy)_2(OAc)_2$, **5-67**

Pt(1)-C(22)	2.002(4)	C(22)-Pt(1)-O(1)	89.82(16)
Pt(1)-C(11)	2.008(4)	C(11)-Pt(1)-O(1)	88.50(15)
Pt(1)-N(2)	2.024(4)	N(2)-Pt(1)-O(1)	170.10(14)
Pt(1)-O(1)	2.026(3)	C(22)-Pt(1)-N(1)	175.04(15)
Pt(1)-N(1)	2.137(4)	O(1)-Pt(1)-N(1)	92.31(14)
Pt(1)-O(3)	2.168(4)	C(11)-Pt(1)-O(3)	176.28(14)
		O(1)-Pt(1)-O(3)	88.17(13)

A close examination of the crude reaction mixture indicated the presence of a second high oxidation state platinum complex. Quantities of this unidentified complex were quite small and could not be isolated under the standard conditions used to prepare

5-67. However, intriguingly, when the reaction was carried out under N_2 (as opposed to the presence of ambient air and moisture) and stirred for 2 days (rather than 15 h), this new complex was the sole product observed. A series of control experiments revealed that both the increased reaction time and the absence of air are contributing factors in the formation of this new species.

This product was initially identified as *cis*-$Pt^{IV}(phpy)_2(OAc)Cl$, **5-68**, by X-ray crystallography (Scheme 5.36 and Figure 5.4). Selected bond lengths and angles are listed in Table 5.6. The structure in Figure 5.4 confirms that the chlorine atom is *trans* to the σ-aryl group of a 2-phenylpyridine ligand. Several other isomers of this complex are possible, but presumably the only complex observed was **5-68** due to the *trans* effect. The structure of **5-68** was further confirmed by re-examining the ^1H NMR spectrum. The most downfield proton signal of **5-68** in $CDCl_3$ appeared at 9.99 ppm. This corresponds to the proton bonded to C(12) in Figure 5.4. In the case of the platinum(IV) diacetate complex, **5-67**, this proton would have been in the environment of an acetate group, which would not be expected to shift it significantly downfield. For example, the most downfield proton signal of **5-67** in $CDCl_3$ is 9.34 ppm. However, being in the environment of a chlorine atom is expected to have a greater shift effect. Additionally, the most downfield proton signal of the palladium(IV) dichloride compound, **3-32**, is 9.90 ppm, significantly closer to the value of 9.99 ppm.

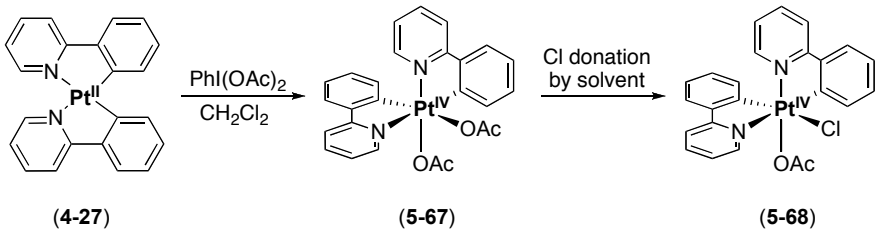


(**4-27**) (**5-68**)

Scheme 5.36 – Synthesis of *cis*-$Pt^{IV}(phpy)_2(OAc)Cl$, **5-68** with $PhI(OAc)_2$

A mechanistic theory for the formation of **5-68** would involve initial generation of the platinum(IV) diacetate complex. The *trans* effect then dictates that the most labile

acetate will be *trans* to the carbon. Increasing the reaction time allows for substitution of the labile acetate group with a chlorine atom obtained from solvent. Literature precedent, in Barnard's research, is already established for this type of substitution by a chlorinated solvent with $PhI(OAc)_2$ as the oxidant (Scheme 5.34).



Scheme 5.37 – Proposed Theory of Formation of **5-68**

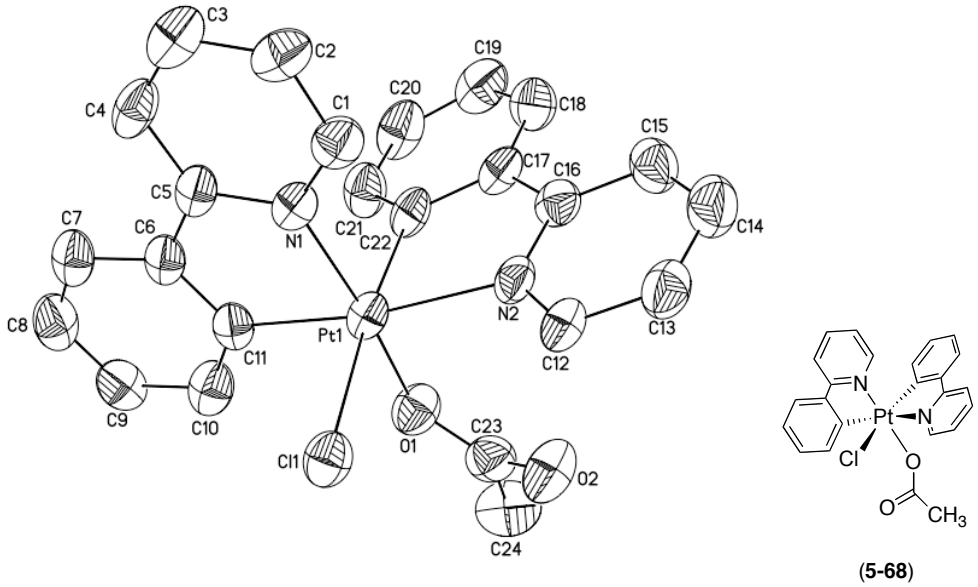
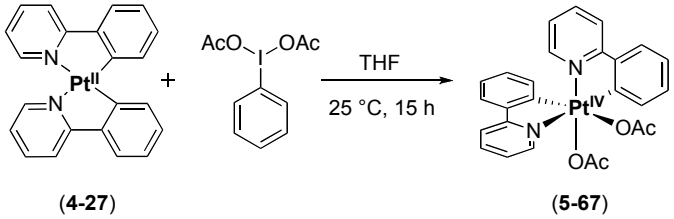


Figure 5.4 - ORTEP View of *cis*-$Pt^{IV}(phpy)_2(OAc)Cl$, **5-68**

Table 5.6 – Selected Bond Lengths (Å) and Angles (°) for *cis*-$Pt^{IV}(phpy)_2(OAc)Cl$, **5-68**

