**Reaction Mechanisms**

1. A mechanism is a theory deduced from the available experimental data. The experimental results are the facts; the mechanism is conjecture based upon these facts.

2. A mechanism the simplest rationalization that is consistent with all of the available data.

3. A mechanism should provide experimentally testable predictions and can only be disproved, never proven.

**Elementary organometallic reactions can usually be classified as one of the following:**

- **MLₙ → ligand dissociation → MLₙ₋₁ + L**
  - Δ e- count: -2
  - Δ ox. state: 0

- **LₙMₓ → reductive elimination → LₙM + X—Y**
  - Δ e- count: -2
  - Δ ox. state: -2

- **MLₙ → σ bond metathesis → LₙM — R**
  - Δ e- count: 0
  - Δ ox. state: 0

- **LₙMₓ → 4-centered reaction → X — M’**

- **LₙMₓ → insertion → LₙM — L — R**
  - Δ e- count: -2
  - Δ ox. state: 0

- **LₙMₓ → de-insertion → LₙM — E — Nu**
  - Δ e- count: 0
  - Δ ox. state: 0
Organometallic Reaction Mechanisms

1. Ligand Association/Dissociation

\[
\begin{array}{c}
\text{ML}_n \quad \text{ligand dissociation} \\
\text{ML}_{n-1} + L \quad \text{ligand association}
\end{array}
\]

Example:

\[
\begin{array}{c}
Pd(PPh_3)_4 \quad \text{Pd(PPh_3)_3} + PPh_3 \quad \text{Pd(PPh_3)_2} + PPh_3
\end{array}
\]

\[
\begin{array}{c}
18\text{ e-} \quad 16\text{ e-} \quad 14\text{ e-}
\end{array}
\]

Topics Discussed

1. **Associative**

2. **Dissociative**
Ligand Exchange Mechanisms

**Associative ligand substitution**: is often called square planar substitution because 16 e-, d8 square planar complexes generally undergo ligand substitution via an associative mechanism (the M-Nu bond is formed before the M-X bond breaks). The intermediate is 18e- and therefore provides a lower energy route to the product than a 14e- intermediate formed via dissociative substitution (the M-X bond is fully broken before the M-Nu bond begins to form). Analogous in many ways to S_N2 reactions.

**Dissociative ligand substitution** is most favored in coordinatively saturated 18e- complexes (e.g. d^{10} tetrahedral, d^{6} octahedral). In the dissociative mechanism, the M-X bond is fully broken before the M-Nu bond forms thereby avoiding an energetically unfavorable 20e- intermediate. Analogous in many ways to S_N1 reactions.

**Note** that in all ligand substitution processes, there is no oxidation state change at the metal center.
**MO Description of σ bonding in ML₄ square planar**

*Metal Valence Orbitals*

- **a₂u**
- **eₜ**
- **a₁g**
- **b₁g**
- **eₙ**
- **b₂g**

*Linear Combinations of Ligand σ Donor Orbitals*

- **LUMO**
- **HOMO**

16 e⁻ Rule:
The square planar geometry is favored by d⁸ metals (e.g. Ni (II), Pd (II), Pt(II), Ir (I), Rh(I)).

A stable electronic configuration is achieved at 16 e⁻, where all bonding and non-bonding orbitals are filled. Spin-paired compounds display diamagnetic behavior (i.e. weakly repelled by magnetic fields) and may be readily characterized by NMR.

When combining orbitals, the resulting MO's must be symmetrically dispersed between bonding and antibonding. Thus, combining 3 orbitals (i.e. a₁g's) requires one of the orbitals to be non-bonding.

In a square planar ligand field, the degenerate d orbitals split into orbitals of a₁g, b₁g, eₙ, and b₂g symmetries. The degenerate p orbitals split into orbitals of eₜ and a₂u symmetries.
**Associative Substitution: the nucleophile**

$$\text{Rate} = \frac{-d[\text{PtCl}_2]}{dt} = k_1[\text{PtCl}_2] + k_2[\text{Nu}][\text{PtCl}_2]$$

$k_1$: first order rate constant that arises from substitution of leaving group by solvent.

$k_2$: second-order rate constant for bi-molecular attack of Nu on metal complex.

