UNDERSTANDING THERMODYNAMICS AND KINETICS OF ORGANOMETALLIC COMPLEXES FOR TAILORING ANALOGOUS IMMOBILIZED METAL CATALYSTS

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by

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Abstract

We use isothermal titration calorimetry (ITC) to study the metal-ligand binding equilibria for a series of monodentate P ligands and bidentate P-P, N-N, and P-N ligands to PdCl$_2$(solv)$_2$ in various solvents at 25°C. For all ligands, we discuss differences in the obtained thermodynamic parameters ($K$, $\Delta G$, $\Delta H$, and $\Delta S$) and differences in binding modes with the Pd center. For bulky ligands and poor electron donating ligands (monodentate), only one equivalent of ligand was able to bind to the Pd center. Two equivalents of all other ligands were able to bind the Pd center. Strong electron donating solvents such as pyridine coordinated to the Pd center and allowed only one equivalent of ligand to bind. For bidentate ligands, we observed large, exothermic enthalpies accompanied by large, negative (unfavorable) entropies upon binding to the Pd center. We discuss solvent reorganization for the binding of bidentate ligands to PdCl$_2$(solv)$_2$ and how it manifests itself as enthalpy-entropy compensation.

The next phase of our study focuses on the homogeneous activity of Wilkinson’s catalyst for terminal olefin hydrogenation in different solvents. We characterize the resulting Rh species in each solvent using $^{31}$P NMR spectroscopy and solution calorimetry in order to determine possible changes in the active Rh structure and test each solvent system for its activity toward the hydrogenation of 1-heptene and 1-octene in a differential batch reactor at 0°C. We interpret the kinetic results (i.e. turnover frequencies) in terms of the Rh species present in each solvent as well as the electron donating and accepting properties of each solvent. Strong electron donating solvents such as pyridine inhibited the hydrogenation reactions due to coordination to the Rh centers.
We transition to studying homogeneous and heterogeneous catalytic results for Wilkinson’s catalyst and a series of supported analogs. First, we graft different functional groups (primary amines, secondary amines, and diphenylphosphines) onto SBA-15 silica surfaces. We then immobilize Wilkinson’s catalyst on each of the three types of functionalized SBA-15 and rigorously characterize each supported Rh species using a variety of spectroscopic techniques, most notably 2D $^{31}$P{$^1$H} HETCOR (heteronuclear correlation) NMR. Using these spectroscopic results, we propose structures for the most likely surface Rh species. When used for hydrothiolation reactions, these catalysts exhibit switches in stereoselectivity (though retaining high regioselectivity for the anti-Markovnikov product) based on the type of functional group (and, therefore, the local Rh structure). Conversely, for hydrosulfonation, all three supported Rh catalysts are regioselective in favor of the Markovnikov product. We then focus on the phosphine-functionalized SBA-15 silica as a control surface in order to examine the effect of the nature of the grafting solvent on the resulting grafted Rh species. We compare the homogeneous activity and selectivity of Wilkinson’s catalyst in each grafting solvent (acting as the reaction solvent) for the hydrothiolation of phenylacetylene by thiophenol as a model reaction to the heterogeneous activity and selectivity of each supported Rh catalyst (grafted in each of the different solvents). We found solvents that were highly active for homogeneous hydrothiolation (e.g. THF) produced heterogeneous Rh catalysts that were barely active and poorly selective when used as grafting solvents. We also observed solvents that were not as active for homogeneous hydrothiolation (e.g. toluene, DCE), yet produced highly active, regio- and stereoselective catalysts when used as grafting solvents.
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Chapter 1

Introduction

1.1 The Importance of Organometallic Complexes in Organic Synthesis – Carbon-Heteroatom (C-X) Bond Activation as a Route to Efficient Techniques

One of the challenges in modern synthetic chemistry is the ability to synthesize novel organic compounds from starting materials that are plentiful and, in many cases, otherwise unreactive. There has been a movement toward understanding the reactivity of catalysts that are capable of performing bond activation of compounds whose bonding does not contain “activated” bonds. However, we must learn how to develop catalysts that can selectively activate these inactive bonds. The ability to access new classes of substrates for organic synthesis represents an exciting avenue for the development of new chemistries because it removes previous constraints of using starting materials that are more expensive and specialized. Thus, being able to utilize materials such as hydrocarbons and fluorocarbons, previously considered to be unsuitable synthetic starting materials, necessitates the activation of bonds such as C-H\(^{[1-6]}\) and carbon-heteroatom (C-X) bonds such as C-O\(^{[7-10]}\), C-F\(^{[11-13]}\), and C-S\(^{[14-17]}\), among others, in homogeneous catalysis. In practice, the activation of such bonds is not facile, so the development of organometallic complexes that selectively activate these bonds is critical. Organometallic complexes are a natural choice as the main tools for C-X bond activation because of the myriad of transition metals and ligands available to synthetic chemists which allows for the design of the most appropriate homogeneous catalysts that must accommodate a specific set of substrates for activation. The omnipresence and wealth of elementary
reactions in organometallic chemistry, such as oxidative addition (breaking of a bond by insertion of a metal complex into the bond) and reductive elimination (the extrusion of a bond from the coupling of two ligands on a metal complex, which is the reverse of oxidative addition), is the core of the robustness of transitional metal complexes for their ability to facilitate chemical transformations in homogeneous catalytic processes.\textsuperscript{[18]}

Advances in the field of C-X bond activation primarily revolve around the design of new organometallic species that are capable of performing specific bond activations under amenable reaction conditions, such as lower catalyst loading and lower temperatures. These design strategies focus on the appropriate choices of metal center and ligands in order to impart the necessary electronic and steric properties at the center of the organometallic complex that gives it its unique catalytic activity. Bergman noted in a discussion of C-H activation that one of the main issues facing catalyst design is the fact that very few organometallic complexes can be applied to broad classes of substrates while emphasizing the importance of obtaining new mechanistic information in order to tailor new catalysts to exploit useful mechanistic data regarding bond activation (see Figure 1.1).\textsuperscript{[19]} Hartwig further elaborated on the importance of understanding the specific factors that contribute to elementary steps in catalytic cycles for carbon-heteroatom activations (and formations) in order to guide new catalyst design strategies based on which elementary steps are rate-limiting for a particular catalytic mechanism.\textsuperscript{[20]}

In order to accelerate the understanding of C-X bond activation, it is necessary to explore the factors that contribute to the observed activities and selectivities of organometallic complexes and to determine which factors of the entire catalytic process dominate the elementary steps of the observed catalytic mechanisms such that new catalysts may be
synthesized to take advantage of these controlling factors. Some of these controlling factors are more obvious, such as the inherent energetics and stabilities of organometallic complexes based on their metal-ligand configurations (i.e. structure-function relationships in which the structure of the catalyst dictates its activity and selectivity for certain classes of reactions), while others are more subtle, such as the role of solvent in the catalytic mechanism and the degree to which solvent stabilizes the reactive intermediates or transition states, thereby enhancing the activity of the catalyst.

The most versatile and robust application of carbon-heteroatom bond activation is the cross-coupling of hydrocarbon substrates, which allows for the formation of C-C bonds (and other important carbon-heteroatom bond formations) via the metal center of an organometallic complex. C-C bond formation is a critical step in the synthesis of pharmaceuticals and drugs such as Taxol®[21] and morphine[22] and natural products such as Pumiliotoxins A and 225F, which are natural toxins found in the skin of poison dart frogs and are used to study how they selectively target and interact with receptors such as enzymes.[23] The need for mild and facile synthetic strategies for valuable chemical products that require C-C bond formation has led to the development of a wide range of cross-coupling reactions. Perhaps the most famous and widely studied cross-coupling reaction is the Mizoroki-Heck reaction, generally referred to as the Heck reaction, which was first used to couple aryl halides with olefins using a Pd catalyst such as palladium acetate, Pd(OAc)₂.[24, 25] There are several reviews regarding the applications and advances in the Heck reaction, such as catalytic processes that use metals other than Pd,[26] intramolecular coupling reactions[27-29], and studies on the overall mechanism.[30] Oestreich recently edited a comprehensive review of the Heck reaction, including
Figure 1.1. Mechanisms of C-H activation. (a) Simple abstraction of a proton using a base (pictured, X⁻), or hydride in the case of an electrophile (X⁺), or hydrogen atom in the case of a free radical (X·). (b) Insertion of a metal complex, M, into the C-H bond during an oxidative addition reaction. (c) Two-step oxidative addition in which the metal complex weakly coordinates to the C-H bond prior to insertion. Adapted from Bergman.¹⁹
innovations in reaction media (e.g. using ionic liquids and supercritical fluids as solvents) and extensive discussions of ligand design. Other types of coupling include Sonogashira coupling (coupling of terminal alkynes with aryl halides using a dual Pd-Cu catalyst system), Suzuki-Miyaura coupling (coupling of organoboron compounds with aryl halides using a Pd catalyst), and Negishi coupling (coupling of organozinc compounds with aryl halides or triflates using Ni or Pd catalysts). Figure 1.2 summarizes these C-C coupling chemistries using chemical equations. While this list of cross-coupling reactions is by no means exhaustive, it illustrates the rich chemistry associated with carbon-heteroatom bond formations in the sense that it is equally important to understand how to access new materials (C-X activation) in order to synthesize new materials (C-X formation) as efficiently as possible (i.e. the principle of microscopic reversibility).

1.2 The Role of Ligand Design in Homogeneous Catalysis

The choice of appropriate ligands in the design of an organometallic catalyst is paramount to optimizing its activity and selectivity for a particular reaction. Ligands are frequently chosen for the electronic and steric properties that they impart on the metal center of an organometallic complex, which give the complex its inherent activity and selectivity for a certain catalytic reaction. Quantifying the electronic contributions to the strengths of metal-ligand bonds for various classes of ligands allows chemists to assess the reactivity of such complexes and subsequently determine the effects of the ligands on catalytic processes. Ligand field theory comprises the study of metal-ligand electronic interactions in coordination complexes using concepts from molecular orbital theory and
Figure 1.2. Common C-C coupling chemistries: (a) Heck reaction, (b) Sonogashira coupling, (c) Suzuki coupling (note: a boronic acid is pictured as it is one of the most common substrates, but other reagents such as boronic esters can be used), and (d) Negishi coupling (note: halide groups, $X_1$ and $X_2$, can be different among the two substrates). $R_1$ and $R_2$ denote the carbon-containing fragments that are coupled to form the final products.
allows ligands to be classified electronically as acids and bases with respect to their inherent abilities to form stable complexes with metal centers.\textsuperscript{18} Specifically, ligands are categorized as being electron acceptors (acids) or donors (bases) to $\sigma$ and $\pi$ orbitals of organometallic complexes. In the 1960s, Pearson developed the Hard and Soft Acid and Base theory (HSAB), which was designed to establish empirical trends in metal-ligand bond strength by treating both the metals and ligands as Lewis acids and bases, respectively.\textsuperscript{38} He described “hard” acids and bases as smaller non-polarizable species that are highly electronegative and do not share electrons easily, while “soft” acids and bases are larger polarizable species that are less electronegative than hard species and share electrons more easily.\textsuperscript{39, 40} His main conclusion was that hard acids were more likely to bind to hard bases and that soft acids preferred to bind with soft bases. While imperfect, HSAB helped to establish periodic trends in the reactivity of transition metals with many different classes of ligands.

Early studies of ligand effects revolved around electronically and structurally simple ligands, such as CO and halides, but the development of new synthetic strategies required more sophisticated ligands capable of imparting innovative electronic and structural effects to organometallic complexes in order perform the desired chemical transformations. Polydentate ligands, especially bidentate ligands, are frequently used to provide structural effects to metal centers of organometallic complexes that monodentate ligands cannot because the presence of two or more donor atoms on polydentate ligands allows them to coordinate with the metal more than once (chelation).\textsuperscript{41} The most common use for polydentate ligands is to constrain the number of binding sites on an organometallic complex which forces reactants to conform to a smaller number of
potential geometries on the metal center (ideally just one), enhancing its selectivity for a particular reaction.\textsuperscript{[42, 43]} The bite angle of a chelating ligand, which is the most commonly assessed steric effect of polydentate ligands on catalytic activity and selectivity, is defined as the angle that spans from the donor atoms of the ligand using the metal center as the vertex of the angle (see Figure 1.3).\textsuperscript{[44]} These bite angle effects have been studied for C-C coupling reactions\textsuperscript{[45, 46]}, olefin hydroformylation\textsuperscript{[47, 48]}, aryl halide amination\textsuperscript{[49]}, and allylic alkylation\textsuperscript{[50]}, among others. Modern computational organometallic chemistry focuses on developing libraries of steric (and electronic) information for bidentate ligands and relating these parameters, such as the bite angle, to experimentally observed parameters, such as catalytic activity and selectivity, in order to establish trends among tested bidentate ligands so that these trends may be applied to a wide range of catalytic reactions in order to quantify their structure-function relationships.\textsuperscript{[51, 52]}

Ligand design is critical in tuning the selectivity of an organometallic complex because increasing the efficiency of a chemical transformation with a highly selective catalyst ensures that the reactants are transformed to the desired product, which could potentially reduce the costs associated with separating unwanted byproducts from the reaction mixture. Asymmetric, or chiral, catalysis is a specialized field of homogeneous catalysis that employs chiral ligands to enhance the selectivity, most notably enantioselectivity and stereoselectivity, of a particular organometallic complex by imparting structural asymmetry at the metal center that achiral ligands cannot.\textsuperscript{[53]} As an example, one of the most widely used chiral ligands for asymmetric catalysis is 2,2\textprime{-}bis(diarylphosphino)-1,1\textprime{-}binapthyl (BINAP – see Figure 1.4), owing to its
Figure 1.3. Schematic of the bite angle, θ, of a bidentate ligand. The bite angle is defined as the angle spanning from one donor atom (L) to the other (L’) with the metal center (M) acting as the vertex of the angle.
Figure 1.4. Enantiomers of BINAP. The aryl backbone can be chemically modified to impart different electronic and steric effects, making it a valuable chiral bidentate ligand for many synthetic techniques.
conformational flexibility which allows it to bind to a wide range of transition metals and its aryl backbone that can be modified with functional groups to impart different effects\textsuperscript{[54]} and has been used for C-N bond formations via cross-couplings of aryl halides and amines (the famous Buchwald-Hartwig amination).\textsuperscript{[55]} Asymmetric catalytic techniques are not limited to phosphine ligands such as BINAP and include such groups as bisoxazolines\textsuperscript{[56-58]} (oxazolines are five-membered heterocycles with an O atom and a hard N donor atom) and derivatives of 2,2′-binaphthol\textsuperscript{[59, 60]} (BINOL, which binds via O atoms). Some other examples of asymmetric catalytic processes include olefin hydrogenation\textsuperscript{[61-63]}, ketone hydrogenation\textsuperscript{[64]}, and epoxide-ring opening.\textsuperscript{[65]}

1.3 Kinetic, Thermodynamic, and Structural Effects of Solvents in Homogeneous Catalysis

Choosing the most appropriate solvent for a homogeneously catalyzed reaction is not trivial due to the wealth of electronic and thermodynamic properties inherent to individual solvents which dictate how solvent molecules interact with solutes (i.e. the reactants, ligands, and catalysts). These solute-solvent interactions can dramatically affect the activity and selectivity for a particular catalytic reaction, so it is imperative to thoroughly understand the role of the solvent in the catalytic process in order to choose the solvent that facilitates the most efficient reaction under the mildest possible conditions. There are two common ways solvents affect reaction rates: solvent molecules are capable of either stabilizing reaction intermediates or transition states (as well as the reactants and products themselves), which lowers the activation energy barrier for the reaction, or altering the catalytic structure of the organometallic species, which
subsequently alters its activity and selectivity (see Figure 1.5).[66, 67] Solvent effects are most commonly quantified by running the catalytic reaction in different solvents under otherwise identical conditions. Differences in reaction rates are then assessed in terms of the magnitudes of the inherent electronic properties of the tested solvent, such as its relative permittivity or dielectric constant ($\varepsilon_r$, which is a measure of the polarity of the solvent) and its dipole moment ($\mu$).[66] For example, Dodds et al examined the Heck reaction of iodobenzene and styrene using a bromo-bridged Pd dimer and determined that polar, non-protic (i.e. molecules that do not act as potential proton sources) solvents (e.g. acetonitrile and $N,N$-dimethylformamide) led to high conversions, while a non-coordinating, non-polar solvent such as toluene was able to achieve the highest initial reaction rate.[68] In their study of asymmetric Heck cyclization of alkenyl triflates via a Pd(OAc)$_2$/(R)-BINAP catalyst system, Ohrai et al concluded that polar solvents such as dimethyl sulfoxide and $N$-methylpyrrolidone gave the desired cyclic enantiomer in poor yield with poor enantioselectivity, while non-polar toluene produced an 82% enantiomeric excess (ee) for the same alkenyl triflate.[69]

Additionally, solvent molecules can act as ligands and coordinate with the metal center of an organometallic complex, which can contribute to the catalytic mechanism; that is, a particular solvent molecule may displace an endogenous, labile ligand which subsequently makes a pair of electrons on the metal center available for activating reactants (see Figure 1.6). As an example, Hussey and Takeuchi studied olefin hydrogenation using Wilkinson’s catalyst, RhCl(PPh$_3$)$_3$, in different solvents and used deuterium-labeling experiments to study the mechanism of hydrogenation.[70, 71] In agreement with Wilkinson’s original observation, they found that olefin had to displace a
Figure 1.5. Potential energy diagram of a hypothetical unsolvated reaction compared to the same reaction in a solvated environment. Solvation is capable of lowering the activation energy for the reaction and stabilizing the reactants and products, as indicated by the shift of the curve to a lower free energy.
solvent molecule bound to the Rh center in one step of the mechanism, but that the mechanism also required a solvent molecule to displace one of the endogenous triphenylphosphine ligands (PPh$_3$), forming the catalytically active 14-electron intermediate in an earlier step (see Figure 1.6). They concluded that the optimal solvent was one that had moderate coordinating power (e.g. nitrobenzene and cyclohexanone were highly active while chloroform and benzonitrile were completely inactive) while also being capable of dissolving a large concentration of molecular hydrogen. Candlin and Oldham studied competitive olefin and alkyne hydrogenation using Wilkinson’s catalyst in a series of mixed solvents (equal volumes of benzene and co-solvent) and found that more polar co-solvents, especially acidic alcohols, were able to selectively hydrogenate the alkyne by promoting intermolecular hydrogen bonding of the alcohol with the alkyne which subsequently facilitated the catalysis.

In addition to their dielectric constants and dipole moments, solvents have other electronic properties that characterize how they interact with solutes, which helps to characterize such solute-solvent interactions from a thermodynamic perspective. An important characteristic of solvents is how well they stabilize solutes, either by acting as electron donors or acceptors. Two empirical parameters, the donor number (DN) and acceptor number (AN), are used to describe these abilities. The donor number is the empirical ability of a solvent to donate electrons to a solute and is determined experimentally by the enthalpy of reaction of 1:1 adduct formation with SbCl$_5$ at 25°C in 1,2-dichloroethane (DCE), which has no electron-donating capabilities of its own. The acceptor number is a dimensionless quantity that measures the ability of a solvent to accept electrons from solutes and is measured experimentally by 1:1 adduct formation
Figure 1.6. Mechanism for olefin hydrogenation using Wilkinson’s catalyst.\textsuperscript{[72]} The boxed species have solvent molecules coordinated to them which must be displaced during the catalytic reaction, demonstrating the role that solvent can play in a catalytic cycle.
with triethylphosphane oxide (Et₃PO) in DCE using $^{31}$P NMR to measure the chemical shift of the adduct, which is then related to the chemical shift of the Et₃PO-SbCl₅ adduct (assigned a reference value of $AN = 100$). These $DN$ and $AN$ values quantitatively illustrate the interactions between solutes and solvent molecules in terms of how effectively particular solvents are capable of solvating solutes of various electronic characteristics and how solvents behave with solutes after they are solvated. For instance, a solvent with a high $AN$ is likely to solvate a solute with a lone pair of electrons more favorably than another solvent with a low $AN$.

Solute-solvent interactions are more clearly understood in the context of solvent reorganization, which is the exchange of solvent molecules between the bulk solvent and the solvation shells of the solutes (i.e. the solvent molecules directly surrounding and interacting with the solutes). Solvent reorganization is present in any chemical process that occurs in the liquid phase and is especially prevalent in solvents that exhibit strong hydrogen bonding characteristics. Chervenak and Toone examined the binding thermodynamics of a series of systems, including protein-peptide and protein-carbohydrate binding equilibria, in H₂O and D₂O and determined that the binding enthalpy was largely driven by solvent reorganization, which contributed 25-100% of the observed enthalpies of binding. They reached this conclusion based on the differences in observed enthalpies between H₂O and D₂O due to the respective hydrogen bonding abilities (O-H vs. O-D) of the two solvents. Furthermore, they observed nearly identical $\Delta G$ values for each binding system, regardless of solvent, but noticed that less negative $\Delta H$ values in D₂O led to compensating values in $\Delta S$, otherwise known as enthalpy-entropy compensation. As Grunwald and Steel proved through a rigorous thermodynamic
derivation, solvent reorganization is accompanied by enthalpy-entropy compensation. They demonstrated that solutes (e.g. organometallic complexes and ligands) exist in two environments: either enclosed in cages of solvent molecules or acting as part of a solvent cage surrounding an arbitrary solvent molecule (see Figure 1.7). They constructed a thermodynamic model consisting of two parts: the nominal contribution to the Gibbs free energy ($\Delta G_{\text{nom}}$) consists of solutes enclosed in cages reacting with one another (a typical chemical reaction, such as a ligand binding to a metal center) and the environmental contribution to the Gibbs free energy ($\Delta G_{\text{env}}$) consists of solutes as part of solvent cages reacting with one another as part of solvent reorganization. At equilibrium, the environmental contribution is equal to zero, meaning that the observed Gibbs free energy of the reaction ($\Delta G_{\text{obs}}$) is equal to the nominal contribution ($\Delta G_{\text{obs}} = \Delta G_{\text{nom}}$). However, the enthalpic and entropic contributions to $\Delta G_{\text{env}}$ are non-zero and contribute to $\Delta G_{\text{obs}}$, meaning that, for chemically reacting systems in which environmental contributions to $\Delta G_{\text{obs}}$ are significant, enthalpy-entropy compensation accompanies solvent reorganization. Ultimately, the presence of solvent reorganization allows for a unique way to consider how the choice of solvent for a particular catalytic system may thermodynamically contribute to stabilizing the catalytic species.

1.4 Immobilization of Organometallic Complexes on Functionalized Supports: Combining the Efficiency of a Homogeneous Catalyst with the Flexibility of a Heterogeneous Catalyst

The main disadvantage of industrial applications of homogeneous catalysts is that separating the organometallic species from the reaction mixture for recycling purposes is
Figure 1.7. Schematic of the nominal and environmental components of solvent reorganization. The metal precursor (M), ligand (L), and bound metal-ligand complex (M-L) are treated as solutes and are either encased in cages of solvent molecules or become part of the solvent cages. The nominal contribution to the Gibbs free energy is the traditional binding event (solvated metals and ligands binding to each other) and the environmental contribution manifests itself as the exchange of solvent molecules in the bulk with the solvent cages surrounding the solutes during the binding event.
both challenging and costly, making heterogeneous catalysts more desirable from an engineering perspective.\textsuperscript{[80]} From an organometallic perspective, heterogenized versions of homogeneous catalysts are designed to exploit the advantages of both the homogeneous precursor (high activity and selectivity) and the resulting immobilized catalyst (separable and recyclable materials). However, the main disadvantage with heterogeneous catalysts is that the catalytically active sites are not as clearly defined structurally as their homogeneous counterparts, which reduces their activities and selectivities.\textsuperscript{[81]} There is considerable interest in the design of single-site heterogeneous catalysts, that is, catalysts with structurally uniform active sites that are evenly distributed on the surface of the support, in order to synthesize heterogeneous catalysts that mimic the activity and selectivity of an analogous homogeneous catalyst.\textsuperscript{[82]} There are several methods available to deposit catalytically active species onto the surface of a support which are primarily classified according to the type of interactions, noncovalent and covalent, between the catalytic species and the surface (see Figure 1.8). Physisorption is the physical adsorption of a catalytic species on the surface of a support via van der Waals forces.\textsuperscript{[83]} Electrostatic interactions use Coulombic forces between oppositely-charged surfaces and catalytic precursors in order to adsorb the precursors directly to the surface.\textsuperscript{[84]} Another noncovalent preparation is entrapment, in which the organometallic precursor is immobilized within the pores of the support in order to prevent leaching of the metal in the presence of solvent.\textsuperscript{[85]} With respect to organometallic complexes, one of the most common methods of synthesizing supported homogeneous analogs is to dissolve the organometallic precursor in an appropriate grafting solvent containing the desired support, which is frequently functionalized with a special tethering agent, and allowing
Figure 1.8. Schematics of noncovalent and covalent interactions for immobilizing organometallic complexes onto supports. Noncovalent interactions (van der Waals forces, electrostatic interactions, entrapment) are weaker in nature than covalent interactions from the donor atoms of the tethering agents that are functionalized on the surface of the support.
the metal centers to link to the surface via covalent interactions over an extended period of time.\textsuperscript{86} In forming these covalent bonds, the tethering agents impart electronic and steric effects similar to the endogenous ligands of the organometallic precursor. In this regard, the functionalized support can be treated as a ligand in its own right. Regardless of the preparation method, the resulting supported organometallic complex must be thoroughly characterized using a variety of spectroscopic techniques in order to determine its correct structure-function relationship for a particular catalytic reaction.\textsuperscript{87, 88} These spectroscopic analyses, and subsequent assignment of the proper structure-function relationship, are significantly easier if the synthesized supported complex is, indeed, a single-site catalyst.

The choice of appropriate support for a surface organometallic catalyst is critical for two main reasons: the reactivity of each of the inherent or chemically modified (i.e. functionalized) surface groups contributes to the final structure(s) of the grafted species and the physical properties of the support (e.g. porosity, thermal stability, etc.) are also critical factors to consider when designing robust, stable surface organometallic catalysts. Mesoporous silicas such as MCM-41 and SBA-15 are extremely popular choices as supports because of their thermal stabilities and customizable, uniform pore distributions, ranging from 20-300 Å in size.\textsuperscript{89} Silica surface chemistry focuses on the interactions of organometallic precursors with two main functional groups: siloxanes and surface hydroxyls (silanols).\textsuperscript{90} In particular, there are several types of silanols common to silica surfaces, which, along with siloxanes, are depicted in Figure 1.9. Silanols are classified as isolated (a single -OH group on a Si atom), geminal (two -OH groups on the same Si atom, also known as silanediols), and vicinal (-OH groups on different Si atoms that are
Figure 1.9. Types of silanols and siloxanes common to silica surfaces. Silanols are divided into three main groups: isolated, geminal, and vicinal. Each surface species is presented with its $Q^n$ notation, where $Q$ represents a silicon atom bonded to four oxygen atoms. The superscript, $n$, ranges from 0 to 4 and is equal to the number of other $Q$ units to which the silicon atom is attached via other oxygen atoms.\[^{91}\]
close enough to each other so that the -OH groups exhibit hydrogen bonding). Basset et al reviewed a variety of surface reactions for inorganic oxides, including silica, and discussed potential differences in grafted structures depending on the types of siloxanes and silanols on each surface for the same organometallic precursor. A relevant example from this review is the grafting of Rh(η^3-C_3H_5)_3 onto partially dehydroxylated silicas that resulted in the total amount of Rh grafted onto the surface being dependent on the number of surface hydroxyl groups present for each type of amorphous silica. There was also formation of two different types of Rh species as determined by ^16O and ^18O labeling experiments: one in which the Rh was coordinated to an oxygen atom and a hydroxyl group attached to the same silicon atom and another where the Rh was coordinated to an oxygen atom and a hydroxyl group on different silicon atoms (see Figure 1.10). The porosity of the support is also an important design parameter because the size of the pores controls which types of reactants can pass through and which types of organometallic species can be grafted in the pores, similar to zeolite catalysis. Additionally, a primary concern of the industrial application of heterogeneous catalysts is the possibility of mass transfer limitation of the reaction kinetics if the pores of the support are too small (assuming that mixing is sufficient), which may play a role in the choice of the support.

One of the most common disadvantages to the implementation of supported organometallic catalysts is the possibility of leaching the active metal species that are grafted to the surface of the support due to the immersion of the support in an appropriate reaction solvent. It is paramount to determine if the active species for the catalytic reaction remains immobilized on the surface or detaches and enters the liquid phase in
Figure 1.10. Grafted Rh complexes on silica. The presence of different types of Si species on the surface allows for the same precursor, Rh(η³-C₃H₅)₃, to adopt different structures. The Rh species is capable of adopting (a) a bridged structure between two different Si atoms and (b) a highly-strained structure using two oxygen bonds on the same Si atom.[⁹⁴]
order to assess the stability and recyclability of the supported catalyst. If the leached metal is the true active species, then either the synthesis of the original catalyst must be redesigned to strengthen the bonds or forces that link the organometallic species to the surface or the reaction solvent must be changed to a solvent that is less likely to leach the active species. Lempers and Sheldon demonstrated the issues associated with leaching in their study of the catalytic oxidation of α-pinene using tert-butyl hydroperoxide as the oxidizing agent over a Cr-substituted aluminophosphate-5 (CrAPO-5) acting as the catalyst.\textsuperscript{100, 101} After 30 min of reaction time at the reaction temperature (80°C), they filtered the reaction solvent and allowed the filtrate to react further at the same temperature to avoid readsorption of the metal species and found that the filtrate reacted at the same rate as an unfiltered catalyst under otherwise identical conditions. This method, referred to as the hot filtration method or the split test, is applicable to a wide range of systems, though, as previously discussed in the literature, it is possible that even trace amounts of metal in solution may catalyze the reaction or that the leached metals redeposit on the support so quickly, which is common for Pd-catalyzed processes such as heterogeneous Heck reactions, that detection of leached species in either case is difficult, if not impossible.\textsuperscript{102-105}

The advantage of a supported organometallic catalyst is retaining the (ideal) activity and selectivity of its homogeneous precursor in immobilized form while simultaneously having the flexibility of a heterogeneous catalyst in terms of significantly simpler product separation with catalyst recyclability. Generally, the supported complexes are not as active and selective as their homogeneous counterparts, but there are examples in which the supported catalyst outperforms the homogeneous catalyst.
McKittrick and Jones synthesized site-isolated Ti catalysts for the polymerization of ethylene on amino-functionalized SBA-15 using aminosilane spacing agents with bulky trityl groups to ensure that species were not grafted to adjacent sites (Figure 1.11).\(^\text{[106]}\) After capping the unreacted surface silanol groups and selectively hydrolyzing the imine bonds of the spacing agents to remove the trityl groups, tetrakis(diethylamino)titanium was grafted to the surface and subsequently treated with trimethylsilyl chloride to produce the active Ti species, which are more active than their homogeneous counterparts.\(^\text{[107]}\) The authors attributed this increased activity to the isolated nature of the Ti sites, as determined by solid-state NMR and other spectroscopic techniques, when compared to similar materials prepared by other methods that produced various types of non-isolated Ti sites on their respective supports.\(^\text{[108]}\) Supported organometallic catalysts are also capable of enantioselective reactions. Corma et al synthesized chiral Cu(II) bisoxazoline supported catalysts on silica and MCM-41 for the Friedel-Crafts reaction of 1,3-dimethoxybenzene with 3,3,3-trifluoropyruvate and were able to obtain higher ee values, up to 92\%, using their immobilized complexes when compared to the homogeneous analogs\(^\text{[109]}\) and verified that leaching did not occur due to the stability of the long chains of the 3-mercaptopropyl linking agents.\(^\text{[110]}\) Raynor et al synthesized a Pd catalyst derived from 1,1′-bis(diphenylphosphino)ferrocene supported on MCM-41 that was more than three times as active and more enantioselective for the formation of ethyl nipecotinate from ethyl nicotinate than its homogeneous counterpart due to fact that the chiral ligand on the Pd catalyst was tethered to the support, which stabilized the active species.\(^\text{[111-113]}\)
Figure 1.11. Supported Ti catalysts for ethylene polymerization. The unfunctionalized surface silanol groups were capped between grafted Ti centers to minimize the possibility that the Ti precursors were grafted to species other than the amino-linking agents. Adapted from McKittrick and Jones.[107]
While these particular systems are exceptions to the rule that the supported organometallic complexes are inferior to their homogeneous counterparts, they serve as examples that there is promise for the development of highly active and selective immobilized organometallic catalysts.

