

Fundamentals of Organometallic Catalysis

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Fundamentals of Organometallic Chemistry

Structure and Bonding in Organometallic Complexes

Introduction to d-orbitals. The organic chemistry that we have encountered thus far has relied only on s- and p-orbitals (and hybrid orbitals that arise from the mixing of these orbitals). We have seen many examples of reaction selectivity that arises because of predictable interactions of these simple orbitals. For example, we understand the backside attack in the S_N2 reaction as occurring due to the geometry of the C-X σ^* orbital of our electrophile (Figure 1).

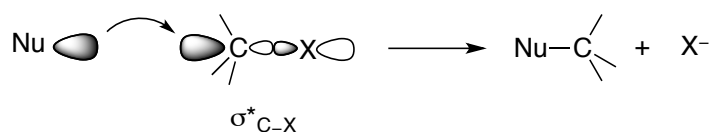


Figure 1. S_N2 reaction proceeds with backside attack due to favorable overlap of nucleophile and C-X σ^* .

Organometallic chemistry is the study of compounds and reactions that arise from interaction of carbon-based molecules with transition metal complexes. Transition metals are notable because the valence orbitals (thus the orbitals most involved in bonding and reaction chemistry) are d-orbitals. There are chemistries that are available to us with the presence of d-orbitals that are not available to elements that only have s and p orbitals. For example, how can we add nucleophiles to olefins? How can we use simple molecules, like CO, to generate valuable products like carbonyl derivatives? These questions can all be answered by understanding the role that d-orbitals and transition metals play in organic reactions.

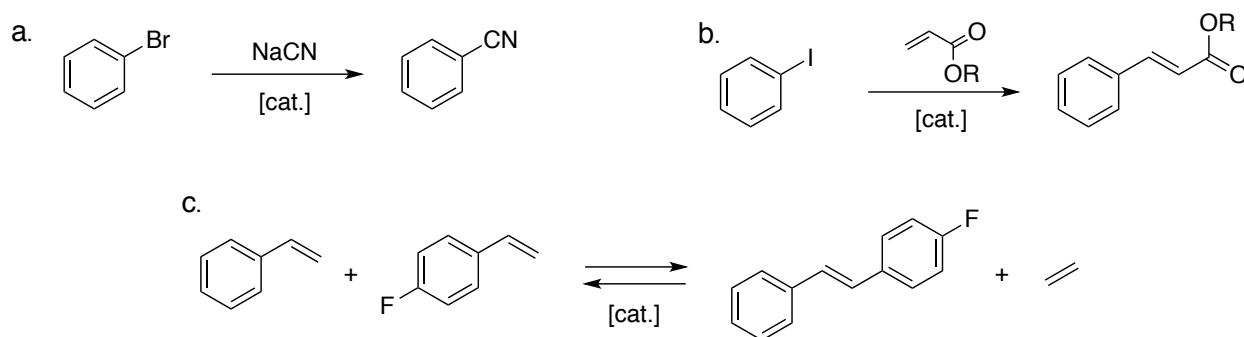


Figure 2. Examples of organic reactions that can be accomplished using transition metal catalysts.

One notable aspect of transition metals, and a critical aspect of understanding organometallic reaction chemistry, is that transition metals can access multiple oxidation states at the metal. We will spend the next section understanding how to assign the oxidation state of typical organometallic complexes.

Determining the Oxidation State of a Metal Ion

The oxidation state is dictated by 1) the identity of the ligands attached to the metal center and 2) by the charge of the transition metal complex.

1. The identity of the ligands attached to the metal:

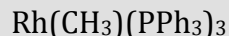
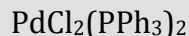
- *X-type ligands*: anionic donors that contribute +1 to the oxidation state of a metal, *i.e.* Cl^- , F^- , OH^- , CH_3^- .

What is the oxidation state of each of the following metal ions?



- *L-type ligands*: neutral donors that do not effect that calculation of the oxidation state of a metal, *i.e.* PPh_3 , ethylene, ethers.

What is the oxidation state of each of the following metal ions?



- *Z-type ligands*: electron acceptors that contribute -1 to the oxidation state of a metal. Examples of Z-type ligands would be the binding of a metal to the empty p-orbital of a borane. These are rarely encountered in organometallic chemistry and we will not examine them in this chapter.
- *Complex ligands*: multidentate ligands, which bind to the transition metal via multiple donor interactions, can be characterized as combinations of simple ligand types. For example, allyl ligands can be considered XL-type ligands.

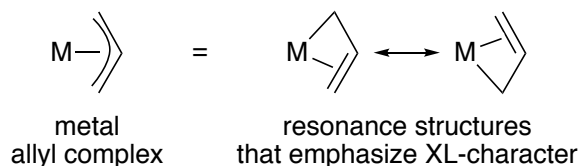
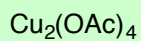
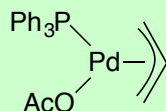
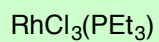
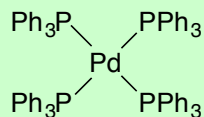


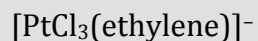
Figure 3. Multidentate ligands, such as an allyl ligand, can be described as combinations of X, L, and Z-type ligands. The allyl ligand can be classified as an XL ligand.

Practice Problem 1 Determine the oxidation state of the metal in the illustrated neutral coordination complexes.