Basicity of the incoming ligand (nucleophile) plays only a minor role in its reactivity for soft metal centers. In general, the softest (i.e. most polarizable) nucleophiles react fastest with soft metals like Pt(II) via associative substitution. Steric hinderance at the nucleophile (i.e. picoline vs pyridine) can retard the rate of substitution.

<table>
<thead>
<tr>
<th>Nu</th>
<th>relative rate</th>
<th>Nu</th>
<th>relative rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOH</td>
<td>1</td>
<td></td>
<td>1549</td>
</tr>
<tr>
<td>$\text{CH}_3\text{CO}_2^-$</td>
<td>&lt;100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO</td>
<td>&lt;100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F$^-$</td>
<td>&lt;158</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{Py}$</td>
<td>158</td>
<td></td>
<td>2754</td>
</tr>
<tr>
<td>$\text{CH}_3\text{O}^-$</td>
<td>&lt;250</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Et)$_3\text{N}$</td>
<td>1175</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{Cl}^-$</td>
<td>1096</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{NH}_3$</td>
<td>1175</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{Br}^-$</td>
<td>15,000</td>
<td>$\text{I}^-$</td>
<td>$2.9 \times 10^5$</td>
</tr>
<tr>
<td>$\text{C}<em>6\text{H}</em>{11}\text{CN}$</td>
<td>$2.2 \times 10^6$</td>
<td>(CH$_3$O)$_3\text{P}$</td>
<td>$1.7 \times 10^7$</td>
</tr>
<tr>
<td>$\text{PhS}^-$</td>
<td>$1.5 \times 10^7$</td>
<td>$\text{Ph}_3\text{P}$</td>
<td>$8.5 \times 10^8$</td>
</tr>
<tr>
<td>$\text{Et}_3\text{P}$</td>
<td>$9.8 \times 10^8$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Assessive Substitution: Sterics

Sterically shielding the positions above and below the plane of the square planar complex can lead to significant decreases in the rates of associative substitution.

\[ k_2 = 100,000 \text{ M}^{-1} \text{ sec}^{-1} \]

\[ k_2 = 200 \text{ M}^{-1} \text{ sec}^{-1} \]

\[ k_2 = 1 \text{ M}^{-1} \text{ sec}^{-1} \]

as the steric bulk of the imine backbone increases, the aryl groups become more rigidly locked perpendicular to the square plane making their ortho substituents more effective at blocking the axial sites above and below the plane.

\[ \text{ associative second order rate constants for ethylene exchange were examined by } ^1\text{HNMR in CDCl}_2 \text{ at } -85^\circ \text{C} \]

\[ k = \text{too fast to measure even at } -100^\circ \text{C}. \]

Brookhart *JACS* 1995 (117) 6414.
**Brookhart Polymerization Catalysts**

Polymer $M_w = 110,000$

Polymer $M_w = 390,000$

**Mechanism -8-**

Week of September 18th, 2012

Brookhart Polymerization Catalysts

Brookhart JACS 1995 (117) 6414.
**Ligand Exchange: Dissociative Mechanism**

The rate-determining step in a dissociative ligand substitution pathway is breaking the M-L bond. Because of the late, product-like transition state for forming the coordinatively unsaturated intermediate in such a process, the M-L BDE is a good approximation of the activation energy ($E_A$).

The rate of ethylene exchange via dissociative displacement at 25°C is $\sim 10^{14}$ sec$^{-1}$

rate of ethylene exchange via associative displacement at 25°C is $\sim 10^4$ sec$^{-1}$

BDE = 31 kcal/mol

Cramer *JACS* 1972 (94) 5681.

<table>
<thead>
<tr>
<th>PPh$_3$ (mmol)</th>
<th>$k \times 10^4$ sec$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.20</td>
<td>1.65</td>
</tr>
<tr>
<td>1.23</td>
<td>1.73</td>
</tr>
</tbody>
</table>

A 6-fold increase in the concentration of nucleophile does not significantly affect the_rxn rate. Results are consistent with a mechanism where the rate-determining step is ethylene dissociation and is not affected by the concentration of the nucleophile.
Ligand dissociation: sterics

The steric bulk of the bidentate phosphine ligand is thought to weaken the Pd-P bond, thereby favoring ligand dissociation required to form the catalytically active species.