Pt(1)-C(22)	2.019(4)	C(22)-Pt(1)-C(11)	95.31(17)
Pt(1)-C(11)	2.026(4)	C(11)-Pt(1)-O(1)	90.49(16)
Pt(1)-N(2)	2.151(3)	O(1)-Pt(1)-N(1)	170.13(13)
Pt(1)-O(1)	2.028(3)	C(22)-Pt(1)-N(2)	80.05(16)
Pt(1)-N(1)	2.037(4)	C(22)-Pt(1)-Cl(1)	174.26(13)
Pt(1)-Cl(1)	2.4474(12)	O(1)-Pt(1)-Cl(1)	91.53(10)
		N(1)-Pt(1)-Cl(1)	92.88(10)

The origin of the chlorine atom in **5-68** was further confirmed by attempting to synthesize **5-68** with $PhI(OAc)_2$ in non-chlorinated solvents such as THF. As shown in Scheme 5.38, the reaction was successful in producing **5-67** exclusively, and no trace of the mixed complex, **5-68**, was observed in the crude reaction mixture.

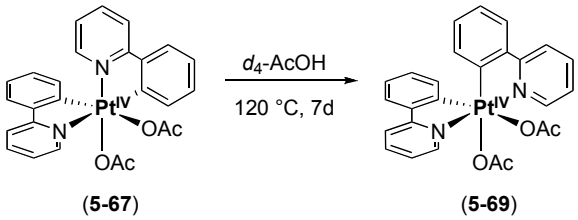


(**4-27**) (**5-67**)

Scheme 5.38 - Oxidation of **4-27** with $PhI(OAc)_2$ in THF

From prior research we were aware of the ability of $Pd^{IV}(phpy)_2(OAc)_2$, **3-50**, to undergo reductive elimination.[38] Our investigation of reductive elimination continued with our newly synthesized platinum analogue, **5-67**. Independent of reductive elimination, complex **5-67** is stable within ambient conditions of air and water. Upon heating in $CDCl_3$ at reflux (100 °C or 150 °C) or d_5-nitrobenzene at 130 °C, no change

was observed in the platinum compound. Heating in d_5-nitrobenzene at 200 °C or d_6-DMSO at 185 °C led to inconclusive results. The first interesting result occurred with thermolysis in d_5-nitrobenzene at 150 °C. New peaks appeared in the 1H NMR spectrum that appeared to correspond with isomerization of complex **5-67** to a *trans* or symmetrical *cis* geometry. As we were still not completely certain of the identity of the new peaks we heated **5-67** in d_4-acetic acid. Over the course of 7 days we observed clear isomerization of **5-67** to what we hypothesize is a symmetrical *cis* geometry, based on diagnostic signals 5.91 ppm and 9.62 ppm. A trans complex would not be expected to have signals markedly downfield or upfield. Notably, reductive elimination of organic products, either the 2-(2-acetoxyphenyl)pyridine or the 2,2'-di(pyridin-2-yl)biphenyl was not observed.



(**5-67**) (**5-69**)

Scheme 5.39 – Isomerization of **5-67** in d_4-acetic acid

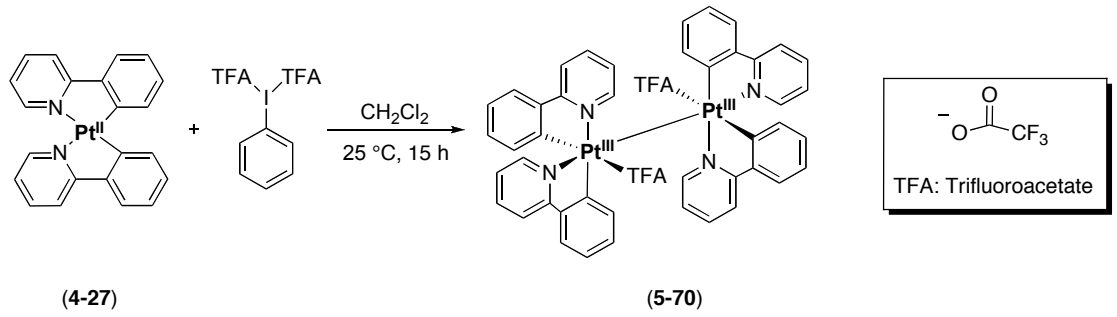
5.6 Oxidation with Iodobenzene Trifluoroacetate

Bis(trifluoroacetoxy)iodobenzene has an identical structure to iodobenzene diacetate, yet different electronic properties due to replacement of the acetate hydrogens with fluorines. We were interested in how oxidative addition would be affected by changing the electronics on the oxidant. Given that fluorine and hydrogen have similar sizes we believed that any differences observed for platinum oxidation would be a result of electronic factors, not steric factors.

Our oxidation of **4-27** with $PhI(C_2F_3O_2)_2$ led us to what we initially believed to be a platinum(IV) complex, based on analogy to oxidations with $PhI(OAc)_2$. Reaction conditions were virtually identical to the oxidations with $PhI(OAc)_2$, with the exception

of a more dilute reaction mixture. Complex **4-27** was combined with approximately one equiv of $PhI(C_2F_3O_2)_2$ in a solution of CH_2Cl_2. After 15 hours of stirring at 25 ºC, the volume was concentrated, and hexanes added to precipitate product.

X-ray crystallographic characterization of a crystal from this reaction mixture showed that the Pt^{III} dimer $[Pt^{III}(phpy)_2(C_2F_3O_2)]_2$ (**5-70** in Scheme 5.39) was produced in this transformation. This change in oxidation state was unexpected, though not unprecedented given the results in Chapter 4. Figure 5.5 displays the solid state structure of **5-70**, which is very similar to that of unsymmetrical complex $[Pt^{III}Cl(phpy)_2]_2$, **4-31**. Distinguishing characteristics include an unsupported platinum-platinum bond, identical ligand environments at each platinum atom, and a *trans* relationship between the fluorinated acetate group and a σ-aryl group. Selected bond lengths and angles are listed in Table 5.7. The Pt-Pt bond length for **5-70**, 2.6703 Å is also comparable to that for $[Pt^{III}Cl(phpy)_2]_2$, **4-31**, at 2.7187 Å.