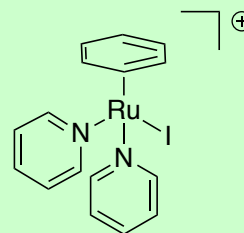
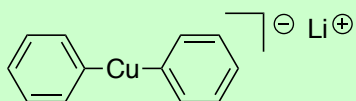


2. The overall charge of the complex: The overall molecular charge is also important to consider. A negative charge is -1 to the oxidation state. A positive charge is $+1$ to the oxidation state.

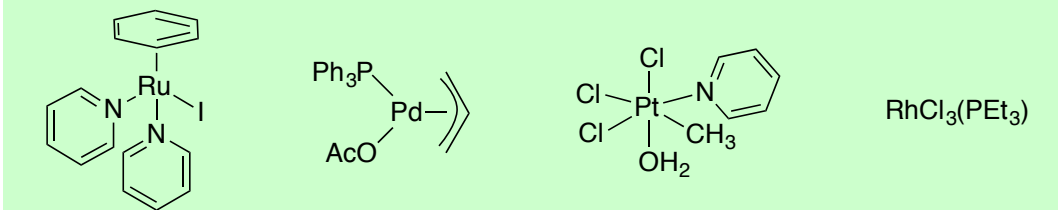
What is the oxidation state of the following metal ions?



Practice Problem 2 Determine the oxidation state of the metal in the illustrated charged coordination complexes.



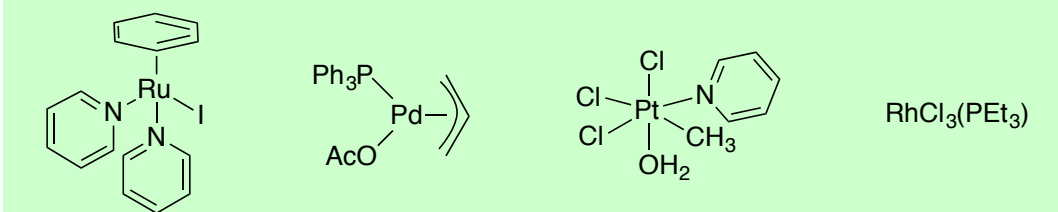
Practice Problem 3 Determine the d-electron counts of the illustrated complexes.



Determining the Electron Supplied by the Ligands

Each L- and X-type ligand that is bound to the metal contributes two electrons to the valence electron count.

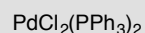
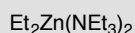
Practice Problem 4 Determine the valence electron count of the illustrated complexes.



Molecular Geometry

Unlike organic molecules, which almost universally display molecular geometries predicted by VSEPR theory, coordination complexes frequently diverge from the geometrical predictions made based on steric minimization. This divergence arises because of *crystal field splitting*, which is a topic you'll have to wait until inorganic chemistry to understand fully. For our purposes, we will only need to know that the geometries of metal complexes with partially filled d-orbitals is not always what you might expect based on VSEPR. Simple geometrical models do hold for d^0 and d^{10} metal complexes because these compounds are not subject to crystal field stabilization.

Would you expect the illustrated complexes to display VSEPR-predicted geometries?



Organometallic Transformations

Just like the chemistry of carbon, transition metal ions participate in a set of well-defined transformations. If we understand each of the individual steps, we can string them together to accomplish synthetic goals. Here, instead of writing multi-step organic synthesis schemes, we will be writing multi-step catalysis cycles.

Oxidative Addition. Oxidative addition is the simple addition of a small molecule to a metal center. The metal provides two electrons, which are donated to an anti-binding orbital of the substrate. In so doing, the A–B bond is broken, the metal is oxidized by two electrons, and new M–A and M–B bonds are formed.

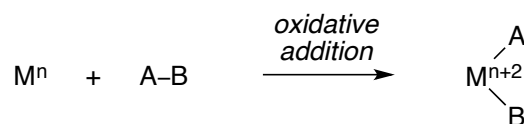


Figure 5. Oxidative addition is a transformation in which a metal ion inserts into an A–B bond and results in the formation of new M–X and M–C bonds in the product.

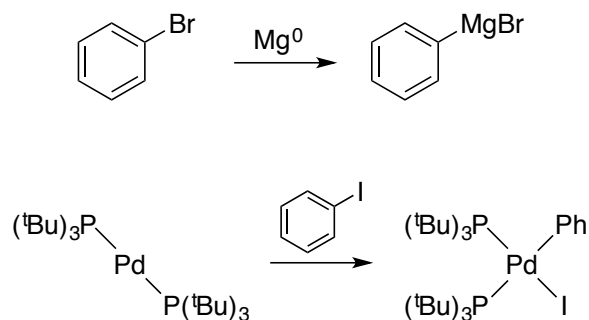


Figure 6. Insertion of Mg^0 into a C–Br bond to generate a Grignard reagent is an example of an oxidative addition. Another common reaction step that will be important to this course is the insertion of Pd^0 into the C–X bond of aryl electrophiles.

A variety of mechanisms are available for oxidative addition reactions, and differentiation depends on the trajectory of interaction between the metal center and the incoming substrate. Both $\text{S}_{\text{N}}2$ and three-centered transition states are common. Others are possible (*i.e.* radical reactions), but we will not see these processes in this course.

Reductive Elimination. Reductive elimination is the chemical reverse of oxidative addition. Overall the metal center is reduced by two electrons and a new A–B bond is formed. Reductive elimination is the product-forming step in many catalytic cycles.

