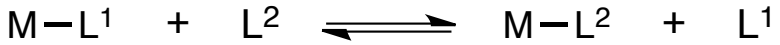
Reaction Mechanisms

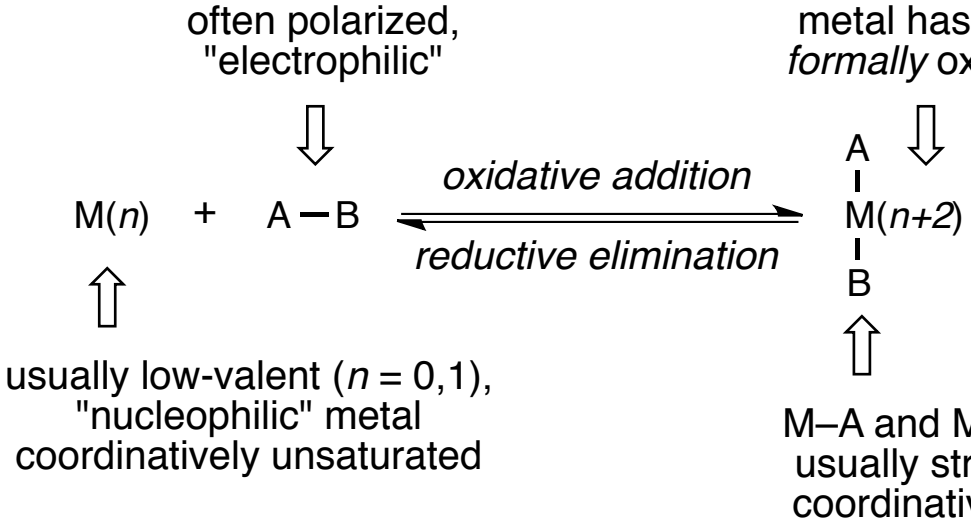
Before we get into the synthetic chemistry it is a good idea to first become familiar with some of the more importatn reaction mechanisms available to transition metals. We will see these again and again as we continue in the course.

I. Ligand Substitution



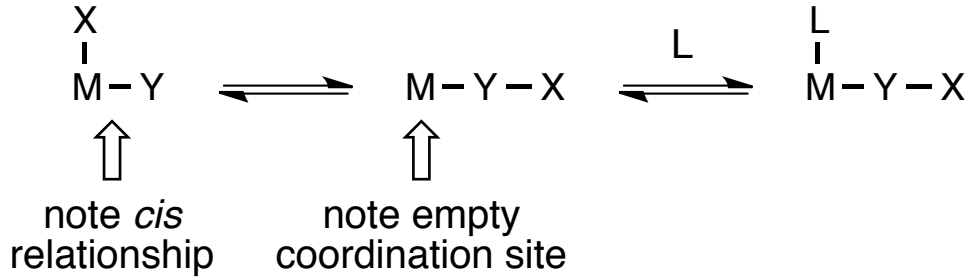
Both associative (S_N2-like) and dissociative (S_N1-like) mechanisms are possible