Scheme 5.40 - Synthesis of **5-70** with $PhI(C_2F_3O_2)_2$ Oxidation

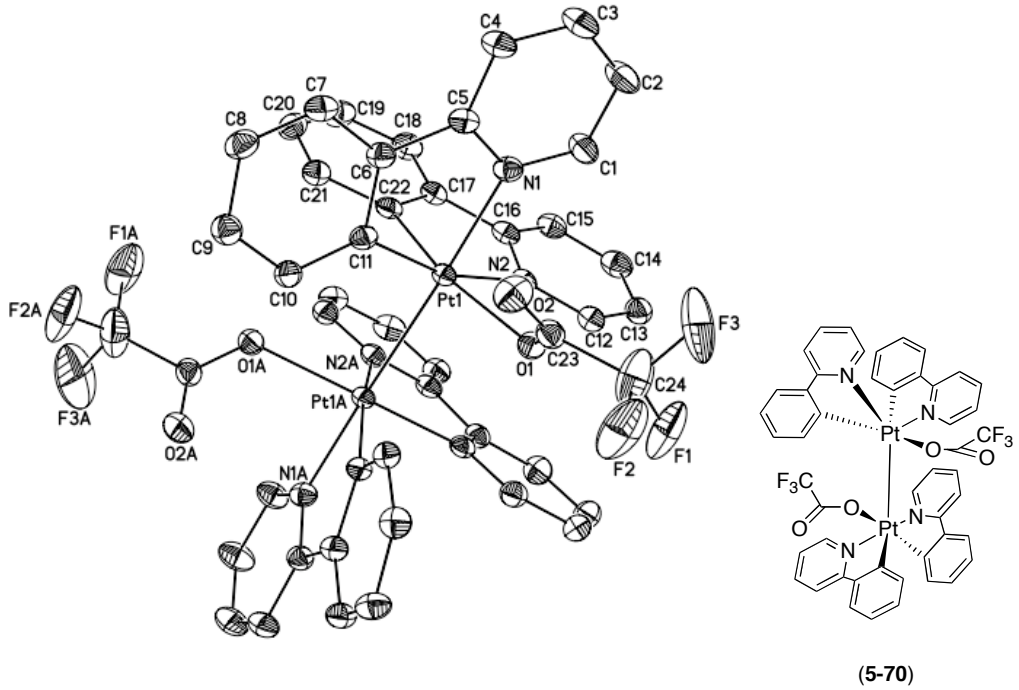


Figure 5.5 - ORTEP View of $[Pt^{III}(phpy)_2(C_2F_3O_2)]_2$, **5-70**

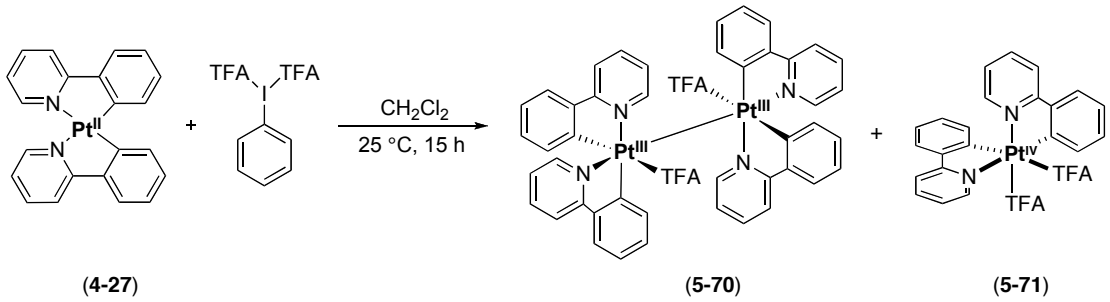
Table 5.7 – Selected Bond Lengths (Å) and Angles (°) for $[Pt^{III}(phpy)_2(C_2F_3O_2)]_2$, **5-70**

Pt(1)-C(22)	1.994(3)	C(22)-Pt(1)-C(11)	89.22(13)
Pt(1)-C(11)	2.028(3)	C(11)-Pt(1)-N(2)	165.52(11)
Pt(1)-N(2)	2.132(3)	C(22)-Pt(1)-O(1)	167.15(12)
Pt(1)-O(1)	2.157(2)	N(2)-Pt(1)-O(1)	86.77(10)
Pt(1)-N(1)	2.156(3)	C(22)-Pt(1)-Pt(1A)	89.50(9)
Pt(1)-Pt(1A)	2.6793(5)	N(1)-Pt(1)-Pt(1A)	177.91(8)
		O(1)-Pt(1)-Pt(1A)	95.84(6)

Importantly, **5-70** was not the only platinum complex in the crude reaction mixture, and we were initially unsure whether it was the major component. Various attempts were made to separate the multiple complexes in solution. Amending the

original conditions allowed us to isolate the major product. Concentration of the reaction solution and slow crystallization in the presence of air over 4 - 6 h afforded a crystalline solid. Careful removal of these crystals provided clean samples of the major product observed by ^{1}H NMR spectroscopy.

Remarkably, crystallographic characterization of this material revealed that the major product of this reaction was, in fact, $Pt^{IV}(phpy)_2(C_2F_3O_2)_2$, **5-71**. Scheme 5.40 reflects the presence of both oxidized products observed in the reaction. Figure 5.6 displays the structure of **5-71**, which is analogous to $Pt^{IV}(phpy)_2(C_2H_3O_2)_2$, **5-67**. Both Pt–O bond lengths for **5-71** have identical values of 2.0947 Å, an intermediate value between the Pt–O bond lengths of 2.026 and 2.1648 for **5-67**. The similarity between these values is unexpected based on the trans influence and cannot be explained at this time. Other selected bond lengths and angles are listed in Table 5.8.



Scheme 5.41 - Isolation and Identification of **5-71** with $PhI(C_2F_3O_2)_2$ Oxidation

Unfortunately attempts to obtain clean samples of Pt^{III} complex **5-70** were unsuccessful. However, the isolation of **5-71** allowed us to distinguish between the major and minor products by NMR spectroscopy. For example, ^{195}Pt NMR spectroscopy showed a signal at –2146 ppm for **5-70**. This is comparable with the signal at –2354 ppm for $[Pt^{III}Cl(phpy)_2]_2$, **4-31**. A signal appears at –1002 ppm for **5-71**, similar to a signal at –930 ppm for $Pt^{IV}(phpy)_2(C_2H_3O_2)_2$, **5-67**. Each platinum atom is symmetrical in complex **5-70** and only one fluorine signal is expected and observed by ^{19}F NMR spectroscopy at

–75.72 ppm. In contrast, the inequivalent trifluoroacetate ligands on **5-71**, lead to two fluorine signals at –74.99 ppm and –75.14 ppm.