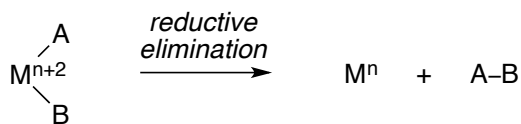


Figure 7. Reductive elimination is a transformation in which a bond (A–B) is eliminated from a transition metal ion. The metal ion is reduced by two electrons during the bond-forming reaction.

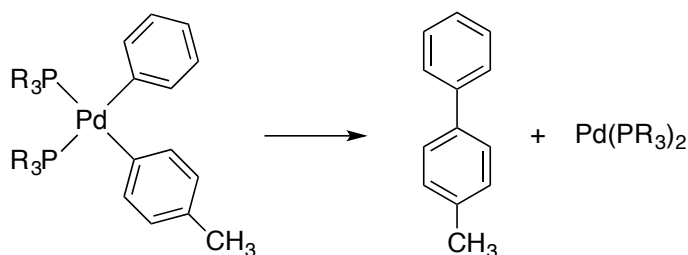


Figure 8. C–C reductive elimination from a diaryl metal complex is an important product-forming step in many transition-metal-catalyzed reactions.

Similar to oxidative addition, the term reductive elimination does not imply a reaction mechanism. Both $\text{S}_{\text{N}}2$ and concerted three-centered reactions are common and radical pathways are possible. For concerted reductive elimination reactions, the participating ligands must be in mutually *cis* coordination sites.

With only oxidative addition and reductive elimination reactions, we have no opportunity to develop useful catalysis; these steps are simply the reverse of one another. In order to develop catalysis, we need methods for ligand exchange chemistry. The two major approaches that we will encounter are transmetalation and migratory insertion reactions.

Transmetallation. Transmetallation is one of the primary organometallic transformations that allows introduction of new ligands to transition metal complexes. In a transmetallation reaction, two metals swap ligands. Transmetallation can proceed between many metals. Typically proceeds under thermodynamic control (*i.e.* reversible); the R group tends to migrate from the more electropositive element to the less electropositive element.

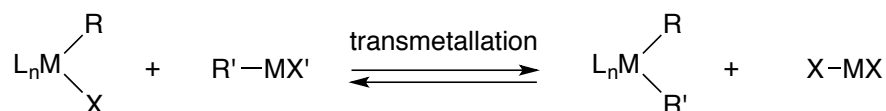
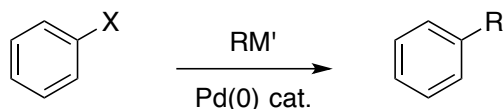


Figure 9. Transmetallation reactions involve the exchange of ligands between two metals.

Cross-Coupling Chemistry: Cross-coupling reactions combine organohalide electrophiles with organometallic nucleophiles in the presence of a transition metal catalyst (Figure 10). Pd(0)/Pd(II) catalytic cycles have emerged as an extremely robust strategy to accomplish cross-coupling chemistry and a wide variety of organometallic reagents can be used in cross-coupling reactions. There are an enormous number of named reactions which are all fundamentally the same cross coupling sequence. They are differentiated only by the metal from which transmetallation proceeds.



<u>Named Reaction</u>	<u>Coupling Partner</u>
Negishi Coupling	RZnCl
Suzuki Reaction	RB(OH) ₂
Stille Reaction	R'SnR ₃
Hiyama Reaction	RSiR ₃
Kumada Reaction	RMgBr

Figure 10. Cross-coupling reactions are a powerful method for building new C-C bonds from aryl halides and organometallic nucleophiles. The organohalide coupling partner is also commonly vinyl or alkynyl. The organometallic coupling partner can also be aryl, vinyl, or alkynyl.

The typical cross coupling catalytic cycle involves oxidative addition of the aryl halide to generate an aryl Pd(II) intermediate, transmetalation to introduce a second M–C bond to the Pd complex, and reductive elimination to generate the targeted C–C bond and regenerate the Pd(0) catalyst (Figure 11). Cross-coupling chemistry is particularly important of the formation of C–C bonds between sp^2 hybridized carbon centers (aryl and vinyl substrates) because these reactions do not present the opportunity for undesired β -hydride elimination reactions to be accomplished (*vide infra*). Recent progress has been made towards alkyl cross-coupling reactions using special ligands that retard β -hydride elimination.

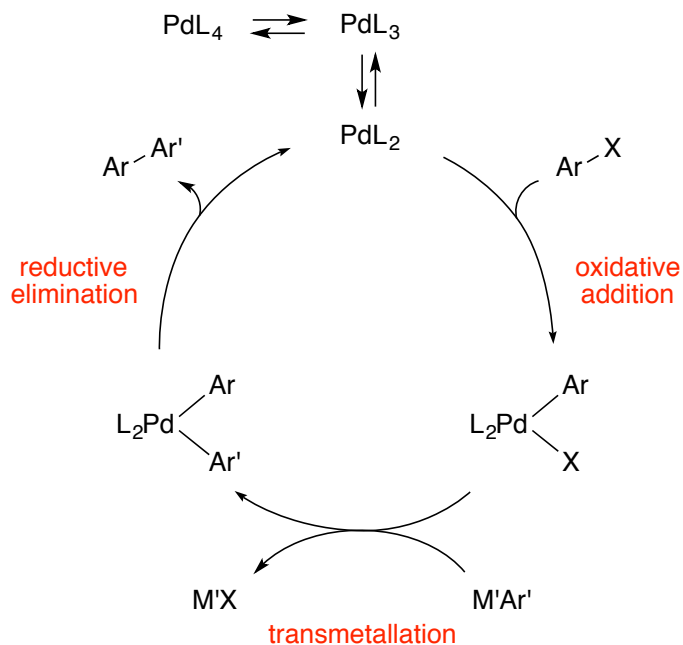


Figure 11. The canonical cross-coupling catalysis cycle proceeds via oxidative addition of an organohalide to PdL_2 , transmetalation, and product-forming reductive elimination.