II. Oxidative Addition/Reductive Elimination

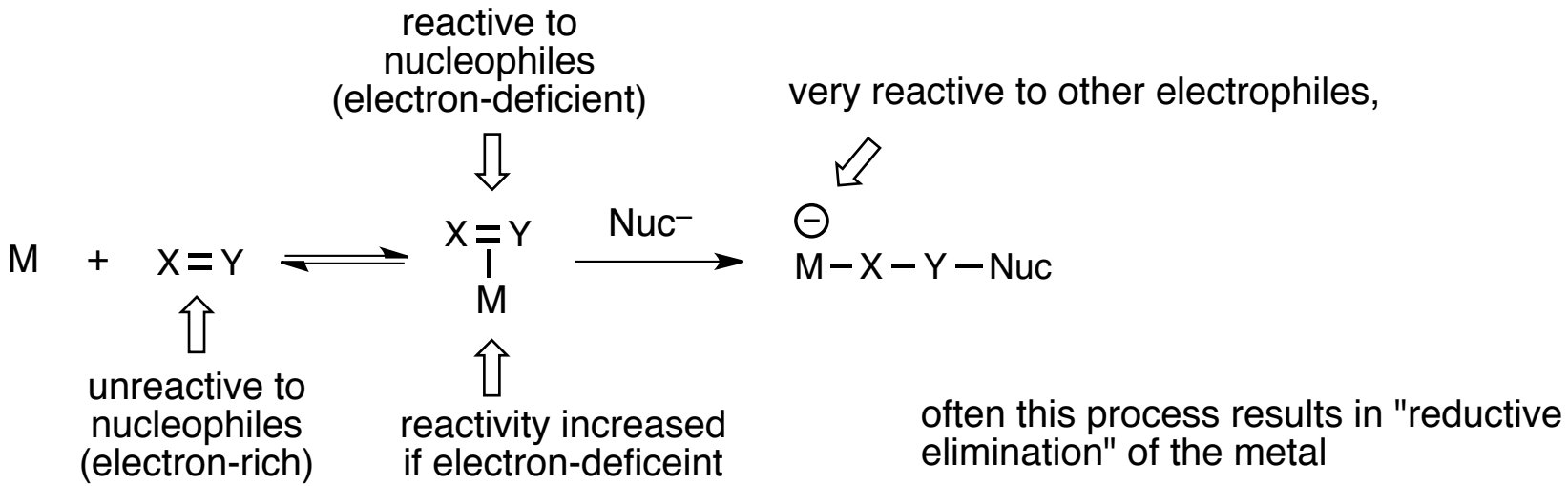


Reaction Mechanisms

III. Migratory Insertion & Elimination

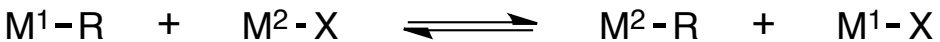


IV. Nucleophilic Attack on Ligands Coordinated to Metal



Reaction Mechanisms

V. Transmetallation

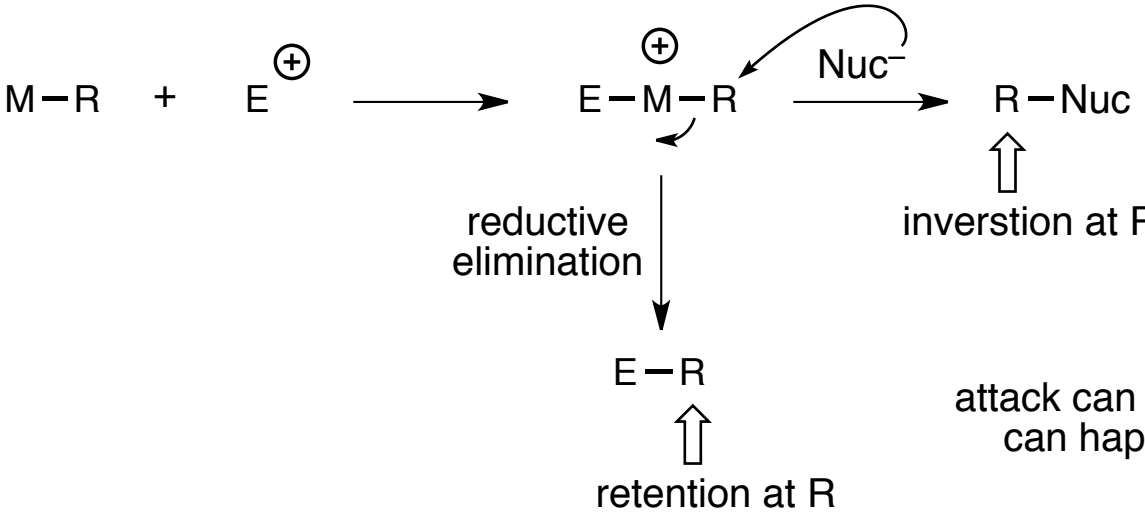


M^1 = Mg, Zn, Zr, B, Hg, Si, Sn, Ge
M^2 = transition metal

almost always the rate-limiting step, usually the culpret when catalytic processes fail

VI. Electrophilic Attack on Metal Coordinated Ligands

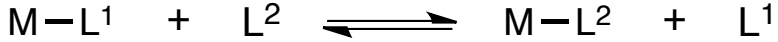
Several different reaction modes are known, will explore further later



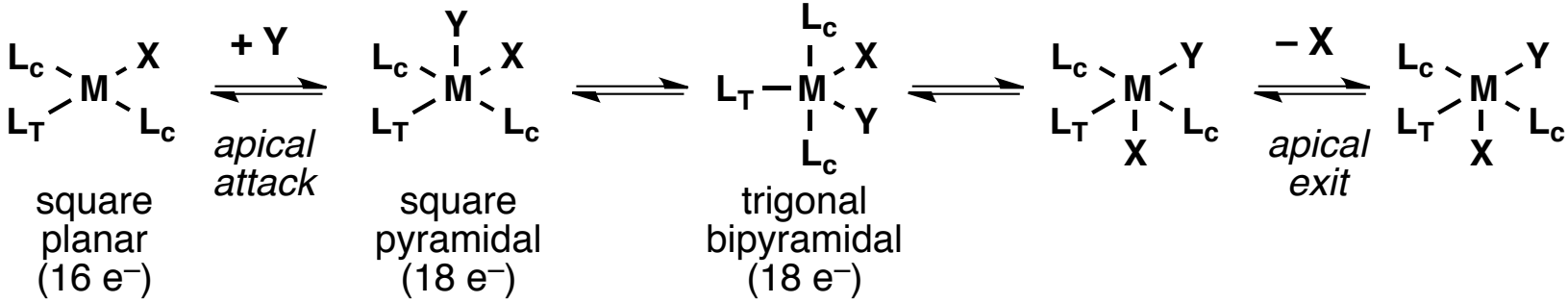
attack can directly cleave M–R bond or can happen α, β, or γ to the metal

Ligand Substitution

Though we will be concerning ourselves more with the reactivity and synthetic utility of organimetallic complexes, understanding the mechanisms available for ligand substitution is critical to understanding how the complexes react.



Associative Mechansim (S_N2-like) – typically occurs with coordinatively unsaturated complexes; exemplified by 16-electron, square planar, d^8 metals (Ni(II), Pd(II), Pt(II), Rh (I), Ir (I))



Factors that influence the rate:

– identity of the metal
– identy of incoming and outgoing ligands
– identy of the *trans* ligand ("trans effect")

Ligand Substitution

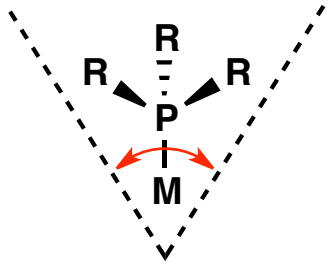
Though we will be concerning ourselves more with the reactivity and synthetic utility of organimetallic complexes, understanding the mechanisms available for ligand substitution is critical to understanding how the complexes react.

$$M{-}L^1 \quad + \quad L^2 \rightleftharpoons M{-}L^2 \quad + \quad L^1$$

Dissociative Mechansim (S_N1-like) – typically occurs with 18 electron coordinatively saturated complexes; often slower that associative substitution; exemplified by M(0) metal carbonyl complexes

$$\underset{(d^{10},\ 18\ e^-)}{\mathbf{Ni(CO)_4}} \overset{\mathbf{-\ CO}}{\rightleftharpoons} \underset{(d^{10},\ 16\ e^-)}{\mathbf{Ni(CO)_3}} \overset{\mathbf{+\ L}}{\rightleftharpoons} \underset{(d^{10},\ 18\ e^-)}{\mathbf{LNi(CO)_3}}$$

The rate can be accelerated by bulky ligands (loss of labile ligand relieves steric strain). This is particularly noticeable with phosphines and can be measured by the "cone angle". The electronics of the phosphine can be changed (idenpendently from sterics) by substitution.



cone angle (Θ)

R	θ	ν_{co} **(cm^{-1})**
OMe	107	2079
OPh	128	2085
Ph	145	2069
o-tolyl	194	–
Cy	170	2056
t-Bu	182	2056

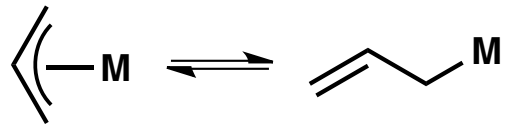
ν_{co} (cm^{-1}) is determined with $Ni(CO)_3L$ and is a measurement of the amount of backbonding. More donating L, more backbonding and ν_{co} decreases.

Hartwig, *Organotransition Metal Chemistry*, 2010, pp 37–38.

