Organotransition metal compounds
Reaction mechanisms

Reaction mechanisms are of fundamental importance for rationalizing the synthesis, stability and reactivity of organotransition metal compounds, and in particular:

- The effect of coordination on the reactivity of organic ligands;
- The effect of the nature of the metal centre;
- The role of the supporting (spectator, ancillary) ligands.

N.B. In the majority of cases, **equilibrium reactions** are taking place.

Dedicated course (II Semester): Meccanismi di Reazione in Chimica Inorganica (Prof. Tubaro)

Substitution reactions

In order to react with a metal centre, organic molecules/fragments must coordinate to it. This takes place through addition or substitution reactions, most commonly the latter.

$L_nX_mM\text{-}\mathbf{Y} + \mathbf{Z} \rightarrow L_nX_mM\text{-}\mathbf{Z} + \mathbf{Y}$

M-Y bond breaking can take place homolytically (generation of radicals) or heterolitically. In the latter case, the bonding electrons can remain with the metal (formal reductive elimination of M) or with the ligand (most common situation):

$L_nX_mM\text{-}\mathbf{Y} \rightarrow L_nX_mM\cdot + \cdot\mathbf{Y}$

$L_nX_mM\text{-}\mathbf{Y} \rightarrow L_nX_mM^{(-)} + \mathbf{Y}^{(+)}$

$L_nX_mM\text{-}\mathbf{Y} \rightarrow L_nX_mM^{(+)} + \mathbf{Y}^{(-)}$

Substitution reactions

Similarly to nucleophilic substitutions reaction in organic chemistry, the mechanism of substitution can be **associative (associative interchange)** or **dissociative (dissociative interchange)** depending on the sequence order in bond breaking/bond formation.

$L_nX_mM\text{-}\mathbf{Y} + \mathbf{Z} \rightarrow L_nX_mM\mathbf{ZY} \rightarrow L_nX_mM\text{-}\mathbf{Z} + \mathbf{Y}$ **associative**

$L_nX_mM\text{-}\mathbf{Y} \rightarrow L_nX_mM + \mathbf{Y} + \mathbf{Z} \rightarrow L_nX_mM\text{-}\mathbf{Z} + \mathbf{Y}$ **dissociative**

The **first reaction step** is generally rate determining.

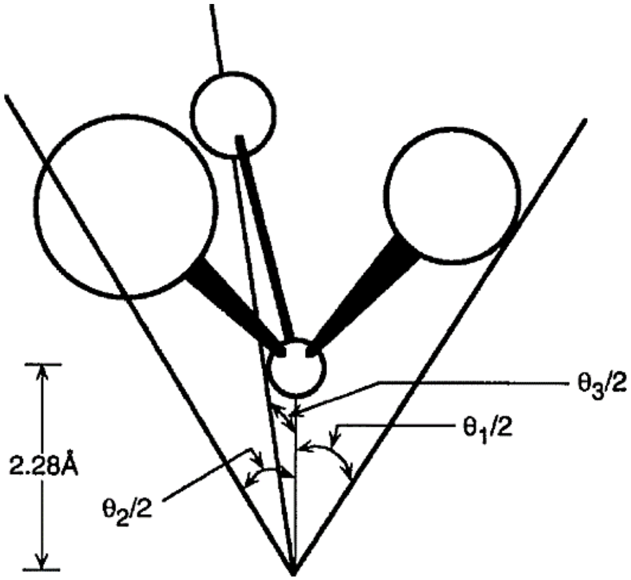
Kinetic effect of the involved ligands

Associative mechanisms:
Strong effect of the incoming ligand, weak effect of the leaving ligand.
The reaction rate increases with the Lewis basicity of the incoming ligand and decreases with increasing steric bulk.

Dissociative mechanisms:
Strong effect of the leaving ligand, weak effect of the incoming ligand.
The reaction rate decreases with the Lewis basicity of the leaving ligand and increases with increasing steric bulk.