Importantly, $Pd(PPh_3)_4$, which is a common catalyst for cross-coupling reactions, is an 18-electron complex and coordinatively saturated. In order to participate in oxidative addition, two phosphine ligands must dissociate from the metal center to afford a 14-electron PdL_2 intermediate that is then poised to react with aryl halides. Significant efforts have been devoted to the development of new, extremely sterically bulky ligands that stabilize PdL_2 intermediates.

Suzuki reactions are particularly important synthetic reactions because aryl boronic acids are widely available and, unlike many organometallic reagents like Grignard and organozinc species, are stable to air and water. Figure 12 illustrates an interesting reaction sequence in which hydroboration is utilized to generate an organoboron species that is a competent reaction partner in subsequent Suzuki coupling.

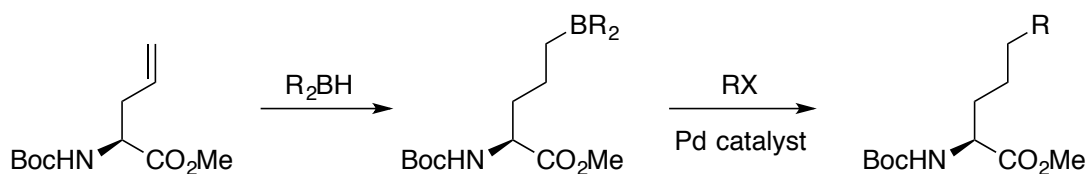


Figure 12. Hydroboration-Suzuki cascade

Sonogashira Chemistry

The Sonogashira reaction is an important cross-coupling reaction that directly couples aryl halides with alkynyl C–H bonds.

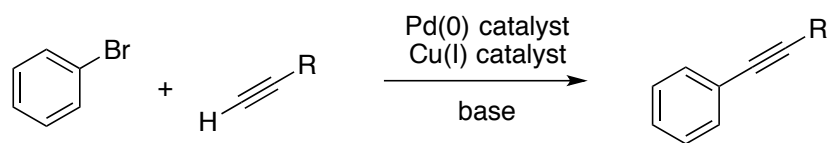


Figure 13. The Sonogashira reaction provides an approach to the direct coupling of aryl halides and terminal alkynes.

The mechanism of the Sonogashira reaction is very similar to that of the aforementioned cross-coupling reactions, except the reaction does not use a pre-formed organometallic nucleophile and thus we need to determine the identity of our transmetalating reagent. Alkynes are not acidic enough to be directly deprotonated by the weak bases employed in Sonogashira reactions (*i.e.* tertiary amines). Instead, interaction with a Cu(I) salt, via a π -complex, sufficiently depresses the pK_a of the alkynyl C–H such that it can be deprotonated in the reaction conditions. There are two catalytic cycles that are simultaneously involved in the Sonogashira reaction – one for the cross coupling and the other to generate alkynyl copper reagents that are responsible for the observed transmetalation reaction.

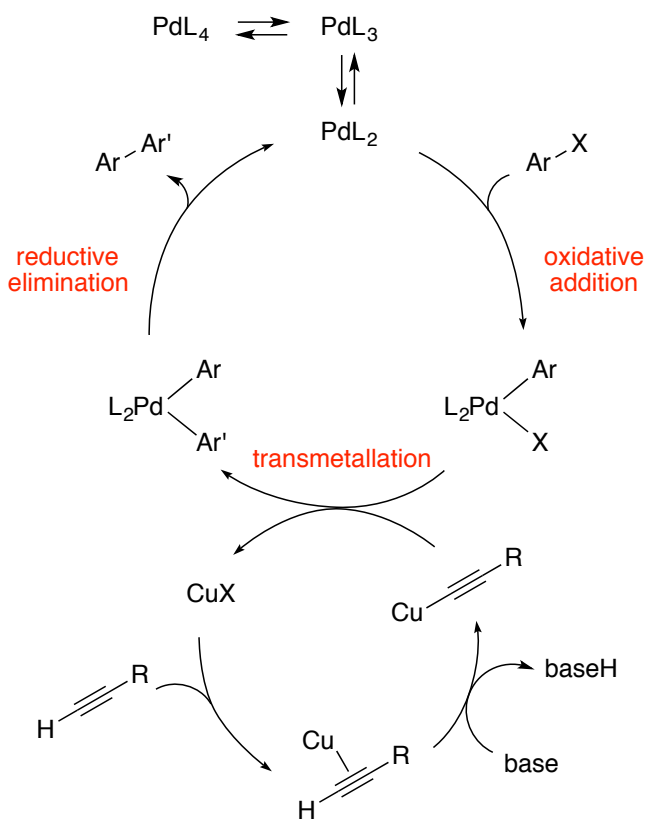


Figure 14. Dual catalysis cycles that are responsible for Sonogashira coupling.

Migratory Insertion. A migratory insertion is a reaction in which an unsaturated ligand inserts itself into an M–X bond. The reaction is redox neutral at the metal and decreases the coordination number of the metal by one. In addition, the valence electron count of the metal decreases by two. There are two common migratory insertion reactions: 1,1- and 1,2-insertion.