Ligand Substitution

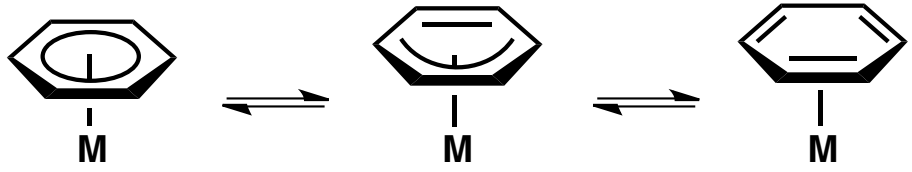
A "full dissociation" is not always necessary to open coordination site on an 18-electron complex. Sometimes a polydendate ligand can "slip" and free up a coordination site.

This can explain some observations seen with ligands such as η^3-allyl, η^5-cyclopentadienyl, and η^6-arene complexes. By slipping to a lower hapticity, a coordination site (or two) is opened.



η^3-allyl
(2 sites)

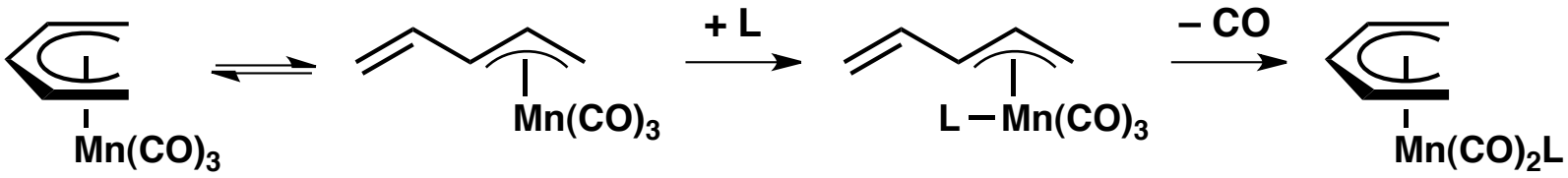
η^1-allyl
(2 sites)



η^6-arene
(3 sites)

η^4-arene
(2 sites)

η^2-arene
(1 site)

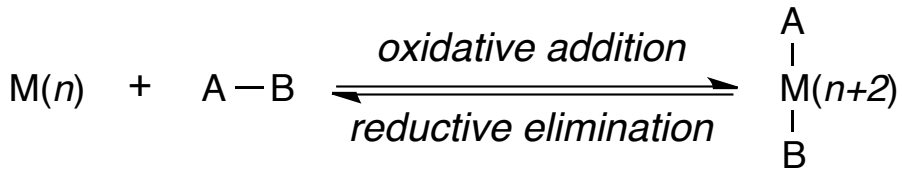


Mn(I), d^6
18 e$^-$

Mn(I), d^6
16 e$^-$

Oxidative Addition/Reductive Elimination

Reactions of this type are central to the synthetic utility of transition metals complexes and relies on the ability of metals to easily and reversably change oxidation states (compare to what is takes to change oxidation state of C).



The terms "oxidative addition" and "reductive elimination" are generic and refer only to the process of changing the oxidation state of the metal. The exact mechanism by which this occurs can vary.

Oxidative Addition (OA)

Metal must be coordinatively unsaturated and relatively electron rich (nucleophilic) and usually in low oxidation state (0, +1). σ-Donor ligands (PR_3, R^-, and H^-) facilitate OA. π-Acceptor ligands (CO, CN^-, alkenes) suppress OA.

By the formalism used to assign oxidation state, the metal has lost two electrons during the above process (the metal has been oxidized)

Metals that most commonly undergo OA reactions (other are certainly known):

d^{10}: Ni(0), Pd(0) $\rightarrow$ d^8: Ni(II), Pd(II)

d^8: Rh(I), Ir(I) $\rightarrow$ d^6: Rh(III), Ir(III)

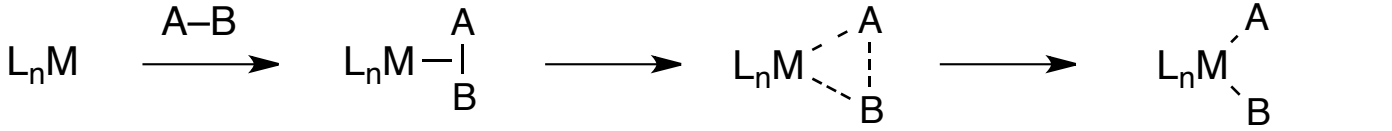
Exact mechanism by which the OA occurs depends on the nature of the substrate.

Oxidative Addition/Reductive Elimination

Nonpolar Electrophiles

Common examples: H_2, R–H, Ar–H, R_3Si–H, R_3Sn–H, R_2B–H, R_3Sn–SnR_3, R_2B–BR_2, 

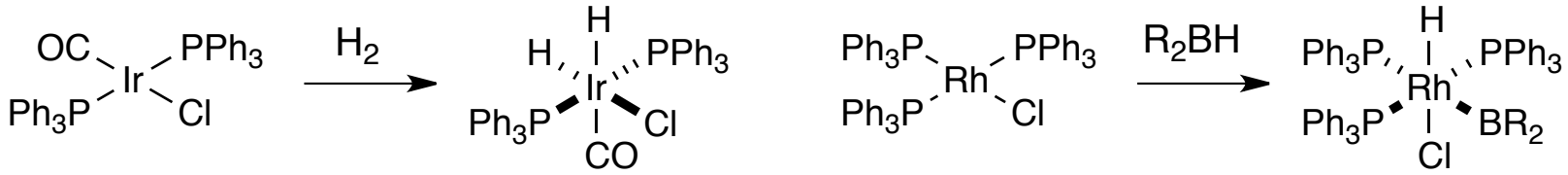
Generally undergo OA by concerted, one-step "insertion" mechanism. The configuration of any stereocenters would be expected to be retained. May require dissociation of a ligand from the initial complex.