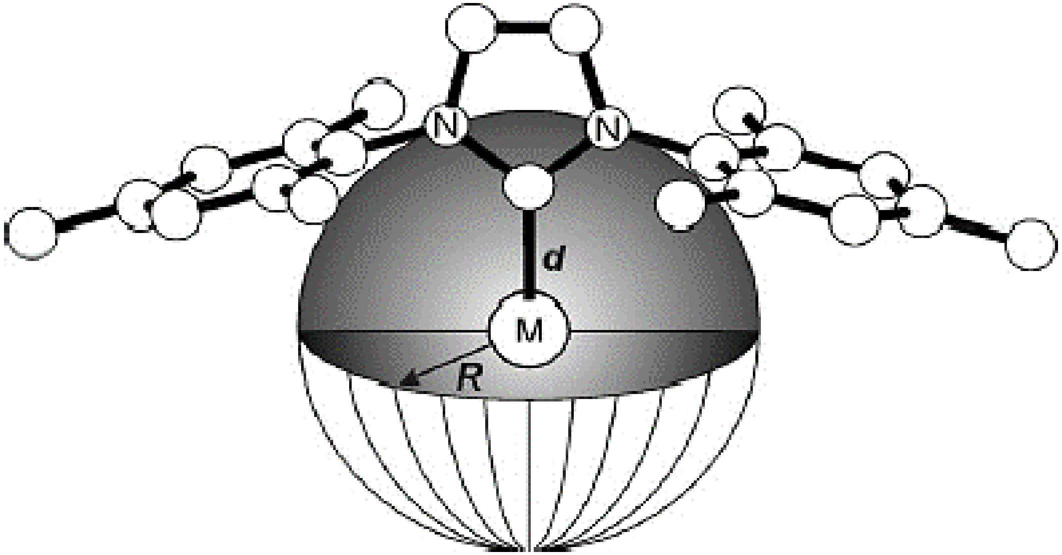
Quantification of Lewis basicity (bond energy) and steric bulk (Tolman “cone angle”, “buried volume”…)

Kinetic effect of the involved ligands



$$\Theta = \frac{2}{3}\sum_{i=1}^{3}\frac{\theta_i}{2}$$

Tolman cone angle



Buried volume

Kinetic effects of the spectator ligands

Steric effects:
The steric bulk of the spectator ligands favours dissociative mechanisms and disfavours associative ones.

Electronic effects:
“Trans effect” of the spectator ligand *trans* to the one being substituted (in square planar complexes)

Kinetic effect of the metal centre

Important for kinetics and mechanism are the no. of e^- in the complex, the electronic configuration at the metal (effect of the ligand field) and the charge of the complex; furthermore, with metals of the **second transition series** the reaction often takes place with the maximum rate.

18 e^- complexes react with dissociative mechanisms, whereas complexes with lower no. of e^- also with associative mechanisms.

Complexes with electron configurations at metal that are particularly stabilized by the ligand field (e.g. low spin d^6, d^3) react slowly.

Cationic complexes easily associate anionic ligands, whereas anionic complexes do dissociate them quite easily.

Kinetic effect of the metal centre

In cases in which the number of e^- in the complex or the electronic configuration at metal does prevent a given substitution reaction, the reaction can nevertheless be facilitated, for example:

- using reagents that selectively remove ligands (the no. of e^- in the complex decreases);

- exploiting redox reactions with reversibly oxidize/reduce the metal (electron transfer catalysis);

- changing the hapticity of ligands coordinated to the metal centre (i.e. allyl hapticity from η^3 to η^1, “ring slippage” of coordinated arenes).

Useful tricks also for other reactions!