1,1-Migratory Insertion. In a 1,1-insertion, the same atom of the migrating ligand forms new bonds with both the M and the X of the M–X bond that is involved.

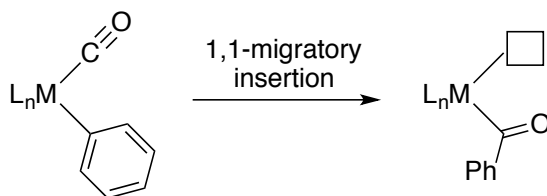


Figure 15. 1,1-Migratory insertion of a carbonyl ligand into an M–X bond. □ = empty coordination site.

Using just the simple oxidative addition, reductive elimination, and migratory insertion reaction steps, we can develop some important catalytic reactions. For example, the Monsanto process combines MeOH and CO under the action of Rh catalysis to generate acetic acid. Historically, the Monsanto process was an important industrial approach to the synthesis of acetic acid.

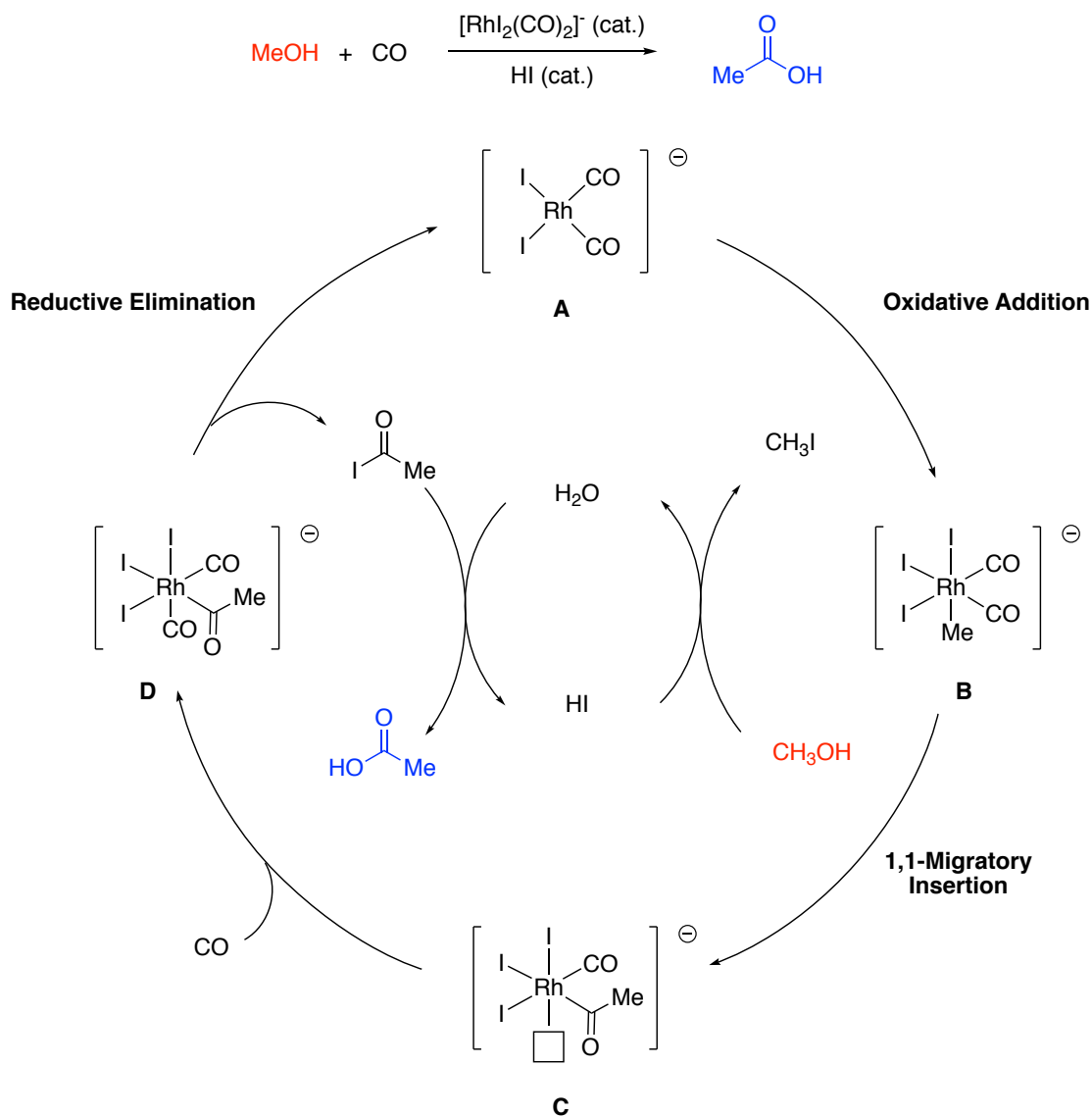


Figure 16. Catalytic cycle for the Monsanto acetic acid synthesis. \square = empty coordination site.

1,2-Migratory Insertion. In a 1,2-insertion, the two atoms of the unsaturated ligand form bonds to the M and the X ligands. A 1,2-migratory insertion reaction of an olefin complex results in the formation of an empty coordination site and a new metal alkyl complex.

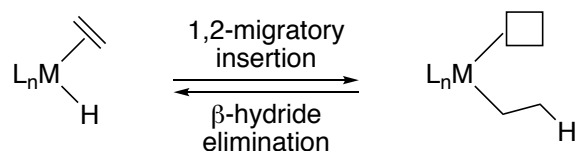


Figure 17. 1,2-Migratory insertion of an olefin into an M–H bond. □ = empty coordination site.