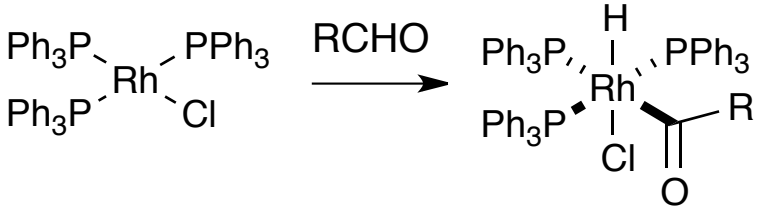


"agostic" interaction
(2 e⁻, 3 center bond)

cis stereochemistry
(kinetic)

Examples:



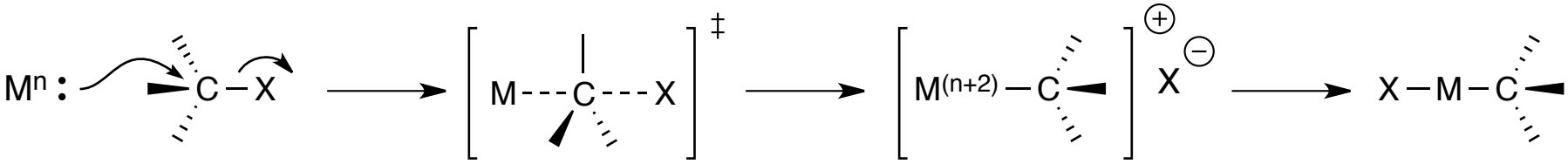


Oxidative Addition/Reductive Elimination

Polar Electrophiles

Common examples: HX, X_2, R–X, R(O)X, Ar–X,

Two mechanisms are possible. One is analagous to reactions with nonpolar electrophiles (direct insertion). The other is an ionic, two-step S_N2 mechanism, where the metal functions as a nucleophile and donates two electrons in the process. The configuration of any stereocenters would be expected to be inverted in this case. The structure of the electrophile determines which is active.



relative rates:

Me > primary > secondary >> tertiary

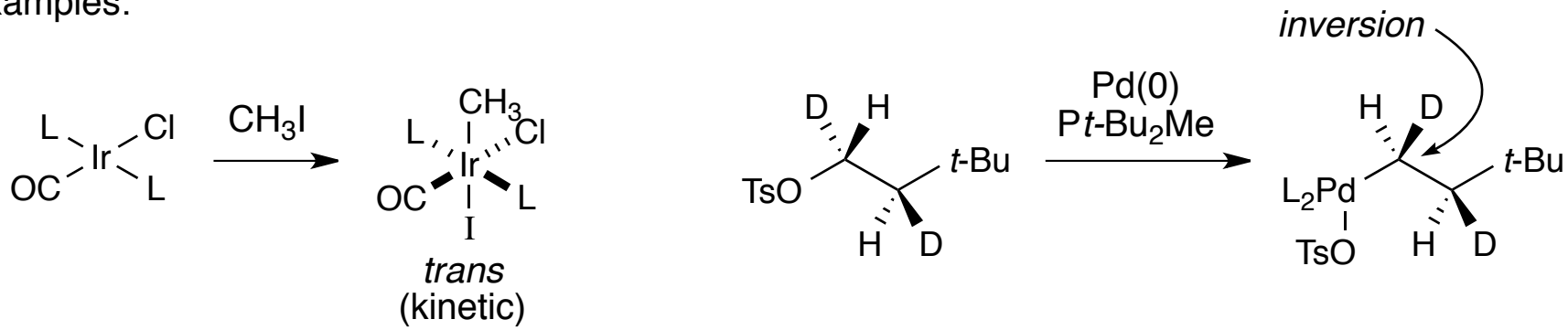
I > Br ~ OTs > Cl >> F

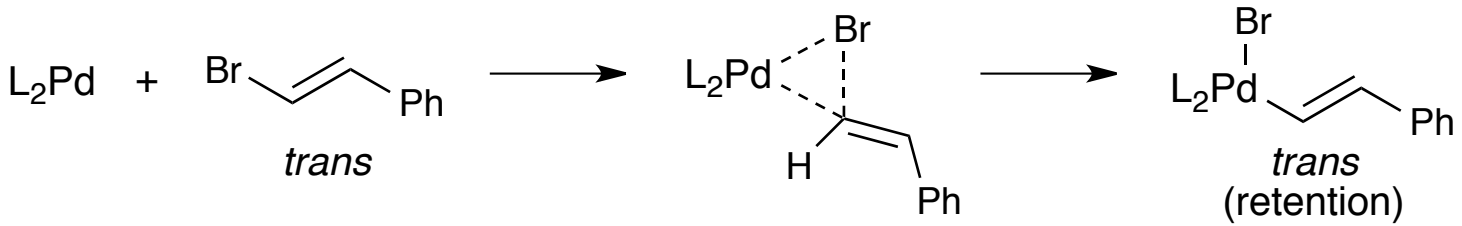
phosphines promote with greater basicity giving faster rates

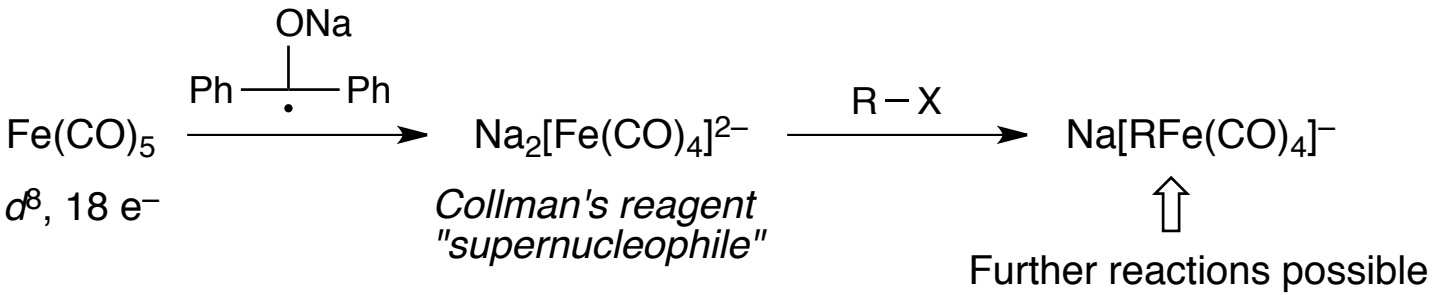
Oxidative Addition/Reductive Elimination

Polar Electrophiles, cont'd

Examples:



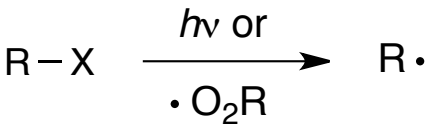


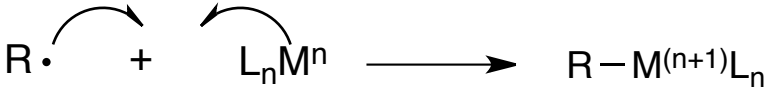


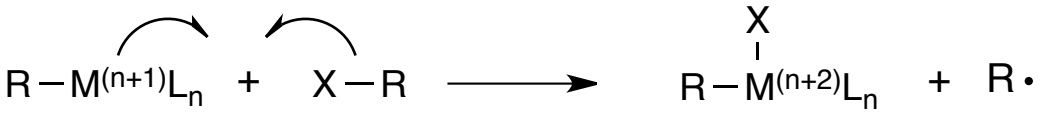
Oxidative Addition/Reductive Elimination

Polar Electrophiles, cont'd

There are also examples of reactions that cannot be explained by either of these mechanisms (concerted or S_N2). These have been rationalized by a radical-chain mechanism.