Thermodynamic effects

Steric and electronic effects influence not only the kinetics but also the thermodynamics of substitution processes:

Example 1: in sterically encumbered complexes (high coordination numbers) the substitution of large ligands with smaller ligands is favoured;

Example 2: in complexes with many π-accepting ligands, the substitution of one of these ligands with a ligand that is only σ-donor is favoured;

In general, substitution of ligands that are weaker Lewis bases with stronger Lewis bases is favoured. However, the **hard/soft character** of the ligands towards the metal centre also matters…

Insertion reactions

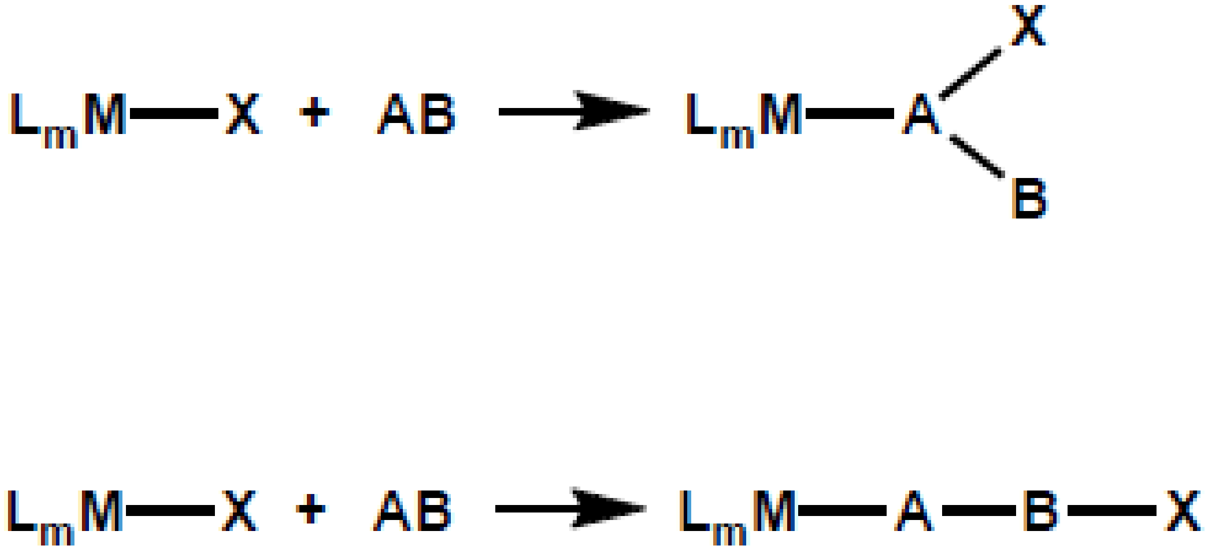
Reaction by which an unsaturated molecule “inserts” into an M-X bond (compare hydro- and carbometallation in main group organometallic chemistry)

$$L_nX_mM\text{-}\mathbf{X} + \mathbf{AB} \rightarrow L_nX_mM\text{-}\mathbf{(AB)}\text{-}\mathbf{X}$$