Hartwig *JACS* 1998 (120) 7369.
**Ligand dissociation: Δ or hv**

Coordinatively and electronically unsaturated complexes capable of oxidatively adding into unactivated C-H bonds.

\[
\text{Rh}^1\text{OC} \xrightarrow{hv \text{ or } \Delta} \text{Rh}^1\text{OC} \xrightarrow{\text{CO}} \text{Rh}^\text{III}\text{OC} \xrightarrow{\text{H}} \text{Rh}^1\text{OC}
\]

Light-promoted ligand dissociation

\[
\begin{align*}
\text{M-CO} & \quad \text{M-CO} \\
\sigma^* & \quad \sigma^* \\
\sigma & \quad \sigma \\
\text{bond order = 1} & \quad \text{bond order = 0}
\end{align*}
\]

Bergman *JACS* 1994 (116) 9585.
Ligand dissociation: weakly coordinating solvents

First generation Crabtree hydrogenation catalyst

\[
\text{Ir} \quad \text{P(PhMe)}_2 \quad (\text{PF}_6^-) \\
\text{Ph}_2(\text{Me})\text{P} \quad \text{Ir} \quad \text{P(PhMe)}_2 \quad (\text{PF}_6^-) \\
\text{S} \quad \text{H} \quad \text{S} \quad \text{R}
\]

A glimpse into the catalytic cycle

Catalytically active species

Solvent (S) | Turnover Frequency (TOF) |
---|---|
\[\text{CH}_2\text{Cl}_2\] | 5100, 3800, 1900 |
\[\text{CO}\] | 10, 0, 0 |

TOF = mol reduced substrate/mol catalyst/h

Crabtree *Acc Chem Res* 1979 (12) 331.
Organometallic Reaction Mechanisms

2. Oxidative Addition / Reductive Elimination

\[
\text{L}_n\text{MXY} \xrightleftharpoons{\text{reductive elimination}} \text{L}_n\text{M} + \text{X} \xrightarrow{\text{oxidative addition}} \text{X} \rightarrow \text{Y}
\]

Topics Discussed

1. *OA mechanism and trends*

2. *RE mechanism and trends*

3. *Mechanistic probes*
Oxidative Addition/Reductive Elimination

**Oxidative Addition (OA):** metal mediated breaking of a substrate σ-bond and formation of 1 or 2 new M-L σ bonds. OA requires removal of 2 electrons from the metal's d electron count. This is reflected in a two unit increase in the metal's oxidation state. The formation of 1 or 2 new M-L σ bonds is accompanied by an increase in the metal's coordination number by 1 or 2 units respectively. The latter results in a 2 unit increase in the electron count of the metal complex (e.g. 16 e⁻ to 18 e⁻). Currently, OA of low valent, electron rich metals to polar substrates is the best way to form M-C σ bonds within the context of a catalytic cycle. *The term oxidative addition confers no information about the mechanism of the reaction.*

![Oxidative Addition and Reductive Elimination Diagram](image)

**Reductive elimination (RE):** microscopic reverse of oxidative addition where two M-L σ bonds are broken to form one substrate σ bond. RE results in the addition of two electrons into the metal d electron count. This is reflected in a two unit decrease in the metal's oxidation state. The breaking of 2 M-L σ bonds is accompanied by a decrease in the metal's coordination number by 2 units. The result is a 2 unit decrease in the electron count of the metal complex (e.g. 18e⁻ to 16 e⁻). The two M-L σ bonds undergoing reductive elimination must be oriented *cis* to each other. Currently, RE is the most common way to form C-C bonds *via* transition metal complexes.

**General OA Mechanisms:**

- **Concerted (generally for non-polar substrates):**
  
  ![Concerted Mechanism Diagram](image)

- **Nucleophilic displacement (generally for polar substrates):**
  
  ![Nucleophilic Displacement Mechanism Diagram](image)

- **Radical (both non-polar and polar):**
  
  ![Radical Mechanism Diagram](image)
**Oxidative Addition**

**Metal Complex:** electron rich metals in low oxidation states, with strong donor ligands and a site of coordinative unsaturation.

\[ d^{10}, \text{tetrahedral, } 18\text{ e}^{-} \rightarrow d^{10}, \text{ML}_{2}, \ 14\text{ e}^{-} \rightarrow d^{8}, \text{ML}_{4}, \text{square planar, } 16\text{ e}^{-} \quad (\text{e.g. } \text{Ni}^{0}, \text{Pd}^{0}, \text{Pt}^{0}) \]

**Substrates:** two groups segregated into non-polar and polar. Currently, the most facile way to form C-M σ bonds is with polar substrates (e.g. alkyl, aryl, and vinyl halides).

