Chapter 2
The Elementary Steps in TM Catalysis

- **Ligand Exchange**
  \[ [M] - L + [M] \rightleftharpoons [M] + L \]

- **Oxidative Addition** → **Reductive Elimination**
  \[ [M]^n + A-B \rightleftharpoons [M]^{n+2} \]

- **Oxidative Coupling**
  \[ [M]^n \rightleftharpoons \text{[cyclic compound]} \]

- **Transmetallation**
  \[ [M] - X + RM' \rightleftharpoons [M] - R + M' - X \]

- **Migratory Insertion** → **(Carbo-, Hydro-metalation)**
  \[ [M] - R \rightleftharpoons [M] + R \]
  \[ \beta\text{-elimination} \leftarrow \]
  \[ \text{(Decarbo-, Dehydro-metalation)} \]
The Elementary Steps in TM Catalysis

- (CO) insertion
- Nucleophilic addition at coordinated ligand
- Electrophilic addition at coordinated ligand

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Ligand Substitution

Similarities with organic nucleophilic displacement reactions

Associative $S_N2$-like processes are the most popular: ligand exchanges of coordinatively unsaturated $16\text{e}^- \cdot d^8$ square planar complexes: $[\text{Ni (II)}, \text{Pd (II)}, \text{Pt (II)}, \text{Rh (I)}, \text{Ir (I)}]$

Substitution reactions proceeding via single electron transfer also exist ($S_{RN2}, S_{RN1}$)
2e⁻ Associative Processes

2\textsuperscript{nd} order rate depending on:

Incoming ligand Y: $R_3P > Py > NH_3, Cl^- > H_2O > OH^-$

Leaving ligand X: $NO_3^- > H_2O > Cl^- > Br^- > I^- > N_3^- > SCN^- > NO_2^- > CN^-$

*Trans* ligand: $R_3Si^- > H^- > CH_3^- > CN^- >$ olefins $> CO > PR_3 > NO_2^- > I^- > Br^- > Cl^- >$ $RNH_2 > NH_3 > OH^- > NO_3^- > H_2O$

* Ligand trans with respect to the one being displaced

The rate of the ligand exchange can be accelerated by bulky ligands, since loss of one ligand leads to release of steric strain.

\[
\text{Ni(CO)}_4 \xrightarrow{\text{slow}} \text{Ni(CO)}_3 + \text{CO} \xrightarrow{\text{fast}} \text{LNi(CO)}_3
\]

\[v = k [\text{Ni(CO)}_4] = 1^{\text{st}} \text{ order rate}\]

The ability to control the bulk of the ligand permits to tune the reactivity of the metal complex. For example, if the dissociation of the phosphine ligand is the first step in a reaction, the reaction can be accelerated by utilizing a larger phosphine ligand. Likewise, if dissociation is a problem, then a smaller phosphine can be used.
Some Examples of Ligand Substitution

R-[Pd]−X \xrightarrow{R′-M} R′-[Pd] + MX

Nucleophilic addition of main group organometallic reagents. Especially useful with M = Zn, Sn, B

R-[Pd]−X \xrightarrow{Y} R-[Pd] − X \xrightarrow{Y}

Nucleophilic addition of anionic nucleophiles Y⁻: H⁻, NC⁻

R-[Pd]−X \xrightarrow{HNR₂} R-[Pd] + HX

Nucleophilic addition of amines

X[Pd] \xrightarrow{RM} [Pd] + MX

Nucleophilic addition of organometallic reagents (Sn) and hydrides to a π-allyl-Pd(II) complex
Anion Capture

The nucleophilic addition at palladium is usually followed by the reductive elimination, and the combination of these two elementary steps is known as the anion capture. The transiently generated σ-alkylpalladium complexes can be alkoxy carbonylated, with concomitant regeneration of Pd(0), by treatment with carbon monoxide in the presence of an alcohol (usually methanol) or amines.