AB = alkene, alkyne, CO, CO_2, O_2, SO_2…

X = H, R, OR, NR_2, SR, OOCR, halides…

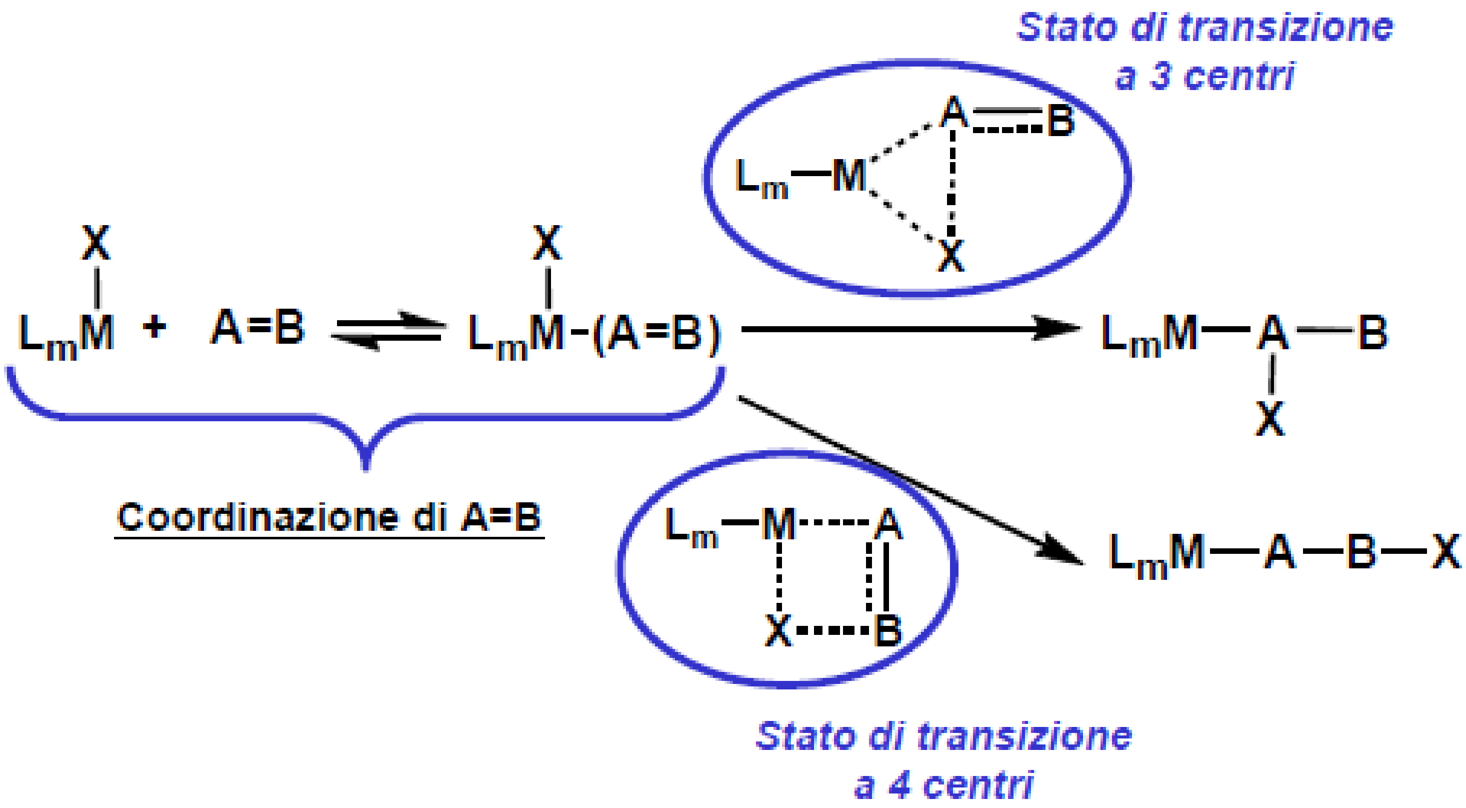
Insertion reactions



Insertion reaction can be in principle categorized into 1,1- (above) and 1,2-insertions (below).

Only SO_2 reacts yielding both these insertion types…

Insertion – Reaction mechanism



Stato di transizione
a 3 centri

Coordinazione di A=B

Stato di transizione
a 4 centri

Addition/substitution of AB to the metal centre followed by transposition of X to AB (migratory insertion). In the last step, the complex decreases the number of e^- by 2 units and the coordination number by one unit: often an additional incoming ligand molecule is useful…

Insertion reactions

- The involved ligand must precoordinate in *cis* position!

- X "migrates" on the unsaturated ligand with retention of configuration (anionotropic migration);

- Alkene/alkyne insertions (1,2-insertions) are generally **slower** than CO insertion (1,1-insertion), since in the former case the AB molecule must assume a suitable orientation related to M-X;

- Insertion into M-H kinetically more facile than in M-R;

- Facility of the insertion in M-R follow the trends for anionotropic migration of R (important for chemoselectivity).