Olefin migratory insertion reactions are critical steps in olefin hydrogenation. An early seminal report of olefin hydrogenation was disclosed by Sir Geoffrey Wilkinson, who showed that homogeneous Rh coordination complexes are efficient catalysts for olefin hydrogenation. Wilkinson's work resulted in the Nobel Prize in 1973 and chemists still refer to $\text{RhCl}(\text{PPh}_3)_3$ as Wilkinson's catalyst.

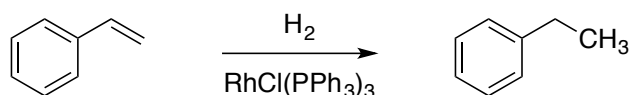


Figure 18. Rh-catalyzed olefin hydrogenation chemistry.

Hydrogenation with Wilkinson's catalyst commences with dissociation of a phosphine ligand from Rh to generate 14-electron intermediate that reacts with H_2 (Figure 19). Olefin binding to metal, 1,2-migratory insertion, and reductive elimination afford the hydrogenated organic product and regenerate the reactive 14-electron catalyst intermediate.

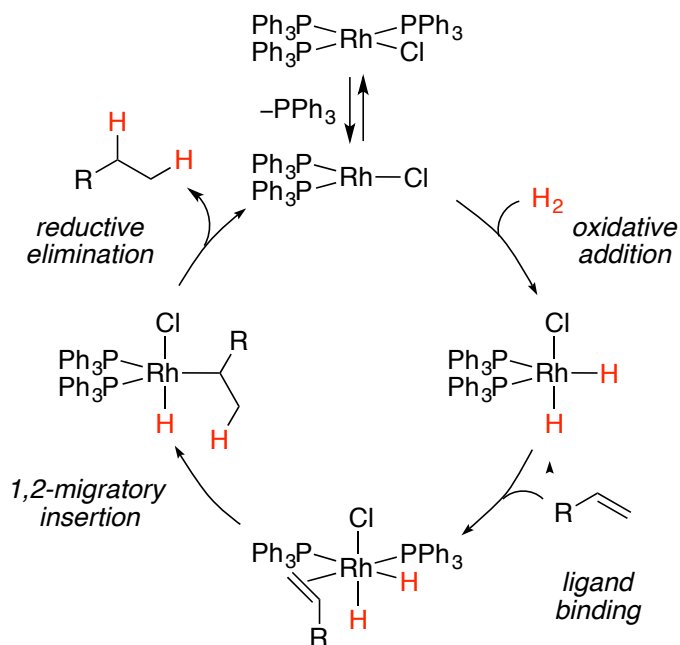


Figure 19. Catalysis cycle for olefin hydrogenation using Wilkinson's catalyst.

1,2-Migratory insertion reactions are reversible. The reverse of a migratory insertion is a β -elimination reaction. The β -hydride elimination is a ubiquitous version of the β -elimination and results in the formation of a metal hydride and an olefin (Figure 17). 1,2-Migratory insertion and β -hydride elimination reactions are important elementary reaction steps in a variety of metal-catalyzed olefin functionalization reactions.

A classic olefin functionalization reaction, and an important synthetic method, is the Heck reaction, in which an aryl halide and an olefin are combined with a Pd catalyst.

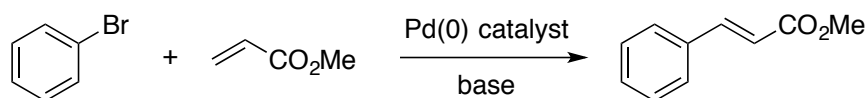


Figure 20. A Heck olefination reaction between an aryl halide and an electron deficient olefin is a powerful method for olefin arylation.

The mechanism of the Heck reaction is pictured in Figure 21. The key steps of a Heck reaction are 1) oxidative addition of Pd(0) into the C-X bond of an aryl halide to generate an organometallic Pd(II) intermediate, 2) 1,2-migratory insertion of an olefin to generate a Pd(II) alkyl intermediate, 3) β -hydride elimination to generate an olefin and a metal hydride, and 4) HX reductive elimination from the Pd(II) catalyst intermediate to regenerate the Pd(0) species that is required to engage with the next equivalent of substrate.