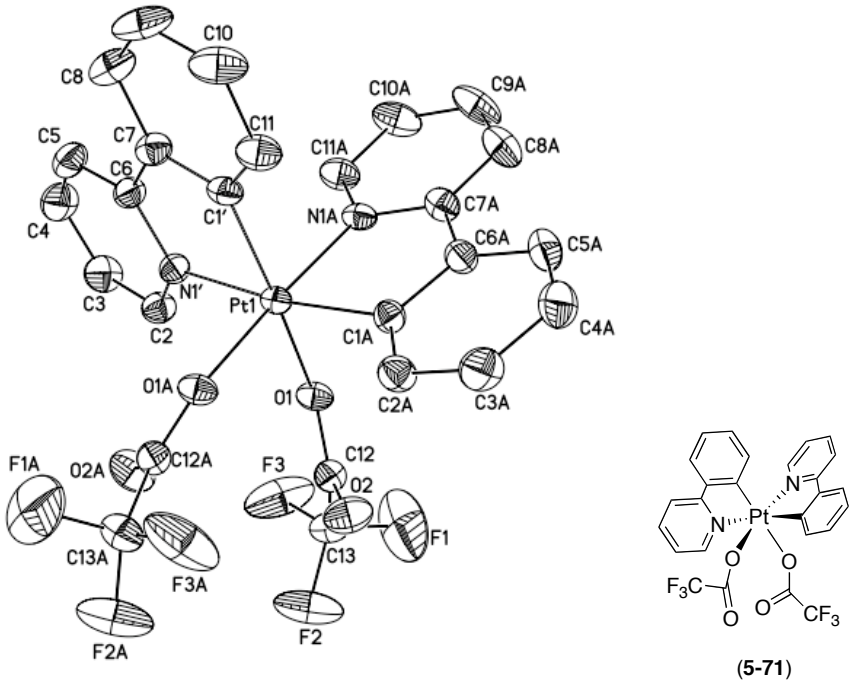


Figure 5.6 - ORTEP View of *cis*-$Pt^{IV}(phpy)_2(C_2F_3O_2)_2$, **5-71**

Table 5.8 – Selected Bond Lengths (Å) and Angles (°) for *cis*-$Pt^{IV}(phpy)_2(C_2F_3O_2)_2$, **5-71**

Pt(1)-N(1A)	2.011(2)	N(1A)-Pt(1)-C(1')	87.96(14)
Pt(1)-C(1')	2.011(2)	C(1')-Pt(1)-C(1A)	93.36(10)
Pt(1)-C(1A)	2.071(3)	C(1A)-Pt(1)-N(1')	172.80(13)
Pt(1)-N(1')	2.071(3)	C(1')-Pt(1)-O(1A)	170.11(9)
Pt(1)-O(1)	2.0947(19)	N(1A)-Pt(1)-O(1A)	170.11(9)
Pt(1)-O(1A)	2.0947(19)	N(1')-Pt(1)-O(1A)	95.43(9)
		O(1')-Pt(1)-O(1A)	95.71(10)

Clearly, changing the electronic nature of the oxidant produced a distinguished effect on platinum oxidation. It is interesting to note that only one oxidation state is observed with the less electron deficient oxidant, iodobenzene diacetate, while two are observed with bis(trifluoroacetoxy)iodobenzene. This electron poor oxidant seems to provide more options for platinum oxidation in the carboxylate hypervalent iodine systems. This statement cannot be expanded to all hypervalent iodine oxidants due to the sole observation of platinum(IV) complexes in chapter 4 with the use of iodobenzene dichloride. Even with the current limitations of scope for the prior statement, electronics clearly induce an effect on the final complex.

5.7 Conclusion

In conclusion, we have been able to demonstrate the oxidative addition of a wide variety of oxidants to the platinum(II) complex $Pt^{II}(phpy)_2$. The halogens, Br_2 and I_2, provided platinum(IV) complexes comparable to others observed in literature, obtained by a similar oxidative addition process. Xenon difluoride was an effective oxidant for the fluorination of platinum(II) with carbon- and nitrogen-donor ligands. While the identities of the halide complexes in this chapter were anticipated, their geometries were not. The mechanism for oxidative addition to a platinum(II) square planar complex predicts that *trans* products should form preferentially over *cis* products. Literature precedent for bromine and iodine support this, however our research indicates that the geometry of oxidative addition is not straightforward. In a comparison of platinum(IV) halide complexes formed in Chapters 4 and 5, iodine and bromine complexes only formed *cis* products. Chlorine complexes were isolated as both *cis* and *trans* products, with the *cis* complex being the major product. The fluorine complex was exclusively isolated as a *trans* product. An analysis of this data would suggest that halide size correlates with the observed geometry, with larger halides exhibiting a preference for the thermodynamic, *cis* products.

Organic carboxylate oxidants additionally offered high oxidation state platinum complexes. The observance of successful oxidation is important in view of the application of platinum to palladium model systems that use identical types of oxidants.

Our results suggest that indeed platinum oxidation studies may be able to model palladium systems. The exact number and types of palladium systems remains unspecified, though we can hypothesize that greater accuracy in modeling may be observed for systems with two-electron oxidants, rather than one-electron. Every oxidant in this chapter is believed to be a two-electron oxidant, whereas the one known divergence of platinum and palladium in our system occurred with a one-electron oxidant, *N*-chloro succinimide. The observance of one oxidation state in the acetate system and two oxidation states in the trifluoro-acetate system is an interesting highlight of the effect of electronics on homologous oxidants. The observed electronic effect may be unique to platinum, due to its higher ability to access an oxidation state of three, and serve as another dichotomy between platinum and palladium.

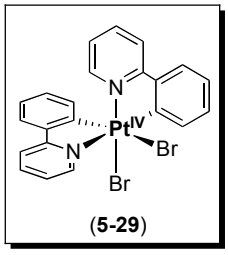
Reductive elimination has also been examined from the halide and carboxylate platinum compounds. Reductive elimination cannot serve as a model for palladium with the use of carbon- and nitrogen-donor ligands. Organic reductive elimination was not visible in any of the examples. Isomerism from *cis* to *trans* or *trans* to *cis* was observed. Additionally, isomerism from one *cis* complex to another was observed. The stability of platinum complexes in general is enhanced greatly by carbon- and nitrogen-donor ligands, allowing for more practical examinations of oxidative addition to platinum(II) versus reductive elimination from platinum(IV).