1.6 Summary of the Dissertation

This section briefly describes the contents in each of the chapters of this dissertation in order. Chapter 1, the present chapter, elaborates on fundamentals of organometallic chemistry and aspects of solvent effects as they relate to homogeneous catalysis, leading up to the implementation of organometallic complexes as precursors in the synthesis of surface organometallic catalysts. This introductory chapter discusses important factors regarding homogeneous catalyst activity and supported organometallic catalyst design and synthesis. Chapter 2 contains a thermodynamic analysis of metal-ligand binding equilibria between a model compound, PdCl$_2$(solv)$_2$, where solv represents a molecule of the organic solvent used for each binding reaction, and a series of monodentate phosphorus ligands using isothermal titration calorimetry (ITC). The thermodynamic information obtained ($K_i$, $\Delta G_i$, $\Delta H_i$, and $\Delta S_i$) for each binding event is discussed in terms of the electronic and steric properties of the different ligands as well as the inherent electronic properties of the solvents. Chapter 3 presents a thermodynamic study of metal-ligand binding equilibria using the same Pd compound in the same organic solvent, acetonitrile, with bidentate ligands having phosphorus and nitrogen as the donor atoms. This calorimetric analysis complements the analysis from Chapter 2 by examining how the thermodynamic parameters ($K_i$, $\Delta G_i$, $\Delta H_i$, and $\Delta S_i$) change for bidentate ligands,
some of which are shown to form chelate compounds with the Pd center, and how solvent reorganization participates in the binding equilibria due to the observation of enthalpy-entropy compensation amongst the tested bidentate ligands. Chapter 4 discusses the structural changes in Wilkinson’s catalyst in various solvents using $^{31}$P NMR and solution calorimetry and how the distribution of Rh species within each solvent affects the hydrogenation of terminal olefins in each solvent. Chapter 5 establishes the protocol for synthesizing supported Rh catalysts using Wilkinson’s catalyst as the organometallic precursor and functionalized SBA-15 silica as the support. Each catalyst is shown to have its own, unique structure using a variety of spectroscopic techniques, most notably solid-state NMR and extended x-ray absorption fine structure (EXAFS), and exhibits its own activity and selectivity for the hydrothiolation of phenylacetylene by thiophenol. Chapter 6 explores the effect of the nature of the grafting solvent on the structure-function relationship of supported Rh catalysts, again using Wilkinson’s catalyst as the precursor and phosphine-functionalized SBA-15 silica as the support. Each grafting solvent is used as the reaction solvent for the homogeneous hydrothiolation of phenylacetylene and thiophenol and is spectroscopically examined for the Rh species present in order to determine if the most active solvents for homogeneous hydrothiolation indeed lead to grafting the most active heterogeneous catalysts. Chapter 7 draws the appropriate conclusions from the preceding chapters and establishes the basics for future work in obtaining new thermodynamic information as it relates to C-I bond activation and in using different types of linking groups to examine the effect of the rigidity of the tethering agent on the activity, selectivity, and stability of supported organometallic catalysts.
1.7 References


Chapter 2

Characterization of Sites of Different Thermodynamic Affinities on the Same Metal Center via Isothermal Titration Calorimetry

2.1 Introduction

The most important factors when considering the activity and selectivity of a homogeneous catalyst are how electronic and steric effects of ligands affect the coordination and electronic characteristics of the metal center. As such, the choice of ligands greatly impacts the types of reactions for which the catalyst is best suited. Phosphorus ligands are ubiquitous in organometallic chemistry and are studied extensively to relate ligand properties to catalytic activities and selectivities.[1-3] Experimental data, such as enthalpies of reaction, rate and equilibrium constants, and spectroscopic data are frequently correlated with the electronic and steric properties of phosphorus ligands in order to predict trends in reactivity for other phosphorus ligands. Perhaps the most famous and useful parameters for describing phosphorus ligands are the Tolman cone angle (θ) and the Tolman electronic parameter (TEP, ν_{CO}). The cone angle is an empirical measure of the overall steric bulk of a phosphorus ligand while the TEP is an empirical measure of the ability of a phosphorus ligand to donate electrons to a metal.[1] Models such as QALE[4] (Quantitative Analysis of Ligand Effects) and ECW[5] (named for the E, C, and W parameters in the model itself) emphasize the σ- and π-acidities and basicities as well as the steric bulk of the tested ligands such that the inherent properties of the ligands may be used to understand trends in kinetics and thermodynamics of organometallic processes (i.e. a structure-function relationship). The
main issue with these parameters is that correlations between the observed kinetic and thermodynamic data and the ligand properties themselves are indirect. It would be more informative to measure the interactions between metal centers and ligands in solution directly such that contributions from other factors, namely the solvent, may be considered in the metal-ligand binding equilibria. Solvent is often implicated in catalytic mechanisms due to the fact that solvent molecules interact with metal centers and ligands in solution, but its exact role in a given mechanism is usually unknown and merely implied.[6, 7]

Calorimetry is an excellent medium for ascertaining data with respect to understanding catalytic activity and metal-ligand binding equilibria from a thermodynamic perspective. Obtaining thermodynamic data in the liquid-phase for a variety of metal-ligand interactions allows organometallic chemists to design new chemical syntheses because the data reveals vital information regarding the stability of the resulting organometallic complexes and how the sterics and electronics of the metal center may influence the reaction pathway for a particular class of substrates.[8] Isothermal titration calorimetry (ITC) is a technique capable of characterizing receptor-ligand interactions in solvated systems by measuring the equilibrium binding constants, enthalpies of reaction, and reaction stoichiometries in a single experiment.[9] Briefly, ITC experiments consist of a sample cell containing a solution of the receptor (in our case, this is the metal complex PdCl$_2$(solv)$_2$) and reference cell containing the solvent that are held at the same temperature. The titrant solution, a solution of ligand, is then titrated into the sample cell once the power rating supplied to the sample cell is constant (note: the power rating is the thermal compensation of the calorimeter that is applied to the sample.
cell to keep it at the same temperature as the reference cell). Heat is then evolved or absorbed due to the metal-ligand binding and the controller compensates for these heat effects to maintain the cell at a constant temperature. Ligand is injected into the cell until the system is saturated, that is, no additional heat is evolved or absorbed due to ligand binding, only heat of mixing is present, and the resulting peaks are integrated to determine the total amount of heat released per injection. These integrated heats are then fit to an appropriate binding model in order to obtain the equilibrium binding constant, enthalpy of reaction, and reaction stoichiometry. ITC is widely used in biological and supramolecular systems because the thermodynamic information reveals how the guests (ligands) interact with the hosts (receptors) such that optimal ligands and receptors may be designed for specific processes. Modern calorimeters are capable of measuring equilibrium constants as high as $10^9 \text{ M}^{-1}$ due to their nW level of sensitivity. This information is critical in any field where molecular recognition is a central topic, such as drug design, metalloenzymes, and protein-ligand interactions, among others, in which the objective is to maximize a host’s affinity for a specific guest. There are extensive reviews of the ITC literature over the last decade, including how ITC is used to obtain kinetic data via heat evolution as well as new types of systems, such as zeolites and nanoparticles, which are being investigated calorimetrically.

This study aims to determine the thermodynamics of ligand binding to a model compound, PdCl$_2$(MeCN)$_2$ (1), in acetonitrile (MeCN) using various phosphorus ligands (see Table 2.1 for ligand properties) and to determine the effect of solvent on the thermodynamics of binding triphenylphosphine, PPh$_3$, to PdCl$_2$(solv)$_2$ (2), where solv is a molecule of solvent. We use ITC to characterize the metal-ligand interactions for each
Table 2.1. Cone angle (θ) and Tolman electronic parameter (TEP) data for the phosphorus ligands used in this study. There is no reported value for the TEP for PFu₃ in the literature. All other values are taken from the literature.[1]

<table>
<thead>
<tr>
<th>Phosphine</th>
<th>Abbreviation</th>
<th>Cone Angle, θ (degrees)</th>
<th>TEP, ν₃CO (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(C₆H₅)₃</td>
<td>PPh₃</td>
<td>145</td>
<td>2068.9</td>
</tr>
<tr>
<td>P(p-FC₆H₅)₃</td>
<td>P(p-FC₆H₅)₃</td>
<td>145</td>
<td>2071.3</td>
</tr>
<tr>
<td>P(C₂H₂O)₃</td>
<td>PFu₃</td>
<td>133</td>
<td>-</td>
</tr>
<tr>
<td>P(OC₆H₅)₃</td>
<td>P(OPh)₃</td>
<td>128</td>
<td>2085.3</td>
</tr>
<tr>
<td>P(o-CH₃C₆H₄)₃</td>
<td>P(o-tolyl)₃</td>
<td>194</td>
<td>2066.6</td>
</tr>
</tbody>
</table>
solvated system and discuss our results in terms of the known electronic and steric properties of the ligands and the inherent properties of the solvents. We supplement our calorimetric analysis with $^{31}$P NMR characterization of the reaction intermediates and products and UV-Vis spectroscopy to verify reaction stoichiometry so that we may adequately describe the binding equilibria occurring in the ITC and validate the appropriate choice of binding model. Furthermore, we consider the solvation and desolvation of the solutes (1, 2, and the phosphorus ligands) and solvent reorganization manifesting themselves in metal-ligand binding equilibria.

2.2 ITC Theory

ITC theory is well-developed in the literature, but due to the fact that there are very few studies of solution-phase calorimetry that attempt to discern different binding modes between metals and ligands in organometallic chemistry using thermodynamic data, we briefly introduce the main concepts behind ITC theory and emphasize the mathematics that are the most pertinent to our work. First, we consider the binding of a single type of ligand, $L$, with a metal receptor, $M$, in solution:

$$M + nL \leftrightarrow ML_n$$

(1)

where $n$ represents the total number of ligands (i.e. the binding stoichiometry) that bind to the metal and $ML_n$ is the final complex that forms between the metal and $n$ ligands. In our systems, $M$ represents $\text{PdCl}_2(\text{solv})_2$ and $L$ represents the series of phosphorus ligands. We will only consider two types of binding within the scope of this work, though interested readers are referred elsewhere for additional information with respect to the establishment of different binding models as well as full derivations of these models.\cite{19}
The first type of binding is independent binding, in which the metal may have several binding sites, but each site is thermodynamically identical and has the same thermodynamic affinity for the ligand. We can write the general equilibrium binding constant, $K_i$, for each binding step as

$$K_i = \frac{[ML_i]}{[ML_{i-1}][L]}$$

where the terms in brackets represent concentrations of the respective species, $ML_i$ represents a metal center with $i$ ligands bound to it, and $ML_{i-1}$ represents a metal center with $i - 1$ ligands bound to it, extending from $i = 0$ to $i = n$. The second type of binding is multiple-site binding, in which the metal has two thermodynamically different types of sites. Specifically, each site has its own affinity for the same ligand, but the occupancy of one site does not affect the affinity of the other, that is, the sites do not exhibit cooperative binding behavior. For our systems, we can model this behavior by considering the sequential binding of the same type of ligand to the same metal center twice ($n = 2$):

$$M + L \leftrightarrow ML$$

$$ML + L \leftrightarrow ML_2$$

For Eqs. (3) and (4), the equilibrium constants are given by Eqs. (5) and (6), respectively

$$K_1 = \frac{[ML]}{[M][L]}$$

$$K_2 = \frac{[ML_2]}{[ML][L]}$$
With full expressions for the respective equilibrium constants, it is now possible to combine these expressions with mass balances on each component:

\[
[M]_T = [M] + [ML] + [ML_2]
\]  
(7)

\[
[L]_T = [L] + [ML] + 2[ML_2]
\]  
(8)

Eqs. (7) and (8) can be extended to any binding system of \( n \) ligands, noting that \([M]_T\) and \([L]_T\) are the total concentrations of metal and ligand in the calorimeter cell. These mass balances can be substituted into the expressions for the equilibrium constants, such that only the total concentrations (i.e. measurable quantities) appear in the final ITC equations. This flexibility allows the experimenter to track the progress of the binding equilibria by calculating the molar ratio, the total amount of ligand in the calorimeter cell to the total amount of metal in the cell, as the independent variable. The dependent variable in ITC experiments is the total amount of heat released per injection of ligand, \(dQ\):

\[
dQ = V \sum_i \Delta H_i d[ML_i]
\]  
(9)

where \(V\) is the volume of the calorimeter cell, \(\Delta H_i\) is the enthalpy of binding for the formation of \(ML_i\), and \(d[ML_i]\) is the incremental amount of complex, \(ML_i\), formed during the injection. Eq. (9) may be extended to any number of complexes in solution. Substituting Eqs. (5)-(8) into Eq. (9) allow \(dQ\) to be written explicitly in terms of \(K_i\), \(\Delta H_i\), \([M]_T\), and \([L]_T\), meaning that the heats from each injection can be fit to a statistical model as a function of the molar ratio that determines the binding parameters (\(K_i\), \(\Delta H_i\), and \(n_i\)) in a single experiment. The full form of Eq. (9) for independent binding that is used to fit the integrated heat data from ITC experiments is given as
\[
\frac{dQ}{d[L]_T} = \frac{1}{2} V \Delta H \left[ 1 - \frac{[L]_T}{[M]_T} - n + \frac{1}{K[M]_T} \sqrt{\left( \frac{[L]_T}{[M]_T} \right)^2 + \left( n + \frac{1}{K[M]_T} \right)^2 - 2 \frac{[L]_T}{[M]_T} \left( n - \frac{1}{K[M]_T} \right)} \right]
\]  

(10)

This form of the equation accounts for any stoichiometry, \(n\).\(^{21}\) The full form of Eq. (9) for multiple-site binding is given in closed-form

\[
Q = V[M]_T \left( \frac{n_1 \Delta H_1 K_1[L]}{1 + K_1[L]} + \frac{n_2 \Delta H_2 K_2[L]}{1 + K_2[L]} \right)
\]  

(11)

where the free concentration of \(L\) is given as

\[
[L] = [L]_T - [M]_T \left( \frac{n_1 K_1[L](1 + K_2[L]) + n_2 K_2[L](1 + K_1[L])}{(1 + K_1[L])(1 + K_2[L])} \right)
\]  

(12)

Eq. (12) is cubic in \([L]\), therefore its solutions can be written as

\[
[L] = 2(-y)^{1/2} \cos \left( \frac{\theta}{3} \right) - \frac{B}{3A}
\]  

(13)

\[
\theta = \arccos \left( \frac{-x}{(-y^3)^{1/2}} \right)
\]  

(14)

\[
x = \left( \frac{B}{3A} \right)^3 - \frac{BC}{6A^2} + \frac{D}{2A}
\]  

(15)

\[
y = \frac{C}{3A} \left( \frac{B}{3A} \right)^2
\]  

(16)
\[ A = K_1K_2 \]

\[ B = K_1 + K_2 + K_1K_2 ([M]_T (n_1 + n_2) - [L]_T) \]

\[ C = 1 + [M]_T (n_1K_1 + n_2K_2) - [L]_T (K_1 + K_2) \]

\[ D = -[L]_T \]

There is only one physically possible solution to this set of equations which is the one used to fit the integrated heat data.\[^{[10]}\]

### 2.3 Experimental

#### 2.3.1 Materials and Solution Preparations

PdCl\(_2\) and the phosphorus ligands P(o-tolyl)\(_3\), PF\(_3\), and P(p-FC\(_6\)H\(_4\))\(_3\) were obtained from Alfa Aesar. P(OPh)\(_3\) was obtained from TCI and PPh\(_3\) was obtained from Sigma. MeCN and pyridine were obtained from EMD while DMSO was obtained from BDH and DMF was obtained from Sigma. All chemicals were used without further purification.

All 1-5 mM solutions of PdCl\(_2\)(solv)\(_2\) were prepared by dissolving 8.9-44.3 mg of anhydrous PdCl\(_2\) in 50 mL of the appropriate degassed solvent and stirred vigorously overnight with gentle heating. The structures of PdCl\(_2\)(solv)\(_2\) for each solvent are trans as reported in the literature.\[^{[22, 23]}\] All phosphorous ligand solutions were prepared immediately before each titration by dissolving the appropriate amount of ligand in the desired degassed solvent followed by vigorous stirring.
2.3.2 ITC Experimental Procedure for Binding Phosphorus Ligands to PdCl$_2$(solv)$_2$

ITC experiments were performed using a NanoITC III calorimeter (TA Instruments, New Castle, DE) equipped with hastelloy cells (V = 1.056 mL). All titrations were carried out at 25°C using a 250 μL syringe at a stirring rate of 250 rpm. The sample cell contained PdCl$_2$(solv)$_2$ and the reference cell contained the chosen solvent. All solvents were degassed prior to titration. The “heat flow” baseline was allowed to equilibrate once the reference and sample solutions were loaded into the cells. The titrations began after equilibration of the power rating. Titrations were run as an incremental series of injections of the appropriate phosphorus ligand into the PdCl$_2$(solv)$_2$ solution. Blank experiments were conducted under identical conditions with only solvent in the sample cell to experimentally determine the heat of mixing of the phosphorus ligands with the pure solvent. These blanks were subtracted from the experiments with PdCl$_2$(solv)$_2$ in the cell and integrated to isolate the heat evolved from metal-ligand interactions. Data analysis was performed using NanoAnalyze v2.1 from TA Instruments using the Independent Sites algorithm (see section 2.2 for derivations of the appropriate models).\textsuperscript{[19]} We used a modified version of the Multiple Sites model in Microsoft Excel in order to account for the inability of NanoAnalyze to fit integrated heat data near zero accurately. We used the Solver function in Excel to minimize the sum of the squares of the differences between the measured heat and the calculated heats. The first integrated heat point in each data set is omitted from each fit because the syringe allows for a miniscule amount of ligand to mix before the experiment starts which makes the first data point unreliable. Error analysis was also performed using NanoAnalyze v2.1 via its Statistics function. The uncertainties in the parameters obtained from the fits are
calculated by adding perturbations to the optimized fits and then refitting the models for a set number of trials. Each perturbation obeys a Gaussian distribution with the same standard deviation generated from the original fit. The error in each data set was determined within one standard deviation for 1000 trials. The error values reported in the tables for the $K$ values are also multiplied by the factor outside of the parentheses. For example, a $K$ value of $(5.99 \pm 0.01) \times 10^5$ means that the error is $0.01 \times 10^5$, or 1000. Independent verification of $K$ values was unsuccessful due to poor detection of species by UV-Vis and $^{31}$P NMR spectroscopies over the most appropriate ranges of concentrations. Specifically, as Hirose details, higher $K$ values require lower concentrations of metal and ligand in order to detect the resulting complexes reliably, and for our systems, we could not detect appreciable signals at the recommended concentrations (less than 1 $\mu$M for metal and ligand for $K$ values in excess of $10^5$ M$^{-1}$).[24]

2.3.3 $^{31}$P NMR Characterization of Reaction Intermediates and Products

Mixtures of one or two equivalents of phosphorus ligand to one equivalent of PdCl$_2$(solv)$_2$ were prepared in advance and allowed to stir at room temperature for 1 h. An aliquot of the Pd solution was mixed with an equal volume of deuterated solvent (Cambridge Isotope Laboratories) in an NMR tube. Samples were run on a Bruker AV-360 at room temperature with proton decoupling. Each sample was run for 128 scans and each spectrum was observed for the chemical shifts of the Pd complexes.

2.3.4 Solution Calorimetry
Solution calorimetry experiments were performed in a TAM III microcalorimeter (TA Instruments) at 25°C. Samples of PPh$_3$ and P(OPh)$_3$ were placed into glass ampoules and sealed with wax to prevent premature mixing of solvent with the ligands. Sealed ampoules were immersed in 25 mL of MeCN in a reaction cell and stirred at 600 rpm. Ampoules were then broken and the ligand (solute) was allowed to mix with the solvent for 1 h while monitoring the heat flow. An electronic heat pulse was applied to the reaction cell before and after dissolution to calibrate the heat capacity in each instance. An empty ampoule (blank) was broken to account for the heat evolved due to breaking the ampoule. The total heat evolved or absorbed during each experiment was obtained using the Analyze Experiment function in the SolCal v1.2 software (TA Instruments). Each heat value was then corrected for the blank experiment and then normalized to the total amount of moles of solute dissolved to calculate the enthalpy of dissolution. The uncertainty for each value originated from the average difference between the evolved heats for multiple experiments.

2.3.5 UV-Vis Spectroscopy Experiments (Continuous Variation Method).

The continuous variation method experiments were performed using a Shimadzu UV-3600 UV-Vis-NIR spectrophotometer at room temperature. For each system, 0.5 mM stock solutions of PdCl$_2$(MeCN)$_2$ and the appropriate phosphorus ligands were prepared in advance. All chemical species were calibrated to find their molar absorptivities, though only PdCl$_2$(MeCN)$_2$ was found to have an appreciable molar absorptivity at the wavelength of interest, 343 nm (highest signal-to-noise ratio). Each analytical sample contained a different total mole fraction of solute, PdCl$_2$(MeCN)$_2$, to vary from 0.1-1 and
was measured for total solution absorbance at 343 nm. The continuous variation method allows for the determination of the binding stoichiometry between two chemical species in solution and was utilized to validate the stoichiometric relationships obtained via ITC. The observed absorbance can be expressed as

\[ A_{\text{obs}} = A_M + A_L + A_{\text{ML}} \]  \hspace{1cm} (21)

where \( A_{\text{obs}} \) is the observed absorbance of the sample, \( A_M \) is the absorbance of the metal \((\text{PdCl}_2(\text{MeCN})_2)\), \( A_L \) is the absorbance of the phosphorus ligand, and \( A_{\text{ML}} \) is the absorbance of the formed organometallic complex \((\text{PdCl}_2(\text{PR}_3)(\text{solv}) \text{ or } \text{PdCl}_2(\text{PR}_3)_2)\). Substitution of the appropriate mass balances and absorbance expressions from Beer’s Law gives

\[ A_{\text{obs}} - \varepsilon_M [M]_T - \varepsilon_L [L]_T = (\varepsilon_{\text{ML}} - a\varepsilon_M - b\varepsilon_L) [\text{ML}] \]  \hspace{1cm} (22)

where \( \varepsilon_i \) is the molar absorptivity of species \( i \), \( a \) is the stoichiometric coefficient of \( M \), \( b \) is the stoichiometric coefficient of \( L \), and the bracketed terms are molar concentrations. Note that the concentrations of \( M \) and \( L \) are expressed as total concentrations, rather than free concentrations. After a lengthy derivation\(^{[24]}\), the maximum of the left-hand side of Eq. (14) as a function of the mole fraction of \( M \), \( x_M \), is found to be

\[ x_M = \frac{a}{a+b} \]  \hspace{1cm} (23)

This point dictates the binding stoichiometry between the specific metal and ligand in solution. If absorbance values are plotted from 0 to 1, \( a \) represents the distance from 0 to where \( x_M \) is a maximum and \( b \) represents the distance from the maximum \( x_M \) to 1. For example, if the binding ratio is two ligands to one metal center, then \( x_M \) will equal 0.333.
2.4 Results and Discussion

2.4.1 $^{31}$P NMR Results for Phosphorus Ligand Binding to PdCl$_2$(solv)$_2$

Figure 2.1a shows the $^{31}$P NMR data for the final bis-ligated complexes and Figure 2.1b shows $^{31}$P NMR data for the intermediate mono-ligated complexes formed (applicable for the complexes in which no free ligand was observed in the presence of two equivalents of ligand). For two equivalents, PdCl$_2$(PPh$_3$)$_2$ ($\delta$ = 23.4 ppm) and PdCl$_2$(P(p-FC$_6$H$_4$)$_3$)$_2$ ($\delta$ = 21.2 ppm) exhibited downfield singlets characteristic of the trans complex while PdCl$_2$(PFu$_3$)$_2$ ($\delta$ = -22.2 ppm) exhibited the upfield singlet characteristic of the cis complex $^{[25, 26]}$. A mixture of PdCl$_2$(MeCN)$_2$ and P(OPh)$_3$ displayed singlets at $\delta$ = 83.0 ppm indicative of the complex PdCl$_2$(P(OPh)$_3$)(MeCN) and at $\delta$ = 128.2 ppm indicative of free P(OPh)$_3$, which agreed with the ITC results. Both PdCl$_2$(PPh$_3$)$_2$ in DMSO ($\delta$ = 23.0 ppm) and DMF ($\delta$ = 23.0 ppm) showed singlets characteristic of the trans complex. The addition of two equivalents PPh$_3$ to PdCl$_2$(py)$_2$ produced two singlets: one at $\delta$ = 28.1 ppm, indicative of the mono-ligated complex PdCl$_2$(PPh$_3$)(py), and one at $\delta$ = -6.8 ppm, indicative of free PPh$_3$. Dissolution of pure PdCl$_2$(PPh$_3$)$_2$ into py yielded an identical spectrum to the solution of PdCl$_2$(py)$_2$ and PPh$_3$ while a solution of pure oxidized triphenylphosphine, OPPh$_3$, produced a singlet at $\delta$ = 24.8 ppm, leading to the conclusion that only one equivalent of PPh$_3$ binds to PdCl$_2$(py)$_2$ in py. A broad resonance was observed for mixtures of PdCl$_2$(MeCN)$_2$ and P(o-tolyl)$_3$ at $\delta$ = 21.7 ppm, which is shifted from free P(o-tolyl)$_3$ at $\delta$ = -31.6 ppm. ITC results show that only one equivalent of P(o-tolyl)$_3$ was able to bind, so we attribute this broad resonance to the existence of PdCl$_2$(P(o-tolyl)$_3$)(MeCN). No evidence of chloro-bridged Pd dimers or ionization isomers was observed for any of the tested ligands and solvents.
Figure 2.1. (a) $^{31}$P NMR spectra of PdCl$_2$(solv)$_2$ and 2 equivalents of phosphorus ligand as synthesized in the ITC. (b) $^{31}$P NMR spectra of PdCl$_2$(solv)$_2$ and 1 equivalent of phosphorus ligand for verification of the intermediates is presented in Figure 2.2. The resulting Pd-P complexes, along with the reaction solvents, are listed for each spectrum.
For one equivalent of ligand, PPh$_3$ ($\delta = 31.2$ ppm), $\text{P}(p$-$\text{FC}_6\text{H}_4)_3$ ($\delta = 28.8$ ppm), and PF$_3$ ($\delta = -24.7$ ppm) have different resonances than their respective two equivalent (cis or trans) complexes. The PPh$_3$ resonance corresponds to coordinated ligand with a bound MeCN molecule trans to it, meaning that the difference in shifts for the one equivalent complexes compared to the two equivalent complexes is due to the coordination of the second ligand as originally reported by Colacot et al.[27] Based on these $^{31}$P NMR results, we present Figure 2.2 as a description of the binding equilibria that occur in the ITC experiments. Figure 2.2 is a specific representation of Eqs. (3) and (4) and describes both independent (just the $K_1$ equilibrium reaction) and multiple-site binding. For our systems, we observed one equivalent of bound ligand for the independent cases while we observed two equivalents of bound ligand for the multiple site cases.

2.4.2 ITC Results for Binding Phosphorus Ligands to PdCl$_2$(MeCN)$_2$

Figures 2.3-2.7 show thermograms for binding ligands to 1 in MeCN at 25°C and the integrated heats and the best-fit binding models for each system as measured by ITC; best fit parameters are compiled in Table 2.2. Note that $n_1$ and $n_2$ refer to the step-by-step stoichiometries presented in Eqs. (3) and (4) and the overall binding equilibria presented in Figure 2.2 ($n = n_1 + n_2$). Additionally, we provide the ITC experimental conditions in Table 2.3. The ligands exhibited two binding modes with Pd: either two ligands were able to bind to the same Pd atom, each ligand with its own thermodynamic affinity for the Pd center as expressed in Eqs. (3) and (4), or only one ligand was able to bind to Pd as described by Eq. (3) only (independent binding). The difference in affinities between sites on the same Pd atom is due to the presence of bound phosphorus ligand after the
**Figure 2.2.** Illustration of metal-ligand equilibria in solution. For each equilibrated step, a PR₃ ligand displaces a bound solvent molecule (solv). For cases where two equivalents of ligand bind, either the *cis* (PFu₃) or *trans* (PPh₃ and P(p-FC₆H₄)₃) product is formed exclusively.
Figure 2.3. (a) Real-time ITC thermogram for PPh$_3$ binding to 1 in MeCN at 25°C with (b) the integrated heat data with fitted model. “Power” refers to the thermal compensation of the calorimeter to keep the sample at a constant temperature (positive peaks are exothermic – the heat evolved reduces the power compensation resulting in a positive value when the baseline is subtracted).
Figure 2.4. (a) Real-time ITC thermogram for $P(p$-FC$_6$H$_4)_3$ binding to 1 in MeCN at 25°C with (b) the integrated heat data with fitted model.
Figure 2.5. (a) Real-time ITC thermogram for PFu$_3$ binding to 1 in MeCN at 25°C with (b) the integrated heat data with fitted model.
Figure 2.6. (a) Real-time ITC thermogram for P(OPh)$_3$ binding to 1 in MeCN at 25°C with (b) the integrated heat data with fitted model.
Figure 2.7. (a) Real-time ITC thermogram for P(o-tolyl)$_3$ binding to 1 in MeCN at 25°C with (b) the integrated heat data with fitted model.
Table 2.2. Thermodynamic parameters for the binding of PR$_3$ ligands to 1 in MeCN at 25°C. Errors were calculated using the statistics function in NanoAnalyze (see section 2.3.2).

<table>
<thead>
<tr>
<th>Ligand</th>
<th>$K_1$</th>
<th>$\Delta G_1$</th>
<th>$\Delta H_1$</th>
<th>$T\Delta S_1$</th>
<th>$n_1$</th>
<th>$K_2$</th>
<th>$\Delta G_2$</th>
<th>$\Delta H_2$</th>
<th>$T\Delta S_2$</th>
<th>$n_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPh$_3$</td>
<td>(1.20 ± 0.01) $\times 10^9$</td>
<td>-51.8 ± 8.6</td>
<td>-62.4 ± 0.2</td>
<td>-10.6 ± 8.6</td>
<td>1.03 ± 0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2.13 ± 0.01) $\times 10^7$</td>
<td>-41.8 ± 5.6</td>
<td>-37.0 ± 0.2</td>
<td>4.8 ± 5.6</td>
<td>1.32 ± 0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>P($p$-FC$_6$H$_4$)$_3$</td>
<td>(1.06 ± 0.01) $\times 10^8$</td>
<td>-45.8 ± 3.2</td>
<td>-64.1 ± 0.1</td>
<td>-18.3 ± 3.2</td>
<td>1.02 ± 0.01</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>(2.20 ± 0.01) $\times 10^6$</td>
<td>-36.2 ± 8.7</td>
<td>-37.5 ± 0.1</td>
<td>-1.3 ± 8.7</td>
<td>1.34 ± 0.01</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>PFu$_3$</td>
<td>(2.27 ± 0.01) $\times 10^5$</td>
<td>-30.6 ± 1.4</td>
<td>-36.7 ± 0.5</td>
<td>-6.1 ± 1.5</td>
<td>1.46 ± 0.01</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>(3.15 ± 0.01) $\times 10^7$</td>
<td>-42.8 ± 4.2</td>
<td>-46.2 ± 0.5</td>
<td>-3.4 ± 4.2</td>
<td>1.03 ± 0.01</td>
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<tr>
<td>P(OPh)$_3$</td>
<td>(2.91 ± 0.01) $\times 10^6$</td>
<td>-36.9 ± 10.9</td>
<td>-123.6 ± 1.0</td>
<td>-86.7 ± 11.0</td>
<td>0.82 ± 0.01</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>P($o$-tolyl)$_3$</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
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*The values for $\Delta G$ and $T\Delta S$ were calculated from the given $K$ and $\Delta H$ values. *aThe integrated heats for each titration were analyzed using either the multiple sites model or the independent model to obtain binding constants ($K_i$), enthalpies of binding ($\Delta H_i$), and binding stoichiometries ($n_i$).
Table 2.3. Experimental conditions for ITC experiments. All ITC experiments were performed at 25°C. For each experiment listed, the PdCl$_2$(solv)$_2$ and ligand concentrations are provided, along with the volume of each injection ($V_{\text{inj}}$), the total number of injections ($N_{\text{inj}}$), and the duration of each injection ($t_{\text{inj}}$). Note that $t_{\text{inj}}$ refers to the amount of time that elapses after an injection in order to allow the baseline to equilibrate.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Solvent</th>
<th>[PdCl$_2$(solv)$_2$] (mM)</th>
<th>[Ligand] (mM)</th>
<th>$V_{\text{inj}}$ (μL)</th>
<th>$N_{\text{inj}}$</th>
<th>$t_{\text{inj}}$ (s)</th>
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<tbody>
<tr>
<td>PPh$_3$</td>
<td>DMSO</td>
<td>1</td>
<td>25</td>
<td>6</td>
<td>25</td>
<td>900</td>
</tr>
<tr>
<td>PPh$_3$</td>
<td>DMF</td>
<td>1</td>
<td>25</td>
<td>6</td>
<td>25</td>
<td>700</td>
</tr>
<tr>
<td>PPh$_3$</td>
<td>Pyridine</td>
<td>1</td>
<td>25</td>
<td>6</td>
<td>30</td>
<td>900</td>
</tr>
<tr>
<td>PPh$_3$</td>
<td>MeCN</td>
<td>1</td>
<td>25</td>
<td>6</td>
<td>20</td>
<td>700</td>
</tr>
<tr>
<td>$\text{P(p-FC}_6\text{H}_4\text{)}_3$</td>
<td>MeCN</td>
<td>1</td>
<td>25</td>
<td>6</td>
<td>20</td>
<td>600</td>
</tr>
<tr>
<td>PFu$_3$</td>
<td>MeCN</td>
<td>1</td>
<td>25</td>
<td>6</td>
<td>25</td>
<td>600</td>
</tr>
<tr>
<td>$\text{P(OPh)}_3$</td>
<td>MeCN</td>
<td>1</td>
<td>10</td>
<td>6</td>
<td>25</td>
<td>900</td>
</tr>
<tr>
<td>$\text{P(o-toly)}_3$</td>
<td>MeCN</td>
<td>5</td>
<td>30</td>
<td>8</td>
<td>31</td>
<td>1200</td>
</tr>
</tbody>
</table>
first equilibrium step, which changes the ground-state thermodynamics of the intermediate complex relative to 1, resulting in two distinct equilibrium constants for identical ligands ($K_1$ and $K_2$).\cite{28} As seen in section 2.4.1, two equivalents of PPh$_3$, PFu$_3$, and P(p-FC$_6$H$_4$)$_3$ were able to bind to 1 in MeCN, while only one equivalent each of P(OPh)$_3$ and P(o-tolyl)$_3$ were able to bind. $^{31}$P NMR confirmed that PPh$_3$ and P(p-FC$_6$H$_4$)$_3$ formed the trans product only while PFu$_3$ formed the cis product only in MeCN (Figure 2.1a). Redfield and Nelson studied the thermodynamics of the cis-trans isomerization of Pd(II)-phosphine complexes and found the cis isomer was generally the most stable by as many as two orders of magnitude in $K$.\cite{29} For the trans complexes, this instability is reflected in lower $K_2$ values, while the more stable cis complex has a higher $K_2$ value. We are not ascribing these differences in $K_2$ between the cis and trans complexes to the well-known trans influence because both chloride ligands remain bound in the cis complex. The trans influence is the ability of a ligand already bound to a metal center to weaken the bond of the ligand trans to it, altering the ground-state thermodynamics of the complex itself.\cite{28} Empirically, phosphorus ligands are better trans directors than Cl ligands, but our $^{31}$P NMR data confirms that the Cl ligands are not substituted, so we attribute the formation of both cis and trans complexes to the inherent weakness of the coordinated MeCN molecules. We confirmed metal-ligand binding ratios using UV-Vis spectroscopy and we provide the data in Figures 2.8-2.12.\cite{24} As discussed in section 2.2, the binding sites on the Pd center are thermodynamically independent and the state of one site, bound or unbound, does not affect the affinity of the other site.\cite{19} This trait is reflected in the shapes of the isotherms as two different sigmoidal regions (see Figure 2.3), for the three ligands for which two equivalents of ligand bind,
Figure 2.8. Continuous variation method analysis for the binding of PPh$_3$ to PdCl$_2$(MeCN)$_2$ at 25°C. The maximum value of the observed absorbance peaks determines the binding ratio.
Figure 2.9. Continuous variation method analysis for the binding of P(\(p\text{-FC}_6\text{H}_4\))_3 to PdCl\(_2\)(MeCN)\(_2\) at 25°C. The maximum value of the observed absorbance peaks determines the binding ratio.
**Figure 2.10.** Continuous variation method analysis for the binding of PFu₃ to PdCl₂(MeCN)₂ at 25°C. The maximum value of the observed absorbance peaks determines the binding ratio.
Figure 2.11. Continuous variation method analysis for the binding of P(OPh)$_3$ to PdCl$_2$(MeCN)$_2$ at 25°C. The maximum value of the observed absorbance peaks determines the binding ratio.
Figure 2.12. Continuous variation method analysis for the binding of P(o-tolyl)$_3$ to PdCl$_2$(MeCN)$_2$ at 25°C. The maximum value of the observed absorbance peaks determines the binding ratio. All systems (Figures 2.8-2.11) are in agreement with the binding stoichiometries as measured by ITC, with the exception being P(o-tolyl)$_3$. Several ITC trials for P(o-tolyl)$_3$ yielded similar results for the reported binding stoichiometry (1:1) in the main text and is the accepted value, rather than the 2:1 value obtained here.
characteristic of multiple-site binding. Conversely, the two ligands for which only one equivalent binds display a single inflection point, characteristic of independent binding. The different binding modes are consistent with the Tolman cone angles and electronic parameters of phosphites as compared to phosphines. \( \text{P(o-tolyl)}_3 \) has the largest cone angle, 194°, so it is logical that only one ligand binds to the Pd centers in solution.\(^{[1]} \) \( \text{P(OPh)}_3 \) is the poorest electron-donor, though being a triarylphosphite, it is a better \( \pi \)-acceptor than the triarylphosphine, \( \text{PPh}_3 \).\(^{[1, 28]} \) It is also a better \( \pi \)-acceptor than \( \text{P(o-tolyl)}_3 \) and has a smaller cone angle, which would explain its larger affinity for binding with 1.\(^{[4, 30, 31]} \) The Tolman electronic parameter (Table 2.1) for \( \text{PPh}_3 \) is less than that of \( \text{P(p-FC}_6\text{H}_4)_3 \), indicating that the overall electron-donating ability of \( \text{PPh}_3 \) is greater.\(^{[1, 28]} \) These two ligands have identical cone angles and the difference in electron-donating ability explains why \( \text{PPh}_3 \) binds more strongly to 1.