**Non-polar substrates:** R-H

- \( \text{H}_2 \), \( \text{R}_3\text{Si-H} \), \( \text{R}_2\text{B-H} \), \( \text{RCH}_2\text{-H} \)

**Polar substrates:** R-X where X = I, Br, Cl, OTf

- \( \text{H-X} \), \( \text{RCH}_2\text{-X} \), \( \text{X} \)
**OA: Concerted 3-centered (non-polar substrates)**

**σ-complex:** intermolecular binding of a substrate via its σ-bond to a metal complex. σ-complexes are thought to be along the pathway for oxidative addition of non-polar substrates to low valent, e-rich metal complexes. Analogous to the Dewar-Chatt-Duncanson model for olefin metal-bonding, σ-bonding is thought to occur via a 2 way donor-acceptor mechanism that involves σ-donation from the bonding σ-electrons of the substrate to empty σ-orbital of the metal and π-backbonding from the metal to the σ* orbitals of the substrate. These bonding principles have been applied to non-polar σ-bonds such as H-H, C-H, Si-H, B-H and even C-C bonds.

**Concerted mechanism:** σ-complex formation precedes an early (little σ-bond breaking), 3-centered transition state where strong π-backbonding results in oxidative addition of the bound substrate to the metal. The concerted mechanism is thought to operate primarily for non-polar substrates (i.e. H-H, C-H, Si-H, B-H) with electron rich, low valent metals. The spectroscopic identification of metal dihydrogen σ-complexes with H-H bond distances stretched between the non-bonding (0.74Å) and dihydride extremes (>1.6Å) provides strong support for this mechanism with H₂.
**sp³C-H OA via σ complex intermediates**

**regioselectivity**: sp² C-H > 1° sp³C-H > 2° sp³ C-H >>> 3° sp³ C-H. There is both a kinetic and thermodynamic preference to form the least sterically hindered C-M σ bond. Kinetic preference: activation barrier to σ-complex formation is lower for less sterically hindered C-H bonds and bonds with more s character. Thermodynamic preference: stronger C-M bonds are formed (see Structure and Bonding, pg. 32).

Evidence in support of a σ-complex intermediate:

Bergman *JACS* 1994 (116) 9585.
**sp³C-H: concerted vs. radical**

crossover experiment: evidence in support of a concerted mechanism.

Less than 7% of the crossover products were observed by $^1$HNMR. This may be indicative of a minor radical pathway.

Bergman *JACS* 1983 (105) 3929.
Agostic interactions: intramolecular σ-complex

An agostic interaction is generally defined as an intramolecular σ-complex that forms between a metal and a C-H bond on one of its ligands.

Brookhart *JOMC* 1983 (250) 395

The strategy of identifying substrates that can act as transient metal ligands has led to the only synthetically useful examples of C-H-> C-M (C-H activation) to date. Like all substrate directed reactions, the scope of such processes is limited.

Trost *JACS* 1995 (117) 5371
Milstein *JACS* 2000 (122) 9848.

**OA: sp³C-sp³C**

Even though BDE's of C-C bonds are lower than those of analogous C-H bonds (e.g. C₆H₅-CH₃: 100 kcal/mol vs. C₆H₅-H: 110 kcal/mol), transition metal mediated OA's into C-C bonds are much more rare than those for analogous C-H bonds. Formation of the σ-complex is kinetically disfavored by steric repulsion between the metal complex and the carbon substituents and by the high directionality of the sp³C-sp³C bond that localizes the σ bonding orbital deep between the carbon nuclei. Milstein and coworkers are able to overcome the kinetic barrier by approximating the C-C bond at the metal center.

![Diagram](image-url)
**OA with $C_{sp^2}$-X bonds: aryl and vinyl halides**

Rate of OA X = I>Br>Cl>>F

**Three main mechanisms to consider for this process:**

1. Concerted process with unsymmetrical, minimally-charged, 3-centered transition state

2. $S_N$Ar-like with highly charged transition state

3. Single-electron transfer processes with oppositely-charged, radical intermediates
Nucleophilic displacement (generally for polar substrates)

\[
L_xM^n + \begin{array}{c}
A \\
\delta^+
\end{array} \xrightleftharpoons{X} \begin{array}{c}
L_xM^n - A - - X \\
\delta^-
\end{array} \rightarrow \begin{array}{c}
[L_xM^{(n+2)} - A]^+ \\
\delta^-
\end{array} + X^-
\]

"Stereochemistry is the single most valuable type of mechanistic evidence in reactions that make or break bonds to tetrahedral carbon." G.M. Whitesides (*JACS* 1974 (96) 2814).