5.8 Experimental Procedures

General Considerations. NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for ^{1}H; 125.70 MHz for ^{13}C) or a Varian Inova 400 (399.96 MHz for ^{1}H; 100.57 MHz for ^{13}C) spectrometer. ^{1}H NMR chemical shifts are reported in parts per million (ppm) with the residual solvent peak used as an internal reference. ^{195}Pt NMR spectra were obtained on a Varian Inova 500 (107.25 MHz for ^{195}Pt). ^{195}Pt chemical shifts are reported in parts per million (ppm) and were referenced using the frequency of the lock signal and the estimated chemical shift of the solvent, DMF-d_7, according to IUPAC recommendations (Ξ = 21.496784).[41] Multiplicities are reported as follows: singlet (s),

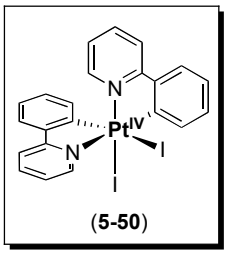
doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet (t), triplet of doublets (td), triplet of triplets (tt), multiplet (m), and broad resonance (br). IR spectra were obtained on a Perkin-Elmer "Spectrum BX" FT-IR spectrometer. Mass spectral data were obtained on a Micromass magnetic sector mass spectrometer.

Materials and Methods. K_2PtCl_4 was purchased from Pressure Chemical, Br_2 from Acros, I_2 from Acros, XeF_2 from Strem Chemicals, $PhI(OAc)_2$ from Acros, and $PhI(C_2F_3O_2)_2$ from Acros. All reagents were used as received. $Pt^{II}(phpy)_2$, **4-27**, was synthesized from 2-(*o*-bromophenyl)pyridine [42] and $PtCl_2(SEt_2)_2$ [43] according to a published procedure.[44] Solvents were obtained from Fisher Scientific and used without further purification. Unless otherwise noted, all reactions were carried out on the bench top in the presence of ambient air and moisture.



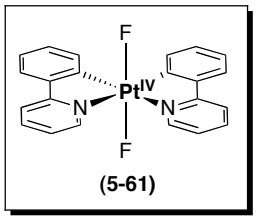
(**5-29**)

$Pt^{IV}(phpy)_2Br_2$ (5-29) - Complex **4-27** (80 mg, 0.16 mmol, 1.0 equiv) and Br_2 (9 μL, 0.17 mmol, 1.1 equiv) were combined in CH_2Cl_2 (8 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 15 h. The reaction mixture was concentrated to 1 mL and hexanes (20 mL) was added to precipitate the product. The resulting precipitate was collected by filtration, washed with hexanes (100 mL) and dried under vacuum to afford **5-29** (75 mg, 71 %) as a light yellow powder. ^{1}H NMR (DMSO-d_6): δ 9.81 (d, J = 4.5 Hz, 1H), 8.50 (d, J = 8.0 Hz, 1H), 8.31 (m, 3H), 8.02 (m, 3H), 7.86 (t, J = 6.5 Hz, 1H), 7.50 (d, J = 6.0 Hz, 1H), 7.39 (m, 2H), 7.21(t, J = 6.0 Hz, 1H), 7.07 (t, J = 7.0 Hz, 1H), 6.93 (t, J = 7.0 Hz, 1H), 6.15 (d, J = 8.0 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 164.06, 160.92, 149.24, 146.47, 142.82, 142.06, 141.83, 141.61, 141.50, 137.70, 133.41, 132.50, 131.72, 130.98, 126.59, 126.50, 126.23, 126.10, 125.98, 125.44, 122.02, 121.95. FTIR (KBr, cm^{-1}) 3052, 1606, 1583, 1569, 1484, 1441. HRMS-electrospray (*m/z*): $[(Br)_2(phpy)_2Pt]^+$ calcd for $C_{22}H_{16}N_2{}^{195}Pt^{79}Br^{81}Br$, 661.9229; Found, 661.9229.



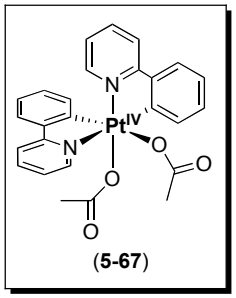
(**5-50**)

$Pt^{IV}(phpy)_2I_2$ (5-50) - Complex **4-27** (120 mg, 0.24 mmol, 1.0 equiv) and I_2 (67 mg, 0.26 mmol, 1.1 equiv) were combined in CH_2Cl_2 (8 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 15 h. Precipitate formed in the reaction was removed by filtration. The filtrate was concentrated to 1 mL and hexanes (20 mL) was added to precipitate the product. The resulting precipitate was collected by filtration, washed with hexanes (100 mL) and dried under vacuum to afford **5-50** (134 mg, 74 %) as an dark orange powder. ^{1}H NMR (DMF-d_7): δ 10.22 (d, J = 5.6 Hz, 1H), 8.82 (d, J = 7.2 Hz, 1H), 8.56 (d, J = 8.0 Hz, 1H), 8.33 (m, 2H), 8.07 (m, 3H), 7.84 (t, J = 5.6 Hz, 1H), 7.61 (d, J = 6.0 Hz, 1H), 7.39 (m, 2H), 7.28 (t, J = 6.0 Hz, 1H), 7.05 (m, 2H), 6.23 (d, J = 7.6 Hz, 1H). ^{13}C NMR (DMF-d_7): δ 164.20, 152.07, 145.58, 141.88, 141.31, 141.08, 140.94, 137.44, 132.73, 131.17, 130.63, 126.19, 126.05, 125.82, 125.01, 124.41, 121.77, 121.67. FTIR (KBr, cm^{-1}) 3059, 1604, 1581, 1567, 1480, 1440. HRMS-electrospray (*m/z*): $[(I)_2(phpy)_2Pt]^+$ calcd for $C_{22}H_{16}N_2{}^{195}PtI_2$, 756.9051; Found, 756.9059.