Selectivity in 1,2-insertions (alkenes/alkynes)

The regioselectivity depends on both steric and electronic factors, but steric factors generally prevail for insertions into M-H or M-R bonds, given their low polarity. In this case, M binds to the less substituted atom (**Markovnikov**). Electronic effects of the substituents may however also become important and cause a reversal in regioselectivity.

The stereoselectivity is **syn**, given the reaction mechanism, but sometimes there is the possibility of a successive isomerization of the insertion product.

Insertion/elimination equilibria

The reversibility of insertion is not always facile, particularly when X is a ligand at carbon (a strong C-C bond is formed): in this case, the reaction is much more easily reversible with CO than with an alkene, for which β-elimination of an H atom is much more facile.

Following an elimination, the number of e^- in the complex increases by two units and the coordination number increases by one unit. Furthermore, an X-type ligand which is generally a pure σ-donor (alkyl, acyl) is transformed into a new X-type σ-donor ligand (H, R) and an L-type π-accepting ligand (alkene, CO).

Consequently, the position of this equilibrium can be influenced by acting on the steric and electronic properties of the complex (e.g. insertion favoured by steric crowding, high coordination numbers, low tendency of the metal centre to retrodonate electrons).

Insertion/elimination equilibria

Analogous factors influence also the kinetics of the process (see the next lesson) together with other factors such as the nature of the metal (β-elimination rate: **Ni < Pd >> Pt**)

Oxidative additions

$$L_nX_mM + \mathbf{AB} \rightarrow \mathbf{A}\text{-}L_nX_mM\text{-}\mathbf{B}$$
$$L_nX_mM + \mathbf{AB} \rightarrow L_nX_mM\text{-}\mathbf{A}^+ + \mathbf{B}^-$$
$$2L_nX_mM + \mathbf{AB} \rightarrow L_nX_mM\text{-}\mathbf{A} + L_nX_mM\text{-}\mathbf{B}$$

AB = H_2, X_2, O_2, HX, RX, alkenes...

The metal centre is formally oxidized by 1 or 2 units; the coordination number increases by 1 or 2 units.

Electron-rich metal centres are required (low formal oxidation states, absence of π-accepting ligands, presence of σ-donating ligands), with not too high coordination numbers.

Reaction favoured with metal of the first < second < third transition series.

Oxidative addition

Equilibrium reaction, generally very shifted to the right or to the left depending on the energy of the bonds that break/form (e.g. R-H, shifted towards the hydrocarbon; R-X, shifted towards the metal complex); single C-C bonds do NOT undergo oxidative addition apart from the cases in which there is an extra energetic bonus (e.g. through relief of steric strain: cyclopropane, biphenylene…).

The ease of reversibility of the reaction depends on the position of the equilibrium and on the peculiar mechanism at play; furthermore, the groups that undergo the reverse reaction (reductive elimination) can be different from those that underwent the direct oxidative addition…

Mechanisms of oxidative addition

Concerted (three-centered)

$$L_mM^n + R\text{-}X \xrightarrow{L_mM\overset{\cdot\cdot R}{\underset{\cdot\cdot X}{}}} L_mM^{n+2}(R)(X)$$

Nucleophilic attack (S_N2)

$$L_mM^n + R\text{-}X \xrightarrow{L_mM\cdots R\cdots X} L_mM^{n+2}(R)(X)$$

Ionic

$$L_mM^n + \underset{(H^+)}{R^+}X^- \longrightarrow [L_mM^{n+2}(R)]^+ + X^- \longrightarrow L_mM^{n+2}(R)(X)$$