**Ozawa** *JACS* **2002** (124) 10968.
Reductive elimination is a key transformation in transition metal mediated catalysis, often representing the product forming step in a catalytic cycle.

**General trend for reductive elimination from \(d^8\) square planar complexes:**

\[
\begin{align*}
&MH > M\text{C}(\text{sp}) > M\text{C}(\text{sp}^2) > M\text{C}(\text{sp}^3) \\
&M\text{C}(\text{sp}^3) \quad M\text{C}(\text{sp}^3)
\end{align*}
\]

Orbitals with more s character are less directional and lead to better overlap in the transition state for reductive elimination (RE). Note: *cis* orientation of the ligands is required for RE to occur.

**Best overlap**

- Metal dihydride
- Transition state (TS)
- Calculated \(\Delta E^\ddagger = 1.55\) kcal/mol
- Pd-H bond is stretched only 2% in TS

**Worst overlap**

- Hydrido(alkyl)metal complex
- Transition state (TS)
- Calculated \(\Delta E^\ddagger = 10.4\) kcal/mol
- Metal dimethyl
- Transition state (TS)
- Calculated \(\Delta E^\ddagger = 22.6\) kcal/mol
- Pd-H bond is stretched ~10% in TS

Computational studies suggest that the spherical symmetry of the s orbitals of H allows the simultaneous breaking of the M-L \(\sigma\) bonds while making the new \(\sigma\) bond of the product.

**Goddard** *JACS* 1984 (106) 8321.

**Dedieu** *Chem. Rev.* 2000 543.
RE: Bite Angle Effects

RE can be promoted by:

**Increasing the bite angle of the ligand**
- Increasing electrophilicity of metal center (e.g., π-acids)
- Ligand dissociation

![Diagram of Pd(II) complex with bite angles and reaction kinetics]

Large bite angles of diphosphines have been shown to enhance the rates of reductive elimination from square planar complexes presumably by bringing the two departing ligands closer together.

Moloy *JACS* 1998 (120) 8527.
**RE: \( \pi \)-Acid Effects**

*RE can be promoted by:*

- Increasing the bite angle of the ligand
- **Increasing electrophilicity of metal center** (e.g. \( \pi \)-acids)
- Ligand dissociation

---

**Chemistry Reaction**

\[
\begin{align*}
\text{Bu} & \quad \text{PentZn} \\
\text{O} & \quad 10 \text{ mol\%} \\
\text{Bu-} & \quad \text{I} \\
\text{F}_3\text{C} - & \quad \text{50 mol\%} \\
\text{Ni}^{II} & \quad \text{possible intermediate} \\
\text{O} & \quad 70\% \text{ yield, 1h} \\
\text{Bu} & \quad \text{Pent} \\
\end{align*}
\]

w/out \( \pi \)-acid: 20%, 15h

---

*Knochel* *ACIEE* 1998 (37) 2387.
Organometallic Reaction Mechanisms

3. Transmetallation

\[
L_nM \rightarrow X + M'R \rightarrow L_nM \rightarrow R + M'-X
\]

- X = leaving group (halide, triflate)
- M' = usually main group metal (boron, tin, zinc)

Example:

\[
\begin{array}{c}
\text{Ph} \quad \text{PPh}_3 \\
\text{Pd} \quad \text{Br} \\
\text{Ph}_3\text{P}
\end{array} + \begin{array}{c}
\text{Bu}_3\text{Sn} \\
\text{Ph} \quad \text{PPh}_3 \\
\text{Pd} \quad \text{Ph}_3\text{P}
\end{array} \rightarrow \begin{array}{c}
\text{Ph} \quad \text{PPh}_3 \\
\text{Pd} \quad \text{Br} \\
\text{Ph}_3\text{P}
\end{array} + \begin{array}{c}
\text{Bu}_3\text{Sn} \quad \text{Br}
\end{array}
\]

Topics Discussed

1. *What is it? (sigma bond metathesis)*

2. *Mechanism*

3. *Complex examples*
Transmetalation: Definition and Utility

Definition: the transfer of an organic group from one metal center to another. The process involves no formal change in oxidation state for either metal.