2.4.3 ITC Results for Binding \( \text{PPh}_3 \) to \( \text{PdCl}_2(\text{solv})_2 \)

Figures 2.13-2.15 show the ITC results for the binding of \( \text{PPh}_3 \) to 2 in dimethyl sulfoxide (DMSO), \( \text{N,N-dimethylformamide (DMF)} \), and pyridine (py) at 25°C while the best fit parameters for all tested solvents are in Table 2.4. The structures of 2 are \textit{trans} as reported in the literature and were prepared as reported (see section 2.3.1).\(^{[22, 23]} \) Multiple-exchanged \( \text{Pd(DMSO)}_n \) species \((n > 1)\) have been observed, such as \( \text{[Pd(DMSO)}_4]^{2+} \), but their formation requires silver perchlorate, \( \text{AgClO}_4 \) (our synthesis does not use silver perchlorate)\(^{[32]} \), while our preparation for \( \text{PdCl}_2(\text{py})_2 \) is identical to that of Gupte and Chaudhari\(^{[33]} \) and the formation of \( \text{PdCl}_2(\text{py})_2 \) was structurally verified via XRD by Liao and Lee.\(^{[34]} \) Therefore, we do not expect formation of either \( \text{Pd(DMSO)}_n \) or \( \text{Pd(py)}_n \).
Figure 2.13. (a) Real-time ITC thermogram for PPh₃ binding to 2 in DMSO at 25°C with (b) the integrated heat data with fitted model.
Figure 2.14. (a) Real-time ITC thermogram for PPh$_3$ binding to 2 in DMF at $25^\circ$C with (b) the integrated heat data with fitted model.
Figure 2.15. (a) Real-time ITC thermogram for PPh$_3$ binding to 2 in py at 25°C with (b) the integrated heat data with fitted model.
Table 2.4. Thermodynamic properties for the binding of PPh$_3$ to 2 in various solvents at 25°C. Errors were calculated using the statistics function in NanoAnalyze (see section 2.3.2).

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$K_1$</th>
<th>$\Delta G_1$</th>
<th>$\Delta H_1$</th>
<th>$T \Delta S_1$</th>
<th>$n_1$</th>
<th>$K_2$</th>
<th>$\Delta G_2$</th>
<th>$\Delta H_2$</th>
<th>$T \Delta S_2$</th>
<th>$n_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeCN</td>
<td>(1.20 ± 0.01) × 10$^9$</td>
<td>-51.8 ± 8.6</td>
<td>-62.4 ± 0.2</td>
<td>-10.6 ± 8.6</td>
<td>1.03 ± 0.01</td>
<td>(2.13 ± 0.01) × 10$^7$</td>
<td>-41.8 ± 5.6</td>
<td>-37.0 ± 0.2</td>
<td>4.8 ± 5.6</td>
<td>1.32 ± 0.01</td>
</tr>
<tr>
<td>DMSO</td>
<td>(2.55 ± 0.01) × 10$^8$</td>
<td>-48.0 ± 3.3</td>
<td>-41.0 ± 0.1</td>
<td>6.9 ± 3.3</td>
<td>1.06 ± 0.02</td>
<td>(1.75 ± 0.01) × 10$^5$</td>
<td>-29.9 ± 9.8</td>
<td>-33.2 ± 0.3</td>
<td>-3.3 ± 9.8</td>
<td>1.17 ± 0.01</td>
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<tr>
<td>DMF</td>
<td>(2.51 ± 0.01) × 10$^7$</td>
<td>-42.2 ± 1.3</td>
<td>-62.8 ± 0.2</td>
<td>-20.5 ± 1.4</td>
<td>0.90 ± 0.01</td>
<td>(7.64 ± 0.01) × 10$^4$</td>
<td>-27.9 ± 1.4</td>
<td>-35.5 ± 0.1</td>
<td>-7.7 ± 1.4</td>
<td>1.09 ± 0.02</td>
</tr>
<tr>
<td>py</td>
<td>(2.08 ± 0.01) × 10$^4$</td>
<td>-24.6 ± 7.0</td>
<td>-12.5 ± 0.3</td>
<td>12.1 ± 7.0</td>
<td>1.29 ± 0.02</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
For DMSO and DMF, two equivalents of ligand bind as seen in MeCN. In py, only one ligand binds, which is attributed to two factors. It has a high donor number \((DN)\) which is an empirical measure of the ability of a solvent to donate electrons to a solute, PdCl\(_2\).\(^{[35]}\) This evidence indicates that a py molecule \((DN = 138.5\ \text{kJ/mol}, \ AN = 14.2\ \text{(unitless)}, \ \text{see below for definition of \(AN\)})\) binds to the Pd center, occupying one of the sites as seen by ITC. The other factor can be traced to a calorimetric study of the thermodynamics of ligand exchange for PdCl\(_2(C_7H_8N)_2\) to determine relative displacement energies (RDE) comparing the intrinsic binding strength of one ligand to another, which found that py has an RDE less than that of PPh\(_3\), which means that displacing PPh\(_3\) has a more unfavorable contribution to \(\Delta G\).\(^{[36]}\) We tested py binding to 1 in MeCN using ITC and found that only one equivalent of py binds (shown in our other study\(^{[37]}\)), agreeing with the RDE study. For our system, PdCl\(_2\)(py)\(_2\) is in excess py, whereas the previous study was conducted in dichloromethane, so it is reasonable to attribute the presence of only one bound PPh\(_3\) ligand to the excess of py relative to unbound PPh\(_3\) (Figure 2.15). The binding is strongest in MeCN (highest \(K\) values) and weakest in DMF (lowest \(K\) values). In terms of \(DN\) and acceptor number \((AN, \ \text{which is an empirical measure of the ability of a solvent to accept electrons from solutes})\), MeCN \((DN = 59.0\ \text{kJ/mol}, \ AN = 18.9)\) is the weakest electron donor and a better electron acceptor than DMF \((DN = 111.3\ \text{kJ/mol}, \ AN = 16.0)\), so bound MeCN molecules are more easily displaced by free PPh\(_3\).\(^{[35]}\) The best fit values of binding in DMSO \((DN = 124.7\ \text{kJ/mol}, \ AN = 19.3)\) and DMF are similar in terms of the orders of magnitude of the obtained \(K\) values due to having similar \(DN\) and \(AN\) values (note: all \(DN\) and \(AN\) values are taken from the literature\(^{[35, 38]}\)).
2.4.4 Understanding the Contributions to the Enthalpy and Entropy of Binding

The obtained $\Delta H$ and $\Delta S$ values provide insight as to what the dominant effects are for a given set of metal-ligand interactions. The obtained ITC parameters are observed values, rather than intrinsic values. The observed enthalpy includes the loss of solute-solvent bonds in the form of solvent reorganization ($\text{PdCl}_2$ and ligand are solutes), the loss of van der Waals forces, solvation and conformational changes at the binding site, and metal-ligand binding.\cite{39, 40} The observed entropy change includes contributions from losses of translational, rotational, and vibrational degrees of freedom and from the solvation and desolvation of the solutes; however, the main contribution to the observed entropy is expulsion of solvent molecules bound to the metal, which normally manifests itself as an increase in entropy.\cite{39, 40} From Table 2.2, ligand binding is enthalpy-driven because of the large, exothermic enthalpies and small entropies. The ligands for which two equivalents bind to 1 all have an increase in entropy after the first ligand is bound, which is attributed primarily to the displacement of the last bound solvent molecule. It is noteworthy that py has nearly equal enthalpy and entropy contributions. Regarding the large RDE of py, it makes sense that the observed $\Delta H$ decreased in magnitude relative to the other solvents because the displacement of the bound py contributes unfavorably to $\Delta G$.\cite{36, 41} For MeCN and DMF, the entropic contributions increase after the second ligand binds, in agreement with the trend from the different ligands. The DMSO system decreases in entropy after the second ligand binds because it has the highest $AN$ of the tested solvents; it is the best electron acceptor and the desolvation of the $\text{PPh}_3$ ligand, which has a lone pair of electrons on the P atom, is not as favorable as it is in the other solvents. Solvent molecules can form adducts with the ligands, which would change their
overall polarity and subsequently change the enthalpy of solvation of the products (Pd-P complexes). Partenheimer et al studied this effect for acid-base systems in cyclohexane and CCl₄ and noticed more cyclohexane molecules formed adducts with the base, dimethylacetamide, than did CCl₄ which explained the differences in the observed enthalpies of acid-base reactions between the solvents. Overall, ligand binding is enthalpy-driven, that is, the large enthalpy values indicate that solvent reorganization contributes greatly to the observed enthalpies, as originally noted by Chervenak and Toone. Solvent reorganization includes the loss of solute-solvent interactions (in the solvation shells around the solutes) during the binding event that is necessarily accompanied by new solvent-solvent interactions that occur once the expelled solvent molecules reenter the bulk. In their study, Chervenak and Toone used ITC to measure the binding thermodynamics of several systems, such as protein-carbohydrate and protein-peptide binding equilibria, in both H₂O and D₂O and determined that decreased ΔH values in D₂O were compensated by changes in ΔS, practically leaving ΔG constant. They assumed that intrinsic ligand-receptor binding was invariant of the nature of the solvent, meaning that solvent reorganization accounted for 25-100% of the observed binding enthalpies for the systems studied.

The drastic variation in thermodynamic values obtained for P(OPh)₃ relative to the other P ligands warrants further discussion. The other ligands in this study have rigid aryl groups connected directly to the P atom, whereas the phenyl groups in P(OPh)₃ are linked to the P atom by O atoms, which allows for more rotational freedom when the ligand is unbound. All ligands will lose translational and rigid-body rotational entropy upon binding, but P(OPh)₃ would seem to suffer the largest penalty. The enthalpies of
dissolution for both ligands, PPh\textsubscript{3} (26.21 \pm 0.04 kJ/mol) and P(OPh)\textsubscript{3} (6.86 \pm 0.01 kJ/mol), are endothermic. In both cases, there are intermolecular forces that must be overcome in order for dissolution to occur. The enthalpy of solution for PPh\textsubscript{3} is larger in magnitude because its lattice energy must be overcome in order for it to dissolve (it is a solid) while P(OPh)\textsubscript{3} is a liquid and has no such energy. If the enthalpy of fusion for PPh\textsubscript{3} (19.69 kJ/mol)\textsuperscript{[45]} is taken into account as a crude approximation of its lattice energy, then dissolution of a hypothetical PPh\textsubscript{3} liquid would be difference between the enthalpy of dissolution and the enthalpy of fusion, which is 6.52 kJ/mol, slightly smaller in magnitude than the enthalpy of solution of P(OPh)\textsubscript{3}, which is 6.86 kJ/mol. Since the enthalpy of dissolution for P(OPh)\textsubscript{3} is positive, overcoming its own intermolecular forces and breaking up solvent-solvent intermolecular forces are larger in combined magnitude than solute-solvent interactions. The inability of P(OPh)\textsubscript{3} to overcome these forces which, along with its enormous rotational entropy penalty, explains why P(OPh)\textsubscript{3} has such a large, negative entropy of binding.\textsuperscript{[46]} Searle and Williams estimate an entropy loss of 8.8-44.8 kJ/mol (for T\Delta S) at 25°C for the binding of small molecules to proteins in solution due to lost rigid-body entropy, noting that the larger losses in entropy are associated with larger increases in enthalpy, i.e enthalpy-entropy compensation.\textsuperscript{[47]} The desolvation of the \pi-acidic P(OPh)\textsubscript{3} upon binding would decrease entropy due to the nature of MeCN being a good electron acceptor.

### 2.5 Conclusions

We have provided detailed analysis of the thermodynamics of the binding of P ligands to 1 and the effect of different solvents on the thermodynamics of binding to PPh\textsubscript{3}.
to 2. We observed via $^{31}$P NMR spectroscopy that one or two equivalents of ligand bind to the Pd centers. For bulkier ligands and poor electron-donating ligands, only a single ligand was able to bind to 1. Our ITC experiments demonstrated that ligands interact with the Pd center in two binding modes: either two equivalents of ligands bind to sites of different affinity on the same Pd center or only one equivalent of ligand binds. For the bis-ligated complexes, the addition of the second ligand proved to be more stable when forming a cis complex when compared to the trans complexes. The electronic influences of the different solvents also affected the binding ability of PPh$_3$. MeCN was the most easily displaced due to its weak-coordinating ability coupled with its strong electron-accepting ability. The strong electron-donating ability and RDE of py restricted binding to a single PPh$_3$ ligand while two equivalents of PPh$_3$ were able to bind in the other three solvents (MeCN, DMSO, and DMF).

We found that these metal-ligand interactions are enthalpy-driven. These large, exothermic enthalpies indicate that solvent reorganization likely contributed greatly to the observed enthalpies and played an active role in the metal-ligand equilibria. We attributed the ability of the solvent molecules to interact with the solutes as another contributor to the observed enthalpies of binding. All ligands for which two equivalents bind to 1 had an increase in entropy after the second ligand was bound, likely due to displacement of a bound solvent molecule. The largest decrease in observed entropy was seen for P(OPh)$_3$ and was attributed to a loss of translational and rigid-body rotational entropies.
2.6 References


[40] A. Bronowska, in *Thermodynamics - Interaction Studies - Solids, Liquids, and Gases* (Ed.: J. C. Moreno-Pirajan), InTech, **2011**.


Chapter 3

Elucidating the Roles of Enthalpy, Entropy, and Donor Atom in the Chelate Effect for Binding Different Bidentate Ligands on the Same Metal Center

3.1 Introduction

The design of sophisticated homogeneous catalysts relies on knowledge of different classes of ligands, such that the chosen ligands impart the desired activity and selectivity for a given chemistry. Altering the electronic and steric characteristics of the metal centers in organometallic complexes dictates the most likely reaction paths during catalytic processes. Polydentate ligands are frequently employed to provide thermodynamic stability via chelation to organometallic complexes, known as the chelate effect, that is unattainable with monodentate ligands.\[^1\] As such, a great variety of polydentate ligands, primarily bidentate ligands, have been synthesized and studied in order to understand their effects on catalytic activity and selectivity. Bidentate ligands also impart steric effects unobtainable with monodentate ligands, which affect the activity and selectivity in ways that monodentate ligands cannot.\[^2\] There is a great interest in quantifying the effects of bidentate ligands on the activities and selectivities of catalytic centers in solution in order to determine if there are trends that can be applied across different classes of ligands. Additionally, these trends enable chemists to design new ligands that exploit these observed enhancements in catalytic activities and selectivities. From a steric standpoint, the catalytic activity and selectivity are controlled primarily by two factors: the bite angle, the angle the ligand forms with the metal center, and the conformational flexibility of the ligand, the ability of a ligand to assume a variety of bite
angles with the metal center so long as the energy of the complex does not vary significantly from the most stable form of the complex.\[^3\] Recently, there has been considerable effort in performing DFT calculations to study the electronics and energetics of bidentate ligands commonly used in homogeneous catalysis.\[^4, 5\] Primarily, these studies aim to quantify the energies of the HOMO and LUMO of each ligand, while considering each donor atom of the ligand as a separate entity, and calculating the bond dissociation energies from model complexes such as ZnCl\(_2\) and PdCl\(_2\) for a series of P-P and P-N ligands.\[^4, 5\]

Bidentate ligands, particularly those containing phosphorus and nitrogen donor atoms, are used in a wide variety of chemical transformations, owing to their unique abilities to enhance catalytic activity while controlling selectivity. Mixed bidentate ligands, such as P-N ligands, represent an intriguing avenue for combining two different types of donor atoms on the same ligand, which allows for moieties that have hard and soft basic properties simultaneously.\[^6\] Blaser et al discussed the roles of P-P and P-N bidentate ligands for the hydrogenation of a great number of substrates such as alkenes, ketones, aromatics, and nitriles, all while highlighting the variety of metal centers available for these hydrogenations and their chemo-, enantio-, and stereoselectivities.\[^7\]

Chelating N-heterocyclic carbenes (NHCs) are a class of strong electron donor ligands via N atoms and are used in C-C bond formation reactions such as Heck reactions, Suzuki couplings, Sonogashira couplings and other reactions such as transfer hydrogenations and hydrosilylation of terminal alkynes.\[^8, 9\] McCarthy and Guiry reviewed a variety of chiral P-P, N-N, and P-N bidentate ligands, among others, for use in designing asymmetric
organometallic complexes for the asymmetric synthesis of enantiomerically pure compounds.\textsuperscript{[10]}

The main difficulty with ligand design is that amassing an exhaustive library of ligands for a certain class of catalytic reactions is both time-consuming and largely ineffective in terms of the number of ligands that must be studied in order to draw reasonable conclusions regarding catalytic performance from a class of ligands. Combinatorial chemistry and high-throughput screening are the main techniques for determining the ability of a synthesized ligand to alter catalytic activity and selectivity. In short, each ligand is determined to have a series of physical and chemical properties and is then tested for its catalytic performance, which is then measured against other ligands.\textsuperscript{[11, 12]} The ligands that best enhance the catalytic activity and selectivity are compared to one another in order to determine which ligand properties contribute most to the observed catalytic enhancements. This methodology is by no means uninformative, but difficulties in synthesizing bidentate ligands frequently requires a great deal of effort and, to a large degree in its own right, serendipity in order to compose the optimal ligand(s) for a specific catalytic reaction.\textsuperscript{[2]}

In an effort to broaden the understanding of the effects of bidentate ligands on stabilizing metal centers in solution, we use calorimetry to quantify the thermodynamics of the chelate effect by examining the binding equilibria between a model compound, PdCl$_2$(MeCN)$_2$, in acetonitrile (MeCN) and various bidentate ligands (P-P, N-N, and P-N) and comparing the results to similar monodentate ligands, triphenylphosphine (PPh$_3$) and pyridine (py). We use isothermal titration calorimetry (ITC) to measure the equilibrium binding constants ($K_i$), binding enthalpies ($\Delta H_i$), and reaction stoichiometry
(n_i), all in a single experiment. Calorimetry is a natural complement to the DFT data available in the literature regarding the energetic of ligand binding to metal centers.\cite{4, 5} ITC is an appropriate technique because modern calorimeters are capable of measuring binding constants on the order of 10^9 M^{-1} due to their nW level of sensitivity.\cite{13} In particular, our analysis can be extended to understand these systems in situ, whereas DFT calculations cannot fully account for solvent effects and often treats reactive species in a vacuum. We supplement our thermodynamic analysis with NMR and UV-Vis characterization and analysis of the reaction products and rationalize the obtained thermodynamic parameters, specifically ΔH and ΔS, with respect to the chelate effect, inherent properties of the tested ligands, as well as the subtle roles that solvation and solvent-solute (i.e., PdCl_2(MeCN)_2 and ligand are treated as solutes) interactions play in contributing to the stability of chelated complexes. We also discuss the presence of enthalpy-entropy compensation and how solvent reorganization manifests itself as a favorable contribution to enthalpy for all three types of ligands.

3.2 Experimental

3.2.1 Materials and Solution Preparations

PdCl_2 was obtained from Alfa Aesar, 1,2-bis(diphenylphosphino)ethane (diphos) was obtained from Strem, and MeCN was obtained from EMD. Pyridine (py), 1,5-bis(diphenylphosphino)pentane (dpppe), 2,2'-bipyridine (bpy), 4-(dimethylamino)phenyl(diphenylphosphine (dmap), o-phenylenediamine (opd), and PPh_3 were obtained from Sigma while (R)-N,N-dimethyl-1-[(S)-2-(diphenylphosphino)ferrocenyl]ethylamine ((R)-(S)-PPFA)) and (S)-N,N-dimethyl-1-[(R)-
2-(diphenylphosphino)ferrocenyl]ethylamine ((S)-(R)-PPFA)) were obtained from Alfa Aesar. All chemicals were used without further purification.

All 0.75-2 mM solutions of PdCl$_2$(MeCN)$_2$ were prepared by dissolving 6.6-17.7 mg of anhydrous PdCl$_2$ in 50 mL of degassed MeCN and stirred vigorously overnight with gentle heating. The structure of PdCl$_2$(MeCN)$_2$ is trans as reported in the literature.[14] All ligand solutions were prepared immediately before each titration by dissolving the appropriate amount of ligand in degassed MeCN followed by vigorous stirring.

3.2.2 ITC Experimental Procedure for Binding Bidentate Ligands to PdCl$_2$(MeCN)$_2$

ITC experiments were performed using a NanoITC calorimeter (TA Instruments, New Castle, DE) equipped with hastelloy cells ($V = 1.056 \text{ mL}$). All titrations were carried out at 25°C using a 250 μL syringe at a stirring rate of 250 rpm. The sample cell contained PdCl$_2$(MeCN)$_2$ and the reference cell contained pure MeCN. The “heat flow” baseline was allowed to equilibrate once the reference and sample solutions were loaded into the cells. Titrations began after equilibration of the power rating (note: the power rating is the thermal compensation of the calorimeter that is applied to the sample cell to keep it at the same temperature as the reference cell). Titrations were run as an incremental series of injections of the appropriate ligand into the PdCl$_2$(MeCN)$_2$ solution. Blank experiments were conducted under identical conditions with only solvent in the sample cell to experimentally determine the heat of mixing of the ligands with pure MeCN. These blanks were subtracted from the experiments with PdCl$_2$(MeCN)$_2$ in the cell and integrated to isolate the heat evolved from metal-ligand interactions. Data
analysis was performed using NanoAnalyze v2.1 from TA Instruments using the Independent Sites algorithm (see Chapter 2.2 for derivations of the models discussed within the present work).\cite{15,16} We used a modified version of the Multiple Sites model in Microsoft Excel in order to account for the inability of NanoAnalyze to fit integrated heat data near zero accurately. We used the Solver function in Excel to minimize the sum of the squares of the differences between the measured heats and calculated heats. The first integrated heat point in each data set is omitted from each fit because the syringe allows for a miniscule amount of ligand to mix before the experiment starts which makes the first data point unreliable. Error analysis was also performed using NanoAnalyze v2.1 via its Statistics function. The uncertainties in the parameters obtained from the fits are calculated by adding perturbations to the optimized fits and then refitting the models for a set number of trials. Each perturbation obeys a Gaussian distribution that has the same standard deviation generated from the original fit. The error in each data set was determined within one standard deviation for 1000 trials. The error values reported in the main text for the $K$ values are also multiplied by the factor outside of the parentheses. For example, a $K$ value of $(5.99 \pm 0.01) \times 10^5$ means that the error is $0.01 \times 10^5$, or 1000.

3.2.3 \textit{\textsuperscript{31}P and \textsuperscript{1}H NMR Characterization of Reaction Intermediates and Products}

Mixtures of one or two equivalents of phosphorus ligand to one equivalent of PdCl$_2$(MeCN)$_2$ were prepared in advance and allowed to stir at room temperature for 1 h. Concentrations were increased by an order of magnitude from the ITC experiments in order to improve the signal-to-noise ratio. An aliquot of the Pd solution was mixed with an equal volume of deuterated solvent (Cambridge Isotope Laboratories) in an NMR
tube. Samples were run on a Bruker AV-360 at room temperature with proton decoupling for $^{31}$P NMR. Each sample was run for 16 ($^1$H) or 128 scans ($^{31}$P) and each spectrum was observed for the chemical shifts of the Pd complexes.

3.2.4 UV-Vis Spectroscopy Experiments (Continuous Variation Method)

The continuous variation method experiments were performed using a Shimadzu UV-3600 UV-Vis-NIR spectrophotometer at room temperature. For each system, 0.5 mM stock solutions of PdCl$_2$(MeCN)$_2$ and the appropriate ligands were prepared in advance. All chemical species were calibrated to find their molar absorptivities, though only PdCl$_2$(MeCN)$_2$ was found to have an appreciable molar absorptivity at the wavelength of interest, 368 nm (highest signal-to-noise ratio). Each analytical sample contained a different total mole fraction of PdCl$_2$(MeCN)$_2$ and was measured for total solution absorbance at 368 nm. The continuous variation method allows for the determination of the binding stoichiometry between two chemical species in solution and was utilized to validate the stoichiometric relationships obtained via ITC (see Chapter 2.3.5 for the derivation equations used). These experiments were performed only for opd because there were no appreciable NMR resonances such that we could independently determine its binding stoichiometry with PdCl$_2$(MeCN)$_2$.

3.3 Results and Discussion

3.3.1 $^{31}$P NMR Results for P-P Ligand Binding to PdCl$_2$(MeCN)$_2$

We begin by identifying the species that are present during the titrations of each ligand so that we may confirm the ITC results and choose the most appropriate binding
model for each system. Figure 3.1 shows the $^{31}$P NMR spectra for the complexes formed from the P-P bidentate ligands diphos and dpppe. One equivalent of diphos was able to bind to PdCl$_2$(MeCN)$_2$, forming a mono-ligated complex at $\delta = 65.9$ ppm, in agreement with Sanger’s original observation of PdCl$_2$(diphos) in solution.$^{[17]}$ The addition of another equivalent (two total) of diphos produced a different resonance at $\delta = 56.1$ ppm, indicative of a trans bis-ligated complex, PdCl$_2$(diphos)$_2$, as reported by Lindsay et al.$^{[18]}$ One equivalent of dpppe was able to bind to PdCl$_2$(MeCN)$_2$, forming a trans-bridging Pd dimer that resonated at $\delta = 17.2$ ppm.$^{[19, 20]}$ For all NMR results, there was no evidence of chloro-bridged Pd dimers or ionization isomers. We therefore propose Figure 3.2 as a description of the binding equilibria that occur in the ITC experiments based on these $^{31}$P NMR results.

### 3.3.2 $^1$H NMR Results for N-N Ligand Binding to PdCl$_2$(MeCN)$_2$

Figure 3.3 shows the $^1$H NMR for the complexes formed in the presence of the bidentate N-N ligand, bpy. There were no observable signals in the $^1$H NMR spectra for the opd ligand. We performed UV-Vis spectroscopic experiments for opd to confirm a 1:1 metal-to-ligand binding ratio and the results are presented in Figure 3.4. The opd complex is most likely a cis configuration because of the rigidity of the aromatic backbone of the ligand.$^{[21]}$ One equivalent of bpy was able to bind with PdCl$_2$(MeCN)$_2$ to form a cis complex, in accordance with the experimental procedure reported by Newkome et al.$^{[22]}$ The shift in the $^1$H peaks of the chelated complex from the peaks of the free bpy ligand in solution indicated that the ligand was coordinated to the Pd center.$^{[23]}$ We also synthesized a py complex, PdCl$_2$(py)(MeCN), as a comparison for a
Figure 3.1. $^{31}$P NMR spectra of PdCl$_2$(MeCN)$_2$ in the presence of one equivalent of diphos, two equivalents of diphos, and one equivalent of dpppe, all in MeCN as solvent. The metal-to-ligand ratios are necessary to confirm the proposed species in Figure 3.2 and the observed thermograms from the ITC experiments. The resulting Pd-P complexes are listed above each spectrum.
Figure 3.2. Schematic of metal-ligand binding equilibria in solution for bidentate P-P ligands. Two equivalents of diphos bind successively to the Pd center while dpppe ligands bridge two Pd centers to form Pd dimers. The $K$ values correspond to the data obtained from ITC experiments.
Figure 3.3. $^1$H NMR spectra of PdCl$_2$(MeCN)$_2$ in the presence of one equivalent of bpy and one equivalent of py. Free bpy and py are included to demonstrate the peak shifts upon ligand coordination to the Pd center. The metal-to-ligand ratios are necessary to confirm the proposed species in Figure 3.5 and the observed thermograms from the ITC experiments. The resulting Pd-N complexes are listed above each spectrum.
**Figure 3.4.** Continuous variation method for opd binding to PdCl$_2$(MeCN)$_2$. The maximum value of the observed absorbance peaks shows that the binding ratio is 1:1, in agreement with the ITC results.
monodentate N ligand. When comparing the NMR spectrum of the complex to that of the free ligand, the peaks characteristic of free py are shifted in the complex, along with unbound py (only one equivalent of py was able to bind as determined by ITC). Figure 3.5 summarizes the binding equilibria of the bidentate N-N ligands that occur in the ITC experiments based on this spectroscopic information.

3.3.3 $^{31}$P NMR Results for P-N Ligand Binding to PdCl$_2$(MeCN)$_2$

Figure 3.6 shows the $^{31}$P NMR for the complexes that formed in the presence of the bidentate P-N ligands dmap, (R)-(S)-PPFA, and (S)-(R)-PPFA. In the presence of one equivalent of dmap, the mono-ligated complex PdCl$_2$(dmap)(MeCN) ($\delta = 31.6$ ppm) formed via the coordination of the P atom of the ligand. In the presence of two total equivalents of dmap, the bis-ligated complex PdCl$_2$(dmap)$_2$ formed at $\delta = 21.7$ ppm in a trans configuration as reported by Sarmah et al.$^{[24]}$ Once again, the dmap ligand coordinated by the P atom exclusively. The chiral ferrocenyl P-N ligands, (R)-(S)-PPFA, and (S)-(R)-PPFA, both formed cis complexes, chelating via both the P and N atoms. Our $^{31}$P NMR results for the cis complexes are identical at $\delta = 13.1$ ppm, shifted from $\delta = -23.4$ ppm of each free ligand.$^{[25, 26]}$ We summarize these NMR results in Figure 3.7 as a description of the binding equilibria that occur in the ITC experiments for the bidentate P-N ligands.

3.3.4 ITC Results for Binding Bidentate Ligands to PdCl$_2$(MeCN)$_2$ in MeCN

Figures 3.8 and 3.9 show thermograms for binding diphos and dpppe to PdCl$_2$(MeCN)$_2$ in MeCN at 25°C, respectively, and the integrated heats and the best-fit
**Figure 3.5.** Schematic of metal-ligand binding equilibria in solution for bidentate N-N ligands. One equivalent of bpy and opd each binds with the Pd center to form a *cis*-chelate. The $K$ values correspond to the data obtained from ITC experiments.
Figure 3.6. $^{31}\text{P}$ NMR spectra of PdCl$_2$(MeCN)$_2$ in the presence of one equivalent of dmap, two equivalents of dmap, one equivalent of (R)-(S)-PPFA, and one equivalent of (S)-(R)-PPFA. The metal-to-ligand ratios are necessary to confirm the proposed species in Figure 3.7 and the observed thermograms from the ITC experiments. The resulting Pd-P and Pd-P-N complexes are listed above each spectrum.
Figure 3.7. Schematic of metal-ligand binding equilibria in solution for bidentate P-N ligands. Two equivalents of dmap bind to the Pd center successively, forming a \textit{trans} complex (non-chelating). One equivalent each of (\textit{R})-(\textit{S})-PPFA and (\textit{S})-(\textit{R})-PPFA binds with the Pd centers via both P and N donor atoms to form \textit{cis}-chelates. The $K$ values correspond to the data obtained from ITC experiments.
Figure 3.8. (a) Real-time ITC thermogram for diphos binding to PdCl$_2$(MeCN)$_2$ at 25°C with (b) as the respective integrated heat data with fitted model. Note that “Power” refers to the thermal compensation of the calorimeter to keep the sample at a constant temperature (positive peaks are exothermic).
Figure 3.9. (a) Real-time ITC thermogram for dpppe binding to PdCl$_2$(MeCN)$_2$ at 25°C with (b) as the respective integrated heat data with fitted model.
binding models for each system as measured by ITC (note: the molar ratio is the ratio of the total amount of ligand to the total amount of metal in the calorimeter cell). The sigmoidal character of the integrated heats is indicative of the binding of a single ligand and the presence of two sigmoidal regions represents binding of two equivalents of ligand. The ITC experimental conditions for all systems are provided in Table 3.1. All thermodynamic parameters obtained from the ITC experiments are presented in Table 3.2. We previously discussed the appropriate binding models and background ITC theory, but we will highlight the most important concepts here.\[^{[16]}\] For our systems we observe two types of binding: independent binding, in which the metal center may have several binding sites (maximum of two for PdCl\(_2\)(MeCN)\(_2\)), but each site has the same thermodynamic affinity for the ligand, and multiple-site binding in which each type of site on the metal center has its own affinity for the same ligand, but the occupancy of one site does not affect the affinity of the ligand for the other site.\[^{[15]}\] The \(K_i\) values are the equilibrium binding constants for independent binding (\(K_1\) only) and multiple-site binding (\(K_1\) and \(K_2\)). The \(\Delta H_i\) values are the enthalpies of binding for each independent step (\(\Delta H_1\) only) and each step in the multiple-site model (\(\Delta H_1\) and \(\Delta H_2\)). Finally, each \(n_i\) value represents the binding stoichiometry of each step, used as a fitting parameter for all ITC experiments. For independent binding, only \(n_1\) applies, while \(n_1\) and \(n_2\) both apply for multiple-site binding (the total stoichiometry is \(n = n_1 + n_2\)). For the cis complexes, each ligand binds as a single entity and behaves thermodynamically as if it were a monodentate ligand binding with a single site on the Pd center. The diphos complex exhibits multiple-site behavior: each ligand binds to a site of different affinity on the Pd center. Interestingly, there is a slight increase in the exothermic heats evolved for the first
Table 3.1. Experimental conditions for ITC experiments. All ITC experiments were performed at 25°C. For each experiment listed, the PdCl$_2$(MeCN)$_2$ and ligand concentrations are provided, along with the volume of each injection ($V_{\text{inj}}$), the total number of injections ($N_{\text{inj}}$), and the duration of each injection ($t_{\text{inj}}$). Note that $t_{\text{inj}}$ refers to the amount of time that elapses after an injection in order to allow the baseline to equilibrate.