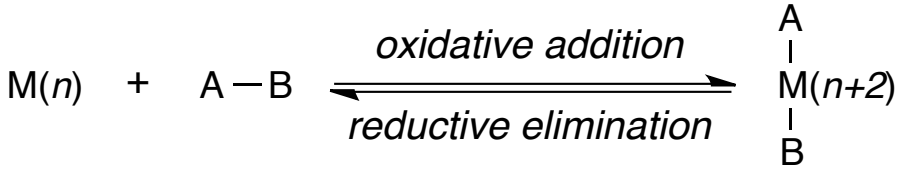






sequential 1e⁻ oxidations,
net 2e⁻ oxidation of metal

Oxidative Addition/Reductive Elimination



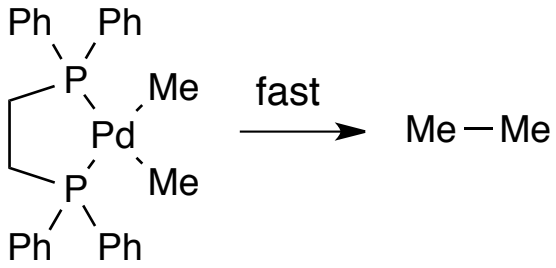
Reductive Elimination (RE)

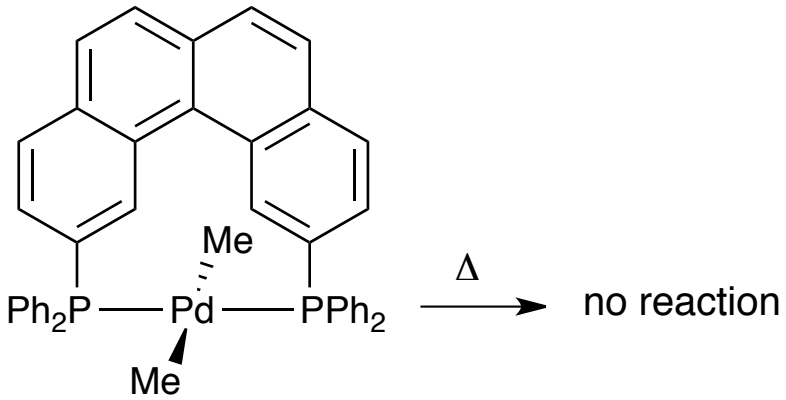
The reverse of oxidative addition. Concerted mechanism proceeds with retention of any stereochemical information. Nucleophilic attack on the ligand would invert the configuration.

Factors that influence:

– First row metals faster than second row, faster than third row
– Electron-poor complexes react faster than electron-rich
– Sterically hindered complexes reacter faster
– H reacts faster than R
– complexes with 1 or 3 L-type ligands faster than 2 or 4

Geometry of the complex is also quite important

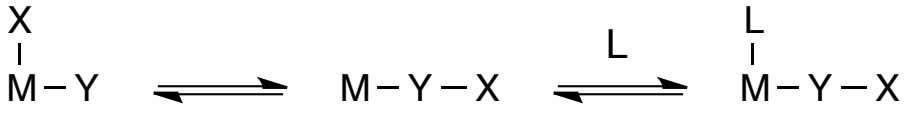




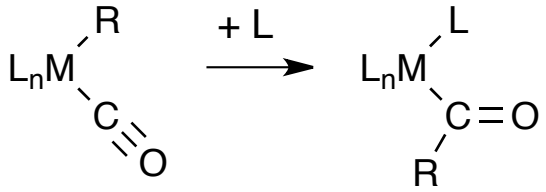
Migratory Insertion & Eliminations

Migratory Insertion

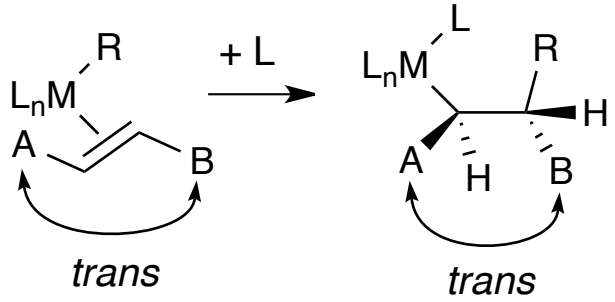
In this process an unsaturated ligand (CO, RNC, alkene, alkyne) inserts into an existing M-ligand bond. The two ligands involved must be *cis* to one another. These are usually reversible processes. At the end of the reaction the metal is left with an empty coordination site.

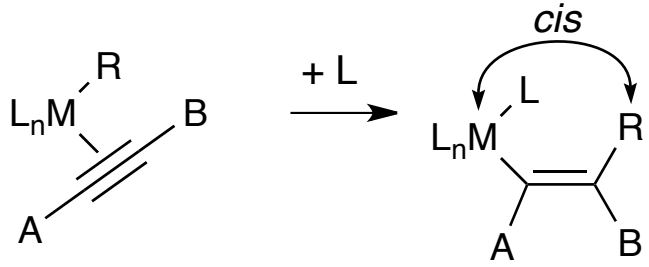


General examples:



R = aryl, alkyl, H



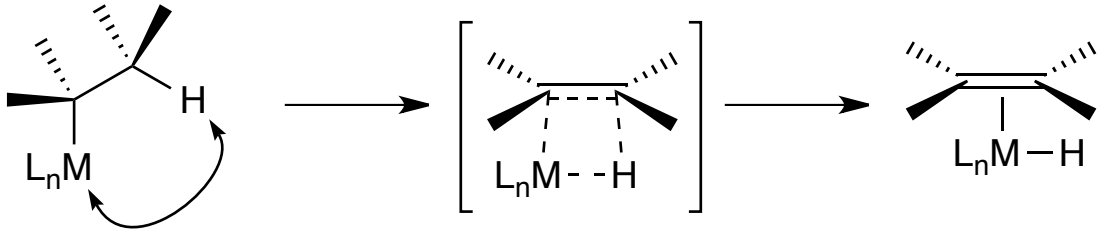


Migratory Insertion & Eliminations

Eliminations are the reverse reaction of migratory insertion and can occur one after the other. The group being eliminated does not have to be the one that participated in the insertion. There are several types of eliminations.