Ligand Exchange via Slippage

\[
\begin{align*}
\text{Mn}^1; \text{d}^6; 18 \text{ e}^- & \quad \text{saturated} \\
\text{Mn}^1; \text{d}^6; 16 \text{ e}^- & \quad \text{unsaturated} \\
\text{Mn}^1; \text{d}^6; 18 \text{ e}^- & \quad \text{saturated (isolated)} \\
\text{Mn}^1; \text{d}^6; 18 \text{ e}^- & \quad \text{saturated}
\end{align*}
\]

\[
\begin{align*}
\text{η}^3\text{-allyl} & \quad (2 \text{ sites}) \\
\text{η}^1\text{-allyl} & \quad (1 \text{ site}) \\
\text{η}^5\text{-Cp} & \quad (3 \text{ sites}) \\
\text{η}^3\text{-Cp} & \quad (2 \text{ sites}) \\
\text{η}^1\text{-Cp} & \quad (1 \text{ site})
\end{align*}
\]

\[
\begin{align*}
\text{η}^6\text{-arene} & \quad (3 \text{ sites}) \\
\text{η}^4\text{-arene} & \quad (2 \text{ sites}) \\
\text{η}^2\text{-arene} & \quad (1 \text{ site})
\end{align*}
\]

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Nucleophilic Attack on Coordinated Ligands

Alkenes: direct attack at the ligand, anti to the metal, usually at the most substituted carbon atom

Allyles: stabilized nucleophiles attack the ligand, anti to the metal. Regioselectivity depends on the nature of the nucleophile and of the ancillary ligands.
Chemically Promoted Substitution

- Tetrahedral
- Trigonal bipyramidal
- Octahedral

These complexes undergo only promoted ligand substitution

### Amine N-oxide promoted ligand dissociation

\[
\begin{align*}
\text{[M]} &= \text{C} \equiv \text{O} \\
\text{O} - \text{NR}_3 &\xrightarrow{\text{fast}} \text{[M]} \xrightarrow{\text{L}} \text{[M]} - \text{L}
\end{align*}
\]

### Phosphine-oxide promoted ligand dissociation

\[
\begin{align*}
\text{[M]} &= \text{C} \equiv \text{O} \\
\text{O} - \text{PR}_3 &\xrightarrow{\text{fast}} \text{[M]} \xrightarrow{\text{L}} \text{[M]} - \text{L}
\end{align*}
\]

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Oxidative Addition
Oxidative Addition

Pd(0) is electron rich and has a nucleophilic character. This transformation often represents the first step of a catalytic cycle and its mechanism depends on the nature of the metal as well as on the substrate involved. An increase of 2 in the formal oxidation state of the metal and of the coordination number is observed.

\[ [M]^n + A-B \leftrightarrow [M]^{n+2} \]

The most commonly encountered systems:

(d^{10} / d^8): Ni(0) / Ni(II), Pd(0) / Pd(II)

(d^{8} / d^6): Co(I) / Co(III), Rh(I) / Rh(III), Ir(I) / Ir(III)
Homogeneous Pd(0): The Seminal Paper

Malatesta and Angoletta: J. Chem. Soc. 1957

231. Palladium(0) Compounds. Part II.1 Compounds with Triarylphosphines, Triaryl Phosphites, and Triarylarsines.

By L. Malatesta and (Miss) M. Angoletta.

The preparation of a number of complex compounds of zero-valent palladium with phosphorus donors is described. They can be prepared from Pd(R•NC)₂ and donor, or by reduction of palladium(II) compounds in the presence of excess of donor.

Three types of complexes have been isolated: (R•NC)(L)₃Pd, PdL₄, and PdL₅ (L = triarylphosphines and triaryl phosphites). The compounds PdL₄ are largely dissociated in solution.

The triphenylarsine complex (Ph₃As)₄Pd has also been obtained.

Previously we mentioned ¹ the reaction between diisocyanopalladium(0) and tri-ρ-chlorophenyl phosphite which yielded a mixed phosphite–isocyanide complex. This is a general reaction, and is shown by triaryl phosphites, triarylphosphines, and triarylarsines. Its course, however, varies with the isocyanide which forms complexes with palladium(0) and the substituting ligand (e.g., phosphines, arsines, and various para-substituted triphenyl phosphites).
Oxidative Additions to Palladium(0)

By P. Fitton, M. P. Johnson, and J. E. McKeon

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The oxidative addition of chloro-olefins to palladium(0)–phosphine complexes, described in the preceding Communication, has now been extended to other organic compounds which contain a carbon–halogen bond, and has been found to be a general method for the preparation of palladium(II) complexes, difficult to prepare by other methods.