<table>
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<tr>
<th>Ligand</th>
<th>[PdCl$_2$(MeCN)$_2$] (mM)</th>
<th>[Ligand] (mM)</th>
<th>$V_{\text{inj}}$ ($\mu$L)</th>
<th>$N_{\text{inj}}$</th>
<th>$t_{\text{inj}}$ (s)</th>
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<td>20</td>
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</tr>
<tr>
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<td>20</td>
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Table 3.2. Thermodynamic parameters for the binding of bidentate P-P, N-N, and P-N ligands and two reference monodentate ligands, PPh₃ and py, to PdCl₂(MeCN)₂ in MeCN at 25°C. Errors were calculated using the statistics function in NanoAnalyze.

<table>
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<tr>
<th>Ligand</th>
<th>$K_1$</th>
<th>$K_2$</th>
<th>$ΔG_1$ (kJ/mol)</th>
<th>$ΔH_1$ (kJ/mol)</th>
<th>$TΔS_1$ (kJ/mol)</th>
<th>$n_1$</th>
<th>$ΔG_2$ (kJ/mol)</th>
<th>$ΔH_2$ (kJ/mol)</th>
<th>$TΔS_2$ (kJ/mol)</th>
<th>$n_2$</th>
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<td>diphos (P-P)</td>
<td>(1.42 ± 0.01) × 10⁹</td>
<td>(3.16 ± 0.01) × 10⁹</td>
<td>-52.2 ± 7.3</td>
<td>-123.3 ± 2.2</td>
<td>-71.1 ± 7.6</td>
<td>1.05 ± 0.02</td>
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<tr>
<td></td>
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<td>-52.2 ± 7.3</td>
<td>-123.3 ± 2.2</td>
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<tr>
<td>dpppe (P-P)</td>
<td>(5.59 ± 0.02) × 10⁵</td>
<td></td>
<td>-32.8 ± 9.0</td>
<td>-116.3 ± 1.3</td>
<td>-83.5 ± 9.0</td>
<td>1.03 ± 0.01</td>
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<td></td>
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<td>-32.8 ± 9.0</td>
<td>-116.3 ± 1.3</td>
<td>-83.5 ± 9.0</td>
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<td>-52.2 ± 8.6</td>
<td>-41.8 ± 5.6</td>
<td>-10.6 ± 8.6</td>
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<td>PPh₃ (P)</td>
<td>(1.20 ± 0.01) × 10⁹</td>
<td>(2.13 ± 0.01) × 10⁷</td>
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<td>-62.4 ± 0.2</td>
<td>-10.6 ± 8.6</td>
<td>1.03 ± 0.01</td>
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<tr>
<td></td>
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<td></td>
<td>-51.8 ± 8.6</td>
<td>-62.4 ± 0.2</td>
<td>-10.6 ± 8.6</td>
<td></td>
<td>-41.8 ± 5.6</td>
<td>-37.0 ± 2.5</td>
<td>4.8 ± 5.6</td>
<td>1.32 ± 0.01</td>
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<tr>
<td>bpy (N-N)</td>
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<td>opd (N-N)</td>
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<td>py (N)</td>
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<td>-46.6 ± 0.9</td>
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<td>-29.2 ± 5.3</td>
<td>-46.6 ± 0.9</td>
<td>-17.4 ± 5.3</td>
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<td>-45.1 ± 0.7</td>
<td>0.6 ± 3.8</td>
<td>1.12 ± 0.01</td>
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<tr>
<td>dmap (P-N)</td>
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<td>(3.03 ± 0.01) × 10⁶</td>
<td>-45.7 ± 3.8</td>
<td>-45.1 ± 0.7</td>
<td>0.6 ± 3.8</td>
<td>1.12 ± 0.01</td>
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<td>-45.7 ± 3.8</td>
<td>-45.1 ± 0.7</td>
<td>0.6 ± 3.8</td>
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<td>-37.0 ± 8.3</td>
<td>-32.6 ± 0.9</td>
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<td>1.45 ± 0.02</td>
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<tr>
<td>(R)-(S)-PPFA (P-N)</td>
<td>(1.67 ± 0.01) × 10⁷</td>
<td></td>
<td>-41.2 ± 6.3</td>
<td>-82.9 ± 0.5</td>
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<tr>
<td></td>
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<td>-41.2 ± 6.3</td>
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<td>-41.7 ± 6.3</td>
<td></td>
<td>-41.9 ± 6.6</td>
<td>-93.9 ± 0.8</td>
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<td>0.91 ± 0.01</td>
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</table>

*The values for $ΔG$ and $TΔS$ were calculated from the given $K$ and $ΔH$ values. $b$The integrated heats for each titration were analyzed using either the multiple sites model or the independent model to obtain binding constants, enthalpies of binding, and binding stoichiometries.
few injections of diphos into the PdCl\(_2\)(MeCN)\(_2\) solution, which causes the fit of the data to be off from these points. We attribute this increase in heat to the inner-sphere rearrangement of the diphos ligands at the Pd center because the first equivalent of ligand must conform to the bite angle necessary for the most stable arrangement of the ligand, which manifests itself as an increase in enthalpy.\(^{[27, 28]}\) The dpppe ligands exhibited peculiar behavior, in that two ligands are required to form the final complex, yet the ITC results demonstrated that ligand binding is thermodynamically independent (i.e. dpppe ligands interact with Pd centers with identical affinities) at a binding stoichiometry of \(n_1 = 1.03\). This evidence likely indicates that the kinetics of ligand binding are sufficiently rapid such that the binding of the first P atom is indistinguishable from the second one from a calorimetric perspective. In other words, if there is a second, faster binding step, it evolves very little heat or occurs so quickly that no additional signal from the calorimeter is observed. Once a dpppe ligand forms a bridge between two Pd centers, another dpppe ligand binds to the remaining sites.

Figures 3.10-3.12 show the binding of bpy, opd, and py, respectively, to PdCl\(_2\)(MeCN)\(_2\) in MeCN at 25°C and the integrated heats and the best-fit binding models for each system as measured by ITC. Each bidentate N-N ligand exhibits independent binding with PdCl\(_2\)(MeCN)\(_2\) with one equivalent of each ligand binding to form cis-chelated complexes. These results indicate that each ligand binds as a single entity and behaves thermodynamically as if it were a monodentate ligand binding with a single site on the Pd center. Figures 3.13-3.15 show the binding of bidentate P-N ligands dmap, (\(R\))-\((S)\)-PPFA, and \((S)-(R)\)-PPFA, respectively, to PdCl\(_2\)(MeCN)\(_2\) at 25°C and the integrated heats and the best-fit binding models for each system as measured by ITC. As discussed
Figure 3.10. (a) Real-time ITC thermogram for bpy binding to PdCl$_2$(MeCN)$_2$ at 25°C with (b) as the respective integrated heat data with fitted model.
Figure 3.11. (a) Real-time ITC thermogram for opd binding to PdCl$_2$(MeCN)$_2$ at 25°C with (b) as the respective integrated heat data with fitted model.
Figure 3.12. (a) Real-time ITC thermogram for py binding to PdCl₂(MeCN)₂ at 25°C with (b) as the respective integrated heat data with fitted model.
Figure 3.13. (a) Real-time ITC thermogram for dmap binding to PdCl$_2$(MeCN)$_2$ at 25°C with (b) as the respective integrated heat data with fitted model.
Figure 3.14. (a) Real-time ITC thermogram for \((R)-(S)\)-PPFA binding to \(\text{PdCl}_2(\text{MeCN})_2\) at 25°C with (b) as the respective integrated heat data with fitted model.
Figure 3.15. (a) Real-time ITC thermogram for $(S)$-$(R)$-PPFA binding to PdCl$_2$(MeCN)$_2$ at 25°C with (b) as the respective integrated heat data with fitted model.
in Chapter 3.3.3, the dmap ligands bind to PdCl$_2$(MeCN)$_2$ via the P atoms only, exhibiting multiple-site binding in the same manner of monodentate P ligands, such as PPh$_3$, which we previously described.$^{[16]}$ The chiral ferrocenyl ligands form cis structures and act analogously to the bidentate N-N ligands, binding to the Pd centers in one step, exhibiting independent binding behavior.

### 3.3.5 Thermodynamic Contributions to The Chelate Effect

The obtained thermodynamic parameters for the bidentate P-P ligands, most notably $\Delta H$ and $\Delta S$, challenge some of the conventions of the chelate effect. The chelate effect is empirically assumed to be an entropic effect because it is implied that enthalpic contributions (i.e. formation of metal-ligand bonds) are nearly identical for comparable monodentate and bidentate ligands, meaning that any changes in $\Delta G$ result directly from changes in $\Delta S$ via displacement of solvent molecules bound to the metal center, favorably contributing to entropy.$^{[29]}$ If we are able to describe how ligand properties and solvation phenomena contribute to $\Delta H$ and $\Delta S$ of binding, then we can develop a more quantitative understanding of the chelate effect as it relates to the enhanced stability of chelated complexes. The ITC results for diphos, when compared to ITC results for PPh$_3$ binding to PdCl$_2$(MeCN)$_2$, contradict this notion of the chelate effect. The $\Delta H$ for the binding of the first diphos ligand is twice as large in magnitude as it is for binding the first PPh$_3$ ligand, while the $\Delta G$ values (and therefore, $K$) for both ligands for both binding steps are nearly identical. It is tempting to attribute this factor of two to the simple fact that the bidentate ligand has two P atoms compared to the one P atom of the analogous monodentate ligand, but the results for our bidentate N-N ligands dispels this notion. The $\Delta H$ values for bpy...
and opd are not twice that of the monodentate py ligand, despite the fact that two N atoms coordinate to the Pd center for the two bidentate ligands. Additionally, extensive computational research in the field of monodentate and bidentate ligand energetics has shown that binding of a wide range of P, P-P, and P-N ligands to model substrates (most notably, PdCl₂) can vary from ligand to ligand and is dependent on the functional groups attached to the donor atoms. The overwhelmingly large, negative ΔS₁ value that results for diphos appears to be confusing in light of the chelate effect. Zhang and Breslow studied the binding of ditopic substrates to cyclodextrins in water and calorimetrically determined that chelated complexes were dominated by enthalpic effects (i.e. improved, or more favorable solvation) that compensated for unfavorable entropic contributions, demonstrating that the chelate effect need not be entropically-controlled.

While surveying the literature, Martell considered the number, arrangement, and size of chelate rings (i.e. the form the ligand takes upon chelation) as well as changes of solvation on complex formation to be the most important entropic contributions to the chelate effect. Myers later posited that the entropies of solvation of both the ligand and the final complex, especially larger complexes, were also important entropic contributions via gas phase calculations and complied data from the literature. ITC results are observed quantities, rather than intrinsic, meaning other phenomena besides metal-ligand binding contribute to the observed ΔH and ΔS values. The observed entropy includes losses of translational, rotational, and vibrational degrees of freedom, the solvation and desolvation of the solutes (PdCl₂ and ligand), and expulsion of solvent molecules bound to or surrounding the metal center. The addition of two diphos ligands displaces coordinated (and surrounding) solvent molecules from the Pd center,
which increases the entropy, so the other factors are the likely cause of this negative $\Delta S_1$ value. Upon binding diphos (or any ligand) to the metal center, it loses both translational and rotational entropy. The alkyl backbone of diphos (and dpppe) affords it rotational freedom not exhibited by other ligands, especially rigid ones such as bpy, which explains the large decrease in the observed $\Delta S$. Based on its structure, PPh$_3$ does not lose nearly as much rotational entropy upon binding as diphos does, which accounts for the difference in $\Delta S_1$. Martell affirmed this notion and stipulated that tighter binding, which reduces the rotational entropy, actually results in a more exothermic binding (a large, negative enthalpy) to compensate for this entropy penalty.$^{[32]}$ Our ITC results for diphos and dpppe (large, negative entropies compensated by larger, negative enthalpies) agree with this argument. Williams also discussed the contribution of enthalpy to the stability of chelated complexes formed in aqueous solution as a function of temperature and noted that it has a much larger role in the chelate effect than what was originally proposed.$^{[34]}$ Specifically, this favorable enthalpic contribution is attributed to the fact that it is easier to overcome the electrostatic repulsions between donor atoms when they are brought together to bind to the metal center if they are linked as a polydentate ligand, rather than as separate monodentate ligands.

The chelate effect for the bidentate N-N ligands is less dramatic than it is for the P-P ligands, but it follows the trend of being more enthalpically-controlled than entropically-controlled, given that the obtained $\Delta H$ values are similar and greater in magnitude than the respective $T\Delta S$ values. The monodentate ligand py was used as a comparison and, from Table 3.2, only one equivalent was able to bind and exhibited the lowest binding affinity (lowest $K$ value) of all N ligands. This result is unsurprising due
to the chelate effect of the other N-N ligands, yet warrants further discussion. The $\Delta H$ values for bidentate N-N ligands are all more exothermic than monodentate py, consistent with the P-P ligands. All N ligands exhibit entropic penalties on binding, though not as severe as those observed for the P ligands. While the more rigid structures of the N ligands likely do not suffer the same rotational entropy losses as the P ligands, there are entropic losses associated with ligands conforming to the exact geometry of the binding sites.\[35, 36\] The ligand opd has the highest $K$ value, which is attributed to having the least sterically hindered N groups (-NH$_2$) of the tested ligands, while also having the most favorable enthalpic contribution. It is logical that bpy has an affinity less than opd because its N atoms are more sterically hindered. Hancock observed via gas phase studies that increasing basicity of N ligands may also contribute favorably to binding enthalpies and, indeed, the more basic bpy ($pK_b = 9.60$) and opd (9.54) have the highest $K$ values and the smaller entropic penalties (compared to py) while opd also has the most favorable enthalpic contribution when compared to the less basic py ($pK_b = 8.75$).\[37\] Additional evidence of enthalpy contributing a larger role to the chelate effect comes from a DFT study by Davydova et al of the substitution of py in Group 14 complexes in the gas phase by bidentate ligands, namely bpy. They showed that structural trans-cis reorganization of the bpy complex was largely endothermic due to the $\sim$32 kJ/mol necessary to restructure the complex, which subsequently overshadowed the entropic benefit presumed to originate from the chelate effect.\[38\]

The bidentate P-N ligands serve as the bridge to understanding the effect of the P and N donor atoms in their respective roles in the chelate effect. The obtained ITC parameters for each chiral ligand, $(R)$-(S)-PPFA and $(S)$-(R)-PPFA, are close in value
(ΔG and TΔS values agree directly within experimental error) and, in each case, only one ligand binds most likely due to the steric bulk of the ferrocenyl group. The placement of the P and N atoms on the rigid cyclopentadienyl ring is the most logical reason for why the N atoms of the chiral ferrocenyl ligands are able to bind to PdCl₂(MeCN)₂, whereas the rigidity of the phenyl group linking the -PPh₂ and -NH₂ groups of dmap constricts the flexibility and rotation of the entire ligand so only the P atom (i.e. the group that contributes most favorably to ΔH) binds. The most remarkable trait of these chiral P-N ligands is that they mirror the stronger chelate effect of P-P ligands, that is, they are enthalpically-controlled with ΔH values closer to the ones obtained for the bidentate P-P ligands rather than the bidentate N-N ligands. Both chiral ligands have ΔH values nearly twice as large in magnitude as their respective TΔS values while having virtually identical ΔG values. Thermodynamically, the presence of one P atom emphasizes the favorable contribution to ΔH via chelation, which is only compounded upon linking two P atoms together on the same ligand. This evidence reveals a trend for bidentate ligands contributing favorably to binding enthalpy increasing in the order of N-N, P-N, and P-P ligands.

3.3.6 Role of Enthalpy-Entropy Compensation and Solvent Reorganization

There is much confusion in the literature regarding the nature of enthalpy-entropy compensation, primarily because there are several definitions, which requires a thorough understanding of the system in question. Grunwald and Steel proposed a model of solvent reorganization and is the most applicable model to determine if any enthalpy-entropy compensation exists in our systems. Briefly, the binding thermodynamics are
partitioned into nominal thermodynamics (binding of the solvated ligands and solvated Pd centers) and environmental thermodynamics (effects of solvent molecules that participate in solvation and desolvation of species during binding). For dilute solutions (treating the reactants, metal center and ligand in our case, as solutes, not pure fluids), $\Delta G$ for the environmental effects (i.e. solvent reorganization, the exchange of solvent molecules between the bulk solvent and the solvation shells of solutes) is equal to zero, meaning that $\Delta H$ and $\Delta S$ for the environmental effect may exhibit enthalpy-entropy compensation.\(^{[39]}\) Thus, if we can demonstrate that this enthalpy-entropy compensation exists for bidentate ligands, we can show that the stability of the chelated complexes, in terms of enthalpy and entropy, depends on solvent reorganization. Figure 3.16 shows the correlation between $\Delta H_1$ and $\Delta S_1$ for the chelating bidentate ligands only. The $\Delta H_2$ and $\Delta S_2$ values for diphos are not included to keep the reactions identical, that is, just one equivalent binds to the Pd center. According to Grunwald and Steel, the closer the slope of the line is to the experimental temperature, the stronger the effects of solvent reorganization in enthalpy-entropy compensation.\(^{[39]}\) The slope of the fit is 304 K, only a 2% difference from the reaction temperature (298 K), indicating that solvent reorganization contributes greatly to the observed $\Delta H_1$ and $\Delta S_1$ values. In a review of enthalpy-entropy compensation, Liu and Guo addressed the concerns of correlations between enthalpy and entropy being mathematical artifacts by determining that simple inclusion of the experimental errors or confidence intervals on the correlation plot demonstrates the validity of the fit.\(^{[40]}\) Additionally, there have been several concerns of high correlation between thermodynamic values obtained during Arrhenius and van’t Hoff analyses because there is no external measurement to double check the validity of
Figure 3.16. Enthalpy-entropy compensation among chelated complexes. The $\Delta H_1$ and $\Delta S_1$ values, and respective errors, are taken directly from Table 3.2. The slope of the linear fit is 304 K, only a 2% difference from the experimental temperature, 298 K, meaning that there is a strong effect of solvent reorganization on the observed enthalpies and entropies of binding ($R^2 = 0.95$).
the parameters (i.e. the $K$ values obtained from a van’t Hoff analysis are used to determine $\Delta H$ values).\textsuperscript{[41, 42]} The utility of ITC is critical to the enthalpy-entropy compensation analysis because the direct measure of the heat evolution of the binding equilibria ensures that the enthalpy values obtained from calorimetric measurements do not have a strong correlation with the $K$ values that come from fitting the ITC data. The vertical error bars in Figure 3.16 are small due to the nW-level sensitivity of the ITC, ensuring that the $\Delta H$ values are accurate. Figure 3.16 is also a visual aid in demonstrating how the P donor atoms of the bidentate ligands contribute more favorably to the binding enthalpies than the N donor atoms do, but it also shows that solvent reorganization is a stronger contributor to the binding enthalpies of bidentate P-P ligands than it is for bidentate N-N ligands. This enthalpy-entropy compensation shows that the chelate effect is not the dominant factor for the stability of the chelated complexes formed in this study.

3.4 Conclusions

We presented a detailed analysis of the binding thermodynamics of bidentate ligands to PdCl$_2$(MeCN)$_2$ and the resulting implications for understanding the chelate effect in terms of the observed $\Delta H$ and $\Delta S$ values. We observed the bidentate N-N ligands formed cis-chelates with PdCl$_2$(MeCN)$_2$ and had higher $K$ values than the corresponding monodentate ligand, py. The increased basicity of the bidentate N-N ligands contributed favorably to the measured binding enthalpies when compared to the monodentate py. Our ITC results for bidentate P-P ligands demonstrated that enthalpy can actually be the dominant factor regarding the stability of chelated complexes when compared to analogous monodentate complexes. Losses of translational and rotational entropies for
bidentate P-P ligands upon binding to PdCl₂(MeCN)₂ contributed unfavorably to the binding entropies. Our study of mixed bidentate P-N ligands revealed that the presence of P groups on bidentate ligands contributed more favorably to binding enthalpies than N groups. Additionally, we observed enthalpy-entropy compensation for the chelated complexes, which we attributed to solvent reorganization. We conclude that favorable contributions to binding enthalpy (and, subsequently, the chelate effect) increases in order for N-N, P-N, and P-P bidentate ligands. Overall, we found that chelation was more dependent on favorable enthalpic contributions than on entropic contributions, due to enthalpy-entropy compensation for the ligands tested.
3.5 References


Chapter 4

The Effects of Solvent on the Structure of Wilkinson’s Catalyst and the Subsequent Effects on Homogeneous Hydrogenation of Terminal Olefins

4.1 Introduction

As discussed in Chapter 1, Wilkinson’s catalyst is a powerful hydrogenation catalyst, but has numerous uses in a variety of other homogeneous catalytic reactions. Wilkinson’s catalyst has been used for polymerization reactions such as the formation of poly(methyl methacrylate) (PMMA) and is capable of 100% conversion of methyl methacrylate in THF at 60°C after 24 h without deactivation of the catalyst. Another possible use is in hydroboration reactions of a variety of substrates, including olefins, alkynes, and silyl ethers using catecholborane (HBO₂C₆H₄) as the hydroborating agent. Wilkinson’s catalyst is also a versatile cycloaddition catalyst than can facilitate inter- and intramolecular additions. Witulski and Alayrac used Wilkinson’s catalyst in the inter- and intramolecular cycloadditions of diynes and terminal alkynes to form carbazoles and were able to achieve high yields (71-98%, depending on the substrates) within 24 h and, in some cases, at room temperature. Grigg et al also studied intermolecular cycloadditions between diynes and alkynes using Wilkinson’s catalyst and noted that polar solvents accelerated the reaction rates which they attributed to the potential loss of the chloride ligand of one of the catalytic intermediates in order to accommodate the steric bulk of the alkynyl substituents. Bedford et al used Wilkinson’s catalyst in conjunction with Cs₂CO₃ as a co-catalyst for the intermolecular ortho-selective arylation of phenols and achieved good to excellent yields using toluene as a solvent. Another
pertinent example of the applicability of Wilkinson’s catalyst to a wide range of systems is the cyclization of aromatic imines (i.e. C-H activation to form C-C bonds using heterocyclic substrates). These types of reactions frequently require higher temperatures, typically 125-160°C, though the presence of Wilkinson’s catalyst ensures high selectivity in activating the desired C-H bonds of the aromatic imines.\textsuperscript{[7-10]}

While Wilkinson’s catalyst has a variety of uses, its complete behavior in solution is not always addressed in kinetic studies, which can often lead to confusion regarding its role in a particular catalytic cycle. The monomer, RhCl(PPh\textsubscript{3})\textsubscript{3}, is known to convert to an electronically unsaturated intermediate that is the most active catalytic species (compared to the monomer and the chloro-bridged dimer, [RhCl(PPh\textsubscript{3})\textsubscript{2}]\textsubscript{2}, that forms in solution) toward molecular hydrogen (in the case of olefin hydrogenation) due to dissociation of one of the PPh\textsubscript{3} ligands.\textsuperscript{[11]} The monomer-dimer equilbria occurs through this intermediate, RhCl(PPh\textsubscript{3})\textsubscript{2}, and can be reversed to favor the original monomer if the catalyst is exposed to an excess of PPh\textsubscript{3} in solution (see Figure 4.1).\textsuperscript{[12]} Halpern and Wong spectrophotometrically determined that the 14-electron intermediate is over 10\textsuperscript{4} times more reactive toward molecular hydrogen than the monomer in benzene.\textsuperscript{[13]} In particular, the monomer-dimer behavior is relevant for the synthesis of supported organometallic catalysts in which Wilkinson’s catalyst is used as the precursor for the grafting process because the catalytically inactive dimer may be grafted onto the surface instead of the most active species. In order to ensure that the most active species is present for a homogenous catalytic reaction or for the synthesis of a supported organometallic catalyst, it is imperative to understand the behavior of the organometallic precursor in solution such that the most appropriate solvent is chosen for a particular
Figure 4.1. Overall reaction of the monomer-dimer equilibria observed for Wilkinson’s catalyst in solution. One of the PPh₃ ligands from the monomer dissociates to form the 14-electron intermediate, RhCl(PPh₃)₂, which reacts with another intermediate to form the chloro-bridged dimer.
process. This study examines the structural changes of Wilkinson’s catalyst upon dissolution in a variety of solvents using $^{31}$P NMR, supplemented with a thermodynamic analysis of enthalpies of dissolution of Wilkinson’s catalyst in different solvents, and the activity of each system for the hydrogenation of terminal olefins, 1-heptene and 1-octene, in a differential batch reactor at 0°C in order to establish relationships between the Rh species present, the inherent properties of the solvents, and the turnover frequencies (TOFs) for the hydrogenation reactions.

4.2 Experimental

Wilkinson’s catalyst was obtained from Sigma. Benzene, pyridine, tetrahydrofuran (THF), and toluene were obtained from EMD while ethanol was obtained from Koptec. All solvents were used as received.

$^{31}$P NMR samples were run on a Bruker AV-360 at room temperature with proton decoupling and were prepared under an inert atmosphere. Wilkinson’s catalyst was dissolved fully in each deuterated solvent. All deuterated versions of the reaction solvents were obtained from Cambridge Isotope Laboratories. Each sample was run for 128 scans in a J. Young NMR tube and compared to known spectra of Wilkinson’s catalyst in order to determine the Rh species present.

Solution calorimetry experiments were performed in a TAM III microcalorimeter (TA Instruments) at 25°C. Samples of Wilkinson’s catalyst were placed into glass ampoules and sealed with epoxy to prevent premature mixing of solvent and catalyst. The ampoules were then immersed in 25 or 100 mL of the desired solvent in the reaction cell and stirred at 600 rpm. Ampoules were then broken and the catalyst (acting as a solute)
was allowed to mix with the solvent while monitoring the heat flow. An electronic heat pulse was applied to the reaction cell before and after dissolution to calibrate the heat capacity in each instance. An empty ampoule was broken to account for the heat evolved due to breaking the ampoule in each experiment. The total heat evolved during each experiment was obtained using the Analyze Experiment function in the SolCal v1.2 software (TA Instruments). Each heat value was then corrected for the blank experiment and the normalized to the total amount of moles of solute dissolved to calculate the enthalpy of dissolution. For each solvent tested, the reaction mixture was examined immediately after the experiment to ensure that all of the catalyst was dissolved completely.

Olefin hydrogenation experiments were conducted on a Schlenk line in a three-necked 50 mL flask in an ice bath at 0°C. Prior to each experiment, the flask was charged with 37 mg of catalyst and a magnetic stir bar (40 mmol) and then purged for 1 h and then filled with inert gas. 20 mL of solvent (2 mM concentration of catalyst) was injected through a septum and allowed to dissolve the catalyst with vigorous mixing. Once dissolved, hydrogen (99.999%) was admitted to the flask in direct contact with the reaction mixture and allowed to equilibrate for 1 h in order to ensure that all active Rh species were hydrogenated (i.e. mass-transfer was not limiting, nor did differences in Henry’s constants at 0°C among the tested solvents limit the reaction). Hydrogen was admitted to the reactor for the duration of the reaction (5 h). Olefin was then injected to achieve an initial concentration of 1 mM (2.84 mL of 1-heptene, 3 mL 1-octene). Every 0.5 h, 200 μL of the reaction mixture was withdrawn via syringe and added to 25 μL of \textit{n}-dodecane (Alfa Aesar) for use as an internal standard in GC analysis. Samples were
analyzed using an Agilent 7890A gas chromatograph equipped with an FID detector and HP-5 column. Pure samples of the reactants and products were calibrated using the same temperature profile ($T = 30^\circ$C for 5 min, ramp of 120$^\circ$C/min for 1 min, $T = 150^\circ$C for 2 min) to determine their respective retention times and response factors. Samples of the reaction mixtures were analyzed using the same temperature profile to determine the total numbers of mmol of the products and reactants as functions of time in order to calculate TOFs.

### 4.3 Results and Discussion

#### 4.3.1 Elucidation of Structural Changes of Wilkinson’s Catalyst upon Solvation via $^{31}$P NMR Spectroscopy

Figure 4.2 shows the $^{31}$P NMR spectra of Wilkinson’s catalyst in the hydrogenation reaction solvents: benzene, benzene-ethanol (a 1:1 mixture by volume), pyridine, THF, and toluene. With the exception of pyridine, both the monomer and dimer were present in the reaction solvents, along with free $\text{PPh}_3$ and oxidized triphenylphosphine, $\text{OPPh}_3$, which is a common contaminant in commercially-made Wilkinson’s catalyst.[14-16] The peaks attributed to the monomer are the doublet of triplets appearing from $\delta = 45-49$ ppm and the doublet of doublets ranging from $\delta = 29-32$ ppm, depending on the solvent (denoted as “b” in Figure 4.2). The peaks attributed to the dimer are the doublet of singlets ranging from $\delta = 49-54$ ppm, again depending on the solvent. The $^{31}$P NMR peaks of Wilkinson’s catalyst in benzene-ethanol are worthy of clarification. The peaks in the doublet of triplets are significantly broader in benzene-
Figure 4.2. $^{31}$P NMR spectra of Wilkinson’s catalyst in different solvents. Each solvent is listed directly above its respective spectrum. The dimer resonates as a doublet of singlets and is marked (a) in the toluene spectrum. The monomer resonates as a doublet of triplets and a doublet of doublets, each of which is marked (b) in the toluene spectrum. The sharp singlets indicate the presence of OPPh$_3$, which is also marked for clarity in the toluene spectrum.
ethanol than in the other three solvents (benzene, THF, and toluene) that contain the monomer. Additionally, the peak for OPPh$_3$ appears directly in the middle of the doublet of doublets (also indicative of the monomer), whereas these peaks are isolated from one another in the other solvents. These changes are most likely due to the presence of the ethanol (compared to the spectrum in pure benzene). The only solvent that does not contain the monomer (and, therefore, the catalytically active 14-electron intermediate) is pyridine, which has free OPPh$_3$ and a doublet of singlets around $\delta = 33$ ppm. In a previous study, Heaton et al examined the reactions of Wilkinson’s catalyst with pyridine and observed the same NMR signal and were unable to assign it a complete structure, though additional $^{31}$P NMR experiments involving the cis and trans isomers of RhCl(pyridine)$_2$(PPh$_3$)$_2$ demonstrated that these did not produce the observed doublet near $\delta = 33$ ppm.$^{[17]}$

4.3.2 Determination of the Thermodynamic Parameters of Catalyst Dissolution via Solution Calorimetry

Wilkinson’s catalyst was dissolved in the five reaction solvents at 25°C in order to measure the molar enthalpy of dissolution in each solvent (Table 4.1). From the results, the solvent with the highest enthalpy of dissolution is THF, which also promotes dimerization as seen by $^{31}$P NMR. The next highest enthalpy of dissolution is attributed to an equal volume mixture of benzene and ethanol, which was reported to inhibit the dissociation of the PPh$_3$ ligands and is reflected in the $^{31}$P NMR spectrum due to the lack of peaks that are characteristic of the dimer, though Figure 4.2 refutes this claim.$^{[18]}$ Among the lower enthalpies of dissolution is pyridine, which was originally reported to
coordinate strongly to the Rh center of the catalyst, thus completely inhibiting hydrogenation.\textsuperscript{[19]} Toluene has the second-lowest enthalpy of dissolution, which is interesting considering that it contains the same Rh and P species as benzene, benzene-ethanol, and THF, in accordance with Figure 4.2. Another factor to consider is the donor number, $DN$, of each solvent (see Table 4.1). The donor number is an empirical measure of a solvent’s ability to act as a Lewis base when interacting with a solute (Wilkinson’s catalyst, in this case) and is determined by measuring the heat evolution for the 1:1 formation between SbCl$_5$ and the chosen solvent, all diluted in 1,2-dichloroethane (DCE).\textsuperscript{[20]} For the tested solvents, benzene and toluene have the lowest $DN$ and two of the lowest enthalpies of dissolution. Both ethanol and THF have much higher $DN$ values and also have the highest enthalpies of dissolution. Interestingly, pyridine has the highest $DN$, yet it has the lowest enthalpy of dissolution. As it was previously noted, pyridine is thought to coordinate very strongly to the catalyst, meaning that the removal of pyridine ligands from the Rh center is likely thermodynamically unfavorable. This would explain the absence of both monomer and dimer in the NMR spectra for pyridine, though it also shows that there is no simple relationship the enthalpy of dissolution and the resulting catalytic structures. While these results do not provide specifics regarding catalyst structures, they do help to understand some of the features observed in the $^{31}$P NMR spectra in pyridine.

4.3.3 Comparison of Turnover Frequencies for the Hydrogenation of Terminal Olefins by Wilkinson’s Catalyst in Various Solvents
Table 4.1. Enthalpies of dissolution of Wilkinson’s catalyst in various solvents at 25°C determined by solution calorimetry. The donor number, $DN$, is given for each solvent, noting that the given value for benzene-ethanol is an average for the two solvents.\textsuperscript{[21]} References for $DN$ values are provided.\textsuperscript{[22-25]}

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$\Delta H$ (MJ/mol)</th>
<th>$DN$ (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>-0.13</td>
<td>0.4</td>
</tr>
<tr>
<td>Benzene-Ethanol</td>
<td>-1.14</td>
<td>38.9</td>
</tr>
<tr>
<td>Pyridine</td>
<td>-0.08</td>
<td>138.5</td>
</tr>
<tr>
<td>THF</td>
<td>-1.86</td>
<td>83.7</td>
</tr>
<tr>
<td>Toluene</td>
<td>-0.11</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Kinetic experiments from a differential batch reactor under constant flow of hydrogen at 0°C were compared under identical olefin and catalyst concentrations and analyzed by GC in order to determine TOFs of olefin hydrogenation in different solvents. Kinetic results for 1-heptene and 1-octene hydrogenation are presented in Figures 4.3 and 4.4, respectively. From the given plots of product concentration as a function of time, it is seen that the conditions of the differential reactor are satisfied, as the rates of hydrogenation are linear (i.e. constant during the course of the reaction). Table 4.2 displays the calculated TOFs for each solvent in the two hydrogenation reactions. The results for both sets of reactions follow similar patterns. The hydrogenation reactions were barely active in THF and completely inactive in pyridine, as Osborn et al originally noted for pyridine. The most active solvent for 1-octene hydrogenation is benzene and the most active solvent for 1-heptene hydrogenation is the benzene-ethanol mixture. However, it should be noted that the hydrogenation reactions in benzene-ethanol mixtures are known to allow isomerizations of the olefinic substrate as well as hydrogenation of the benzene solvent molecule and that extraneous product peaks appeared in the GC analysis. As such, the TOFs given are calculated with respect to total reactant conversion in order to establish the best possible comparison.