L\textsuperscript{'}\textsubscript{n}M\textsuperscript{'}\textsuperscript{R'} + L\textsubscript{n}M\textsuperscript{X} \rightleftharpoons L\textsuperscript{'}\textsubscript{n}M\textsuperscript{X} + L\textsubscript{n}M\textsuperscript{R}

Transmetalation is often a reversible process, with the equilibrium favoring the more ionic M-X bond. Subsequent reactivity of one L\textsubscript{n}M-R species can drive the equilibrium in one direction. This is often exploited in cross-coupling reactions, where a transmetalated intermediate undergoes a reductive elimination to generate a new organic product. Subsequent oxidative additions generates a new substrate for transmetalation.

Commonly used transmetalation reagents and their associated cross-coupling reaction

R-M\textsuperscript{1} + X-M\textsuperscript{2} \rightarrow X-M\textsuperscript{1} + R-M\textsuperscript{2}

M\textsuperscript{2} is typically group 10

<table>
<thead>
<tr>
<th>Reagent</th>
<th>R</th>
<th>X-coupling reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>LiR, MgXR</td>
<td>vinyl, aryl, allyl, alkyl</td>
<td>Kumada</td>
</tr>
<tr>
<td>RZrClC\textsubscript{p} \textsubscript{2}</td>
<td>vinyl, alkyl</td>
<td>Negishi</td>
</tr>
<tr>
<td>RZnCl</td>
<td>vinyl, aryl, alkyl</td>
<td>e.g. Sonagashira</td>
</tr>
<tr>
<td>RCU\textsubscript{L}\textsubscript{n}</td>
<td>alkynyl, aryl</td>
<td>Stille</td>
</tr>
<tr>
<td>RSnR\textsuperscript{3}</td>
<td>vinyl, aryl, alkynl</td>
<td>Suzuki</td>
</tr>
<tr>
<td>RB(OR\textsuperscript{'})\textsubscript{2}</td>
<td>vinyl, aryl</td>
<td>Suzuki-Miyaura</td>
</tr>
<tr>
<td>R-9BBN</td>
<td>alkyl</td>
<td></td>
</tr>
<tr>
<td>RSiR\textsuperscript{3}</td>
<td>aryl, vinyl, alkyl</td>
<td></td>
</tr>
<tr>
<td>AlR\textsubscript{2}, AlX\textsubscript{2}</td>
<td>alkyl</td>
<td></td>
</tr>
</tbody>
</table>

In general the rates of transmetalation of R follow the order: alkynyl > aryl, vinyl > alkyl
The mechanism for transmetalation is the least-studied of the basic reaction steps. In a simple picture, the metal accepting the R group is the electrophile and the M-R bond being transferred is the nucleophile. M-R bond formation may or may not be simultaneous with M’-X bond formation, depending on the nature of X and the actual complexes involved.

\[
\begin{align*}
\delta^+ & \quad M & \quad \delta^- \\
\downarrow & \quad X & \quad M' \\
\uparrow & \quad M' & \quad X
\end{align*}
\]

With this model, increasing the nucleophilicity of R by altering the ligands on M’ and increasing the electrophilicity of M through its ligands will facilitate the transmetalation step. For weakly nucleophilic transmetalation reagents, an added nucleophile or base often facilitates the transmetalation.

**Transmetalation with the Suzuki coupling often requires added base**

**F⁻ is thought to activate the organosilicon reagent for transmetalation via formation of a nucleophilic pentavalent silicate in a Hiyama coupling**

**Suzuki Chem. Rev. 1995 (95) 2457.**

**Hiyama Tet. Lett. 1990 (31) 2719.**
Transmetalation with advanced intermediates

Suzuki-Miyaura

\[
\text{O} \quad \text{OBn} \\
\text{BnO} \quad \text{H} \\
\text{BnO} \quad \text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{OTBS}
\]

\[
\text{O} \quad \text{OBn} \\
\text{BnO} \quad \text{H} \\
\text{BnO} \quad \text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{OTBS}
\]

\[\text{THF, rt} \quad 9\text{BBN}\]