The products were obtained in good yield by the addition of the halogenocarbon to a suspension of Pd(PPh₃)₄ in benzene at room temperature. Removal of benzene in vacuo gave a solid which was triturated with ether to remove triphenylphosphine. Recrystallization of the residue from methylene chloride–hexane gave the pure complexes.†

\[
Pd(PPh₃)₄ + R–X \rightarrow Pd \quad \text{Ph₃P} \quad \text{R}\ \\
\text{X} \quad \text{PPh₃} \\
\text{+ 2PPh₃}
\]

variation of \(\nu(\text{Pd–Cl})\) was noted in the complexes derived from chloro-olefins.⁵ The \textit{trans}-configuration of the products does not illuminate the stereochemistry of the oxidative addition. The \textit{cis}-isomers are generally the less stable forms in the palladium series and isomerization is easy, particularly in the presence of excess triphenylphosphine.³

When methyl iodide was added to bis(triphenylphosphine)palladium(0)² the product after recrystallization was identical with that obtained when Pd(PPh₃)₄ was used. This complex (I) gave an n.m.r. spectrum consistent with the proposed structure; the methyl protons appear at 0.18 p.p.m., split into a 1:2:1 triplet by coupling to two phosphorus nuclei \((J = 5.0\ \text{c./sec.})\). Occasionally the reaction of methyl iodide and [Pd(PPh₃)₄]₂ gave an adduct, the n.m.r. spectrum of which contained, in addition to the usual triplet at 0.18, a second 1:2:1 triplet of comparable intensity at -0.10 p.p.m. \((J = 5.0\ \text{c./sec.})\). This was at first attributed to the presence of some
Non-polar Substrates

Oxidative addition of H$_2$ takes place via a 3-center mechanism (central to catalytic hydrogenation and related to C-H bond activation).

\[ [M] + H_2 \rightarrow [M]H_2 \]

"agostic" 2 e$^-$, 3-center bond

The 3-center TS is involved and there is a synergic electron flow:

Proof of the mechanism:

Proof of the structure:

IR: 2 M-H stretching bands (symm and asymm). If trans, only asymm. is expected

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By the Way: Agostic

Agostic interactions:

From the Greek:

to hold one to oneself. It refers to a C-H bond on a ligand that undergoes an interaction with the metal complex.

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Non-polar Substrates

terminal alkynes

\[ \text{R} \equiv \equiv \text{H} \quad \xrightleftharpoons{[\text{Pd(0)]}} \quad \text{R} \equiv \equiv \text{H} \quad \leftrightarrow \quad \text{R} \equiv \equiv \text{H} \quad \xrightleftharpoons{[\text{Pd(II)]}} \quad \text{R} \equiv \equiv [\text{Pd}]\text{H} \]

active methylenes

\[ \text{Me} \quad \text{CO}_2\text{Et} \quad \xrightarrow{[\text{Pd(0)]}} \quad \text{Me} \quad \text{CO}_2\text{Et} \]

alcohols

\[ \text{R-OH} \quad \xrightarrow{[\text{Pd(0)]}} \quad \text{R-O-[Pd]H} \]
Polar Substrates

Halides: If the halide carries a $\beta$-H, dehydropalladation ($\beta$ -H elimination) may be a facile, and normally undesired, process, thereby generating an alkene. Accordingly, the most widely used substrates are vinyl-, aryl or benzyl-halides, whose corresponding $\sigma$-alkyl Pd complexes have no $\beta$-H.