With the known $^{31}$P NMR spectra, it is worth considering that benzene, benzene-ethanol, THF, and toluene all have the exact same phosphorus species in solution in oxygen-free environments, yet there is a marked decrease in catalyst activity from benzene, benzene-ethanol, and toluene to THF. The predominating theory, and the one that Wilkinson’s group originally proposed, is that the solvent molecules coordinate to the Rh center of the catalyst upon solvation. THF has a $DN$ of 83.7 kJ/mol and is two
Figure 4.3. Turnover number (TON) for the hydrogenation of 1-heptene in a differential batch reactor at 0°C using Wilkinson’s catalyst in different solvents. All reactions were conducted with 20 mL of anhydrous solvent with 2 mM of Wilkinson’s catalyst using an initial 1-heptene concentration of 1 M. The fits for each data set are shown and the solvents have the following symbols: benzene (circles), benzene-ethanol (squares), pyridine (diamonds), THF, (open circles), and toluene (open squares).
Figure 4.4. Turnover number (TON) for the hydrogenation of 1-octene in a differential batch reactor at 0°C using Wilkinson’s catalyst in different solvents. All reactions were conducted with 20 mL of anhydrous solvent with 2 mM of Wilkinson’s catalyst using an initial 1-octene concentration of 1 M. The fits for each data set are shown and the solvents have the following symbols: benzene (circles), benzene-ethanol (squares), pyridine (diamonds), THF, (open circles), and toluene (open squares).
Table 4.2. Turnover frequencies (TOFs) for 1-heptene and 1-octene hydrogenation using Wilkinson’s catalyst in different solvents at 0°C. Hydrogen solubilities for each solvent are listed, noting that the value for benzene-ethanol is for ethanol only. All values are taken from the literature.[28-30]

<table>
<thead>
<tr>
<th>Solvent</th>
<th>1-Heptene</th>
<th>1-Octene</th>
<th>H₂ Solubility (mM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>5.79</td>
<td>7.63</td>
<td>2.93</td>
</tr>
<tr>
<td>Benzene-Ethanol</td>
<td>9.71</td>
<td>6.00</td>
<td>3.97</td>
</tr>
<tr>
<td>Pyridine</td>
<td>0.00</td>
<td>0.00</td>
<td>2.00</td>
</tr>
<tr>
<td>THF</td>
<td>0.47</td>
<td>0.70</td>
<td>3.50</td>
</tr>
<tr>
<td>Toluene</td>
<td>3.57</td>
<td>5.05</td>
<td>2.95</td>
</tr>
</tbody>
</table>
orders of magnitude stronger as a donor solvent than either benzene or toluene ($DN = 0.4$ kJ/mol for both in Table 4.1). As discussed previously, the dissociation of a PPh$_3$ ligand is critical to the formation of the 14-electron intermediate such that this electronically unsaturated species is subsequently able to oxidatively add the hydrogen (or bind the olefinic substrate). If the chosen solvent is more likely to donate electrons, as is the case with the two lone pairs on the oxygen atom in THF, then solvent molecules will compete with either the olefin substrate or hydrogen in order to bind with the 14-electron intermediate, explaining the large difference in TOFs from benzene, benzene-ethanol, and toluene to THF in both hydrogenation reactions, despite containing the same catalytic species in each solvent system. While there are critics of the $DN$ method in terms of how the experimental values are obtained and applied, it is a simple way to address the glaring discrepancy in TOF values between the poorly-donating benzene and toluene and the strongly-donating THF.$^{[31]}$

4.4 Conclusions

The kinetics obtained for the hydrogenation of terminal olefins in a differential batch reactor using Wilkinson’s catalyst in different solvents revealed that the electronic properties of the solvent affected the activity of the reaction. $^{31}$P NMR further revealed that pyridine contained no active Rh species (i.e. the monomer) for hydrogenation, which kinetic experiments revealed to be completely inactive. Pyridine had the smallest enthalpy of dissolution for Wilkinson’s catalyst, which suggests that the pyridine molecules are not easily removed from the Rh centers in solution, in agreement with its large $DN$ value and inactivity for hydrogenation. The other four solvent systems,
benzene, benzene-ethanol, THF, and toluene, all contained the catalytically active monomer and exhibited various degrees in activity for the hydrogenation of terminal olefins. THF was the least active solvent for hydrogenation, which was attributed to its large $DN$, indicating that THF molecules were more likely to coordinate to the Rh species in solution, inhibiting the catalysis. Benzene and benzene-ethanol were the most active solvents for olefin hydrogenation, while toluene, similar to benzene in terms of molecular structure and $DN$ value, was less active than the aforementioned solvents.
4.5 References


Chapter 5

Structural Elucidation of Supported Rh Complexes Derived from Wilkinson’s Catalyst Immobilized on Functionalized SBA-15 and Their Catalytic Performance for Carbon-Heteroatom (S, O) Bond Formation

5.1 Introduction

The immobilization of catalytically active species, i.e. organometallic complexes, onto a solid support to produce a molecular heterogeneous catalyst is one potential solution to issues associated with homogeneous catalysis, such as catalyst recyclability and separation from the product mixture.\textsuperscript{[1-3]} The merits of heterogeneous catalysts are derived not only from their ease of separation from reaction media, but also their unique activity derived from their site-isolation and the structure of the catalytically active sites. Functionalization of supports via organic modification provides their surfaces with many favorable properties for various practical applications in gas storage, separation, catalysis, and drug delivery. The immobilization of organometallic complexes through covalent bond formation with functional groups on supports is the most commonly employed method to form heterogenized organometallic catalysts that are applicable for a variety of catalytic chemistries including hydrogenation,\textsuperscript{[4-6]} hydroformylation,\textsuperscript{[7-10]} and hydrosilylation.\textsuperscript{[11, 12]} The chemical bonding between metal complexes and functional groups of the support maintains the isolated nature of metal complexes at dilute complex surface densities, which can influence the catalytic performance in a manner that the analogous homogeneous complex does not exhibit in solution.\textsuperscript{[13-18]} These grafted structures not only reduce metal leaching from the support and subsequent metal
contamination of the products, but in some examples provide an enhancement in activity and selectivity relative to the analogous homogeneous complex.\textsuperscript{[4-10]}

Wilkinson’s catalyst, RhCl(PPh\textsubscript{3})\textsubscript{3}, is one of the most well-known and used homogeneous hydrogenation catalysts in organic synthesis and the production of fine chemicals.\textsuperscript{[19-25]} It has also been immobilized onto supports using various functional groups to form heterogenized catalysts which have shown high activity and stability during catalysis.\textsuperscript{[6, 26-33]} In spite of tremendous effort dedicated to the immobilization of homogeneous complexes over the last two decades,\textsuperscript{[34]} investigations of the local structures of RhCl(PPh\textsubscript{3})\textsubscript{3} upon immobilization on surface-functionalized supports are scarce and there has been no conclusive study to date. Possible structures of immobilized Rh species were proposed previously in the literature,\textsuperscript{[35, 36]} but these studies did not adequately combine spectroscopic characterization(s) of the heterogeneous species that probe both the grafted metal center and local ligand environment. Additionally, the most thorough study to date\textsuperscript{[35]} did not perform catalytic experiments to correlate kinetic behavior with the structure of the grafted organometallic catalyst (i.e. a structure-function relationship). We aim to determine the local structures of immobilized analogs of Wilkinson’s catalyst through rigorous spectroscopic characterization in order to establish structure-function relationships, such that we may use the kinetic and spectroscopic results to assess the effectiveness of each analog, and how to tune synthetic procedures for future studies.

Recently, we reported the highly regio- and stereoselective hydrothiolation of alkynes with thiols to produce valuable vinyl sulfides catalyzed by immobilized Rh complexes with high activity and stability (Figure 5.1).\textsuperscript{[37]} We found the regio- and
Figure 5.1. Product distribution for the hydrothiolation of phenylacetylene and thiophenol over different Rh catalysts. Reaction conditions: 0.5 mmol phenylacetylene, 0.55 mmol thiophenol, 50 mg catalyst (4.5 µmol Rh), 2 mL DCE, room temperature and a reaction time of 45 min for RhCl(PPh₃)₃ and 20 h for the immobilized catalysts.
stereoselectivity for vinyl sulfides is highly dependent on the immobilized Rh complexes derived from the reaction of RhCl(PPh₃)₃ with surface-functionalized SBA-15 bearing different functional groups: primary–amine, secondary–amine, and diphenylphosphine. We believe the local structure of the immobilized Rh complexes is primarily responsible for such differences in stereoselectivity, but did not pursue the origin of these differences in stereoselectivity in our previous work, which motivated us to determine their exact structure with an in-depth characterization study. We extend the use of such immobilized Rh complexes to C-O bond formation chemistry – the addition of alkynes with sulfonic acids (hydrosulfonation) to produce valuable vinyl sulfonates.

In this study, we elucidate the local structure of immobilized Rh complexes, derived from the reaction of Wilkinson’s catalyst with surface-functionalized SBA-15 by systematic characterization using x-ray diffraction (XRD), physical adsorption, high-resolution transmission electron microscopy (HR-TEM), x-ray photoelectron spectroscopy (XPS), multi-nuclear (¹³C,²⁹Si, and ³¹P) solid-state nuclear magnetic resonance (NMR) spectroscopy, ³¹P{¹H} HETCOR (heteronuclear correlation) 2D NMR, and Rh K-edge extended x-ray absorption fine structure (EXAFS) spectroscopy. Such heterogeneously immobilized Rh complexes were further applied for the addition of alkynes with sulfonic acids to produce valuable vinyl sulfonates, demonstrating high activity, excellent regio- and stereoselectivity, broad substrate versatility, and significant stability.

5.2 Experimental

5.2.1 Materials
All operations were performed under an inert atmosphere either in a glovebox or on a Schlenk line. Unless otherwise noted, all chemicals were purchased from Sigma-Aldrich and used as received without further purification. Wilkinson’s catalyst was purchased from Strem and P123 was obtained from BASF.

5.2.2 Preparation of SBA-15

SBA-15 was synthesized according to a published procedure.\textsuperscript{[38]} In a typical run, 4.0 g of P123 (PEO\textsubscript{20}PPO\textsubscript{70}PEO\textsubscript{20}; PEO = poly(ethyleneoxide); PPO = poly(propyleneoxide)) tri-block co-polymer was dissolved in 30 mL of water, followed by the addition of 120 mL HCl (2 M). After stirring at room temperature until the P123 was completely dissolved, 8.5 g of tetraethylorthosilicate (TEOS) was added. After stirring at 35°C for 20 h, the mixture was transferred to an autoclave for condensation at 100°C for 24 h. The as-synthesized samples were collected by filtration and washed with water and ethanol thoroughly. The solid powder was calcined at 550°C for 12 h to remove the surfactants.

5.2.3 Preparation of Cl-SBA-15

The calcined SBA-15 silica (2.0 g) was evacuated at 200°C for 6 h under vacuum, and then refluxed in an anhydrous toluene solution of 3-chloropropyltriethoxysilane (5.33 mL) at 120°C for 24 h under an inert atmosphere. The SBA-15 was filtered and washed with anhydrous dichloromethane and then dried under vacuum for 24 h. The solid powder was labeled as Cl-SBA-15 and stored under an inert atmosphere.
5.2.4 Preparation of N-SBA-15

The calcined SBA-15 silica (1.0 g) was evacuated at 200°C for 6 h under vacuum, and then refluxed in an anhydrous toluene solution of 3-aminopropyltriethoxysilane (APTES) (1.0 mL) at 120°C for 24 h under an inert atmosphere. The SBA-15 was filtered and washed with anhydrous dichloromethane and then dried under vacuum for 24 h. The solid powder was labeled as N-SBA-15 and stored under an inert atmosphere.

5.2.5 Preparation of 2N-SBA-15

The calcined SBA-15 silica (1.0 g) was evacuated at 200°C for 6 h under vacuum, and then refluxed in an anhydrous toluene solution of [3-(2-aminoethylamino)-propyl]triethoxysilane (AEPTES) (1.0 mL) at 120°C for 24 h under an inert atmosphere. The SBA-15 was filtered and washed with anhydrous dichloromethane and then dried under vacuum for 24 h. The solid powder was labeled as 2N-SBA-15 and stored under an inert atmosphere.

5.2.6 Preparation of P-SBA-15

A THF solution of lithium diphenylphosphide (16 mL, 0.5 M) was added to a solid sample of Cl-SBA-15 (1.5 g) under an inert atmosphere. The resulting mixture was stirred at room temperature for 20 h. The solid was filtered and washed with anhydrous dichloromethane and then dried under vacuum for 24 h. The solid powder was labeled as P-SBA-15 and stored under an inert atmosphere.

5.2.7 Preparation of Rh-N-SBA-15
An anhydrous toluene solution of Wilkinson’s catalyst (0.10 g, 0.11 mmol) was added to N-SBA-15 (1.0 g) under an inert atmosphere. The resulting mixture was refluxed for 3 h. The solid was filtered and washed with anhydrous toluene and then dried under vacuum for 24 h. The solid powder was labeled as Rh-N-SBA-15 and stored under an inert atmosphere.

5.2.8 Preparation of Rh-2N-SBA-15

An anhydrous toluene solution of Wilkinson’s catalyst (0.10 g, 0.11 mmol) was added to 2N-SBA-15 (1.0 g) under an inert atmosphere. The resulting mixture was refluxed for 3 h. The solid was filtered and washed with anhydrous toluene and then dried under vacuum for 24 h. The solid powder was labeled as Rh-2N-SBA-15 and stored under an inert atmosphere.

5.2.9 Preparation of Rh-P-SBA-15

An anhydrous dichloromethane solution of Wilkinson’s catalyst (0.15 g, 0.16 mmol) was added to P-SBA-15 (1.5 g) under an inert atmosphere. The resulting mixture was stirred at room temperature for 2 days. The solid was filtered and washed with anhydrous dichloromethane and then dried under vacuum for 24 h. The solid powder was labeled as Rh-P-SBA-15 and stored under an inert atmosphere. Figure 5.2 summarizes the synthesis of the functionalized SBA-15 samples as well as the immobilized Rh complexes.
**Figure 5.2.** Preparation of supported Rh complexes on surface-functionalized SBA-15.
5.2.10 Heterogeneous Hydriothiolation Reactions of Alkynes with Thiols

In a typical catalytic reaction, 50 mg (4.5 μmol Rh) of supported catalyst and 1,2-dichloroethane were combined in a 10 mL Schlenk tube equipped with a magnetic stir bar. Alkyne (0.5 mmol), thiol (0.55 mmol), and CH₂Br₂ (0.5 mmol) as an internal standard were then added under an inert atmosphere. The mixture was stirred at room temperature while aliphatic alkynes and thiols were stirred in an oil bath at 60°C. The progress of the reaction was monitored by ¹H NMR.

5.2.11 Homogeneous Hydrothiolation Reactions with Added Primary and Secondary Amines

In a typical catalytic reaction, 4.5 μmol of Wilkinson’s catalyst and 1,2-dichloroethane were combined in a 10 mL Schlenk tube equipped with a magnetic stir bar. Phenylacetylene (0.5 mmol), thiophenol (0.55mmol), CH₂Br₂ (0.5 mmol as the internal standard) and 2 equivalents of propylamine (9 μmol) or N-ethylethylenediamine (9 μmol) relative to the amount of Wilkinson’s catalyst were added under an inert atmosphere. The reaction was carried out at room temperature and the progress of the reaction was monitored by ¹H NMR.

5.2.12 Heterogeneous Hydrosulfonation Reactions of Alkynes with Sulfonic Acids

In a typical catalytic reaction, 50 mg (4.5 μmol Rh) of supported catalyst and 1,2-dichloroethane were combined in a 10 mL Schlenk tube equipped with a magnetic stir bar. Alkyne (1.0 mmol), sulfonic acid (0.50 mmol), and CH₂Br₂ (0.5 mmol) as an internal
standard were then added under an inert atmosphere. The Schlenk tube was immersed in a 70°C oil bath. The progress of the reaction was monitored by $^1\text{H}$ NMR.

5.2.13 NMR Characterization of Hydrothiolation and Hydrosulfonation Reactions

$^1\text{H}$ and $^{13}\text{C}$ NMR spectra were collected on a Bruker Advance 300 or 400 NMR spectrometer in CDCl$_3$ at room temperature. $^1\text{H}$ and $^{13}\text{C}$ NMR chemical shifts are reported in ppm relative to either the residual solvent peak ($^{13}\text{C}$) ($\delta = 77.00$ ppm) or TMS ($^1\text{H}$) ($\delta = 0.0$ ppm) as an internal standard. Data for $^1\text{H}$ NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. Regioselectivity and stereoselectivity of the product was determined by NMR analysis of the crude product.

5.2.14 Physisorption of N$_2$ on SBA-15 and Functionalized SBA-15 Surfaces

Nitrogen adsorption was performed on a Micromeritics ASAP-2020 analyzer at 77 K. Each sample (150 mg) was degassed at 473 K for 3 h before an adsorption measurement. Surface area calculations were conducted using the BET (Brunauer-Emmett-Teller) method,$^{[39]}$ and the pore diameter calculations were conducted using the BJH (Barrett-Joyner-Halenda) method.$^{[40]}$

5.2.15 Solid-State NMR Characterization

$^{13}\text{C}$, $^{29}\text{Si}$ and $^{31}\text{P}$ solid-state MAS (magic angle spinning) NMR spectra (MAS rate: 5 kHz) were recorded with a Chemagnetics Bruker AV-300 spectrometer operating at 75.5, 59.7, and 121.6 MHz, respectively. $^{13}\text{C}$ MAS NMR spectra with cross polarization (CP) were acquired with a contact time of 3.0 ms. A cross polarization
detection method with hydrogen decoupling was used in $^{29}$Si NMR measurements, using a contact time of 4.0 s. The rotor spin rate was 5 kHz, with the delay time of 5 s ($^{13}$C) or 4 s ($^{29}$Si). Hexanethylenbenzene ($^{13}$C: 17.4 and 132.3 ppm), tetrakis(trimethylsilyl)-silane ($^{29}$Si: -9.7 and -125.2 ppm) and $\text{H}_3\text{PO}_4$ (85% in water, $^{31}$P: 0 ppm) were used as external standards for the calibration of the chemical shift.

5.2.16 XRD Characterization of SBA-15

Low-angle powder XRD patterns were recorded at room temperature on an X’Pert PRO X-ray diffractometer with Cu-Kα radiation at 45 kV and 40 mA. The 2θ angle was scanned from 0.5° to 8° at a rate of 1°/min.

5.2.17 HR-TEM Characterization of SBA-15

High resolution transmission electron microscopy (HR-TEM) was performed on a JEOL JEM-2010F operating at an accelerating voltage of 200 kV. The sample was dispersed in dry ethanol and supported on holey carbon-coated Cu grids.

5.2.18 X-ray Absorption Spectroscopy (XAS) Characterization

X-ray absorption measurements were made on the 10-BM beam line of the Materials Research Collaborative Access Team (MRCAT) at the Advanced Photon Source, Argonne National Laboratory (Argonne, IL). A cryogenically cooled double-crystal Si (111) monochromator was used in conjunction with an uncoated glass mirror to minimize the presence of harmonics. The monochromator was scanned continuously during the measurements with data points integrated over 0.5 eV for 0.05 s per data point.
Measurements were made in transmission mode at the Rh $K$ absorption edge (23.220 keV) with the ionization chambers optimized for the maximum current with linear response (~$10^{10}$ photons detected per second) using a mixture of N$_2$ and He in the incident X-ray detector and a mixture of ~20% Ar in N$_2$ in the transmission X-ray detector. A Rh foil spectrum was acquired simultaneously with each measurement for energy calibration. For each sample, the $k$-range for the Fourier transform and the $R$-range for fitting were 2-10 Å$^{-1}$ and 1.2-2.7 Å, respectively. For each fit, the atom-atom distances were fixed as 2.29 Å, 2.37 Å, and 2.08 Å for Rh-P, Rh-Cl, and Rh-N, respectively. Scattering paths based on FEFF in Artemis (XAS software) were used to model the EXAFS data for each catalysts and to obtain the best fit parameters for the coordination number, $N$, of each scattering path (Rh-X). The coordination parameters were obtained by a least-squares fit in $k$- and $R$-space of the isolated multiple-shell, $k^2$-weighted Fourier transform data.

Catalyst samples were handled in the absence of air using a glovebox purged with N$_2$ and ~20-40 mg of each were pressed into a cylindrical holder of ~5 mm. The sample holder was loaded in a quartz tube (1 in. diameter) and fitted with Swagelok fittings containing Kapton windows for entry and exit of X-rays. X-ray absorption spectra of fresh samples were obtained under an inert atmosphere. The interatomic distances, $R$, for each scattering path (Rh-X) were fixed in each case in order to ensure the results were chemically reasonable and not mathematical artifacts as a result of allowing these distances to compensate or bias during fitting. Each spectrum was analyzed with appropriate references according to XPS and NMR measurements to find the best fit based on the elements confirmed to be present.
5.2.19 Inductively Coupled Plasma – Atomic Emission Spectroscopy (ICP-AES) Characterization

The Rh loading in the supported catalyst and the potential presence of Rh in solution after reaction were detected using a Perkin-Elmer-Optima 5300, Inductively Coupled Plasma Emission Spectrometry (ICP-AES). A 40% hydrofluoric acid solution was used to dissolve the sample. Each catalyst sample was nominally loaded at 1 wt % Rh and the Rh loading in each sample was determined by ICP-AES to be 0.92 (Rh-N-SBA-15), 0.89 (Rh-2N-SBA-15), and 0.91 (Rh-P-SBA-15).

5.3 Results and Discussion

5.3.1 Characterization of SBA-15, Functionalized SBA-15, and Supported Rh Catalysts

The nitrogen adsorption isotherms of pure SBA-15, P-SBA-15, and Rh-P-SBA-15 as representative samples, respectively, shown in Figure 5.3, displayed typical IV type N$_2$ adsorption-desorption isotherms with a clear H1 hysteresis loop, indicating the highly ordered mesoporous channel structures of SBA-15 were preserved upon organic functionalization and subsequent immobilization of Wilkinson’s catalyst within the pores of the silica matrix. The hysteresis loops of SBA-15, P-SBA-15, and Rh-P-SBA-15 gradually shifted to lower relative pressures, especially for Rh-P-SBA-15, indicating a lower relative pressure at which capillary condensation commences, and a significant decrease in their surface areas occurs. This is consistent with changes in pore size distributions, as shown in Figure 5.3. We observed similar behavior for the amine-functionalized SBA-15 silica.
Figure 5.3. (A) $\text{N}_2$ adsorption-desorption isotherms and (B) pore diameter distribution of samples: (a) SBA-15; (b) Cl-SBA-15; (c) P-SBA-15; and (d) Rh-P-SBA-15.
Functionalization and immobilization of Wilkinson’s catalyst caused a reduction in the surface area, total pore volume, and mean pore size compared with pure SBA-15, as listed in Table 5.1. The low-angle XRD pattern (Figure 5.4) for all samples showed three well-resolved peaks in the region of 0.6-2θ indexed to (110), (200), and (211) reflections of hexagonal mesoporous arrays and a significant decrease in their reflection intensities compared with pure SBA-15. A positive shift in peak position for the P-SBA-15 and Rh-P-SBA-15 samples was observed relative to the pure SBA-15, owing to the increased thickness of the pore wall. These results demonstrate the organic functional groups and rhodium complex were grafted predominantly onto the internal surface of the pores. The HR-TEM images in Figure 5.5 clearly demonstrate the mesoporous channels were preserved upon functionalization and immobilization of Wilkinson’s catalyst.

In order to further characterize differences in SBA-15 before and after functionalization and immobilization, we conducted 13C and 29Si solid-state NMR experiments. Figure 5.6 shows the 29Si CP-MAS NMR spectra for pure SBA-15, N-SBA-15, 2N-SBA-15, and P-SBA-15, respectively. As shown in Figure 5.6A, three signals around -93, -101, and -110 ppm for the pure SBA-15, characteristic of Q^2, Q^3, and Q^4 silicon sites of the SiO_4-substructures (Q^n = Si(OSi)_n(OH)_{4-n}, n = 2-4) in the silica framework, are present. The structural changes of the silica after the functionalization are visible in Figures 5.6B, C, and D (spectra a, c, e). An additional set of peaks between -50 and -70 ppm, assignable to T^m-site groups (T^m = RSi(OSi)_m(OH)_{3-m}, m = 1-3) is present, indicating the successful incorporation of organic moieties into the silica framework. A significant decrease in the intensity of the Q^3 and Q^2 sites with respect to the Q^4 sites was observed for all samples regardless of grafted organic ligand type. The subsequent
Table 5.1. Structural and textual properties of SBA-15 samples.

<table>
<thead>
<tr>
<th>Sample</th>
<th>(d_{100}) (Å)</th>
<th>(a_0) (Å)</th>
<th>Wall thickness (Å)</th>
<th>(S_{\text{BET}}) (m²g⁻¹)</th>
<th>(D_{\text{BJH}}) (Å)</th>
<th>(V_u) (cm³g⁻¹)</th>
<th>(V_p) (cm³g⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBA-15</td>
<td>90.8</td>
<td>104.8</td>
<td>40.8</td>
<td>587</td>
<td>64</td>
<td>0.046</td>
<td>0.75</td>
</tr>
<tr>
<td>Cl-SBA-15</td>
<td>94.8</td>
<td>109.5</td>
<td>51.1</td>
<td>460</td>
<td>62</td>
<td>0.037</td>
<td>0.56</td>
</tr>
<tr>
<td>P-SBA-15</td>
<td>94.8</td>
<td>109.5</td>
<td>53.5</td>
<td>445</td>
<td>56</td>
<td>0.008</td>
<td>0.54</td>
</tr>
<tr>
<td>Rh-P-SBA-15</td>
<td>95.7</td>
<td>110.5</td>
<td>52.5</td>
<td>315</td>
<td>58</td>
<td>0.007</td>
<td>0.43</td>
</tr>
</tbody>
</table>

\(^a\) XRD (100) interplanar spacing, \(\lambda = 2d_{100}\sin\theta\). \(^b\) Hexagonal unit cell parameter, \(a_0 = \left(\frac{\lambda}{\sqrt{3}}\right)\sin\theta\). \(^c\) Size of wall thickness, wall thickness = \(a_0 - D_{\text{BJH}}\). \(^d\) BET specific surface area. \(^e\) Mean pore diameter. \(^f\) Micropore volume. \(^g\) Total pore volume.
Figure 5.4. Low-angle XRD pattern of (a) SBA-15, (b) Cl-SBA-15, (c) P-SBA-15, and (d) Rh-P-SBA-15.
Figure 5.5. High resolution TEM image of (A) SBA-15 and (B) Rh-P-SBA-15.
Figure 5.6. $^{29}\text{Si}$ solid-state NMR spectra for (A) SBA-15; (B) a: N-SBA-15, b: Rh-N-SBA-15; (C) c: 2N-SBA-15, d: Rh-2N-SBA-15; (D) e: P-SBA-15, f: Rh-P-SBA-15.
immobilization of RhCl(PPh$_3$)$_3$ on the surface-functionalized SBA-15 causes marginal changes in the $^{29}$Si CP-MAS spectra in the lines attributed to the T$^m$ and Q$^n$ groups, as shown in Figures 5.6B, C, and D (spectra b, d, f).

Figure 5.7 depicts the $^{13}$C CP-MAS NMR spectra for the SBA-15 upon organic functionalization and the corresponding catalysts after subsequent immobilization of RhCl(PPh$_3$)$_3$. Peaks corresponding to the pure organic functional linkers (Figures 5.7A, spectrum a, 5.7B, d; and 5.7C, 2g) appear in the $^{13}$C solid-state NMR spectra of the organically functionalized SBA-15 samples and their respective immobilized Rh complexes, indicating the successful grafting and structural retention of the organic linkers on the silica surface. Taking N-SBA-15 as an example, the appearance of peaks at $\delta = 10.8, 18.6, 27.9, 45.4$, and $58.6$ ppm, corresponding to –SiCH$_2$, –OCH$_2$CH$_3$, –CH$_2$CHCH$_2$, –CH$_2$NH$_2$, and –OCH$_2$CH$_3$, respectively, demonstrates the successful grafting of 3-aminopropyl-linkers to the SBA-15 surface through the condensation reaction between -OH and -SiOCH$_2$CH$_3$ (Figure 5.7A, spectrum b). After subsequent immobilization of RhCl(PPh$_3$)$_3$, no significant differences in the $^{13}$C CP-MAS NMR spectra were found among the catalysts with exception of the appearance of a broad peak around $\delta = 128$-132 ppm, assignable to the phenyl group of triphenylphosphine ligands coordinated to rhodium.

Notably, in the case of Rh-P-SBA-15 (Figure 5.7C, spectrum i), the signal intensity of the phenyl group ranging from 128-132 ppm significantly increases, while the same signal for Rh-2N-SBA-15 (Figure 5.7B, spectrum f) is virtually absent in the $^{13}$C CP-MAS spectra. The most likely reason for this observation is due to the complete replacement of the PPh$_3$ ligand with the secondary-amine groups on the silica surface.
Collectively, these results demonstrate the organic functional linkers and RhCl(PPh₃)₃ were successfully immobilized onto the surface of SBA-15. The techniques used thus far demonstrate differences amongst grafted samples, but do not provide significant insight into the local structures of the individual immobilized Rh centers.

5.3.2 Solid-State $^{31}$P NMR Characterization of Supported Rh Complexes

Various attempts towards the covalent immobilization of Wilkinson’s catalyst, RhCl(PPh₃)₃, on a variety of solid supports have been undertaken and the resulting catalysts have high activity and stability during catalysis,[26-33] but little attention has been paid to the structure of the heterogenized catalyst. We deem this a critical element in the synthesis of supported molecular catalysts because knowledge of the local structure allows for the elucidation of structure-function relationships between activity and the structure of the Rh center. To address this shortcoming, we applied a series of techniques in concert to obtain a better understanding of the chemical environment of surface-supported Rh complexes including $^{31}$P CP-MAS NMR, 2D $^{31}$P{$^1$H} HETCOR NMR, XPS, and Rh K-edge EXAFS.

Figure 5.8 is the $^{31}$P CP-MAS NMR spectra for the as-prepared catalysts, Rh-N-SBA-15, Rh-2N-SBA-15, and Rh-P-SBA-15, respectively. The spectrum of Wilkinson’s catalyst upon immobilization on the surface-functionalized SBA-15 differs significantly from the neat complex. The spectrum of the neat complex shows three center-split peaks with isotropic chemical shifts of 48.0, 32.5, and 22.3 ppm, attributable to the three nonequivalent phosphorus atoms in the complex molecule (Figure 5.8A). A single broad symmetric peak at $\delta = 32.0$ ppm was observed upon immobilization of RhCl(PPh₃)₃ onto...
Figure 5.8. $^{31}$P solid-state NMR spectra for (A) RhCl(PPh$_3$)$_3$; (B) a: P-SBA-15, b: Rh-P-SBA-15, c: Rh-2N-SBA-15, d: Rh-N-SBA-15. Note: * represents spinning side bands.
N-SBA-15 (Figure 5.8B, spectrum d), which is in good agreement with previously reported results.\cite{35} After immobilization of RhCl(PPh\textsubscript{3})\textsubscript{3} onto 2N-SBA-15 (Figure 5.8B, spectrum c), a single broad peak centered at $\delta = 28.6$ ppm was detected, albeit with a considerably lower intensity, compared with the other two immobilized Rh complexes under the same experimental conditions, indicating a reduced number of triphenylphosphine groups are ligated to rhodium on the SBA-15 surface, in good agreement with previously discussed $^{13}$C CP-MAS NMR and XPS results mentioned in Chapter 5.3.4.

In sharp contrast, two well-resolved peaks centered at $\delta = 27.0$ and 44.0 ppm were observed upon immobilization of RhCl(PPh\textsubscript{3})\textsubscript{3} onto P-SBA-15 (Figure 5.8B, spectrum b), indicative of two non-equivalent phosphorus groups coordinated to rhodium. Additionally, free grafted diphenylphosphine ligand at $\delta = -15.8$ ppm was also observed. This peak position is in good agreement with the spectrum of P-SBA-15 (Figure 5.8B, spectrum a). There is no indication of an oxidized phosphine peak ($\delta = 38.0$ ppm) or phosphonium species ($\delta = 24.0$ ppm) among all of the as-prepared catalysts.\cite{41, 42} As a consequence, the $^{31}$P CP-MAS NMR results strongly indicate the RhCl(PPh\textsubscript{3})\textsubscript{3} was successfully immobilized onto surface-functionalized SBA-15 with distinct differences in the exact structures of the local Rh complexes.