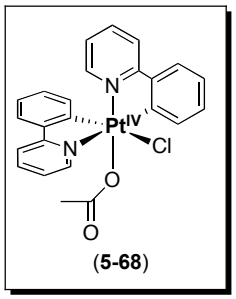
(**5-61**)

$Pt^{IV}(phpy)_2F_2$ (5-61) - Complex **4-27** (100 mg, 0.20 mmol, 1.0 equiv) was added to CH_2Cl_2 (10 mL) in a 25 mL round bottom flask under an inert atmosphere. Xenon difluoride (50 mg, 0.30 mmol, 1.5 equiv) was added to CH_2Cl_2 (10 mL) in a 25 mL round bottom flask under an inert atmosphere. Cannula transfer was used to add the solution of complex **1** to the xenon difluoride solution. The reaction stirred at -40°C under an inert atmosphere for 4 h. The reaction gradually warmed to room temperature and was allowed to stir for another 10 h. The reaction mixture was concentrated to 1 mL and hexanes (20 mL) was added to precipitate the product. The resulting precipitate was collected by filtration, washed with hexanes (100 mL) and dried under vacuum to afford **5-61** (70 mg, 65 %) as a light yellow powder. ^{1}H NMR (DMSO-d_6): δ 9.28 (d, J = 5.2 Hz, 2H), 8.46 (d, J = 8.0 Hz, 2H), 8.25 (t, J = 8.4 Hz, 2H), 8.02 (d, J = 7.6 Hz, 2H), 7.76 (d, J = 7.2 Hz, 2H), 7.72 (t, J = 7.2 Hz, 2H), 7.35 (t, J = 7.2 Hz, 4H). ^{19}F NMR (DMSO-d_6): δ -315.18. FTIR (KBr, cm^{-1}) 3058, 1609, 1583, 1569, 1487, 1442.



(**5-67**)

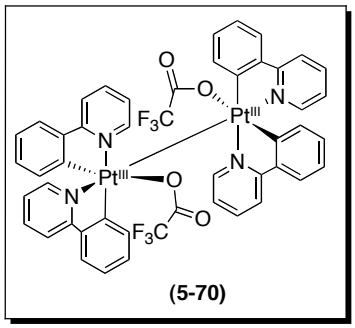
$Pt^{IV}(phpy)_2(C_2O_2H_3)_2$ (**5-67**) - Complex **4-27** (100 mg, 0.20 mmol, 1.0 equiv) and iodobenzene diacetate (71 mg, 0.22 mmol, 1.1 equiv) were combined in CH_2Cl_2 (5 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 15 h. The reaction mixture was concentrated to 1 mL and hexanes (20 mL) was added to precipitate the product. The resulting precipitate was collected by filtration, washed with hexanes (100 mL) and dried under vacuum to afford **5-67** (88 mg, 71 %) as a pale cream powder. ^{1}H NMR ($CDCl_3$): δ 9.32 (d, *J* = 6.0 Hz, 1H), 8.04 (m, 2H), 7.73 (m, 2H), 7.62 (t, *J* = 7.6 Hz, 3H), 7.53 (m, 3H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.81 (m, 2H), 6.30 (d, *J* = 7.6 Hz, 1H), 1.97 (s, 3H), 1.90 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 177.75, 161.55, 150.11, 148.57, 145.11, 141.91, 140,94, 140.14, 140.02, 132.36, 131.74, 130.54, 129.87, 128.82, 126.19, 126.11, 125.92, 125.68, 124.44, 124.41, 123.36, 122.21, 119.51, 119.47, 24.97, 23.79. ^{195}Pt NMR (DMF-d_7): δ –929.85. FTIR (KBr, cm^{-1}) 3056, 1665, 1609, 1585, 1487, 1466, 1443. HRMS-electrospray (*m/z*): $[(C_2H_3O_2)(phpy)_2Pt]^+$ calcd for $C_{24}H_{19}N_2O_2Pt$, 562.1094; Found, 562.1100.



(**5-68**)

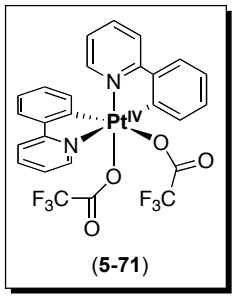
$Pt^{IV}(phpy)_2(C_2O_2H_3)Cl$ (**5-68**) - Complex **4-27** (60 mg, 0.12 mmol, 1.0 equiv) and iodobenzene diacetate (42 mg, 0.13 mmol, 1.1 equiv) were combined in a dry 20 mL glass vial. The vial was brought into an inert atmosphere where CH_2Cl_2 (4 mL), from the columns, was added. The vial was sealed with a Teflon-lined cap, brought out of the inert atmosphere, and allowed to stir at room temperature for 2 days. The reaction mixture was opened to air and concentrated to 1 mL. The reaction was allowed to stir at room temperature for another 15 hours and hexanes (20 mL) was added to precipitate the product. The resulting precipitate was collected by filtration, washed with hexanes (100 mL) and dried under vacuum to afford **5-68** (44 mg, 62 %) as a pale cream powder. ^{1}H NMR ($CDCl_3$): δ 9.99 (d, *J* = 6.0 Hz, 1H), 8.05 (m, 3H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 2H), 7.59 (m, 2H), 7.41 (t, *J* =

7.6 Hz, 1H), 7.25 (m, 2H), 6.91 (m, 2H), 6.38 (d, *J* = 8.0 Hz, 1H), 2.09 (s, 3H). FTIR (KBr, cm^{-1}) 3435, 3054, 1668, 1607, 1584, 1485, 1442, 1360, 1290.



(5-70)

$Pt^{III}_2(C_2O_2F_3)_2(phpy)_4$ (5-70)- Complex **4-27** (20 mg, 0.04 mmol, 1.0 equiv) and [Bis(trifluoroacetoxy)iodo]benzene (19 mg, 0.044 mmol, 1.1 equiv) were combined in CH_2Cl_2 (2 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 15 h. The reaction mixture was concentrated to 1 mL. The concentrated reaction mixture was open to the presence of air for approximately 4 – 6 hours. The precipitate formed was removed and hexanes (20 mL) was added to the remaining filtrate to precipitate the product. The resulting precipitate was collected by filtration, washed with hexanes (100 mL) and dried under vacuum to afford **5-70** as a light yellow powder. ^{1}H NMR (DMSO-d_6): δ 9.07 (d, *J* = 5.2 Hz, 2H), 8.58 (d, *J* = 8.4 Hz, 2H), 8.44 (m, 4H), 8.19 (m, 4H), 8.02 (d, *J* = 6.4 Hz, 2H), 7.92 (t, *J* = 6.4 Hz, 2H), 7.75 (d, *J* = 7.6 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 6.0 Hz, 2H), 7.30 (t, *J* = 6.0 Hz, 2H), 7.19 (t, *J* = 6.0 Hz, 4H), 6.96 (t, *J* = 8.0 Hz, 2H), 6.24 (d, *J* = 8.0 Hz, 2H). ^{195}Pt NMR (DMF-d_7): δ –2148.10. ^{19}F NMR (DMSO-d_6): δ -75.72. FTIR (KBr, cm^{-1}) 3056, 1730, 1605, 1584, 1484, 1441. HRMS-electrospray (*m/z*): $[(C_2F_3O_2)(phpy)_2Pt]^+$ calcd for $C_{24}H_{16}N_2F_3O_2Pt$, 616.0812; Found, 616.0814.