The better the leaving group, the faster the oxidative addition: $\text{N}_2^+ >> \text{TfO} > \text{I} > \text{Br} > \text{OTs} > \text{Cl}$

Jutand, A.; Négri, S. *Organometallics*, 2003, 22, 4229

**vinyl halides: clean retention mechanism is observed**

**aryl halides: the reaction reminds a nucleophilic aromatic substitution**
Polar Substrates

However, in the presence of suitable electron rich bulky phosphines, or heterocyclic carbenes, oxidative addition to Pd(0) becomes so facile that alkyl halides having β-hydrogens can afford the corresponding σ-alkyl complexes under very mild conditions and without subsequent dehydropalladation.

\[
\text{PhCH}_2	ext{Br} \quad \xrightarrow{[\text{Pd}(0)], \text{P(t-Bu)}_2\text{Me, Et}_2\text{O, 0°C (94%)} } \quad \text{PhCH}_2\text{Pd} \quad \text{Me(t-Bu)}_2\text{PBr}
\]


Alkyl halides oxidatively add to Pd(0) via a SN2 like process. Inversion mechanism is observed......but sometimes racemisation via double inversion takes place

Polar Substrates

propargylic systems (X = leaving group)

allylic systems (X = leaving group)
From Pd(II) to Pd(IV)

Alkyl halides may also oxidatively add to R-Pd(II)-R complexes to give a usually unstable Pd(IV) complex.

Reductive Elimination

The reverse of oxidation addition
Reductive elimination produces coordinatively unsaturated metal centers

\[ \begin{align*}
[M^{n+2}] & \rightarrow [M^n] + A\rightleftharpoons B \\
\end{align*} \]

Thermodynamics may be different:

\[ \begin{align*}
[M] & \rightleftharpoons [M] + H-H \quad \text{fast} \quad \text{usually reversible} \\
[M] & \rightleftharpoons [M] + R-H \quad \text{fast} \quad \text{usually reversible} \\
[M] & \rightleftharpoons [M] + R-R \quad \text{slow} \quad \text{usually irreversible} \\
\end{align*} \]

\[ D_{M-R} = \sim 145 \text{ kJ/mol}, \quad D_{R-H} = \sim 420 \text{ kJ/mol}, \quad D_{M-H} = \sim 230 \text{ kJ/mol}, \quad D_{H-H} = \sim 435 \text{ kJ/mol}, \quad D_{R-R} = \sim 375 \text{ kJ/mol} \]
Reductive Elimination

Anything that reduces the electron density at the metal facilitates the reductive elimination.

Methods to reduce electron density are:
- oxidation of the metal
- addition of strong π-acceptor ligands such as:

![Chemical structures showing CO, O=O, and NC=CN](image)

The fragments to be eliminated must occupy cis position on the metal or must rearrange from trans to cis prior to the reductive elimination.

![Chemical reaction diagrams](image)

G. Poli
Transmetalation

Transfer of an R group from a main group organometallic compound to a TM complex.

When combined with reactions which introduce an R group into the Pd complex such as oxidative additions or nucleophilic attack on alkenes, efficient C-C bond forming reactions ensue: cross-coupling (Zn: Negishi-Baba, B: Suzuki-Miyaura, Sn: Migita-Kosugi-Stille, Si: Hiyama,…)

\[
\begin{align*}
R \rightarrow & M + R'[\text{Pd}X] \\
& \downarrow \text{red. elim.} \\
& \text{Zn, B, Sn, Si...} \\
\rightarrow & \rightarrow \\
& R[\text{Pd}]R' + MX \\
& \text{R-R'}
\end{align*}
\]

The main group organometallic must be more electropositive than Pd. The nature of X is also important.
Usually a reversible process, no variation in the oxidation state
Both the metal and the migrating group add to the same face of the olefin (syn addition)
Migratory insertion generates a vacant site. Conversely, dehydrometalation (β-H elimination) requires a vacant cis site on the metal.
When an alkyl group migrates, its stereochemistry is maintained.
Migratory Insertion: Some Examples

alkene or alkyne insertion into RPdX
R = H: hydropalladation; R = C: carbopalladation

alkene insertion into π-allyl-PdX

allene insertion into π-allyl-PdX (R = C, H)

allene insertion into RPdX (R' = C, H)

CO insertion (carbonylation) into RPdX (R = C, H)
alkene insertion into acyl-PdX