5.3.3 2D $^{31}$P/$^1$H HETCOR NMR Characterization of Immobilized Rh Catalysts

Due to the substantial breadth of the 1D $^{31}$P CP-MAS NMR spectra, it prevents an accurate determination of the Rh-P coupling constants and determination of the non-equivalency of the phosphorus atoms. Two-dimensional $^{31}$P/$^1$H HETCOR NMR
experiments were conducted to provide additional information on the phosphorus species grafted to the SBA-15 surface in order to gain better insight into the local structure of the active Rh site. The 2D spectra for the as-prepared catalysts Rh-P-SBA-15, Rh-N-SBA-15, and Rh-2N-SBA-15 are shown in Figures 5.9-5.11, respectively. The $^{31}$P NMR peak at $\delta = -15.8$ ppm from the grafted diphenylphosphine ligands in Rh-P-SBA-15 is strongly correlated to the methylene species ($^1$H NMR peaks ranging from 0.8 to 2.8 ppm) and to the aromatic rings ($^1$H NMR peaks, 7.0-7.5 ppm), as shown in Figure 5.9. An identical correlation was found for the $^{31}$P NMR peak centered at $\delta = 27.0$ ppm to both $^1$H peaks of 0.8-2.8 and 7.0-7.5 ppm, suggesting 1 or 2 PPh$_3$ ligands are displaced when RhCl(PPh$_3$)$_3$ is grafted to P-SBA-15. The $^{31}$P NMR peak centered at 44.0 ppm shows no correlation to the $^1$H NMR peaks ranging from 0.8-2.8 ppm, but does show a correlation to the aromatic protons ($^1$H peaks, 7.0-7.5 ppm), which is attributed to the remaining PPh$_3$ ligated to rhodium. Deconvolution of the $^{31}$P CP-MAS spectrum (Figure 5.8, spectrum b) revealed the intensity ratio of peaks at $\delta = 27.0$ and 44.0 ppm is about 2:1, indicating two equivalents of the tethered diphenylphosphine replaced two PPh$_3$ ligands to coordinate with rhodium upon immobilization of RhCl(PPh$_3$)$_3$ on the SBA-15 surface. The excess grafted diphenylphosphine increased the probability that adjacent free diphenylphosphine groups were available to ligate the same Rh center. In the case of Rh-N-SBA-15, the $^{31}$P NMR peak at $\delta = 32$ ppm, as expected, only has one correlation to the $^1$H peak of the aromatic rings, as shown in Figure 5.10. However, a considerably weaker correlation between the $^{31}$P and $^1$H peaks was found in the case of Rh-2N-SBA-15, in accordance with the result of the 1D $^{31}$P CP-MAS NMR experiment, further confirming the existence
Figure 5.9. $^{31}\text{P}^\ddagger{\text{H}}$ HETCOR NMR for Rh-P-SBA-15.
Figure 5.10. $^{31}$P{\text{^{1}H}}$ HETCOR NMR for Rh-N-SBA-15.
Figure 5.11. $^{31}\text{P}^{[1\text{H}]}$ HETCOR NMR for Rh-2N-SBA-15.
of trace amounts of phosphorus groups, most likely in the form of physically adsorbed RhCl(PPh\textsubscript{3})\textsubscript{3} on the surface even after thorough filtering and washing.

5.3.4 XPS Characterization of Immobilized Rh Catalysts

Figure 5.12 shows the XPS spectra for RhCl(PPh\textsubscript{3})\textsubscript{3}, Rh-N-SBA-15, Rh-2N-SBA-15, and Rh-P-SBA-15, respectively. The binding energy (BE) value of Rh 3d\textsubscript{5/2} in RhCl(PPh\textsubscript{3})\textsubscript{3} was observed at 309.2 eV, in agreement with the literature.\textsuperscript{[43]} Upon immobilization of RhCl(PPh\textsubscript{3})\textsubscript{3} on the surface-functionalized SBA-15, the BE values of Rh 3d\textsubscript{5/2} varied from the homogeneous precursor. The magnitude of each BE shift relative to pure RhCl(PPh\textsubscript{3})\textsubscript{3} depended on the functional groups tethered to the SBA-15 surface. In the case of Rh-P-SBA-15, no distinct deviations in Rh 3d\textsubscript{5/2} BEs were observed. This result is reasonable because the electronic and steric characteristics of the immobilized rhodium complex was intrinsically retained upon immobilization since two PPh\textsubscript{3} ligands were replaced with two equivalent surface-tethered diphenylphosphines, as observed from 2D \textsuperscript{31}P\textsuperscript{[1H]} HETCOR NMR. However, a significant shift to lower values in the BE of the Rh 3d\textsubscript{5/2} peak (307.9 and 307.5 eV) was found in Rh-N-SBA-15 and Rh-2N-SBA-15, respectively, and the shift in the case of Rh-2N-SBA-15 is slightly larger than Rh-N-SBA-15. We attribute the larger shift in Rh-2N-SBA-15 to twice as many amine interactions between the secondary-amine ligands, compared to the primary-amine, and rhodium. Amine ligands (primary and secondary) can replace two or even three PPh\textsubscript{3} ligands to coordinate with Rh during the formation of the immobilized Rh complexes because the surface amine groups are stronger \(\sigma\)-electron donors than PPh\textsubscript{3} ligands. PPh\textsubscript{3} is a stronger \(\pi\)-acid than the amine ligands and the \(d-\pi\) back-donation
Figure 5.12. XPS spectra for (a) RhCl(PPh₃)₃, (b) Rh-N-SBA-15, (c) Rh-2N-SBA-15, and (d) Rh-P-SBA-15. The Rh wt % loading detected by ICP-AES for the immobilized samples is 0.92, 0.89, and 0.91, respectively.
decreases with the replacement of PPh$_3$ by -NH$_2$, thereby shifting the BEs of the Rh 3d$_{5/2}$ peaks to lower values.$^{[44]}$

Table 5.2 summarizes the elemental composition for each catalyst measured by XPS. The observed results for the atomic ratio of P-to-Rh and Cl-to-Rh for RhCl(PPh$_3$)$_3$ matched the expected results of three and unity, respectively, while the atomic ratio of P-to-Rh varied among Rh-P-SBA-15, Rh-N-SBA-15, and Rh-2N-SBA-15. For Rh-N-SBA-15, the atomic ratio decreased to unity, suggesting only one PPh$_3$ remains ligated to rhodium. No significant phosphorus signal was detected for the catalyst Rh-2N-SBA-15, suggestive of nearly complete replacement of PPh$_3$ with the surface-tethered secondary amine groups on SBA-15 surface. The lack of phosphorous signal is likely due to the lower sensitivity of XPS compared to $^{31}$P CP-MAS NMR. In the case of Rh-P-SBA-15, owing to an excess of free tethered diphenylphosphine ligands on the SBA-15 surface, the atomic ratio of P-to-Rh exceeded three. Such a value is reasonable and agrees with the $^{31}$P NMR results (Figure 5.8, spectrum b). The atomic ratio of Cl-to-Rh (1:1) in each as-prepared catalyst is constant at the stoichiometry of the neat complex, demonstrating that Cl is not replaced during immobilization.

5.3.5 EXAFS Characterization of Immobilized Rh Catalysts

Rh $K$-edge EXAFS experiments were conducted to further characterize the local structure of the immobilized Rh complexes. Figure 5.13 is a compilation of the collected spectra and Table 5.3 summarizes the fitting results. In Figure 5.13, solid lines represent the experimental data while the dashed lines represent the phase-corrected fitted models. For each sample, the $k$-range for the Fourier transform and the $R$-range for fitting were 2-
Table 5.2. Elemental composition measured by XPS for different grafted Rh catalysts.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Relative Concentration (atom%)</th>
<th></th>
<th></th>
<th>P/Rh</th>
<th>Cl/Rh</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>P</td>
<td>Cl</td>
<td>Rh</td>
<td></td>
</tr>
<tr>
<td>RhCl(PPh$_3$)$_3$</td>
<td>-</td>
<td>4.90</td>
<td>1.54</td>
<td>1.65</td>
<td>2.97</td>
</tr>
<tr>
<td>Rh-N-SBA-15</td>
<td>3.93</td>
<td>0.68</td>
<td>0.84</td>
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<tr>
<td>Rh-2N-SBA-15</td>
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<td>-</td>
<td>1.06</td>
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<td>-</td>
</tr>
<tr>
<td>Rh-P-SBA-15</td>
<td>-</td>
<td>2.52</td>
<td>0.77</td>
<td>0.72</td>
<td>3.50</td>
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</tbody>
</table>
Figure 5.13. (A) $k^2$-Weighted and (B) Fourier transform of Rh K-edge EXAFS spectra for the supported Rh catalysts.
Table 5.3. Curve-fitting analysis for the Rh $K$-edge EXAFS data.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Path</th>
<th>$N$</th>
<th>$R$ (Å)</th>
<th>$E_0$ (eV)</th>
<th>$\sigma^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-P-SBA-15</td>
<td>Rh-P</td>
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<tr>
<td>Rh-Cl</td>
<td>Rh-P</td>
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<td>2.37</td>
<td>-3.9</td>
<td></td>
</tr>
<tr>
<td>Rh-N-SBA-15</td>
<td>Rh-N</td>
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<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Rh-Cl</td>
<td>2.11</td>
<td>2.37</td>
<td>-5.3</td>
<td></td>
</tr>
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<td>Rh-2N-SBA-15</td>
<td>Rh-N</td>
<td>4.05</td>
<td>2.08</td>
<td>-9.7</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Rh-Cl</td>
<td>0.95</td>
<td>2.37</td>
<td>7.5</td>
<td></td>
</tr>
</tbody>
</table>

*The Debye-Waller factor, $\sigma^2$, is a measure of the thermal disorder in the system. Values in the range of 0.002-0.005 are expected for structures with little disorder due to lack of long range scattering (e.g. molecular complexes).*
10 Å⁻¹ and 1.2-2.7 Å, respectively. For each fit, the atom-atom distances are fixed as 2.29 Å, 2.37 Å, and 2.08 Å for Rh-P, Rh-Cl, and Rh-N, respectively. These numbers are obtained from references[45, 46] and supplemented with our own DFT calculations. For the Rh-P-SBA-15 catalyst, the coordination number, N, was found to be 2.00 for both Rh-P and Rh-Cl scattering paths. Due to the similar interatomic distances and electronic structures of Rh-Cl and Rh-P, it is possible that distinguishing between P and Cl atoms is difficult, so we refit the spectrum by using either the Rh-Cl scattering path or the Rh-P scattering path only in two separate trials. We obtained N values of 3.70 and 4.38, respectively, which support our proposed structure of having four total Rh-X bonds (3 Rh-P contributions and 1 Rh-Cl contribution). For the immobilized Rh-2N-SBA-15 catalyst, we excluded Rh-P scattering for our EXAFS fitting due to the lack of P signals from XPS and NMR results. The fitting for Rh-2N-SBA15 shows N values of 4.05 and 0.95 for Rh-N and Rh-Cl, respectively. These results also support the proposed structure with the local atomic environments consisting of 4 Rh-N bonds and 1 Rh-Cl bond. Finally, for the Rh-N-SBA-15 catalyst, the N values were found to be 0.80, 1.09, and 2.11 for Rh-P, Rh-Cl, and Rh-N, respectively. The ratio of these numbers is close to the proposed structure (1:1:2 for P:Cl:N). Overall, our EXAFS results show that the local atomic structures agree with the proposed structures from our XPS and NMR results, including retention of the Cl ligand of Wilkinson’s catalyst upon immobilization. Based on the above characterization results, the local structures of the immobilized Rh complexes upon the reaction of RhCl(PPh₃)₃ with functionalized SBA-15 bearing primary amine, or secondary amine, or diphenylphosphine groups are described as shown in Figure 5.2.
5.3.6 Heterogeneous Hydrothiolation of Alkynes with Thiols

Several metal-based homogeneous catalysts such as Rh,\textsuperscript{[47-50]} Ir,\textsuperscript{[51]} Ni,\textsuperscript{[52]} Pd,\textsuperscript{[53, 54]} Pt,\textsuperscript{[55]} Au,\textsuperscript{[56]} Zr,\textsuperscript{[57-59]} and f-elements\textsuperscript{[57-59]} have been developed to produce regio- and stereoselective vinyl sulfides, which are versatile intermediates for the synthesis of biologically active compounds, organic building blocks, and new materials. However, highly regio- and stereoselective hydrothiolation of a wide range of alkynes with various thiols catalyzed by a heterogeneous catalyst is still not readily available to date. Given the utility and proficiency of Rh complexes for alkyne hydrothiolation as previously reported,\textsuperscript{[47-50]} we developed immobilized Rh complex catalysts with different grafting ligands for the hydrothiolation of alkynes with thiols (see Table 5.4 for hydrothiolation data).\textsuperscript{[37]} Homogeneous Wilkinson’s catalyst, RhCl(PPh$_3$)$_3$, showed good activity and excellent regio- and stereoselectivity for the addition of phenylacetylene (1a) to thiophenol (1b), achieving up to 98% conversion and 94% selectivity to \textit{E-1ab} along with 6% selectivity to the Markovnikov adduct in DCE at room temperature within 45 min, as shown in Figure 5.1. The immobilized Rh complexes – Rh-N-SBA-15, Rh-2N-SBA-15, and Rh-P-SBA-15 – exhibited similar conversions (around 80%) after 20 h. The stereoselectivity differed depending on the functional groups linked to the Rh complex, as presented in Figure 5.2, though all immobilized catalysts were completely regioselective to the anti-Markovnikov product. The catalyst Rh-N-SBA-15 gave a mixture of anti-Markovnikov ((\textit{E+Z})-(1+2)ab) products with the \textit{Z}-isomer (1ab) as the main product, while Rh-2N-SBA-15 produced \textit{Z-2ab} with 99% stereoselectivity. In sharp contrast, exclusive and reversed stereoselectivity to \textit{E-1ab} was obtained in the presence...
Table 5.4. Screening of alkynes and thiols for catalytic hydrothiolation.

| Reaction conditions: 0.5 mmol alkyn, 0.55 mmol thiol, 50 mg catalyst Rh-P-SBA-15 (4.5 µmol Rh) and 2 mL DCE. Conversion of alkynes and selectivity were determined by 1H NMR analysis of the crude mixture. |
of Rh-P-SBA-15 under otherwise identical reaction conditions. The Markovnikov addition was completely suppressed upon immobilization of RhCl(PPh₃)₃ onto the surface-functionalized SBA-15. Our objective in this work is to rigorously characterize the immobilized Rh catalysts in order to determine their structures, such that we may establish structure-function relationships for each grafted structure for our hydrothiolation (especially regarding the switches in stereoselectivity based on the catalytic structure as shown in Figure 5.1) and hydrosulfonation kinetic data.

In order to better understand the relationship between the local structure and catalytic activity, two equivalents of propylamine with respect to RhCl(PPh₃)₃ were mixed with phenylacetylene and thiophenol in solution. 92.0% conversion with 30/70 of $E/Z$ stereoselectivity to 2ab was observed after 20 h at room temperature (Figure 5.14), which is roughly equal to the activity and stereoselectivity of the Rh-N-SBA-15 catalyst. Likewise, excellent stereoselectivity to Z-2ab (96%) at lower conversion (61.2%) compared to the Rh-2N-SBA-15 catalyst was afforded when 2 equivalents of $N$-ethylethylenediamine were introduced into the reaction under otherwise identical reaction conditions (Figure 5.14). These findings demonstrate the amino functional groups (either primary or secondary) indeed influence the stereoselectivity of alkyn hydrothiolation catalyzed by RhCl(PPh₃)₃. $^{31}$P NMR characterization of two equivalents of propylamine and $N$-ethylethylenediamine relative to RhCl(PPh₃)₃ are presented in Figure 5.15. Mechanistic investigations point to a catalytic cycle initiated by oxidative addition of the thiol with Rh center to generate a hydride thiolate (H-Rh-SR) species and subsequent alkyn insertion into the hydride ligand followed by reductive elimination to afford the anti-Markovnikov ($E$, $Z$, or both) adducts.$^{[50,60]}$ The formation of $Z$-$\beta$-vinyl sulfides
Figure 5.14. Product distribution for the hydrothiolation of phenylacetylene and thiophenol over RhCl(PPh$_3$)$_3$ with 2 equivalents of propylamine or $N$-ethylethylenediamine. Reaction conditions: 4.5 $\mu$mol RhCl(PPh$_3$)$_3$, 0.5 mmol phenylacetylene, 0.55 mmol thiophenol, 2 mL DCE, and room temperature.
Figure 5.15. $^{31}$P NMR spectra for (a) Wilkinson’s catalyst and its reaction with 2 equivalents of (b) propylamine and (c) N-ethylethylenediamine in DCE at room temperature for 2 h. After Wilkinson’s catalyst reacted with 2 equivalents of propylamine in DCE at room temperature for 2 h, the signal for the characteristic $^{31}$P NMR peaks of RhCl(PPh$_3$)$_3$ in DCE decreased, the free PPh$_3$ was released from the complex due to the exchange reaction between propylamine and PPh$_3$ ligands with concomitant formation of a new Rh species at $\delta = 27.8$ ppm. However, after reaction with 2 equivalents of N-ethylethylenediamine, the characteristic $^{31}$P NMR peaks for RhCl(PPh$_3$)$_3$ disappeared with nearly complete release of free PPh$_3$ in DCE. These results are consistent with the observed $^{31}$P solid-state NMR results.
generally requires isomerization of metal alkenyl intermediates prior to reductive elimination.\textsuperscript{[61, 62]} It appears the active Rh species coordinated to amino-groups preferentially favors the isomerization to produce Z-\(\beta\)-vinyl sulfides based on our findings over both homogeneous and heterogeneous N-ligated Rh centers.

5.3.7 Heterogeneous Hydrosulfonation of Alkynes with Sulfonic Acids

Vinyl sulfonates are important and versatile building blocks in organic synthesis, especially for cross-coupling,\textsuperscript{[63-67]} carbylation,\textsuperscript{[68]} and polymerization\textsuperscript{[69]} reactions, and are also attractive intermediates for the formation of vinyl cations or alkylidene carbenes.\textsuperscript{[70]} The most straightforward and atom-economical method to access vinyl sulfonates is via transition-metal catalyzed regioselective intermolecular addition of sulfonic acids to alkynes. Although transition-metal-catalyzed addition of alkynes to various nucleophilic reagents such as water,\textsuperscript{[71-75]} alcohols,\textsuperscript{[76-81]} amines,\textsuperscript{[51, 82-91]} thiols,\textsuperscript{[37, 48, 50, 54, 56-59, 92, 93]} carboxylic acids,\textsuperscript{[94-97]} and sulfonic acids\textsuperscript{[98]} for the formation of regio- and stereo-defined vinyl C-heteroatom products have been developed, only a few catalytic systems have been reported for the regioselective addition of sulfonic acids to alkynes.\textsuperscript{[98, 99]} Previous approaches to synthesize vinyl sulfonates suffered from complicated synthesis of starting materials, tedious work-up procedures, low yield and regioselectivity, and limited substrate versatility.\textsuperscript{[100-104]} Studies documenting regio- and stereoselective additions over supported metal catalysts are not available thus far, to the best of our knowledge. Therefore, development of a stable heterogeneous catalyst that allows for highly regio- and stereoselective addition of alkynes to sulfonic acids to form the corresponding vinyl sulfonates is of great interest.
As discussed above, the regio- and stereoselectivity to the desired vinyl sulfides for hydrothiolation of alkynes with thiols is controlled by the local structure of the immobilized Rh complexes. We tested the ability of Wilkinson’s catalyst to perform hydrosulfonation reactions using 1.0 mol % catalyst in 2 mL DCE at 70°C in the presence of 1.0 mmol phenylacetylene and 0.5 mmol methanesulfonic acid. We achieved 86.2% yield (based on conversion of methanesulfonic acid) of the Markovnikov product after 2 h and were intrigued by the possibilities of heterogeneous hydrosulfonation. We then performed the addition of phenylacetylene with methanesulfonic acid to form vinyl sulfonates catalyzed by Rh-P-SBA-15, Rh-N-SBA-15, and Rh-2N-SBA-15, respectively, in DCE at 70°C. The immobilized catalysts displayed comparable activity and absolute regioselectivity to Markovnikov vinyl sulfonates. The regioselectivity is independent of the local structure of the immobilized Rh complexes, which is completely different and opposite to the anti-Markovnikov adducts that formed during hydrothiolation. We screened the scope of both alkynes and sulfonic acids over Rh-P-SBA-15 and the results are summarized in Table 5.5. A wide range of alkynes were hydrosulfonated with methanesulfonic acid to produce the corresponding Markovnikov vinyl sulfonates in moderate to high conversion with absolute regioselectivity. A group of phenylacetylenes bearing electron-rich (5-8a) and electron-poor substituents (10, 11a) at o-, m-, or p-positions on the phenyl ring, all reacted efficiently with methanesulfonic acid. The electron-poor substituents exhibited a negative effect on the reaction, resulting in considerably lower conversions under otherwise identical reaction conditions. Internal alkynes underwent regioselective hydrosulfonation to afford the corresponding
Table 5.5. Screening of alkynes and sulfonic acids for hydrosulfonation.

| Reaction conditions: 1 mmol alkyne, 0.50 mmol sulfonic acid, 50 mg catalyst Rh-P-SBA-15 (4.5 µmol Rh) and 2 mL DCE, 70 °C. Conversion of sulfonic acids was determined by \(^1\)H NMR analysis of the crude mixture. | 
|---|---|---|
| 1 (2 equiv) | 4 | 4-21ab |
| **4ab**, 93.0% conv.(24 h) | **5ab**, 95.1% conv.(24 h) | **6ab**, 92.1% conv.(24 h) |
| **7ab**, 90.2% conv.(24 h) | **8ab**, 95.9% conv.(24 h) | **9ab**, 94.8% conv.(24 h) |
| **10ab**, 83.4% conv.(24 h) | **11ab**, 78.9% conv.(24 h) | **12ab**, 100% conv (24 h) |
| **13ab**, 82.6% conv.(24 h) | **14ab**, 90.6% conv.(24 h) | **15ab**, 91.6% conv.(24 h) |
| **16ab**, 78.7% conv.(24 h) | **17ab**, 73.2% conv.(24 h) | **18ab**, 92.4% conv.(24 h) |
| **19ab**, 96.3% conv.(24 h) | **20ab**, 56.5% conv.(30 h) | **21ab**, 50.8% conv.(30 h) |
Markovnikov adducts (20, 21ab) with satisfactory conversions, but required longer reaction times.

Aromatic sulfonic acids featuring both electron-donating (16, 17b) and electron-withdrawing groups (18, 19b) could be added to phenylacetylene efficiently to afford the corresponding vinyl sulfonate esters in moderate to high conversions with exclusive regioselectivity. Stronger acids are beneficial to this transformation. The addition of 4-chlorobenzenesulfonic acid to phenylacetylene was converted into the corresponding vinyl sulfonate (18ab) in 92.4% yield after 24 h, while 73.2% yield of 17ab for the addition of 4-ethylbenzensulfonic acid with phenylacetylene was only achieved under otherwise identical reaction conditions. Functional groups on the alkynes such as fluoro, chloro, hydroxyl, and methoxy were compatible with this catalytic system. In all cases listed in Table 5.5, no double bond isomerization occurred.

5.3.8 Stability and Recyclability of the Immobilized Rh Catalysts for Hydrosulfonation

In our previous studies, we found the immobilized Rh complexes to be stable for the hydrothiolation of alkynes with thiols.[37] We also examined the stability of the immobilized Rh complexes during hydrosulfonation reactions. First, to verify whether the observed catalysis was due to the heterogeneous catalyst, Rh-P-SBA-15, or a leached rhodium species in solution, we carried out the addition of phenylacetylene (1a) to methanesulfonic acid (4b) and removed the catalyst from the reaction mixture by hot-filtration at approximately 50% conversion of 4b (Figure 5.16) at 70°C. After removal of Rh-P-SBA-15, the filtrate was again held at the same temperature under an atmosphere of N2. No significant increase in conversion was observed, indicating leached Rh species
Figure 5.16. Comparison of the hydrosulfonation with and without catalyst removal (after 12 h as indicated by the arrow). Methanesulfonic acid conversion with Rh-P-SBA-15 is represented by closed circles while methanesulfonic acid conversion after Rh-P-SBA-15 removal after 12 h is represented by open circles. Reaction conditions: 1.0 mmol phenyacetylene, 0.5 mmol methanesulfonic acid, 50 mg catalyst Rh-P-SBA-15 (4.5 µmol Rh), 2 mL DCE, and 70°C.
from the catalyst (if any) are not responsible for the observed activity. ICP-AES analysis provided further confirmation that no rhodium species were detected in the filtrate (below the detection limit). The Rh-P-SBA-15 catalyst was recovered and could be reused up to four times for the transformation of 1a and 4b without any significant loss of catalytic activity and regioselectivity, as shown in Figure 5.17. Together, these results rule out any contribution to the observed catalysis from a homogeneous rhodium species, confirming the observed catalysis was intrinsically heterogeneous. Additionally, results for $^{31}$P CP-MAS NMR of the grafted catalysts after reaction showed little change in the local structure of the grafted Rh complexes (Figure 5.18).

### 5.4 Conclusions

The structure of immobilized Rh complexes derived from the reaction of Wilkinson’s catalyst with surface-functionalized SBA-15 bearing primary or secondary amine and diphenylphosphine functional groups within the mesoporous channels have been elucidated. Their structures strongly depended on the surface-tethered functional groups replacing two or three PPh$_3$ ligands of RhCl(PPh$_3$)$_3$ on SBA-15 during the transformation, which were structurally and systematically identified by a series of techniques including $^{31}$P CP-MAS NMR, $^{31}$P{$^1$H} HETCOR NMR, XPS, and Rh K-edge EXAFS. The resulting immobilized Rh complexes exhibited high activity for the addition of alkynes with thiols or sulfonic acids, respectively. The regio- and stereoselectivity for hydrothiolation to yield vinyl sulfides depended on the local structures of grafted Rh complexes and the stereoselectivity could be readily switched. In contrast, only Markovnikov vinyl sulfonate esters were produced for the addition of alkynes with
**Figure 5.17.** The recyclability of Rh-P-SBA-15 for hydrosulfonation of phenylacetylene and methanesulfonic acid. Conversion is represented by closed circles and regioselectivity is represented by the open circles.
Figure 5.18. $^{31}$P CP-MAS NMR spectrum of Rh-P-SBA-15 after reaction.
sulfonic acids without such a dependence of the structures of grafted Rh complexes. A wide range of substrates (alkynes, thiols, and sulfonic acids) were added to form their corresponding adducts efficiently. Moreover, such immobilized Rh complexes could be reused several times without significant loss in catalytic activity and regio- and stereoselectivity for hydrothiolation and hydrosulfonation. This study demonstrates that, in order to potentially understand why a particular catalyst is active and selective, it is paramount to determine the local structure of the surface organometallic catalyst, which requires complementary spectroscopic techniques.
5.5 References


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Chapter 6
Quantifying the Effect of Grafting Solvent on the Structure, Reactivity, and Selectivity of Supported Rh Organometallic Catalysts

6.1 Introduction

The immobilization of homogeneous organometallic catalysts onto solid supports combines the advantages of homogeneous catalysts (high activity and selectivity) with the advantages of heterogeneous catalysts (reusability of the catalyst and ease of product separation). The main challenge in the synthesis of supported organometallic catalysts is retaining the inherent activity and selectivity of the analogous homogeneous complex after grafting. Ideally, the grafted species exhibit the same site uniformity of the homogeneous complex due to retention of the electronic and steric properties of the inner-sphere ligands that impart the activity and selectivity of the organometallic precursor in the liquid phase.\[1\] However, the potential loss of endogenous ligands of the homogeneous complex during the grafting process is the most obvious reason for the difference between the activity of the homogenous complex (generally superior) and its immobilized analog. The other reason for reduced activity in the supported catalyst is the loss of fluxionality (i.e. the interchanging of ligands within the inner-sphere of the metal center of the organometallic precursor which facilitates many catalytic reaction steps) upon grafting. In order to mitigate the loss of the endogenous ligands and their inherent fluxionality, the tethering agents that covalently link the organometallic complex to the support are frequently chemically modified to impart effects similar to the effects originally imparted by the lost endogenous ligand(s). In a broad sense, the surface, or at
least the functionalized linking agents on the surface, behaves as a bulky, less fluxional ligand. As an example of the impact of the loss of fluxionality, Huang et al synthesized supported Rh complexes using Wilkinson’s catalyst, RhCl(PPh₃)₃, as the precursor, toluene as the grafting solvent, and amine- and thiol-functionalized MCM-41 as the support for the hydroformylation of cyclohexene.[2] They observed that the immobilized catalysts were stable and resistant to Rh leaching, but less active than the homogeneous catalyst due to the strong Rh-N and Rh-S interactions of the linking agents, which restricted the formation of the Rh-H bond necessary for catalysis, demonstrating the loss of fluxionality of the ligands.

Examples of supported analogs of Wilkinson’s catalyst in the literature demonstrate the differences in activity and selectivity between the heterogeneous and homogeneous catalysts, though rigorous spectroscopic characterization of the active species of the grafted catalysts is quite rare, which subsequently makes assessing the specific differences in structure-function relationships between the homogenous and heterogeneous catalysts rather difficult.[3-8] Grünberg et al provide a detailed study of solid-state NMR characterization of supported version of Wilkinson’s catalyst on amine-functionalized SBA-3 silica using toluene as the grafting solvent.[3] Their study is especially useful because they demonstrated how a more powerful technique, specifically 2D J-resolved ³¹P solid-state NMR, was capable of determining that the grafted Rh species contained only one endogenous PPh₃ ligand and were linked to two amine groups on the surface of the support in comparison to 1D ³¹P solid-state NMR which led to inconclusive results due to broad peaks in the spectrum. A similarly prepared catalyst using SBA-15 silica as the support and toluene as the grafting solvent was studied to test
the metal leaching capabilities of reaction solvents again using solid-state NMR where it was found that more polar solvents such as acetone and methanol had higher leaching rates than less polar solvents such as benzene. In another study using benzene as the grafting solvent, Wilkinson’s catalyst was tethered to MCM-41 silica functionalized with \( N,N\)-bis(diphenylphosphinomethyl)amino moieties, bidentate phosphine linking groups, in which the authors concluded via \( ^{31}P \) solid-state NMR and elemental analysis that the most likely surface Rh species was bound to two phosphine groups as expected for a bidentate ligand (i.e. a 1:2 Rh:P ratio for each catalytic site). This supported catalyst was tested for hydrophosphinylation of a series of alkynes with diphenylphosphine oxide and was found to have similar activity as a homogeneous complex, \( \text{RhBr(PPh}_3\text{_3)} \), though no comparison to Wilkinson’s catalyst was made. As a more direct comparison to the homogeneous precursor, Leitmannová et al synthesized supported analogs of Wilkinson’s catalyst on phosphine- and amine-functionalized MCM-41 and SBA-15 using chloroform as the grafting solvent for the selective hydrogenation of phenylacetylene to styrene. They found the homogeneous precursor was more than twice as active as any of the supported catalysts, though not as selective (63% selectivity to styrene, compared to 68-77% for the heterogeneous catalysts), which they attributed to the formation of monomeric Rh sites on the surfaces of the supports identical to the normal Wilkinson structure, that is, the surface structures were identical to the homogeneous structure (three P bonds and one Cl bond). In spite of spectroscopic data such as \( ^{31}P \) solid-state NMR, UV-Vis, and XRD, the authors do not attempt to draw substantive conclusions regarding the structure-function relationship of the heterogeneous catalyst and why the immobilized (monomeric) catalyst is more selective, but less active, than the homogeneous
(monomeric) catalyst, especially considering they have the same local Rh structure. Huang and Kawi tethered Wilkinson’s catalyst to amine-, thiol-, and phosphine-functionalized Aerosil silicas using toluene as the grafting solvent for the hydroformylation of cyclohexene and determined that the homogeneous precursor was the most active overall, though the amine-functionalized catalyst was nearly as active and all catalysts were highly selective (at least 94%).\[7\] Their $^{31}$P solid-state NMR analysis showed that the immobilized complexes had broad singlets at $\delta = 28.9$ ppm, which they attributed to monomeric Rh species retaining two endogenous PPh$_3$ ligands that were linked just once to the surface, regardless of the type of the functional group, but the original report of this type of catalyst merely proposed these structures and was unable to conclusively determine the exact Rh structures.\[8\] These examples illustrate the inherent difficulties in determining the correct structure-function relationships for specific grafted catalysts and the importance of spectroscopic characterization of the immobilized complexes in order to determine the correct catalytic structures.

In order to optimize the activity and selectivity of a supported organometallic catalyst, it is imperative to consider three factors: choosing the appropriate reagents (e.g. organometallic precursor, tethering agent, etc.), tailoring the synthetic strategy such that site-isolation (structural uniformity amongst grafted metal complexes) occurs, and performing proper spectroscopic characterization of the supported complexes (including connectivities between the metal center, endogenous ligands, and the functionalized surface) such that structure-function relationships may be established for a particular catalytic reaction. If the grafted catalytic species are structurally uniform, elucidating their structures becomes significantly easier from a spectroscopic perspective.
Additionally, single-site catalysts ensure that catalytic activity is due to one type of grafted structure only, which allows for the determination of a rigorous structure-function relationship. The presence of multiple types of catalytic sites on the surface of any heterogeneous catalyst dramatically complicates the elucidation of the correct catalytic mechanism and accompanying rate expression.\textsuperscript{10} However, designing these synthetic techniques and accurately performing the most pertinent spectroscopic techniques is quite challenging. Silica surfaces are common choices for grafting processes because of the variety of siloxane and surface hydroxyl (silanol) groups that allow for the formation of active sites.\textsuperscript{10} A complication of inorganic oxide surfaces is that spectroscopic characterizations become more difficult due to these heterogeneous surface groups, which often broaden peaks and bands observed in common techniques such as infrared (IR) and solid-state NMR spectroscopies and potentially lead to the formation of several types of catalytically active sites.\textsuperscript{11} Anwander reviewed the surface chemistry of periodic mesoporous silicas and how their various features allow for the design of a wide range of supported organometallic catalysts.\textsuperscript{12} Sindorf and Maciel used \textsuperscript{29}Si cross polarization and magic-angle spinning (CP-MAS) NMR to study the dehydration and rehydration of Fisher S-157 silica gel and noted the difficulties in characterizing the surface chemistry using a specific model due to the observed NMR signals not clearly displaying a pattern for a particular surface chemistry.\textsuperscript{13} Another NMR analysis involving dehydration and rehydration of silica gel surfaces used D\textsubscript{2}O to study hydrogen bonding between vicinal silanols.\textsuperscript{14} The authors determined the time-averaged Si-O-D bond angle to be 121° using line-shape analysis and discussed the possibility of nonlinear O-H-O arrangements, in contrast to typical hydrogen bonding of silanols with O-O.
distances of 0.33 nm and linear O-H-O arrangements, which would be weaker to the more typical hydrogen bonds, but still significant enough to affect the molecular dynamics and interaction energies of the other surface species. Scott and Dugens reviewed the types of chemistries often exploited for grafting organometallic complexes onto silica, with particular emphasis on using siloxanes and vicinal silanols to construct the grafted species.\textsuperscript{[10]} Copéret et al reviewed the impact of modern techniques in surface organometallic chemistry as well as the surface chemistry of silicas and placed special emphasis on the importance of spectroscopic characterization of the grafted species.\textsuperscript{[15]}

The heterogeneities that arise from the complex surface chemistry of inorganic oxides requires the application of a variety of spectroscopic techniques, such as solid-state NMR\textsuperscript{[16]}, extended x-ray absorption fine structure (EXAFS)\textsuperscript{[17]}, and IR and Raman spectroscopies\textsuperscript{[18]} such that the structure(s) of the active species is/are properly determined.