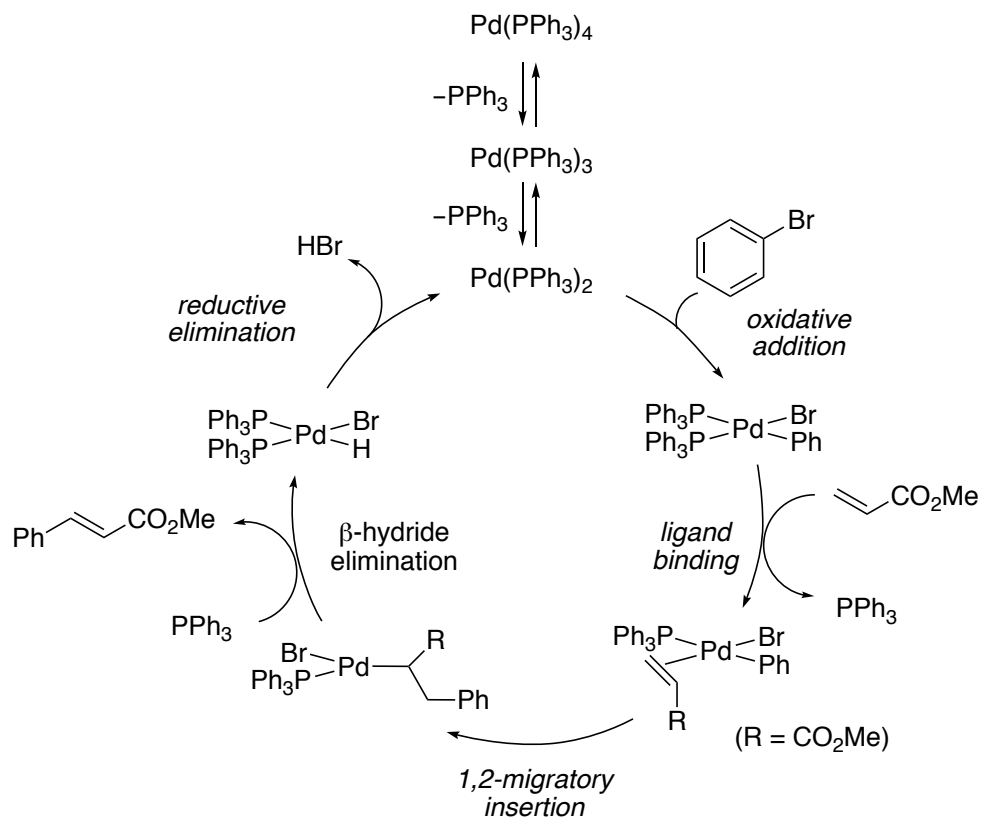


Figure 21. The catalytic cycle of a Heck reaction.

Olefin Metathesis

Olefin metathesis is an incredibly useful reaction in which C=C bonds are cleaved and new C=C are formed. In the presence of many transition metals, the olefin exchange reaction pictured in Figure 22 is observed. The extent of olefin scrambling is typically thermodynamically controlled; a mixture of all available olefins are obtained from these reactions.

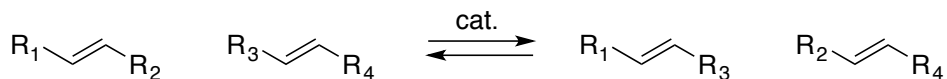


Figure 22. Olefin metathesis results in the scrambling of the termini of C=C bonds.

The importance of olefin metathesis is related to the ubiquity of olefins in organic molecules. Olefin metathesis chemistry has applications in fine chemical synthesis and in large scale commodity chemical synthesis, which we will explore below. The potential utility of olefin metathesis reactions has motivated an enormous effort to develop highly active and highly selective catalysts for application to various methathesis reactions. Figure 23 illustrates some common metathesis catalysts.

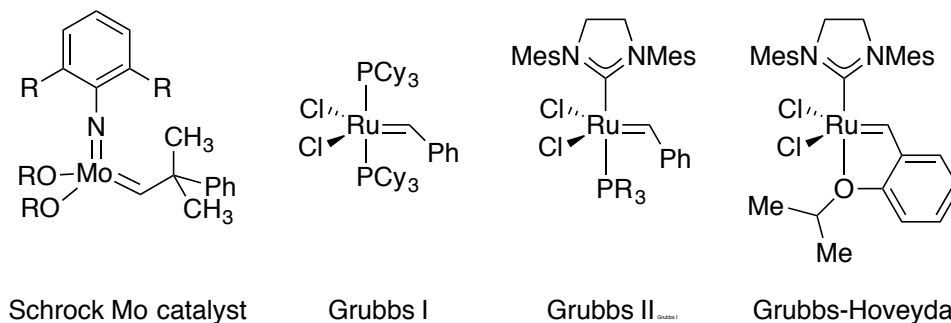


Figure 23. Common olefin metathesis catalysts.

Molybdenum catalysts were popularized by Prof. Dick Schrock and ruthenium-based catalysts were popularized by Prof. Robert Grubbs, who, along with Prof. Yves Chauvin, were awarded the Nobel Prize in chemistry in 2005.

Chauvin's major contribution to the development of olefin metathesis was the suggestion that cycloaddition reactions, and metallacyclobutane intermediates, were involved in the reaction mechanism of olefin metathesis. These metallacycles have subsequently been isolated in some cases and shown to be relevant intermediates in the chemistry. Figure 24 illustrates a typical olefin metathesis catalytic cycle, which is true both for Mo and Ru catalysts.

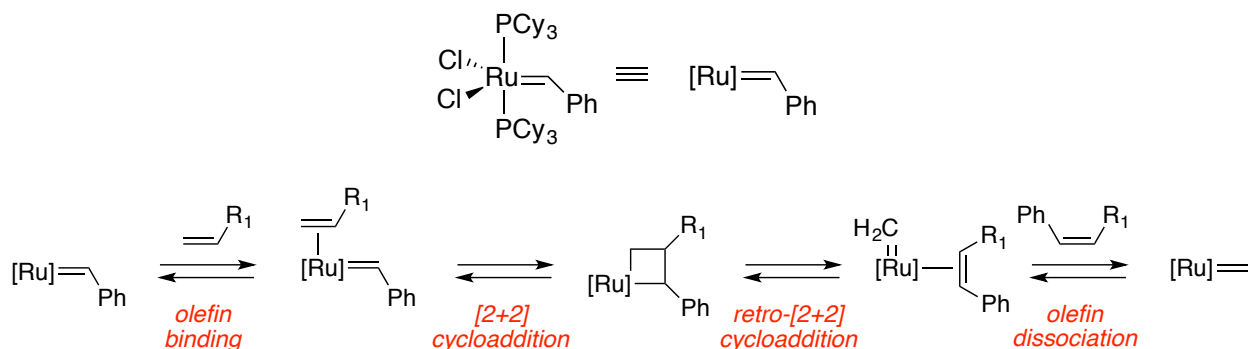


Figure 24. Olefin metathesis reactions proceed via a series of [2+2] cycloadditions between olefins and alkylidene complexes to generate metallacyclobutane intermediates and subsequent retro-cycloaddition reactions which afford olefins and alkylidene complexes; in this figure the Grubbs I catalyst is abbreviated as [Ru]=CHPh.