3M aq. \(\text{Cs}_2\text{CO}_3\), DMF

\[\text{Pd(Ph}_3)_4, \quad 0^\circ\text{C}\]

71%

Synthetic studies on Ciguatoxin

Takakura *ACIEE*, 2001 (40) 1090
Organometallic Reaction Mechanisms

4. Migratory Insertion / De-insertion

Example:

\[
\text{Cp}_2^*\text{Nb} 
\xrightleftharpoons[de-insertion]{insertion} 
\text{Cp}_2^*\text{Nb} - \text{R} 
\xrightleftharpoons[de-insertion]{insertion} 
\text{Cp}_2^*\text{Nb} - \text{COR} 
\xrightarrow{CO} 
\text{Cp}_2^*\text{Nb} - \text{Me} 
\]

Nb(III), 18 e-
Nb(III), 16 e-
Nb(III), 18 e-

Topics Discussed

1. What is it?

2. Mechanism

3. Beta-hydride elimination
**Migratory Insertion/De-insertion: Alkyl, H**

### The π-bonding electrons of the olefin are used in σ-bond formation with a M-alkyl σ*. Formation of the new C-C and M-C σ bonds are thought to occur simultaneously with breaking of the π-bond and alkyl-M σ bond through a 4-centered concerted transition state. Migratory insertion of a hydride into a coordinated olefin (the microscopic reverse of β-hydride elimination) is thought to proceed via the same mechanism. For metal alkyls, the equilibrium lies to the right, whereas for metal hydrides it lies to the left.

---

**β-Hydride Elimination**

A significant decomposition pathway for metal alkyls is β-hydride elimination which converts a metal alkyl into a hydrido metal alkene complex.

β-hydride elimination can occur when:

- *cis* to the alkyl group there exists a site of coordinative unsaturation on the metal which corresponds to a site of electronic unsaturation (empty metal orbital).
- the M-C-C-H unit can take up a coplanar conformation which brings the β-hydrogen in close enough proximity to the metal to form an agostic interaction.
- the metal is electrophilic resulting in an agostic interaction that is primarily electron donative in nature (*i.e.* $\sigma$-donation $\gg \pi$-backbonding).

![Diagram of β-Hydride Elimination](image-url)
Wacker Oxidation

Commercial production of acetaldehyde

Binding specificity: terminal olefins
Regioselectivity: 2 carbon
Remote functionality tolerated
**β-Hydride Elimination**

Computational studies suggest that the higher energy of the Ni(II) vacant d orbital (0.1069 hartree) with respect to that of the analogous Pd(II) complex (0.0505 hartree) results in a weaker donative agostic interaction with the βCH σ bond. The energetically optimized geometries of the agostic complexes show a greater lengthening of the βC-H bond in the Pd(II) complex than in the Ni(II) complex, indicative of greater σ-donation in the former. These computational results are consistent with the experimentally observed greater stability of Ni alkyls towards β-hydride elimination that Pd alkyls and can be rationalized based on the greater electronegativity of Pd(II) vs Ni(II) as reflected in their respective second ionization potentials.

Recall: sp³ C-H is 1.09 Å

**Ni(II): 18.15 eV**

second ionization potential

**Pd(II): 19.9 eV**

second ionization potential

*Morokuma JACS 1985 (107) 7109.*
Migratory Insertion/De-insertion: CO

Mechanism for CO insertion: *via* alkyl migration to coordinated CO

![Mechanism Diagram]

Experimental evidence also suggests that carbonyl insertion occurs *via* alkyl migration (not CO migration)


**Migratory Insertion/De-insertion: CO**

![Chemical structures](image)

(no dimer observed)

Electron donating substituents on aryl R groups promote migrations whereas electron withdrawing substituents inhibit them.

<table>
<thead>
<tr>
<th>R</th>
<th>Monomer</th>
<th>Dimer</th>
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<tr>
<td>N</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>MeO</td>
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<td></td>
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</table>


**Heck Arylation**

**Oxidative Addition**

\[
\text{Pd(PPh}_3\text{)}_4 \text{ cat.} \quad \text{NEt}_3, \text{CH}_3\text{CN} \quad 80^\circ C
\]

**Associative Displacement**

**Migratory Insertion**

**β-Hydride Elimination**

93% yield

\[
(\pm)\text{-FR-900482}
\]

Danishefsky *JACS* 1993 (115) 6094.