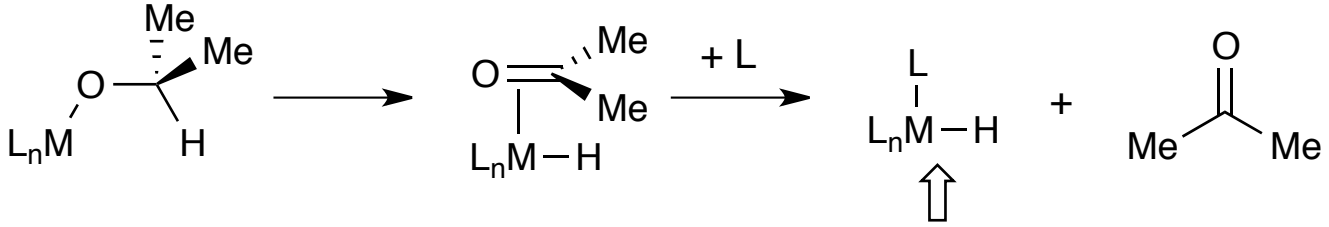
β-Hydride Elimination (BHE)

If an alkyl metal complex has hydrogens b to the metal, then this type of elimination is likely to occur. However, the β-hydrogens usually must be syn coplanar to the metal. Also the metal usually must have an open coordination site.



syn coplanar

BHE from transition metal-alkoxides and -amines are also important



M–H without using H_2

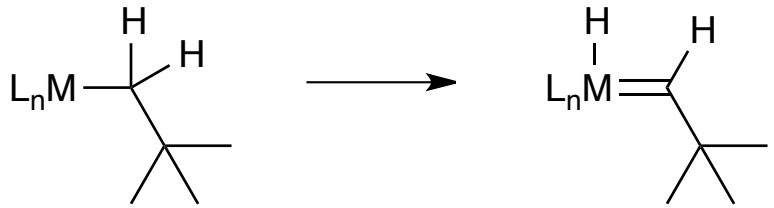
β-Eliminations of alkoxides and halides are known.

Migratory Insertion & Eliminations

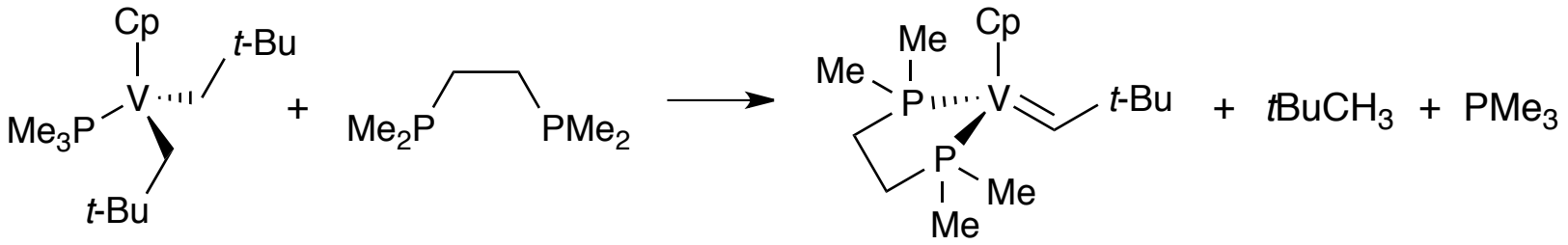
Eliminations are the reverse reaction of migratory insertion and can occur one after the other. The group being eliminated does not have to be the one that participated in the insertion. There are several types of eliminations.

α-Hydride Elimination (AHE)

Elimination of an α-hydrogen from metal alkyl complexes. This forms a carbene. Much slower than β-elimination processes and usually only occur when BHE is not possible. More common with early transition metals (d^0, group 4 and 6), but can happen with later metals.



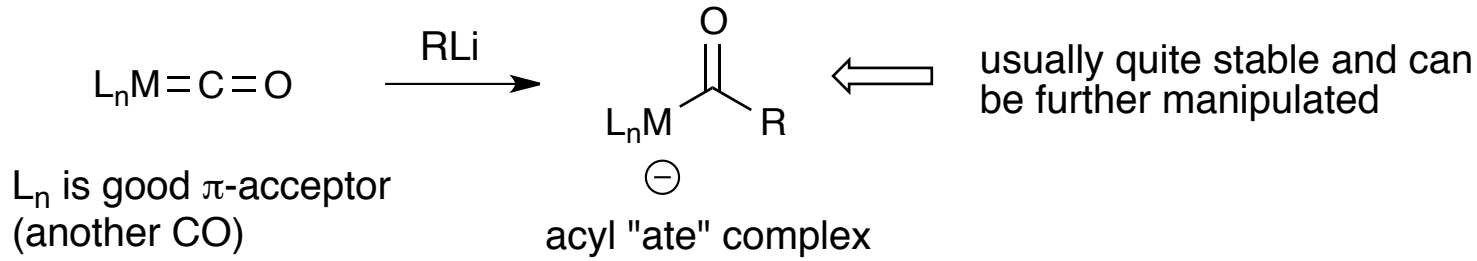
Often induced by ligand exchange processes.