(5-71)

$Pt^{IV}(phpy)_2(C_2O_2F_3)_2$ (5-71)- Complex **4-27** (20 mg, 0.04 mmol, 1.0 equiv) and [Bis(trifluoroacetoxy)iodo]benzene (19 mg, 0.044 mmol, 1.1 equiv) were combined in CH_2Cl_2 (2 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was stirred at room temperature for 15 h. The reaction mixture was concentrated to 1 mL. The concentrated reaction mixture was open to the presence of air for approximately 4 – 6 hours. The precipitate formed was removed, washed with hexanes (100 mL) and dried under vacuum to afford **5-71** (10 mg, 35 %) as a light yellow powder. ^{1}H NMR (DMF-d_7): δ 9.34 (d, *J* = 5.5 Hz, 1H), 8.61 (d, *J* = 8.0 Hz, 1H), 8.44 (m, 2H), 8.16 (t, *J* = 7.0 Hz, 1H), 8.11 (d, *J* = 7.5 Hz, 1H), 8.06 (t, *J* = 8.0 Hz, 1H), 7.98 (t, *J* = 6.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 6.5 Hz, 1H), 7.55 (m, 2H), 7.34

(t, J = 6.0 Hz, 1H), 7.18 (t, J = 6.5 Hz, 1H), 6.98 (t, J = 8.0 Hz, 1H), 6.28 (d, J = 8.0 Hz, 1H). ^{13}C NMR (DMF-d_7): δ 165.71, 160.20, 148.94, 148.92, 148.45, 144.78, 142.58, 142.11, 142.04, 141.88, 141.69, 131.51, 128.51, 127.10, 126.64, 126.05, 126.00, 125.64, 124.85, 124.82, 121.45, 121.37, 121.33, 121.25, 117.62, 115.30. ^{195}Pt NMR (DMF-d_7): δ –1003.38. ^{19}F NMR (DMF-d_7): δ -74.99, -75.14. FTIR (KBr, cm^{-1}) 3077, 1726, 1713, 1607, 1586, 1488, 1444.

X-ray structure determination for *cis*- $Pt^{IV}(phpy)_2Br_2$ (5-29) - Yellow plates of **5-29** were grown from a chloroform/pentane solution at 22 °C. A crystal of dimensions 0.20 x 0.18 x 0.10 mm was mounted on a standard Bruker SMART CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 123(2) K; the detector was placed at a distance 4.980 cm from the crystal. A total of 5190 frames were collected with a scan width of 0.5° in ω and phi with an exposure time of 20 s/frame. The integration of the data yielded a total of 49520 reflections to a maximum 2θ value of 56.62° of which 5902 were independent and 5478 were greater than 2σ (I). The final cell constants (Table 1) were based on the xyz centroids of 9246 reflections above 10σ (I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P1bar with Z = 2 for the formula $C_{42}H_{16}N_2Br_2Pt•(CHCl_3)$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0171 and wR2 = 0.0403 [based on I > 2sigma(I)], R1 = 0.0205 and wR2 = 0.0379 for all data.

X-ray structure determination for *cis*- $Pt^{IV}(phpy)_2(C_2O_2H_3)_2$ (5-67) - Yellow block-like crystals of **5-67** were grown from a dichloromethane/pentane solution at 22 °C. A crystal of dimensions 0.40 x 0.24 x 0.20 mm was mounted on a standard Bruker SMART CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV, 40 mA).

The X-ray intensities were measured at 123(2) K; the detector was placed at a distance 4.980 cm from the crystal. A total of 2642 frames were collected with a scan width of 0.5° in ω and phi with an exposure time of 20 s/frame. The integration of the data yielded a total of 26168 reflections to a maximum 2θ value of 56.62° of which 6195 were independent and 5839 were greater than 2σ (I). The final cell constants (Table 1) were based on the xyz centroids of 9685 reflections above 10σ (I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P1bar with Z = 2 for the formula $C_{26}H_{22}N_2O_4Pt•(CH_2Cl_2)$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0303 and wR2 = 0.0845 [based on I > 2sigma(I)], R1 = 0.0326 and wR2 = 0.0868 for all data.

X-ray structure determination for *cis*- $Pt^{IV}(phpy)_2(C_2O_2H_3)Cl$, (5-68) - Colorless needles of **5-68** were grown from a dichloromethane/pentane solution at 23 °C. A crystal of dimensions 0.22 x 0.08 x 0.08 mm was mounted on a standard Bruker SMART CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 123(2) K; the detector was placed at a distance 4.969 cm from the crystal. A total of 2215 frames were collected with a scan width of 0.5° in ω and phi with an exposure time of 60 s/frame. The integration of the data yielded a total of 41383 reflections to a maximum 2θ value of 52.84° of which 5125 were independent and 3598 were greater than 2σ (I). The final cell constants (Table 1) were based on the xyz centroids of 9795 reflections above 10σ (I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P2(1)/c with Z = 4 for the formula $C_{24}H_{19}N_2O_2ClPt•(CH_2Cl_2)$. The dichloromethane solvate molecule is disordered and was modeled by use of the SQUEEZE subroutine of the PLATON program suite. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0426 and

wR2 = 0.0928 [based on I > 2sigma(I)], R1 = 0.1091 and wR2 = 0.1076 for all data.

X-ray structure determination for $[Pt^{III}(phpy)_2(C_2F_3O_2)]_2$, (5-70) - Pale yellow plates of **5-70** were grown from a dichloromethane solution at 22 °C. A crystal of dimensions 0.38 x 0.32 x 0.14 mm was mounted on a standard Bruker SMART CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 123(2) K; the detector was placed at a distance 4.980 cm from the crystal. A total of 2817 frames were collected with a scan width of 0.5° in ω and phi with an exposure time of 20 s/frame. The integration of the data yielded a total of 53578 reflections to a maximum 2θ value of 56.64° of which 5875 were independent and 5212 were greater than 2σ (I). The final cell constants (Table 1) were based on the xyz centroids of 9969 reflections above 10σ (I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group C2/c with Z = 4 for the formula $C_{48}H_{32}N_4O_4Pt \bullet 2(CH_2Cl_2)$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. The complex lies on a two-fold rotation axis in the crystal lattice. The fluorine atoms of the $-CF_3$ group are disordered. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0210 and wR2 = 0.0552 [based on I > 2sigma(I)], R1 = 0.0272 and wR2 = 0.0585 for all data.