Olefin metathesis reactions proceed by initial binding of olefins to the metal center to form a π -complex. Subsequent [2+2] cycloaddition generates a metallacyclobutane intermediate. You may recall from our studies of pericyclic reactions and cycloadditions that a [2s+2s] cycloaddition is thermally forbidden. This example is a beautiful illustration of the kind of reaction that can take place easily when the d-orbitals are involved in reaction chemistry! The metallacyclobutane that is generated can break down via a retro-[2+2] cycloaddition to either regenerate the starting reactants (reverse of original cycloaddition in Figure 27) or can break down to generate a new olefin and a new alkylidene complex. Via the intermediacy of metallacyclobutane intermediates, olefinic substrates swap the carbon atoms of the C=C bond.

Olefin metathesis chemistry is thermodynamically controlled and in many cases mixtures of olefins are obtained. There are certain cases in which olefin metathesis chemistry can be controlled and can be directed to generate a single product. For example, Figure 28 illustrates two examples of ring-closing metathesis (RCM) chemistry. In these examples, diene substrates undergo an olefin metathesis reaction which generates an equivalent of ethylene. While under equilibrating conditions, the ethylene could participate in a reverse olefin metathesis reaction, it is a gaseous substrate and can be removed by either vacuum or a flow of inert gas through the reaction vessel. These approaches take advantage of Le Chatelier's principle to achieve high-yielding olefin metathesis reactions.

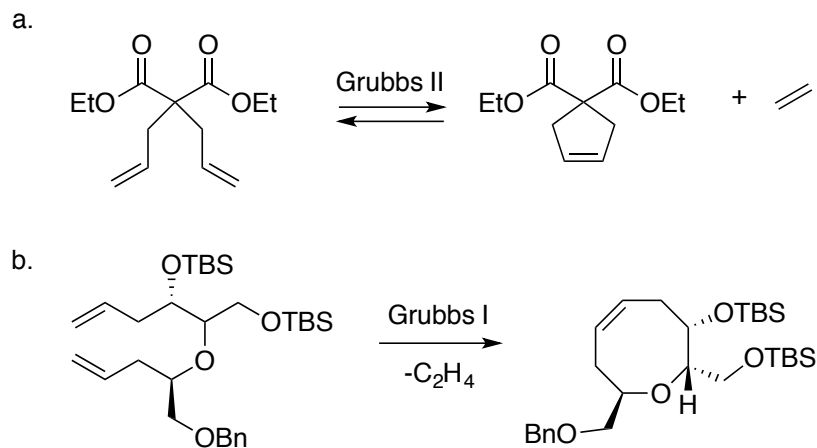


Figure 25. Ring-closing metathesis can be used to generate a variety of ring sizes. These reactions can be selectively driven to completion by removing the evolved ethylene from the reaction vessel.

Another major application of olefin metathesis chemistry is in ring-opening metathesis polymerization (ROMP) chemistry. The driving force to selectively generate polymer and not intractable mixtures of olefins in these reactions is provided by ring strain in the monomers that are used to generate the polymer. For example, in the ROMP of dicyclopentadiene illustrated below, the strained olefin that is part of the norbornene unit is selectively cleaved first. Metathesis of this double bond leads to long polymer chains that are decorated by bicyclic units. Following consumption of the more strained olefin, subsequent cross-metathesis reactions between the remaining cyclopentene groups leads to substantial polymer cross-linking that generates very robust plastics.

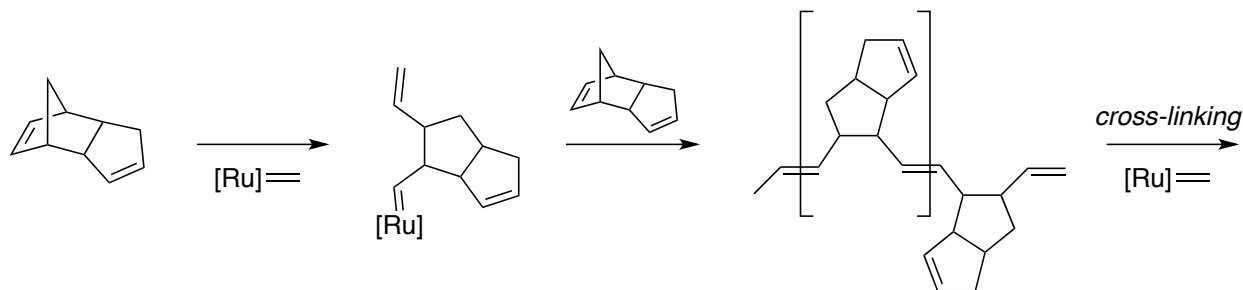


Figure 26. Ring opening metathesis polymerization (ROMP) of dicyclopentadiene.