Perhaps the most overlooked contributor to the synthesis of supported organometallic complexes is the choice of grafting solvent, which is the simplest and most popular medium for transferring the solid organometallic precursor into the liquid phase for its subsequent immobilization onto the support. The main oversight with the choice of the grafting solvent is the ability of a given solvent to alter the catalytic structure of the precursor prior to grafting, which could result in grafting organometallic species that do not exhibit catalytic activity comparable to the original precursor in solution, either in the same grafting solvent or in a different reaction solvent. For example, Wilkinson’s catalyst is known to form chloro-bridged Rh dimers, \([\text{RhCl}(\text{PPh}_3)_2]_2\), in solution, which are less active than the monomeric species and are
nearly inactive for olefin hydrogenation.\cite{19} There have been several studies of the
dissociation of the monomer to form the dimer in benzene using UV-Vis spectroscopy,
all of which agreed the equilibrium constant for the formation of the dimer was on the
order of $10^{-4}$ for temperatures ranging from 20-25°C.\cite{20-22} Other studies involving the
activity of the dimer toward hydrogen determined the dimer to be more likely to
oxidatively add hydrogen to the Rh centers than previously thought by using
parahydrogen induced polarization (PHIP) NMR studies (for making NMR signals easier
to observe).\cite{23-25} Using PHIP, Duckett et al verified the ability of the dimer to activate
hydrogen in benzene as the reaction solvent and reinforced the notion that the dimer is
much slower at activating hydrogen than the monomer, though no rate constants were
given.\cite{23} Future work showed only one Rh atom in the dimer was able to activate
hydrogen (a 1:1 Rh:H ratio), leading to the conclusion that the dimer acted as a hydrogen
reservoir during the course of the reaction.\cite{24, 25} Recently, Goodman et al performed
dynamic NMR experiments of Wilkinson’s catalyst in tetrahydrofuran (THF) and
determined the most labile endogenous PPh$_3$ ligands to be the ones that are cis to the Cl
ligand (and, therefore, trans to each other).\cite{26} This study is particularly relevant because
understanding the exact dynamics of the fluxionality of the monomer may be useful to
numerous processes that employ Wilkinson’s catalyst in determining the structures of
possible reaction intermediates and transition states and how the active Rh species
interact with the substrates during catalytic reactions.

As an alternative example to Wilkinson’s catalyst, Nosova et al used $^1$H and $^{13}$C
NMR to elucidate structural changes of palladium acetate, Pd(OAc)$_2$, a common catalytic
precursor, which exists as a cyclic trimer, [Pd(OAc)$_2$]$^3$.\cite{27} They showed in methanol at -
18°C that methanol molecules react with the precursor to form methoxy-bridged trimers followed by formation of Pd clusters, while at 27°C, the initial Pd(II) is reduced to Pd(0). Additionally, solvent can interact with precursor and coordinate to the metal center, acting as a ligand. A highly efficient catalyst for the aerobic oxidation of alcohols is the Pd(OAc)$_2$/pyridine system (toluene is the reaction solvent, pyridine is a ligand)$^{[28-34]}$, in which equivalents of pyridine (acting in a small quantity as a solute/ligand, not a solvent) with respect to the total amount of Pd are added to the reaction mixture to coordinate to the Pd center to form the active species.$^{[35]}$ However, if the coordination of the solvent to the metal center is too strong, then the reactant must compete to interact with the metal center, which inhibits the catalytic activity. This inhibitory effect is seen with Wilkinson’s catalyst in neat pyridine and neat dimethyl sulfoxide (DMSO) where the solvents coordinate to the Rh center, which causes the organometallic species to be inactive for olefin hydrogenation.$^{[19]}$ These two examples illustrate the positive and negative effects of solvent molecules (or molecules such as pyridine that can be treated as solvents or solutes, depending on concentration) on the activities and selectivities upon coordination to homogeneous catalysts.

This study consists of the synthesis and characterization of supported Rh organometallic catalysts on phosphine-functionalized SBA-15 using Wilkinson’s catalyst as the precursor in order to determine the effect of different grafting solvents on the resulting immobilized active species. The model reaction for this system is the hydrothiolation of phenylacetylene by thiophenol, which allows for the assessment of the catalytic activity and regio- and stereoselectivity of each grafted catalyst.$^{[36-38]}$ We compare the heterogeneous activity and selectivity of each catalyst using a common
reaction solvent, 1,2-dichloroethane (DCE), in order to determine which grafting solvents produce the most active catalysts.\textsuperscript{39} We elucidate the active species present in each catalyst using solid-state NMR spectroscopy and combine these spectroscopic results with our kinetic data in order to establish structure-function relationships. Additionally, we compare the activity and selectivity of Wilkinson’s catalyst in each of the grafting solvents as reaction solvents to determine the activity and selectivity of each of their respective supported analogs to see if the homogeneous kinetic trends correlate with the heterogeneous kinetic trends.

6.2 Experimental

6.2.1 Materials

All procedures were conducted either in a glovebox or on a Schlenk line in the presence of inert gas. All materials, including anhydrous solvents and Wilkinson’s catalyst, were obtained from Sigma, with the exception of P123, which was obtained from BASF. All deuterated solvents were obtained from Cambridge Isotope Laboratories.

6.2.2 Synthesis of SBA-15

SBA-15 silica was prepared according to the literature procedure.\textsuperscript{40} In a standard synthesis, 4.0 g of P123 triblock copolymer, (EO)\textsubscript{20}(PO)\textsubscript{70}(EO)\textsubscript{20}, was added to 30 mL of deionized water. Next, 120 mL of 2 M HCl was added to the mixture, which was stirred vigorously until the P123 was completely dissolved. 8.5 g of tetraethylorthosilicate (TEOS) was added, the mixture heated to 35°C, and stirred for 20 h. Next, the mixture was placed in an oven at 100°C for 24 h. The mixture was then filtered and washed.
thoroughly with deionized water and ethanol. The solid residue was calcined at 550°C for 12 h.

6.2.3 Synthesis of Cl-SBA-15

SBA-15 (2.0 g) was calcined at 200°C for 6 h under vacuum in a Schlenk flask. After evacuation, the flask was filled with inert gas and 5.33 mL of 3-chloropropyltriethoxysilane and 30 mL of anhydrous toluene were added. The flask was then heated to 120°C and refluxed for 24 h under an inert atmosphere. The mixture was filtered and washed with anhydrous dichloromethane several times and then dried under vacuum for 24 h. The resulting solid was labeled Cl-SBA-15 and stored under an inert atmosphere.

6.2.4 Synthesis of P-SBA-15

1.5 g of Cl-SBA-15 and 16 mL of a 0.5 M solution of lithium diphenylphosphide, LiPPh₂, in THF was added to a Schlenk flask under an inert atmosphere and stirred for 20 h at room temperature. The mixture was filtered and washed with anhydrous dichloromethane several times and then dried under vacuum for 24 h. The resulting solid was labeled P-SBA-15 and stored under an inert atmosphere.

6.2.5 Synthesis of Supported Rh Catalysts in Various Grafting Solvents

1.5 g of P-SBA-15 and 150 mg (0.16 mmol) of Wilkinson’s catalyst were charged to a Schlenk flask and filled with inert gas and enough anhydrous grafting solvent (benzene, THF, DMSO, toluene, pyridine, DCE), usually 25-30 mL, to wet the P-SBA-15
and dissolve the Wilkinson’s catalyst. For the catalysts grafted in toluene and DCE with 1 equivalent of DMSO, 11.4 μL (0.16 mmol) of DMSO was also added at this point in the synthesis. The grafting mixture was stirred for 2 days at room temperature and then filtered and washed with the chosen grafting solvent several times. The resulting catalyst was dried under vacuum for 24 h, labeled according to the grafting solvent used, and stored under an inert atmosphere.

6.2.6 Heterogeneous Hydrothiolation Reactions

In a typical catalytic reaction using one of the supported Rh catalysts, 50 mg of catalyst and 2 mL of DCE (the reaction solvent for all heterogeneous catalysts tested) were admitted to a Schlenk flask with a magnetic stir bar under an inert atmosphere. Phenylacetylene (0.5 mmol, 54.9 μL), thiophenol (0.55 mmol, 56.4 μL), and CH₂Br₂ (0.5 mmol, 35.5 μL) as an internal standard for ¹H NMR analysis were subsequently admitted to the flask under an inert atmosphere. Aliquots of the crude reaction mixture were analyzed using ¹H NMR in order to measure turnover numbers (TON) relative to the total amount of Rh as determined by ICP-OES performed by Galbraith Laboratories, Inc.

6.2.7 Homogeneous Hydrothiolation Reactions

For all homogeneous hydrothiolation reactions, 2-3 mg (2.2-3.2 mmol) of Wilkinson’s catalyst was dissolved in 2 mL of each grafting solvent (benzene, THF, DMSO, toluene, pyridine, DCE) under an inert atmosphere. Each catalyst solution was charged with the same amounts of phenylacetylene (0.5 mmol), thiophenol (0.55 mmol), and CH₂Br₂ (0.5 mmol) as the heterogeneous reactions and then thoroughly mixed.
Aliquots of each sample were placed in J. Young tubes to prevent contamination from atmospheric oxygen and analyzed every 5 min by $^1$H NMR. Peaks corresponding to the anti-Markovnikov and Markovnikov products were integrated to determine the total moles of each and normalized to the amount of Rh present as the monomer according to $^{31}$P NMR analysis.

6.2.8 Liquid Phase $^1$H and $^{31}$P NMR Measurements

Liquid phase NMR samples were run on a Bruker AV-360 or Advance 300 at room temperature for 16 scans ($^1$H) or 128 scans ($^{31}$P). Spectra for heterogeneous reactions were recorded in CDCl$_3$ while the homogeneous hydrothiolation reactions were recorded in the deuterated form of each of the grafting solvents. For $^{31}$P NMR spectra of Wilkinson’s catalyst only, the peaks corresponding to the monomer (a doublet of triplets and a doublet of doublets) and dimer (a doublet of doublets) were integrated and normalized to the total number of P atoms native to each Rh species (three for the monomer, four for the dimer). These areas were used to determine the amount of dimer present relative to the amount of monomer in each reaction solvent. 2D $^{31}$P{$^1$H} HETCOR (heteronuclear correlation) solid-state NMR spectra were run on a Bruker AV-300 spectrometer. External standards TMS ($^1$H, $\delta = 0$ ppm) and H$_3$PO$_4$ (85% in water, $^{31}$P, $\delta = 0$ ppm) were used to calibrate the chemical shifts in each spectrum.

6.2.9 XPS Measurements

XPS measurements were recorded using a Kratos Ultra X-ray Photoelectron Spectrometer, equipped with an Al K$\alpha$ x-ray source. Survey and multi-region spectra
were recorded for Rh 3d, C 1s, O 1s, Cl 2p, P 2p, and Si 2p peaks. All binding energies were shifted by defining the C 1s peak at 284.6 eV.

6.3. Results and Discussion

6.3.1 Homogeneous Hydrothiolation Kinetic Experiments using Wilkinson’s Catalyst in Various Solvents

Figure 6.1 shows $^{31}$P NMR spectra of Wilkinson’s catalyst in the chosen grafting solvents (benzene, THF, DMSO, toluene, pyridine, DCE). The catalytically active Rh monomer produces two sets of resonances: a doublet of triplets and a doublet of doublets.$^{[41]}$ The catalytically less active Rh dimer produces a doublet of singlets that is shifted farther downfield than both sets of resonances from the monomer and trace amounts of triphenylphosphine oxide (OPPh$_3$) appear as sharp singlets upfield, which are present as a minor contaminant in commercially available Wilkinson’s catalyst.$^{[42]}$ Both monomer and dimer are present in every solvent except DMSO and pyridine (py). In DMSO, only free PPh$_3$ (not pictured) and OPPh$_3$ are observed, while the appearance of a doublet near $\delta = 33$ ppm in py indicates the presence of a new Rh-P species. Heaton et al observed this complex and were unable to assign it a structure, but they deduced that it was not a monophosphine complex due to its $^{31}$P NMR spectral differences from cis and trans isomers of RhCl(py)$_2$(PPh$_3$).$^{[43]}$ In DMSO, Banerjee and Wong explained the lack of peaks associated with the monomer in the $^{31}$P NMR spectrum to the rapid exchange of PPh$_3$ ligands, which makes the signals unobservable.$^{[44]}$ The presented $^{31}$P NMR results suggest that the solvents with the catalytically active monomer will be the most active for hydrothiolation while DMSO and py will not be as active.
Figure 6.1. $^{31}$P NMR of Wilkinson’s catalyst in various solvents. The common species are the (a) chloro-bridged Rh dimer, [RhCl(PP$_3$)$_2$]$_2$, and the (b) monomer. They are marked in the DCE spectrum for convenience.
Figure 6.2 shows the turnover number (TON) for the hydrothiolation of phenylacetylene and thiophenol using Wilkinson’s catalyst in each of the grafting solvents as the reaction solvents at 25°C. Table 6.1 summarizes the conversions, regio- and stereoselectivities, and the amount of monomer present in each reaction solvent, as determined by $^{31}$P NMR, where applicable. As expected, DMSO was barely active and only formed the Markovnikov product while py was completely inactive. THF and benzene were the most active solvents for hydrothiolation and each solvent achieved 91% regioselectivity toward the anti-Markovnikov product and were 100% stereoselective in favor of the $E$-isomer (note: we define regioselectivity with respect to the anti-Markovnikov product and stereoselectivity with respect to the $E$-isomer for all kinetic analyses, unless otherwise specified). Toluene and DCE were the next most active solvents for hydrothiolation, each with excellent regioselectivity (95% for toluene, 92% for DCE) and 100% stereoselectivity. These results are consistent with a previous report of the preference of homogeneous Wilkinson’s catalyst to form the $E$-isomer, though the $Z$-isomer was favored when the reaction solvent was ethanol.$^{[38]}$ In this same study, DCE was more active than benzene and THF for formation of vinyl sulfides, though the thiol used was 2,2,2-trifluoroethanethiol instead of thiophenol, which likely accounts for the differences in observed activities. From Table 6.1, the solvent that contained the most monomer was DCE (98 mol % Rh as monomer), yet it was most comparable in activity to toluene, which only contained 82% Rh as monomer. Both benzene and THF contained 91% Rh as monomer and displayed identical regio- and stereoselectivities, though THF achieved a higher conversion (66% compared to 49% for benzene). These results
Figure 6.2. Kinetics of homogeneous hydrothiolation of phenylacetylene and thiophenol in different solvents at 25°C. The tested solvents are benzene (circles), THF (squares), DMSO (diamonds), toluene (open circles), py (open squares), and DCE (open diamonds). Samples of the reaction mixture were analyzed by $^1$H NMR using CH$_2$Br$_2$ as the internal standard. Reaction conditions: 0.5 mmol alkyne, 0.55 mmol thiol, 2 mL solvent, 2-3 mg catalyst (TON values are normalized to the mmol of Rh present as monomer or total mmol of Rh if no monomer is present as determined by $^{31}$P NMR).
Table 6.1. Conversion and selectivity of Wilkinson’s catalyst for the homogeneous hydrothiolation of phenylacetylene and thiophenol at 25°C in various solvents. Samples of the reaction mixture were analyzed by $^1$H NMR using CH$_2$Br$_2$ as the internal standard. Reaction conditions: 0.5 mmol alkyne, 0.55 mmol thiol, 2 mL solvent, 2-3 mg catalyst.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Conversion (%)$^a$</th>
<th>Regioselectivity (%)$^b$</th>
<th>Stereoselectivity (%)$^c$</th>
<th>Rh Monomer(mol %)$^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>49</td>
<td>91</td>
<td>100</td>
<td>91</td>
</tr>
<tr>
<td>THF</td>
<td>66</td>
<td>91</td>
<td>100</td>
<td>91</td>
</tr>
<tr>
<td>DMSO</td>
<td>6</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Toluene</td>
<td>27</td>
<td>95</td>
<td>100</td>
<td>82</td>
</tr>
<tr>
<td>Py</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DCE</td>
<td>39</td>
<td>92</td>
<td>100</td>
<td>98</td>
</tr>
</tbody>
</table>

$^a$Calculated from the total moles of product formed compared to the initial number of moles of phenylacetylene. $^b$anti-Markovnikov product. $^c$E-isomer. $^d$Determined by $^{31}$P NMR.
demonstrate that solvents containing the most Rh present as the catalytically active monomer are not necessarily the most active and selective homogeneous reaction media.

6.3.2 Effect of “Inhibiting Solvents” (DMSO and Pyridine) on the Structure and Activity of Wilkinson’s Catalyst in a Common Solvent (DCE)

In an effort to quantify the degree to which DMSO and py inhibit the hydrothiolation reaction, we examined the structural changes in Wilkinson’s catalyst in DCE, a solvent in which both monomer and dimer were observed, using stoichiometric amounts of the two inhibiting solvents relative to the total amount of Rh initially present. Figure 6.3 shows the $^{31}$P NMR of 1 equivalent of Wilkinson’s catalyst in DCE in the presence of 1 equivalent of py and 1 equivalent of DMSO and, considering the lack of activity in both DMSO and py as reaction solvents, the spectroscopic results are quite surprising. In the presence of 1 equivalent of py, there is no monomer or dimer present, only free PPh$_3$ and OPPh$_3$ with an unknown resonance at $\delta = 22.9$ ppm. The large amount of free PPh$_3$ and conspicuous absence of the catalytically active monomer suggests that py completely deactivates the Rh present in solution, which is consistent with the results in Figure 6.2. The results of the addition of 1 equivalent of DMSO to 1 equivalent of Wilkinson’s catalyst are remarkable because the catalytically active monomer is present without any traces of the catalytically inactive dimer. When compared to the $^{31}$P NMR results in Figure 6.1 for pure DMSO, the presence of the catalytically active species with 1 equivalent of DMSO is striking because it implies that DMSO, or any solvent, may have markedly different structural (and fluxional) effects on transition metal complexes when present as a solute (i.e. in a smaller quantity, acting more as a ligand if the solvent
Figure 6.3. $^{31}$P NMR of Wilkinson’s catalyst in the presence of 1 equivalent of py and 1 equivalent of DMSO using DCE as a common solvent (pure Wilkinson’s catalyst in DCE is shown for comparison). The monomer and dimer are absent with 1 equivalent of py present, but the monomer exists without any dimer in presence of 1 equivalent of DMSO. No activity for the hydrothiolation is observed in presence of 1 equivalent of py (no active Rh species is present), but enhanced activity is observed in the presence of 1 equivalent of DMSO (all Rh is present as the active monomer).
coordinates to the metal center) instead of acting as a solvent. In other words, when DMSO is present as a solute in a small quantity, it suppresses dimer formation, but when it is present in excess as a solvent, the rapid exchange of PPh₃ ligands and coordination of solvent molecules dramatically inhibits the hydrothiolation reaction. The absence of the dimer initiated another kinetic study in which we determined the effects of adding varying amounts of DMSO to the hydrothiolation reaction in DCE, the results of which are presented in Figure 6.4 and summarized in Table 6.2. From the figure, the addition of even 1 equivalent of DMSO increased the catalytic activity from that in pure DCE, implying that when DMSO acts as a solute (i.e. a ligand from an organometallic perspective) with the Rh species in solution, it prevents dimerization without coordinating to the Rh too strongly so as to inhibit the catalysis. We performed an identical reaction with 1 equivalent of py and the reaction was completely inhibited, confirming the lack of catalytically active homogeneous Rh species. Each DMSO-enhanced catalyst (1-80 equivalents) exhibits high activity (91-100% conversion after 1 h) with 95% regioselectivity and 100% stereoselectivity. Once larger amounts of DMSO are admitted to the reaction system (i.e. the reaction solvent becomes richer in DMSO), the activity eventually decreases until it is comparable to pure DMSO. In the presence of at least 80 equivalents of DMSO, the ³¹P NMR spectrum for Wilkinson’s catalyst is identical to the spectrum obtained for Wilkinson’s catalyst in neat DMSO (Figure 6.3). Therefore, the reported TON values are normalized to the total amount of Rh present for reactions run in at least 80 equivalents of DMSO, while the other TON values are normalized to the total amount of Rh present as monomer. The kinetic results in the presence of 80 equivalents of DMSO are particularly insightful because they demonstrate
Figure 6.4. Kinetics of homogeneous hydrothiolation of phenylacetylene and thiophenol in DCE with varying equivalents of DMSO (relative to the amount of Wilkinson’s catalyst) at 25°C. Solvent systems tested include pure DCE (circles), 1 equivalent DMSO (squares), 5 equivalents (diamonds), 80 equivalents (open circles), 1000 equivalents (open squares), 10000 equivalents (open diamonds), and pure DMSO (triangles). The addition of DMSO increases the activity of Wilkinson’s catalyst to a constant level (1-80 equivalents) and gradually decreases once the reaction solvent has higher compositions of DMSO. Reaction conditions: 0.5 mmol alkyne, 0.55 mmol thiol, 2 mL solvent (DCE and DMSO combined), 2-3 mg catalyst (TON values are normalized to the mmol of Rh present as monomer or total mmol of Rh if no monomer is present as determined by $^{31}$P NMR).
Table 6.2. Conversion and regioselectivity of Wilkinson’s catalyst for the homogeneous hydrothiolation of phenylacetylene and thiophenol at 25°C in DCE using different equivalents of DMSO relative to the amount of Wilkinson’s catalyst present. Samples of the reaction mixture were analyzed by $^1$H NMR using CH$_2$Br$_2$ as the internal standard. Reaction conditions: 0.5 mmol alkyne, 0.55 mmol thiol, 2 mL solvent, 2-3 mg catalyst. With the exception of the reaction run in neat DMSO, all reactions were completely stereoselective toward the $E$-isomer.

<table>
<thead>
<tr>
<th>Equivalents of DMSO</th>
<th>Conversion (%)$^a$</th>
<th>Regioselectivity (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (Neat DCE)</td>
<td>39</td>
<td>92</td>
</tr>
<tr>
<td>1</td>
<td>94</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>91</td>
<td>95</td>
</tr>
<tr>
<td>80</td>
<td>100</td>
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<tr>
<td>1000</td>
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<td>97</td>
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<td>10000</td>
<td>15</td>
<td>95</td>
</tr>
<tr>
<td>Neat DMSO</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

$^a$Calculated from the total moles of product formed compared to the initial number of moles of phenylacetylene. $^b$anti-Markovnikov product.
the ability of DMSO molecules to interact with the Rh species (i.e. the lack of monomer and dimer due to the fluxionality of the inner-sphere ligands rapidly exchanging in the presence of DMSO) while increasing the catalytic activity to the same degree when using only 1-5 equivalents of DMSO when the monomer is still present in the $^{31}$P NMR spectra. In contrast, when the solvent is composed purely of DMSO, the rapid exchange of PPh$_3$ ligands and interaction of DMSO molecules with Wilkinson’s catalyst dominates the behavior at the Rh centers in solution and is most likely preferable thermodynamically than the hydrothiolation reaction under the same conditions. Based on these kinetic results, we hypothesized that adding 1 equivalent of DMSO during the grafting step of the supported catalyst synthesis would tether more active Rh sites to the surface compared to the catalysts grafted in pure solvents.

6.3.3 Heterogeneous Hydrothiolation Kinetic Experiments using Supported Analogs of Wilkinson’s Catalyst Grafted in Various Solvents

Figure 6.5 shows the activity and selectivity of each supported Rh catalyst grafted in the six different solvents using DCE as a common heterogeneous reaction solvent at 25°C. Table 6.3 summarizes all reaction results, including the Rh wt % of each grafted catalyst. All grafted catalysts were completely regioselective toward the anti-Markovnikov product. Benzene, toluene, and DCE formed the most active supported Rh catalysts with linearly increasing TONs as functions of time and complete stereoselectivity. The catalysts grafted in THF, DMSO, and py were initially an order of magnitude more active than the other catalysts, though they were not completely stereoselective. Figure 6.5b shows that, as time elapses, more of the $E$-isomer is formed,
Figure 6.5. (a) Activities and (b) selectivities of hydrothiolation of phenylacetylene and thiophenol over supported analogs of Wilkinson’s catalyst on phosphine-functionalized SBA-15 in DCE as a common reaction solvent at 25°C. The grafting solvents are benzene (circles), THF (squares), DMSO (diamonds), toluene (open circles), py (open squares), and DCE (open diamonds). Reaction conditions: 0.5 mmol alkyne, 0.55 mmol thiol, 2 mL solvent, 50 mg catalyst (2.8-5.2 μmol Rh).
Table 6.3. Conversion and stereoselectivity of a series of supported Rh catalysts grafted in different solvents for the heterogeneous hydrothiolation of phenylacetylene and thiophenol at 25°C in DCE. Samples of the reaction mixture were analyzed by $^1$H NMR using CH$_2$Br$_2$ as the internal standard. Reaction conditions: 0.5 mmol alkyne, 0.55 mmol thiol, 2 mL solvent, 50 mg catalyst (2.8-5.2 μmol Rh). All supported catalysts were completely regioselective toward the anti-Markovnikov product. The listed values were determined after 5 h unless otherwise specified.

<table>
<thead>
<tr>
<th>Grafting Solvent</th>
<th>Rh wt %$^a$</th>
<th>Conversion (%)$^b$</th>
<th>TOF (h$^{-1}$)$^c$</th>
<th>Stereoselectivity (%)$^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>0.919</td>
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<td>5.05</td>
<td>100</td>
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<tr>
<td>THF</td>
<td>0.806</td>
<td>15</td>
<td>20.17$^f$</td>
<td>88</td>
</tr>
<tr>
<td>DMSO</td>
<td>0.572</td>
<td>18</td>
<td>32.02$^f$</td>
<td>51</td>
</tr>
<tr>
<td>Toluene</td>
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<td>21$^d$</td>
<td>6.39$^d$</td>
<td>100$^d$</td>
</tr>
<tr>
<td>Py</td>
<td>0.71</td>
<td>10$^e$</td>
<td>15.65$^f$</td>
<td>38$^e$</td>
</tr>
<tr>
<td>DCE</td>
<td>0.971</td>
<td>38</td>
<td>8.26</td>
<td>100</td>
</tr>
<tr>
<td>Toluene (1 eq. DMSO)</td>
<td>0.935</td>
<td>34</td>
<td>8.22</td>
<td>100</td>
</tr>
<tr>
<td>DCE (1 eq. DMSO)</td>
<td>1.07</td>
<td>43</td>
<td>9.01</td>
<td>100</td>
</tr>
</tbody>
</table>

$^a$Determined by ICP-OES. $^b$Calculated from the total moles of product formed compared to the initial number of moles of phenylacetylene. $^c$E-isomer. $^d$After 4 h. $^e$After 2 h. $^f$After 1 h.
though the Z-isomer is formed in a larger quantity for the THF, DMSO, and py-grafted catalysts during the first hour. This time dependency of the stereoselectivities of the heterogeneous catalysts is perhaps the biggest difference from the observed homogeneous kinetic experiments. The initial formation of the Z-isomer (the kinetic product) and its subsequent disappearance to form the E-isomer (the thermodynamic product) indicates the possibility of isomerization by the supported Rh catalysts. Furthermore, the catalysts grafted in THF, DMSO, and py all grafted the least amounts of Rh onto the supported catalysts out of all the grafting solvents used (Table 6.3). Figure 6.6 shows the activities of catalysts grafted in toluene and DCE with 1 equivalent of DMSO relative to the total amount of Wilkinson’s catalyst present and the activity of each catalyst with 1 equivalent of DMSO is higher when compared to the catalysts grafted in pure solvents. The initial TOFs are shown in Figure 6.6 and the specific values for these fits are shown in Table 6.3. There is a slight increase in the TOF of the catalyst grafted in DCE with 1 equivalent of DMSO (9.01 h⁻¹) compared to the catalyst grafted in neat DCE (8.22 h⁻¹). The initial TOF for the catalyst grafted in toluene (6.39 h⁻¹) increases by a factor of 1.3 when 1 equivalent of DMSO is added during the grafting process (8.22 h⁻¹). From Figure 6.1 and Table 6.1, Wilkinson’s catalyst in DCE forms a small amount of dimer (98% monomer), especially compared to toluene (82% monomer), which subsequently explains the larger increase in initial TOF for the catalyst grafted in toluene with 1 equivalent of DMSO because a larger amount of monomeric (active) Rh was able to be grafted when compared to grafting in neat toluene. The ICP-OES results for the Rh wt % loadings of these catalysts grafted in the presence of 1 equivalent of DMSO confirm that more total Rh, and likely monomeric Rh, was indeed grafted onto the supports when compared to the
Figure 6.6. Effect of the addition of 1 equivalent of DMSO to grafting solvents on the activities of the resulting supported Rh catalysts. The two most active supported catalysts using pure solvents were grafted in toluene (circles) and DCE (squares), but the addition of 1 equivalent of DMSO in both toluene (open circles) and DCE (open squares) during the grafting process increased the activity of each catalyst. Linear fits of the initial TOFs are shown for each data set as solid lines. Only the $E$-isomer was formed in all four cases.
catalysts grafted in the neat solvents (Table 6.3). These kinetic results confirm our hypothesis that the addition of 1 equivalent of DMSO would enhance the catalytic activities of the supported Rh catalysts.

It is critical to discuss the similarities and differences between the observed activities and selectivities of the homogeneous and heterogeneous reactions in order to draw the appropriate conclusions of the effects of each of the grafting solvents. THF was the most active solvent for homogeneous hydrothiolation and exhibited complete stereoselectivity toward the E-isomer, yet the supported Rh catalyst grafted in THF was not the most active and initially favored formation of the Z-isomer. This result is surprising in the context of the $^{31}$P NMR results of Figure 6.1 because the catalytically active monomer is present in THF. Furthermore, the monomer is present in benzene, toluene, and DCE, which all resulted in grafting more active and stereoselective heterogeneous catalysts. The kinetic results for THF demonstrate two important and related points: the most active solvents for a homogeneous catalytic reaction do not necessarily allow for the grafting of the most active heterogeneous analogs and the grafting solvent may have subtle effects on the solvated transition metal complexes during the grafting step that lead to the formation of unexpected catalytic species and structures that are less active than their homogeneous counterparts. Benzene, toluene and DCE all formed supported Rh catalysts that were completely regioselective (superior to their homogeneous analogs, by comparison) and stereoselective, though it is interesting that benzene was more active for the homogeneous hydrothiolation than either toluene or DCE, but produced a less active heterogeneous catalyst than either toluene or DCE. Furthermore, we achieved a higher Rh loading on phosphine functionalized SBA-15
using benzene (0.919 wt %) compared to toluene (0.896 wt %) as the grafting solvent, yet the catalyst grafted in benzene was not as active as the catalyst grafted in toluene. This result demonstrates the subtlety of the effects of the grafting solvent on the final supported organometallic catalyst, in the sense that it is logical to expect the grafting solvent capable of grafting the most amount of metal species on the surface would produce the most active heterogeneous catalyst, though our results indicate this expectation is not always the case. The catalysts grafted in DMSO and py were poorly active and stereoselective (51% after 5 h for DMSO, 38% after 2 h for py), which is unsurprising due to the lack of catalytically active Rh species present in their respective homogeneous $^3$P NMR spectra (Figure 6.1, Table 6.1). The ICP-OES results in Table 6.3 confirm that DMSO and py grafted the least amounts of Rh onto the SBA-15 support.

6.3.4 Spectroscopic Elucidation of the Structures of the Supported Analogs of Wilkinson’s Catalyst and Subsequent Quantification of the Effects of the Grafting Solvents in Terms of the Observed Catalytic Activities and Selectivities

We obtained XPS spectra for each grafted catalyst in order to confirm the existence of Rh, Cl, and P species on the surface of each catalyst (i.e. elemental analysis). Figure 6.7a shows the XPS results for the six neat grafting solvents, with the Rh 3d, Cl 2p, and P 2p peaks outlined in dashed boxes for clarity. The presence of these three peaks, characteristic of pure Wilkinson’s catalyst, indicates that Wilkinson’s catalyst was, in some form, tethered to each functionalized surface. Figure 6.7b compares the XPS spectra for the catalysts grafted in toluene and DCE to their counterparts grafted in the same solvents with 1 equivalent of DMSO. The intensities of the Rh 3d, Cl 2p, and P 2p
Figure 6.7. XPS spectra of supported analogs of Wilkinson’s catalyst grafted in (a) neat solvents and (b) toluene and DCE with and without 1 equivalent of DMSO relative to Wilkinson’s catalyst. The Rh 3d, Cl 2p, and P 2p peaks are outlined in dashed boxes for clarity.
peaks for the catalysts grafted in the presence of 1 equivalent of DMSO are larger when compared to the catalysts grafted without any added DMSO, especially for toluene. These results are consistent with the ICP-OES analysis (Table 6.3) which demonstrated that more Rh was grafted to the functionalized SBA-15 surface when 1 equivalent of DMSO was added either to toluene or DCE. The most important structural information obtained is the 1:1 atomic ratio of Rh:Cl in each sample, which shows that Cl ligands were not displaced during grafting.

We performed 2D $^{31}$P{$^{1}$H} HETCOR NMR experiments in order to elucidate the supported Rh structures on the functionalized SBA-15 surfaces as a function of the nature of the grafting solvent. The catalysts grafted in benzene, toluene, and DCE, as well as the toluene and DCE catalysts grafted in the presence of 1 equivalent of DMSO (Figures 6.8-6.12, respectively) produced identical spectra, which is consistent with our previously observed results for supported Rh catalysts linked to SBA-15 via diphenylphosphine groups (Figure 6.13).[45] In Figures 6.8-6.12, the peaks near $\delta = -15$ ppm in the $^{31}$P NMR spectra correspond to the free diphenylphosphine ($-\text{PPh}_2$) moieties supported by propyl backbones on the SBA-15 surface. The peaks near $\delta = 28$ and $42$ ppm correspond to the immobilized Rh species linked to two $-\text{PPh}_2$ groups on the SBA-15 surface, with retention of one endogenous $\text{PPh}_3$ ligand and the endogenous Cl ligand. We previously observed these surface Rh species to be highly active for hydrothiolation with complete regioselectivity in favor of the anti-Markovnikov product and complete stereoselectivity in favor of the $E$-isomer.[45] The catalysts grafted in benzene, toluene, and DCE (grafted with or without 1 equivalent of DMSO) exhibit the same activity, regio-,
Figure 6.8. 2D $^{31}\text{P}$$^{1}\text{H}$ HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in benzene.
Figure 6.9. 2D $^{31}$P-$^1$H HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in toluene.
Figure 6.10. 2D $^{31}$P-$^1$H HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in DCE.
Figure 6.11. 2D $^{31}$P/$^1$H HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in toluene with 1 equivalent of DMSO relative to the total amount of Wilkinson’s catalyst.
Figure 6.12. 2D $^{31}$P-$^1$H HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in DCE with 1 equivalent of DMSO relative to the total amount of Wilkinson’s catalyst.
stereoselectivity we previously determined for the supported Rh catalyst presented in Figure 6.13.