X-ray structure determination for *cis*- $Pt^{IV}(phpy)_2(C_2F_3O_2)_2$, (5-71) - Colorless needles of **5-71** were crystallized from a dichloromethane solution at 23 °C. A crystal of dimensions 0.44 x 0.34 x 0.24 mm was mounted on a standard Bruker SMART 1K CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 123(2) K; the detector was placed at a distance 4.969 cm from the crystal. A total of 2300 frames were collected with a scan width of 0.5° in ω and phi with an exposure time of 15 s/frame. The integration of the data yielded a total of 26601 reflections to a maximum 2θ value of 56.72° of which 2660 were independent and 2906 were greater than 2σ (I). The final cell constants (Table 1) were based on the xyz centroids

of 7181 reflections above 10σ (I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group C2/c with Z = 4 for the formula $C_{26}H_{14}N_2O_4F_6Pt$. The complex lies on a two-fold axis in the lattice. The carbon and nitrogen sites bonded to the platinum of the phenyl pyridine ligands are disordered. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0195 and wR2 = 0.0492 [based on I > 2sigma(I)], R1 = 0.0201 and wR2 = 0.0494 for all data.

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Chapter 6

Conclusion

New discoveries and understandings in any area of chemistry invariably open the door for additional questions to be answered. The organometallic research described in this document serves as a representative example of providing key advancements while presenting opportunities for future work.

The polymer oxidation of small molecules in Chapter 2 involved an environmentally benign optimization of an already efficient reaction. Further benefits could be gained by generating the polymer oxidant *in situ*, eliminating the need for step-wise recovery of the polymer by-product and subsequent regeneration of the oxidant. The potential for two parallel catalytic cycles to function simultaneously is of great interest. One cycle would acetoxylate small molecules, while the second cycle would regenerate oxidant in tandem with the first cycle (Figure 6.1). As the first cycle and oxidant regeneration have been demonstrated, the challenge arises with the simultaneous function of the second cycle.

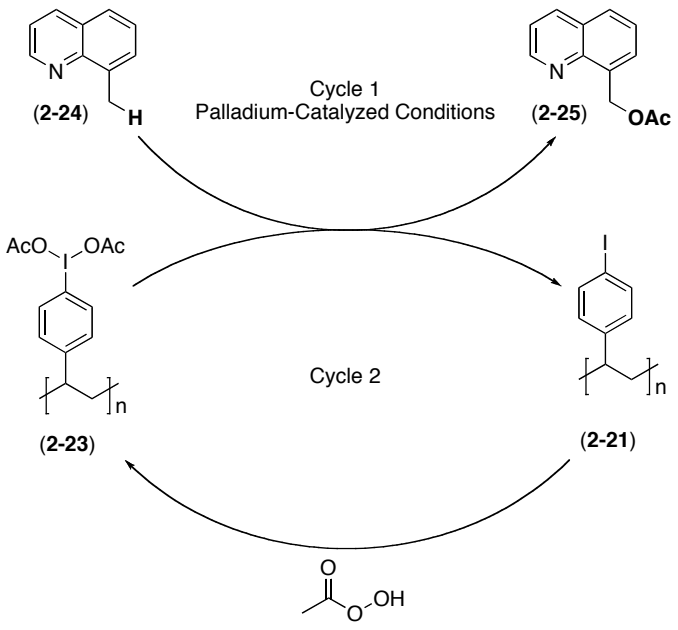
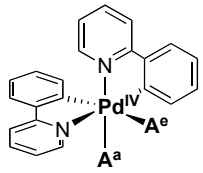


Figure 6.1 – Acetoxylation with *In Situ* Generation of Poly-4-(Diacetoxyiodo)styrene, **2-23**

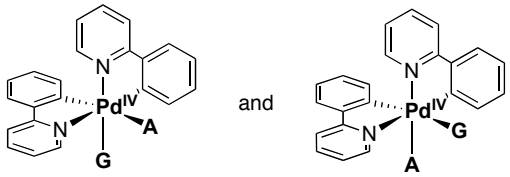
The synthesis of chlorinated palladium(IV) complexes in Chapter 3 was an interesting and significant discovery. Reductive elimination from these complexes produced functionalized organic molecules, yet the mechanism has still not been completely elucidated. Future work should aim to achieve a full understanding of the mechanism of reductive elimination. One question that should specifically be addressed is determining which ligand participates in reductive elimination in situations with identical and different ligands. For a complex with duplicate ligands (A) in different positions, shown in Figure 6.2, the ligand found on the organic product may have been in the axial (A^a) or equatorial (A^e) position.



(**6-1**)

Figure 6.2 – Palladium(IV) Complex with Two Identical Ligands in Axial & Equatorial Positions

Additional work may explore whether the ligand in the organic product, always or preferentially, comes from one site versus another. The answer may also be that an axial or equatorial location has no bearing on the reductive elimination. If true, future work should also continue to explore the preference of different ligands. This would involve expanding the scope of the palladium(IV) mixed isomers series to include more ligand sets for groups A and G in Figure 6.3 is a first step. Researchers may be able to determine the importance of ligand position, ligand identity, and solvent effects relative to one another.



(**3-41**) (**3-42**)

Figure 6.3 – Synthetic Targets for Palladium(IV) Mixed Isomers

Results from attempted reductive eliminations in Chapter 5 were inconclusive in several cases. Future work should definitively determine the identities of the complexes displayed in Figure 6.4. Presumably they represent isomers of platinum(IV) complexes.

Reductive elimination data may also be gathered by the addition of select Lewis acids in an attempt to promote reductive elimination of organic molecules. The stability of platinum(IV) complexes presents a significant challenge, particularly given the enhanced stability offered by carbon-nitrogen donor ligands.

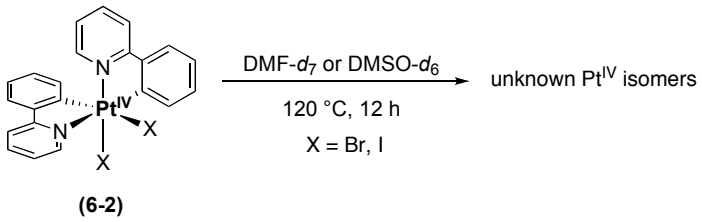


Figure 6.4 – Possible Isomerization of Platinum(IV) Halogen Complexes

The aforementioned research individually and collectively presents challenges within the respective scopes of study and in the greater subfield of organometallic chemistry. However, the research described in Chapters 2 through 5 addressed previous challenges as well. This series of advancements provides key information to address the new challenges and a sense of hope that they indeed may be solved in an effort to further expand the field.