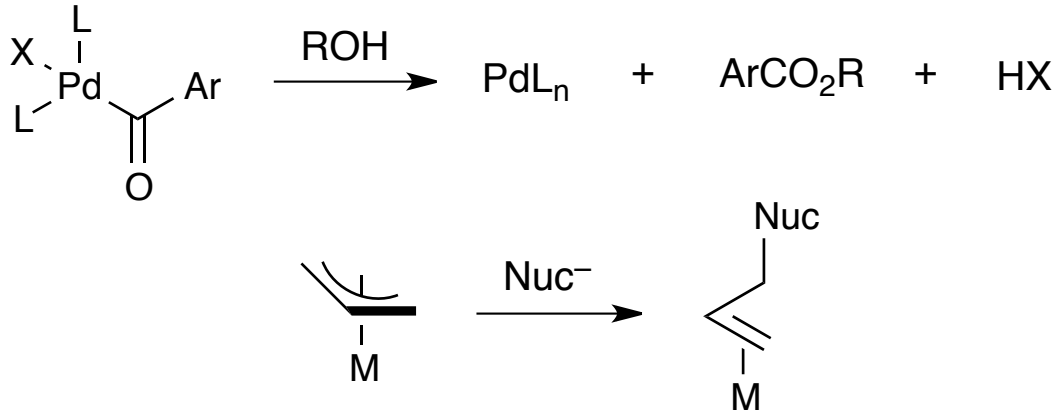
Nucleophilic Attack on Coordinated Ligands

Many different kinds of examples of this. From our prespective the more important ones involve attack on M–CO complexes and M–alkene/alkyne complexes.

Attack on Metal-Bound Carbonyl – The nucleophile is typically strong nucleophiles, like RLi



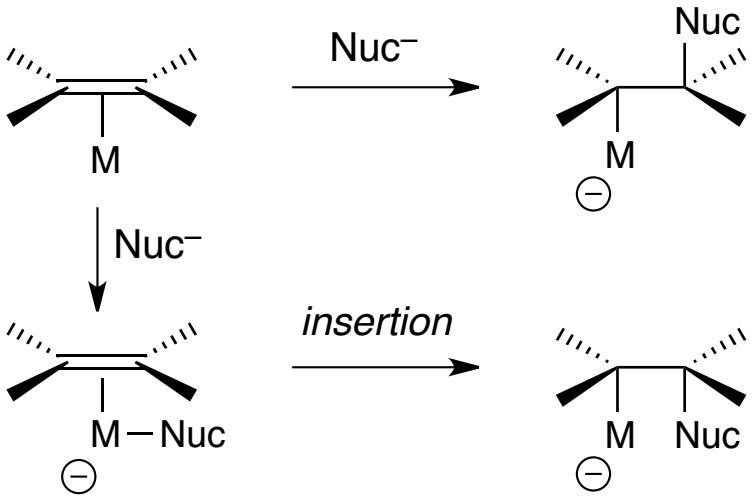
Attack on M–C σ-Bonds – Such bonds are often intermediates in catalytic reactions. The carbon can be sp^2 or sp^3 hybridized. Nucleophilc reactions with η^3-allyl complexes fall in this category. Can also be considered as a "reductive elimination" process.



Nucleophilic Attack on Coordinated Ligands

Many different kinds of examples of this. From our prespective the more important ones involve attack on M–CO complexes and M–alkene/alkyne complexes.

Attack on M–C π-Bonds – By ligating the metal, alkenes and alkynes usually become electrophilic. This makes then susceptible to nucelophilic attack. Depending on how the nucleophile reacts, the addition can be *syn* or *anti*.



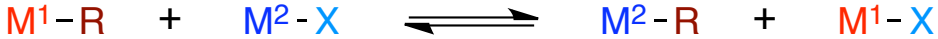
"external" addition of nucleophile
product of *anti* addition
(most common pathway)

"internal" addition of nucleophile
product of *syn* addition

Other nucleophilic reactions will be covered as needed

Transmetallation

Importance is growing as this is a key step in useful methods for constructing C–C bonds, particularly such bonds that are difficult to forge by other means. However, the exact mechanism by which transmetallation occurs is not well understood and seems to be quite dependent on the metal species.

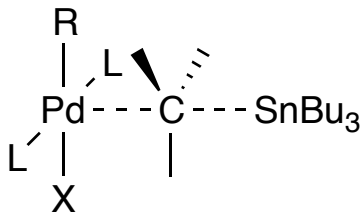


M^1 = Mg, Zn, Zr, B, Hg, Si, Sn, Ge
M^2 = transition metal

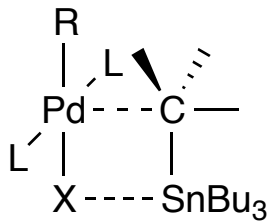
Generally speaking, transmetallation involves replacing the halide or pseudohalide in a transition metal (M^2) complex with the organic group of a "main group" organometallic (M^1) reagent. This step is almost always the rate-limiting step and is usually the culpret when cross-coupling reactions fail.

This is an *equilibrium*, so to ensure success both partners must gain some thermodynamic benefit. Often this can be enhanced by appropriate "activation" of the main group element.

Isomeric integrity (*cis*, *trans*) is usually maintained when R is an olefin. With alkyl metals the situation is more complicated. With polar solvents, alkylstannanes can transmetallate with *inversion* of configuration (open transition state?), but in less polar solvents *retention* is seen (closed transition state?). However, aliphatic organoboron reagents tend to proeed with *retention*.



proposed open t.s.
leading to *inversion*



proposed open t.s.
leading to *retention*

similar mechanisms could be drawn with other metals under apprpriate activation

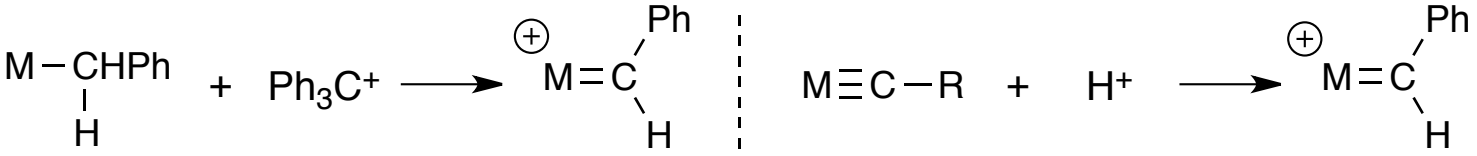
Electrophilic Attack on Coordinated Ligands

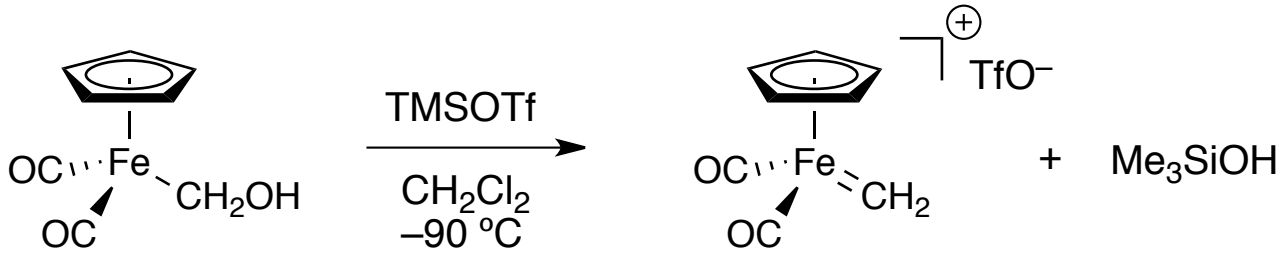
Several different reactivity modes depending on the metal, ligand, and electrophile involved. More specific examples will be discussed as needed.