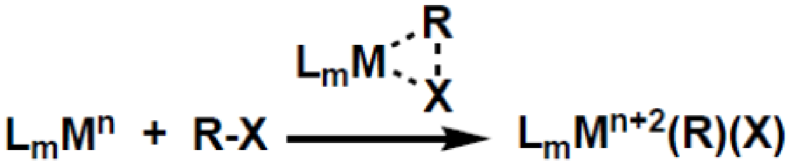
$$L_mM^n + \underset{(H^+)}{R^+}X^- \longrightarrow [L_mM^n(X)]^- + R^+ \longrightarrow L_mM^{n+2}(X)(R)$$

Radicalic

$$L_mM^n + R\bullet \longrightarrow L_mM^{n+1}(R)$$

$$L_mM^{n+1}(R) + X\text{-}R \longrightarrow L_mM^{n+2}(R)(X) + R\bullet$$

Oxidative addition - concerted mechanism



R-X bond breaking and M-R, M-X bond formation take place at the same time.

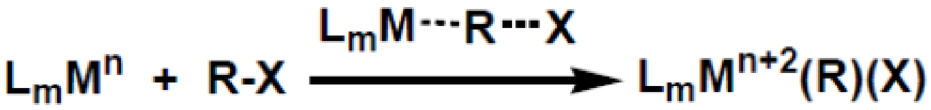
Typical mechanism for oxidative addition of compounds in which the polarity of R-X is zero or small (H_2, X_2, Si-H, C-H…).

RX must **first** coordinate to M, which should consequently be elecrophilic and possess a free coordination site (< 18 e^-).

After coordination, π donation from the metal to the σ^* antibonding orbital of R-X causes bond breaking.

Formation of M-X and M-R can be perfectly synchronous (for homoleptic R-X) or not (the mechanisms tends towards S_N2).

Oxidative addition - S_N2 mechanism



$$L_mM^n + R\text{-}X \xrightarrow{L_mM\cdots R\cdots X} L_mM^{n+2}(R)(X)$$

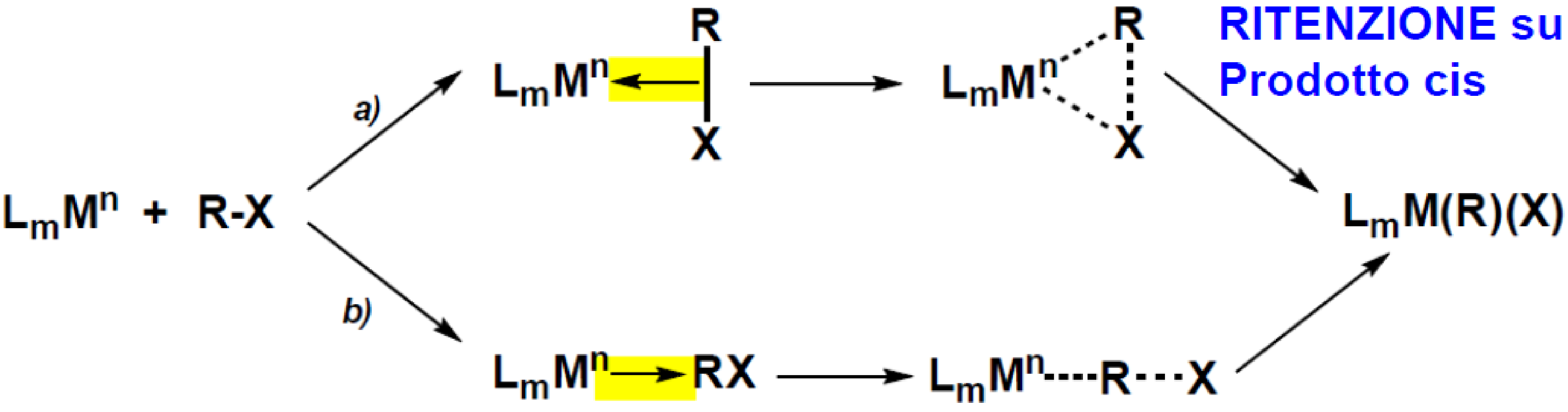
R-X bond breaking and M-R bond formation take place at the same time. M-X bond formation may follow (or not).