Interestingly, the 2D $^{31}\text{P}\{^{1}\text{H}\}$ HETCOR NMR results for the catalysts grafted in THF, DMSO, and py also produced identical spectra (Figures 6.14-6.16, respectively). In each spectrum, there is little-to-no signal indicating the presence of free -PPh$_2$ groups on the SBA-15 surface. In the range of $\delta = 18-40$ ppm for each of these catalysts, there are overlapping peaks, which we attribute to two main contributors: covalently bound Rh to the -PPh$_2$ groups on the SBA-15 surface (the single-site active species in Figure 6.13) and physisorbed Wilkinson’s catalyst. Wilkinson’s catalyst physisorbed on SBA-15 has been detected previously using solid-state $^{31}$P NMR and was observed at a lower value of the chemical shift when compared to the covalently bound Rh species.$^{[4]}$ In a separate control experiment, we observed physisorbed Wilkinson’s catalyst to produce a single peak in $^{31}$P solid-state NMR shifted to $\delta = 24$ ppm instead of the $\delta = 28$ ppm observed for the covalently bound Rh species. It is also possible that, in the range of $\delta = 18-40$ ppm, there are contributions from the interactions of the diphenylphosphine groups with the surface silanols.$^{[4]}$ The presence of physisorbed Wilkinson’s catalyst explains the time-dependent stereoselectivity present in the catalysts grafted in THF, DMSO, and py. Specifically, the lower Rh wt % loadings for each of these catalysts indicate a much lower loading of single-site (i.e. active) Rh, which would explain the rapid initial formation of the kinetic product (the Z-isomer) with eventual isomerization to the thermodynamic product (the E-isomer). The most important qualitative information we obtained from the 2D $^{31}\text{P}\{^{1}\text{H}\}$ HETCOR NMR experiments is the clear distinction between the catalysts with high activity and complete stereoselectivity toward the E-isomer and the less active catalysts
Figure 6.13. Single-site structure of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15. This supported Rh species is the active species for the hydrothiolation of phenylacetylene by thiophenol.
Figure 6.14. 2D $^{31}$P-$^1$H HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in THF.
Figure 6.15. 2D $^{31}\text{P}$-$^{1}\text{H}$ HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in DMSO.
Figure 6.16. 2D $^{31}$P/$^1$H HETCOR NMR of Wilkinson’s catalyst immobilized on phosphine-functionalized SBA-15 grafted in py.
that exhibit time dependent stereoselectivity. The single-site Rh catalysts we observed for the species grafted in benzene, toluene, and DCE (with and without 1 equivalent of DMSO) all exhibited similar NMR spectra, indicative of the same active structure (the single-site Rh species). The catalysts grafted in THF, DMSO, and py also exhibited similar spectra, once again indicating that they have identical Rh structures on the surface, which is consistent with each of these catalysts exhibiting poor long term activity and time dependent stereoselectivity. Each of the bad catalysts also produced peaks in the range of $\delta = 65$-$68$ ppm, which could be due to coordination of the grafting solvent molecules to the immobilized Rh species, causing a shift in the resonances previously observed for the immobilized Rh species linked to two -PPh$_2$ groups ($\delta = 28$ and $42$ ppm). These peaks show strong correlations with the protons from the propyl backbones and the phenyl groups of the endogenous PPh$_3$ ligands of Wilkinson’s catalyst, which indicate a separate surface Rh species from the active, single-site structure observed for the active and completely stereoselective supported catalysts.

6.4 Conclusions

We performed homogenous hydrothiolations in various solvents using Wilkinson’s catalyst as a model compound for determining the effect of the grafting solvent in the synthesis of immobilized organometallic catalysts. Using $^{31}$P NMR, we demonstrated the lack of active Rh species in DMSO and py as homogeneous reaction solvents, which we confirmed via hydrothiolation reactions. We synthesized supported Rh catalysts on phosphine-functionalized SBA-15 and characterized each sample using XPS, ICP-OES, and 2D $^{31}$P{$^1$H} HETCOR NMR and determined that Rh, Cl, and P were
present in all samples. Heterogeneous hydrothiolation experiments showed that solvents that were active and selective for homogeneous hydrothiolation did not necessarily result in grafting the most active and selective Rh species on the functionalized SBA-15. 2D $^{31}$P{$^1$H} HETCOR NMR experiments differentiated between the highly active, regio-, and stereoselective catalysts (single-site Rh structures on the SBA-15 surface) and the less active, time dependent stereoselective catalysts (a mixture of Rh species on the SBA-15 surface, including physisorbed Wilkinson’s catalyst). Including 1 equivalent of DMSO relative to the amount of Wilkinson’s catalyst during the grafting process resulted in more total (and active) Rh being covalently bound to the $\text{-PPh}_2$ groups on the SBA-15 surface. Additionally, we illustrated the importance of exhaustive homogeneous and heterogeneous kinetic and spectroscopic analyses of catalytic materials in order to elucidate the structures of the catalytic species present in each system and, subsequently, to determine the correct structure-function relationship based on the active structures. The results of our study do not apply to homogeneous and heterogeneous catalytic systems only, but any system in which solvent is a necessary medium and may have adverse (or beneficial, as we showed) kinetic and/or structural effects on the reagents which could potentially alter the process in question in undesirable (i.e. lower activity/selectivity) or unexpected (i.e. subtle changes in the final synthesized structure) ways.
6.5 References


Chapter 7
Conclusions and Future Work

7.1 Conclusions of the Dissertation

We examined the binding of monodentate and bidentate ligands to PdCl$_2$(solv)$_2$ in various solvents using ITC and obtained full thermodynamic profiles ($K_i$, $\Delta G_i$, $\Delta H_i$, $\Delta S_i$, $n_i$) for each system. We showed that the inherent electronic and steric properties of the monodentate phosphorus ligands influenced the thermodynamic affinities of the ligands binding to the Pd centers in solution. We observed cases in which either one or two equivalents of monodentate or bidentate ligands were able to bind to the Pd center. In particular, we observed for cases in which two equivalents of ligand were able to bind to the Pd center that the sites were thermodynamically independent from each other and had different affinities for the same ligand, which we attributed to differences in energies of the $d$ orbitals as predicted by crystal field theory. Ligand binding for monodentate and bidentate ligands was enthalpy-driven due to the large, exothermic enthalpies of binding observed in comparison to the large, negative entropic contributions. This conclusion is particularly interesting for the bidentate ligands because the chelate effect is presumed to be an entropy-driven phenomenon, though our results for these specific bidentate ligands demonstrate otherwise. Additionally, the observation of enthalpy-entropy compensation in the bidentate ligand binding experiments demonstrates the role of solvent reorganization in metal-ligand binding equilibria and the chelate effect. Specifically, P donor atoms are more favorable contributors to enthalpy (large, exothermic values) than N donor atoms.
Kinetics of terminal olefin hydrogenation and spectroscopic characterization of Wilkinson’s catalyst, RhCl(PPh₃)₃, in different solvents showed that the solute-solvent interactions have significant effects on the structure, and therefore activity, of the Rh species in solution. Pyridine, the strongest electron donating solvent tested, proved to inhibit the hydrogenation of terminal olefins using Wilkinson’s catalyst, likely due to coordination of pyridine molecules to the Rh centers in solution. THF, also a strong electron donating solvent, was barely active for olefin hydrogenation, even though ³¹P NMR experiments confirmed the existence of the catalytically active Rh monomer. Benzene, toluene, and an equal volume mixture of benzene and ethanol were all active solvents for olefin hydrogenation. Interestingly, benzene was more active than toluene, in spite of their structural similarities and their electron donating abilities.

In our transition from homogeneous catalysis to heterogeneous catalysis, we characterized the local structures of Rh complexes derived from the immobilization of Wilkinson’s catalyst on SBA-15 silica functionalized with primary amine, secondary amine, or diphenylphosphine groups within the mesoporous channels by a series of techniques including XRD, HR-TEM, multinuclear (¹³C, ²⁹Si, ³¹P) solid-state NMR, 2D ³¹P{¹H} HETCOR NMR, XPS, and Rh K-edge EXAFS. The immobilization of RhCl(PPh₃)₃ through covalent bond formation with functional groups grafted to the silica surface led to variations in their local structures, depending on the surface functional groups, that replace two or even three of the PPh₃ ligands in RhCl(PPh₃)₃. The immobilized Rh complexes showed high activity for the addition of alkynes with thiols (hydrothiolation) or sulfonic acids (hydrosulfonation) with excellent regio- and stereoselectivity under mild reaction conditions. A wide range of alkynes reacted with
various thiols efficiently to produce valuable anti-Markovnikov vinyl sulfides with readily switchable stereoselectivity, depending on the local structure of the immobilized Rh complex. A similar group of alkynes added to sulfonic acids exclusively to produce Markovnikov vinyl sulfonates in high yields, independent of the local structure of the immobilized Rh complexes. This work demonstrates that some reactions appear tolerant to the local chemistry around the grafted organometallic metal centers while other reactions depend critically on this chemistry (different structure-function relationships).

We also examined the effect of the grafting solvent on the final structure of supported Rh organometallic catalysts, again using Wilkinson’s catalyst as the precursor and phosphine-functionalized SBA-15 as the model surface. Homogeneous hydrothiolation experiments showed that THF and benzene were the most active solvents, but neither solvent produced the most active and selective supported Rh catalyst. THF produced a poorly active and time-dependent stereoselective heterogeneous catalyst, which was surprising considering the large amount of catalytically active Rh present in neat THF as confirmed by $^{31}$P NMR experiments. Conversely, toluene and DCE were less active as solvents for homogeneous hydrothiolation than either benzene or THF, but both solvents were superior grafting solvents, grafting the most amount of active, regio-, and stereoselective Rh on the surface, leading to the formation of heterogeneous single-site Rh catalysts. We also confirmed the enhancement of homogeneous and heterogeneous catalytic activity when 1 equivalent of DMSO relative to the total amount of Wilkinson’s catalyst was added to homogeneous reaction systems and grafting processes. XPS measurements confirmed the presence of Rh, Cl, and P contributions to each grafted catalyst. 2D $^{31}$P{$^1$H} HETCOR NMR measurements differentiated between
two types of local Rh structures for the active and stereoselective catalysts (single-site Rh catalysts) and the less active and less stereoselective catalysts (physisorbed Rh species). Our results demonstrate that the most active solvents for a catalytic reaction may not necessarily be the best grafting solvents for the synthesis of support organometallic catalysts and that thorough spectroscopic and kinetic characterization of the heterogeneous species is necessary to determine which grafting solvents are best for a particular organometallic precursor.

7.2 Future Work

The formation and cleavage of bonds is critical to developing atom-efficient organic synthetic techniques and new products and is ubiquitous throughout chemistry. Most homogeneous catalyst design philosophies revolve around choosing a metal with a carefully selected set of ligands in order to tune the electronic and steric character of the metal center such that it cleaves or forms the desired bond and then “screening” the designed catalyst(s) for a wide variety of substrates. However, with the innumerable combinations of metals and ligands available as well as an overwhelming number of potential substrates, this philosophy fails to address inherent features common to numerous catalytic processes. Specifically, chemists often focus on reactant conversion and desired product yield instead of obtaining thermodynamic and kinetic data that could explain why certain steps in a catalytic cycle are enhanced or inhibited. The effects of subtler contributions to the activity and selectivity of an organometallic complex, such as the role of solvent in the catalytic mechanism and the thermodynamic stability of the complex itself, are either treated in a cursory fashion or completely ignored. For example,
solvent can alter the structure of the catalytic species, which changes its inherent activity. Nosova et al observed changes in the $^1$H and $^{13}$C NMR spectra of the cyclic trimer palladium diacetate, [Pd(OAc)$_2$]$_3$, and determined that upon dissolution in methanol at -18°C, the trimer reacts with methanol to form methoxy-bridged Pd trimers followed by the formation of soluble and insoluble Pd clusters, while at 27°C, the Pd(II) is reduced to Pd(0).\textsuperscript{[1]} This example serves as a benchmark for the caution that organometallic chemists must exercise in order to be certain that any catalytic species, especially those synthesized \textit{in situ}, are thermodynamically stable and do not alter the structure of the active sites. Muzart’s recent review of $N$,$N$-dimethylformamide (DMF) as a solvent in numerous organic and catalytic processes provides several examples in which it can act as a ligand and coordinate to the metal center of an organometallic catalyst or even direct the selectivity of a reaction.\textsuperscript{[2]} A relevant example from this review is the Pd(PPh$_3$)$_4$-catalyzed selective isomerization of (Z)-1,4-diacetoxy-2-butene to the $E$-isomer in tetrahydrofuran (THF), while the same reaction gives the $E$-isomer and 1,2-diacetoxy-3-butene in DMF, which is attributed to the formation of an $\eta^1$-allylpalladium species in THF as compared to cationic $\eta^3$-allylpalladium species in DMF.\textsuperscript{[3]} These specific examples highlight the substantive effects that solvent can have on the catalytic mechanism (i.e. the active species that perform the catalysis and are represented in the catalytic cycle) as well as the thermodynamic stability of solvated organometallic complexes.

One of the largest discrepancies in homogeneous catalysis is combining theoretical and non-solvated thermodynamic and kinetics data (i.e. DFT calculations and gas-phase measurements) with observations in the liquid-phase where the catalysis
actually occurs. Molecular simulations and gas-phase measurements are capable of determining the most energetically favorable pathways for catalytic mechanisms and optimizing metal-ligand interactions, but often neglect solvent effects or describe them inadequately. Specifically, DFT calculations usually treat solvent molecules as a dielectric continuum, which neglects the other properties of the solvent that may be critical to understanding the activity of an organometallic complex.\textsuperscript{[4-6]} Traditional liquid-phase measurements capture the genuine catalytic behavior due to the thermodynamic contributions of the solvent, but observed kinetic and thermodynamic parameters are global to the entire system and must be properly deconvoluted in order to determine which factors (e.g. solvent reorganization, catalyst stability, etc.) contribute most to the observed catalytic activity and selectivity.

Perhaps the most common route for the activation of carbon-heteroatom bonds is oxidative addition, a common step in homogeneously catalyzed reactions. Oxidative addition is known to occur by a variety of mechanisms, including concerted additions, $S_N2$ reactions, radical mechanisms, and ionic mechanisms.\textsuperscript{[7]} With such a vast array of potential mechanisms, it comes as no surprise that oxidative addition permeates the catalytic cycles of several important synthetic techniques, including Buchwald-Hartwig aminations\textsuperscript{[8-10]}, Heck reactions\textsuperscript{[11, 12]}, and Suzuki coupling\textsuperscript{[13-15]}, among others. Despite the omnipresence of oxidative addition in homogeneous catalysis, it is generally a thermodynamically unfavorable process, especially for C-H bonds.\textsuperscript{[16]} As such, oxidative addition is frequently considered to be the rate-limiting step in a number of catalytic processes. In order to accelerate the rates of these types of reactions, the kinetics and full rate expression for such reactions are fully examined and optimized to overcome these
limitations. However, the actual thermodynamics of oxidative addition, at least from a quantitative standpoint, are rarely considered as a method of accelerating the rate (e.g. ways to stabilize the catalytic intermediate, using enthalpies and entropies of reaction, etc.), though there are experimental and theoretical studies of oxidative addition reactions in terms of why certain reaction pathways are favored and what factors contribute to the activation of certain bonds.\textsuperscript{[17-24]}

Carbon-iodide bonds are a well-studied class of reactions for bond activation due to their relatively low bond dissociation energy in the gas phase ($\text{BDE}_{\text{C-I}} = 209 \text{ kJ/mol at } 25^\circ\text{C}$).\textsuperscript{[25]} In many organic syntheses, it is necessary to cleave a bond and C-I substrates, namely aryl iodides, are a popular choice because of their reactivity, especially compared to analogous aryl bromides and chlorides.\textsuperscript{[26, 27]} As such, organometallic chemists have focused considerable effort in determining the kinetics of oxidative addition of aromatic iodides to a variety of complexes, with emphasis on Pd(0) species.\textsuperscript{[28-38]} We feel that aryl iodides are an excellent candidate for an in-depth study of carbon-heteroatom activation and oxidative addition because of the relative ease of the cleavage of the C-I bond and the strong foundation of information available in the literature regarding Pd(0) complexes that are capable of performing C-I cleavage. We will use this information to our advantage to initiate a study of liquid-phase thermodynamics of C-I activation and oxidative addition in order to capture the effects of solvent that DFT measurements and gas-phase measurements cannot adequately duplicate. Furthermore, we anticipate adapting our proposed work for C-I activation for more difficult systems, namely C-H bond activation. We are especially interested in the C-H activation of aromatic compounds, such as benzene and its monosubstituted derivatives, because the selectivity
of the resulting products of C-C coupling reactions, *meta-* vs. *para*-, is often poor.\(^{[39]}\)

Additionally, the aromatic substrates usually are employed in large excess, generally as the solvent or co-solvent, which changes the thermodynamic interactions of the catalytic species with the reactants. This aspect of this class of C-H activations is not considered from a thermodynamic standpoint and we aspire to apply what we learn from C-I activation thermodynamics to these systems.

Calorimetry is not a method for obtaining thermodynamic data only. As mentioned previously, calorimetry is also useful as a way to measure chemical kinetics and is capable of elucidating complicated rate expressions for homogeneously catalyzed reactions. Reaction progress kinetic analysis has been developed recently as a way to compare rates of reaction with the heat evolution or absorption of the reaction under isothermal conditions in order to deduce the steps in the catalytic cycle and the rate and equilibrium constants that appear in the final rate expression.\(^{[70]}\) Reaction progress kinetic analysis revolves around the fact that the rate of reaction is directly proportional to the heat evolved or absorbed during a chemical reaction, which the calorimeter measures in real time, and is related by the enthalpy of reaction and the volume of the calorimeter.

This analysis is differential in nature, that is, the rate of reaction is the measured variable while reactant conversion is the processed variable. The power of reaction progress kinetic analysis is that it relies on *in situ* measurements and the construction of rate equations to process reaction orders in reactants, catalyst, and potentially products, all while needing few experimental trials to accomplish these goals, as Blackmond details thoroughly in her review.\(^{[40]}\) This technique is used in Pd catalysis for carbon-carbon and carbon-heteroatom bond formations and is applicable to systems in which the heat
response is adequate and the heat flow is representative of the desired products formation (i.e. there is no significant formation of by-products). \cite{41-47}

ITC provides us the benefit of characterizing binding equilibria in solution while reaction progress kinetic analysis allows us to construct rate expressions when necessary. In other words, we can measure all of the thermodynamic state functions ($\Delta G$, $\Delta H$, and $\Delta S$) in the Gibbs equation as well as rate and equilibrium constants ($k$ and $K$, respectively) over a range of temperatures. For kinetic analysis, we can simply inject all of the titrant at once and treat the calorimeter cell as a batch reactor. As a result, we are equipped to handle both reversible and irreversible processes in solution. We feel strongly that, with the robust versatility of ITC as an experimental technique, we can obtain extensive thermodynamic and kinetic data that will allow us to draw conclusions about trends in catalytic activity based on thermodynamic arguments.

Perhaps the most important issue in the development of C-X bond activation chemistry is the inability to apply information learned for a given catalytic system to another, since the vast majority of catalytic studies focus on a specific combination of catalyst, ligand, solvent, and other necessary reaction components. The “screening” method is useful for understanding the nuances of a particular catalytic system and its tested substrates, but the trends learned from within the system may not apply to another catalytic system that uses a different catalyst, ligand, solvent, etc. It would be beneficial to an overwhelming number of catalytic applications to establish trends applicable to a multitude of catalytic systems, rooted in physical chemistry and thermodynamics, in steps common to homogeneous catalysis, such as oxidative addition, based on the properties of the substrates, the solvent, and the organometallic complex itself. With the dearth of
thermodynamic data available for catalytic processes in the liquid-phase (relative to DFT studies and gas-phase measurements), it becomes apparent that obtaining such information will yield new insight into the methodology of designing catalysts (and choosing substrates and solvents) for organic synthesis. Goldman and Goldberg mentioned that “the ‘difficulty’ associated with C-H activation is typically more related to thermodynamics than to kinetics; in those cases where the thermodynamics are favorable, the kinetics are often quite facile”.\[16\] Halpern noted that the intrinsic weakness of metal-carbon bonds was the dominant factor in the less than favorable thermodynamics of C-H activation, specifically mentioning that most thermodynamic information is obtained via the reverse process, reductive elimination, and gas-phase measurements of bond dissociation energies.\[48\]

7.3 Establishing Linear Free Energy Relationships for the Activation of C-I Bonds – Quantifying the Role of the Solvent in the Catalytic Cycle

We will perform oxidative addition reactions with meta and para substituted iodobenzene derivatives over a range of solvents using the same catalyst and ligand precursors, Pd(OAc)$_2$ and PPh$_3$, in the calorimeter in order to determine the enthalpies of oxidative addition, $\Delta H_{OA}$, and rate constants of oxidative addition, $k_{OA}$. We will then construct Hammett plots for each solvent using the obtained rate constants for oxidative addition to determine if solvent has a significant effect on the rate of cleavage of the C-I bond. If solvent accelerates the cleavage of the C-I bond, we expect to see a significant change in the Hammett reaction coefficient, $\rho$, for the exact same set of substrates reacted in the different solvents (Figure 7.1). If solvent does not accelerate the cleavage of the C-
Figure 7.1. Hypothetical Hammett plot for the activation of C-I bonds in different solvents for the same sets of substrates, assuming solvent has a significant effect on C-I cleavage. We expect the slopes of the lines (represented by the solid, dotted, and dashed lines) to change if the solvent affects the activity of the catalyst more than the substituents do. These changes in slopes (the Hammett parameter, $\rho$) would signify changes in the electronic character of the Pd center due to the properties of the solvent.
I bond, we expect to see little change in $\rho$ for the same substrates in different solvents. We will choose -NO$_2$, -OMe, -Cl, -CN, and -Me functional groups for the iodobenzenes because they vary from electron-donating to electron-withdrawing. The variety of substrates allows us to determine if the electronic character of the substrate contributes more to stability of the Pd intermediate, or if solvent can aid in stabilizing the intermediate. Such information would be integral to the design of novel organic syntheses because it would allow for more freedom in choosing the substrates (i.e. the substrates do not need to be chosen for high reactivity with the metal center because the electronic properties of the solvent can stabilize the intermediate instead). We want to study solvents that are common to a myriad of organometallic chemistries while also having a wide range of electronic properties, such as tetrahydrofuran (THF), N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), N-methylpyrrolidone (NMP), dimethylacetamide (DMA), acetonitrile (MeCN), and pyridine (py). We will consider the donor number, $DN$, of each solvent as an experimental variable, which is an empirical measure of a solvent’s ability to donate electrons to solutes (i.e. the substituted iodobenzenes and the Pd(0) complex). Of course, solvents have a range of electronic properties, including dielectric constants ($\varepsilon_r$), dipole moments ($\mu$), and even acceptor numbers ($AN$, an empirical measure of a solvent’s ability to accept electron from solutes), all of which we will consider as possible contributors to observed trends in catalytic activity and stability as they compose the polarity and solvation ability of a given solvent. We hypothesize that less polar (low values of $\varepsilon_r$ and $\mu$) solvents with high $DN$s will result in decreased rates of oxidative addition of iodobenzene derivatives and less favorable enthalpies of oxidative addition. Dodds et al examined solvent effects in the
coupling of iodobenzene and styrene using a Pd dimer and determined that polar, non-
protic solvents led to high conversions and that strongly-coordinating solvents inhibited
the initial reaction rates while a nonpolar solvent such as toluene enhanced the initial
reaction rate. We feel strongly that solvent will affect the rate of oxidative addition due
to reports of different $\rho$ values for various reactions studied in DMF\cite{50, 51} ($\rho < 0$) and
DMA\cite{52-54} ($\rho > 0$). These variations in $\rho$ also demonstrate the importance of Hammett
plots, namely that deviations from linearity and changes in the sign of $\rho$ signify changes
in the state of the intermediates, which subsequently reveals information about the
catalytic mechanism.\cite{55} Jutand’s recent review of mechanistic information known about
the Mizoroki-Heck reaction elaborated on the specific systems in which oxidative
addition was rate-limiting, which is an indication of the utility of our proposed work in C-
X bond activation.\cite{56}

7.4 Establishing the Thermodynamic Effect of the Metal Center in C-I Activation –
Applications of the Brønsted-Evans-Polanyi Relation and Sabatier’s Principle

The difficulty of oxidatively adding C-X bonds across a metal center is
omnipresent in homogeneous catalysis.\cite{29, 30, 57-62} The most common method used to
overcome the difficulties in C-X cleavage in homogeneous catalysis is to study the
electronic and steric properties of the endogenous ligands of the metal centers and
attribute differences in catalytic activity based on their inherent characteristics. In
heterogeneous catalysis, however, there are no ligands, so the emphasis usually revolves
around the electronic characteristics of the metal and how reactants interact with the
metal surface to form the intermediates necessary for catalysis.\cite{63} A common analysis is
to plot the rate of a reaction for different metals as a function of the enthalpy of adsorption of the reactant(s). These so-called volcano plots are a consequence of Sabatier’s principle, which states that the most efficient catalysts are capable of binding the reactant, though not too strongly, while facilitating the reaction once the reactants are adsorbed, that is, the rates of catalyst-substrate binding and product formation (overcoming the activation energy in the transition state) are equal.\[^{64}\] Volcano plots are most commonly constructed using the Brønsted-Evans-Polanyi relation, which states that the changes in activation energies for a family of reactions is linearly related to changes in overall reaction energies.\[^{65}\] The Brønsted-Evans-Polanyi relation is generally solved computationally for a series of metal surfaces for the same reaction because it is easiest to obtain the reaction energy theoretically rather than experimentally. Bligaard et al compiled a list of reaction energies for the dissociation of common species, such as $\text{H}_2$, CO, $\text{CH}_4$, and $\text{NH}_3$ for a variety of transition metals and used volcano curves to determine the optimal dissociative adsorption energies, and by extension, the optimal transition metals.\[^{66}\] Andersson et al studied the formation of $\text{CH}_4$ by the hydrogenation of CO over a series of metallic surfaces and compared calculations for the CO dissociation energy from the Brønsted-Evans-Polanyi relation to experimental data for catalytic activity for the formation of $\text{CH}_4$.\[^{67}\] Their results illustrate how the computation data is transformed into the volcano plot, as depicted in Figure 7.2. In homogeneous catalysis, at least in terms of oxidative addition, the only prerequisites for the metal center are that there is a vacant two-electron site available and that the resulting oxidation state of the metal center is stable.\[^{17}\] As such, there is little distinction in homogeneous catalysis as to which metal centers are best suited to certain processes and catalyst development.
Figure 7.2. Example of the Brønsted-Evans-Polanyi relation calculations (top) and the resulting volcano plot (bottom) for a series of metal and alloy surfaces for the dissociation energy of CO. Adapted from Andersson.\textsuperscript{[67]}
focuses on metal centers that are known to work for such processes, even though these metals may not necessarily be the most efficient class of catalysts.

Palladium is an extremely popular choice for a wide range of organic transformations, especially C-C bond formations, due to its versatility in handling many functional groups, its low toxicity, and its economic costs relative to other noble metals.\[68\] However, the efficiencies of organic syntheses are usually compared to one another by considering catalytic processes with identical metal centers, rather than considering transition metals as a whole. Admittedly, with the innumerable combinations of metal centers and ligands available, compiling an exhaustive database for a class of organic reactions for a large range of organometallic complexes would be folly. This dilemma leads us to believe that a centralized study of structurally similar organometallic complexes (with different metal centers) for the same reaction will allow us to determine trends in activity based on the character of the metal center. We will perform calorimetric titrations of iodobenzene solutions into solutions of different metal centers (Pd, Ni, Co, Ir, Rh, Pt, etc.) with different types of native ligands. Ideally, we will use the same reducing ligand when necessary, PPh$_3$, model compounds that have similar structures and ligands, and a solvent from our first study that dissolves our desired precursors and gives high rates of C-I activation. As before, we will determine the enthalpies of oxidative addition, $\Delta H_{OA}$, and rate constants of oxidative addition, $k_{OA}$, for iodobenzene across the different metal centers. We will then construct volcano plots of turnover frequency (TOF) as functions of $\Delta H_{OA}$ for the oxidative addition of iodobenzene in solution to see if there are trends in the tested metal centers. Specifically, we will use this information to establish which metal centers are \textit{kinetically controlled} (i.e. time-dependent) and which
ones are thermodynamically controlled (i.e. energy-dependent). We hypothesize that metal centers that are the most active for C-I bond cleavage will obey Sabatier’s principle, that is, the most active metal centers will have intermediate enthalpies of oxidative addition for iodobenzene. This analysis will also reveal more about the thermodynamic and kinetic nature of C-I activation. If we find more points to the left of the peak (Figure 7.2), then C-I activation is dictated by weak substrate-catalyst binding and is considered time-dependent. If we find more points to the right of the peak, then C-I activation is limited by the energetics of product formation, that is, the transition states are less stable than the reactants and the activation energy is high.[69]

7.5 Thermodynamics of the Catalytic Cycle – Which Steps Are Thermodynamically Favorable?

It is crucial to understand the steps that belie catalytic mechanisms from thermodynamic and kinetic perspectives because it allows for a higher degree of control of the steps that limit the overall reaction. In all fields of catalysis, it is desirable to formulate an expression for the overall rate law that governs the catalytic mechanism and obtain the rate and equilibrium constants that appear in the expression. While this method is certainly useful from a reaction engineering and design standpoint, there leaves much to be learned about the quantitative thermodynamic stability of the catalytic intermediates involved in the mechanism. Frequently, catalytic intermediates are proposed, though there is no spectroscopic evidence for such species. Therefore, a quantitative thermodynamic characterization of known catalytic species in solution should be able to correlate the stability of catalytic species synthesized in situ with their activities for the
same chemical reaction. Furthermore, studying the thermodynamics of each proposed step in a catalytic cycle would allow for a much more quantitative description of how favorable or unfavorable each step is. Such information could transform how catalytic mechanisms are perceived, in that most investigators aim to determine which step is \textit{kinetically} rate-limiting, but may consider which step is \textit{thermodynamically} rate-limiting instead. This philosophical shift could dramatically change how catalysts are designed in order to address these thermodynamic issues.

We will perform \textit{in situ} reduction of Pd(II) precursors (Pd(OAc)$_2$, Pd(dba)$_2$, Pd$_2$(dba)$_3$, PdCl$_2$, etc.) using calorimetry the same ligand (PPh$_3$) and a solvent from the first study that gives high reaction rates and dissolves our desired precursors to obtain enthalpies of reduction, $\Delta H_{\text{red}}$. If we determine from Chapter 7.4 that another transition metal is worthy of study, we will certainly consider extending this study to such catalysts. We will then titrate solutions of iodobenzene and phenylacetylene into solutions of the Pd(0) catalysts and determine the enthalpies of the C-C coupling reactions, $\Delta H_{\text{rxn}}$. Our objective is to compare the TOFs of the product formation for the various Pd(0) species to their respective enthalpies of reduction in order to determine the relationships between the observed kinetics and thermodynamics. We \textit{hypothesize} that the most favorable thermodynamics (large, exothermic values of $\Delta H_{\text{red}}$) of \textit{in situ} reduction of Pd(II) precursors will produce the most active catalysts for the C-C coupling of iodobenzene and phenylacetylene. This method allows us to examine the steps in a catalytic mechanism using reaction progress kinetic analysis both individually and from a thermodynamic perspective. Kinetics and thermodynamics are inextricably linked, but rarely are quantitative thermodynamics considered to be tunable factors in catalytic
processes. We anticipate this work revealing ways to enhance catalytic activity, and perhaps even control selectivity, simply by considering the thermodynamic stability of the synthesized catalysts and how they translate to catalytic performance.

7.6 The Effect of the Rigidity of the Linking Group on the Catalytic Activity and Selectivity of a Grafted Organometallic Species

The linking group that tethers the organometallic species to the surface of the support can also play a role in the activity and selectivity of a grafted catalyst, in the sense that its rigidity may lead to the formation of single-site catalysts, that is, the more rigid the linking group, the fewer conformations it can adopt on the surface, meaning that the grafted organometallic species is much more likely to be single-site. As an example, Jiang et al synthesized a series of supported Rh catalysts using [Rh(cod)Cl]₂ (cod = 1,5-cyclooctadiene) as the organometallic precursor and derivatives of trans-1,2-diaminocyclohexane, a chiral ligand, as the linking agent to tether the Rh species to the mesoporous silica in order to study the effects of their rigidities on the catalytic activity and selectivity toward the asymmetric transfer hydrogenation of ketones with isopropanol. They used derivatives that had benzyl and propyl groups as linkers and determined that the benzyl linker (93-97% conversion with 26-30% ee) was more active and enantioselective for the transfer hydrogenation of acetophenone than the propyl linker (36% conversion with 8% ee) after 3 h due to the rigidity (site isolation of Rh as confirmed by solid-state NMR, XRD, and diffuse reflectance UV-Vis spectroscopy) and electron-withdrawing characteristics of the benzyl group. We aim to synthesize a series of supported Rh catalysts using various linking agents containing functionalities
such as benzyl and alkynl groups instead of the propyl backbone of the catalysts synthesized according to the procedure outlined in Chapters 5 and 6. The activity and selectivity of each catalyst for the hydrothiolation of phenylacetylene and thiophenol will serve as the model reaction in order to compare these more rigid catalysts to their propyl counterparts as a method of quantifying the effect of the rigidity of the linking agent on the catalytic activity. Similar spectroscopic characterizations for the previously synthesized catalysts will allow us to determine if the rigid linkers lead to the formation of single-site catalysts. We hypothesize that supported catalysts synthesized with more rigid linking agents will be more likely to produce single-site Rh catalysts and will exhibit higher activities and selectivities than analogous catalysts synthesized with more flexible linking agents. We expect this work to complement our study of the effect of the grafting solvent in terms of demonstrating the benefits of controlling as many factors of the synthesis of supported organometallic catalysts as possible in order to ensure that the most active and selective catalytic species are grafted onto the surface of the support.
7.7 References


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Publications


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