Electrophilic cleavage of σ-alkyl metal bonds – Note metal is removed.

retention at R

Attack at α-position – Forms carbenes

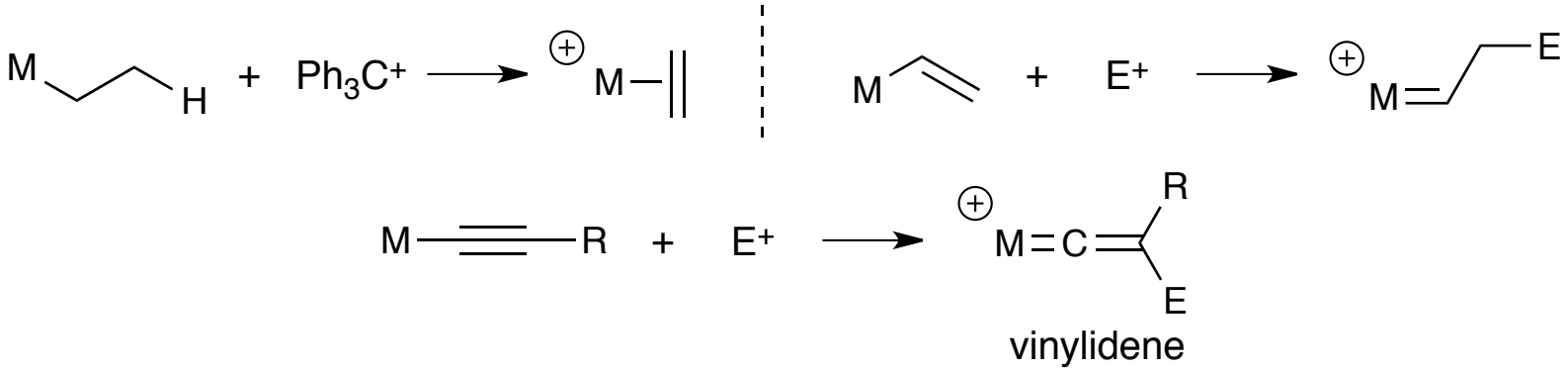


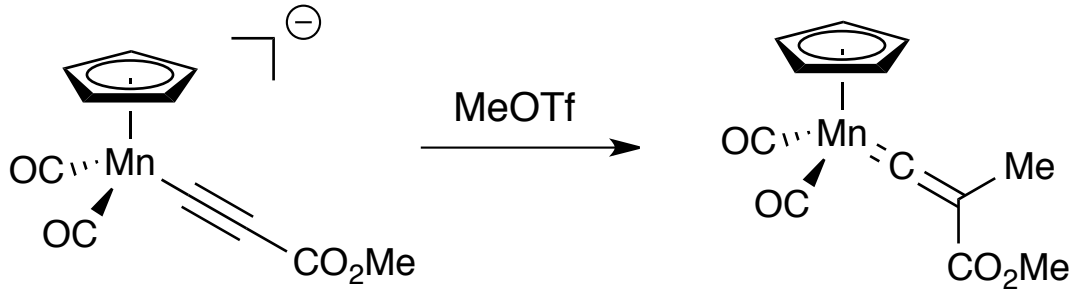


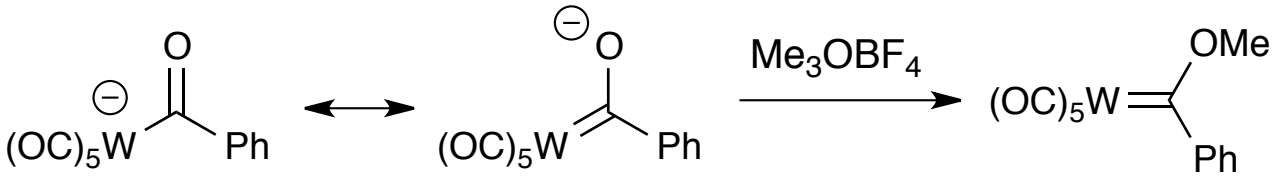
Electrophilic Attack on Coordinated Ligands

Several different reactivity modes depending on the metal, ligand, and electrophile involved. More specific examples will be discussed as needed.

Attack at β-position



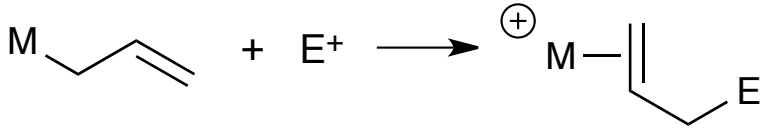


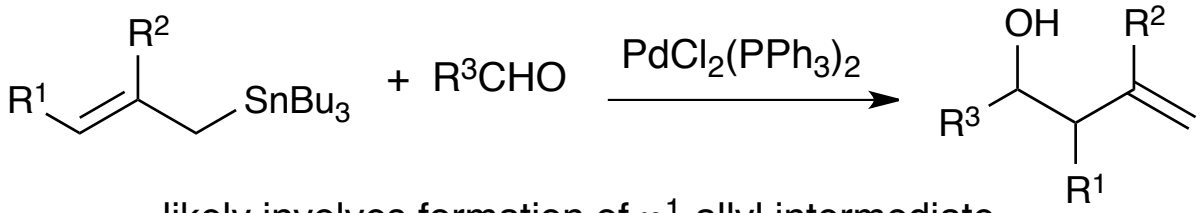


Electrophilic Attack on Coordinated Ligands

Several different reactivity modes depending on the metal, ligand, and electrophile involved. More specific examples will be discussed as needed.

Attack at γ-position





likely involves formation of η^1-allyl intermediate