Typical mechanism for oxidative addition of compounds in which the polarity of R-X is high and X is a good leaving group.

M must be nucleophilic and consequently be electron-rich and possess a high energy electron doublet (low oxidation state, anionic complex, 18 e^-).

After nucleophilic attack on R, X^- can coordinate to M through an addition/substitution reaction or it can remain free in solution.

Concerted vs. S_N2 mechanism



RITENZIONE su R
Prodotto cis

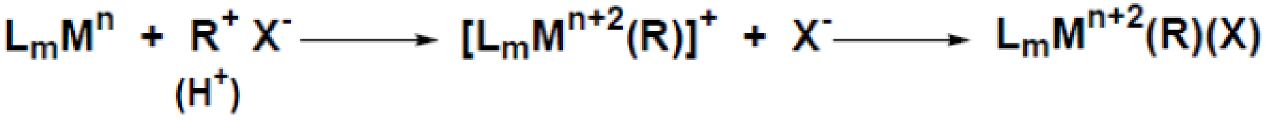
INVERSIONE su R
Prodotto cis e/o trans

Il tipo di interazione iniziale è completamente diverso.

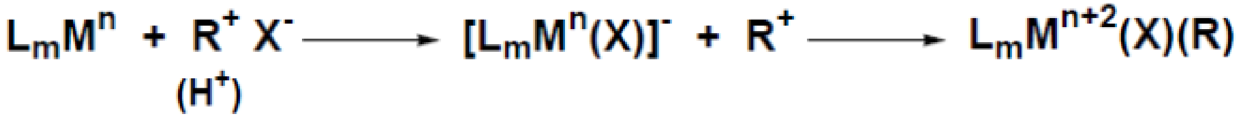
In **concerted mechanism** *a)*, M initially behaves as an <u>electrophile</u>: a low energy LUMO is needed, but also a high energy HOMO for π back donation.

In **S_N2 mechanism** *b)* M behaves as a <u>nucleophile</u>: a very high energy HOMO is needed.

Oxidative addition - ionic mechanism



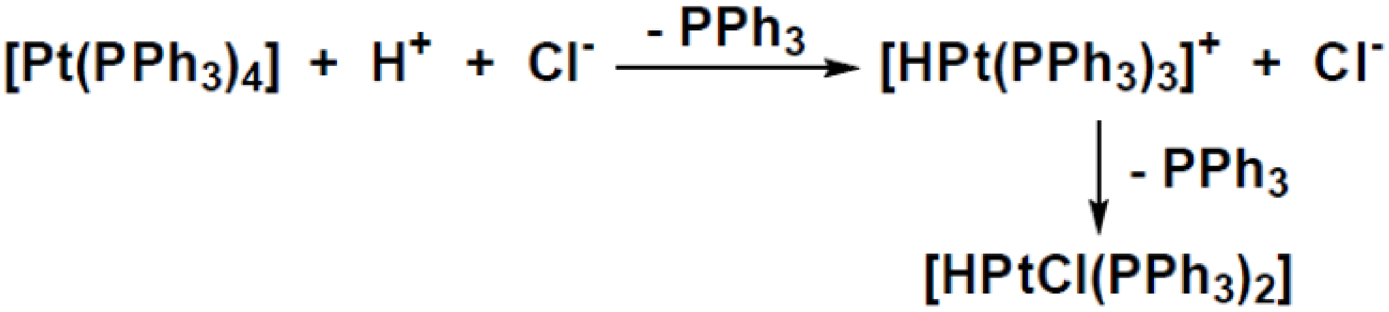
$$L_mM^n + \underset{(H^+)}{R^+}X^- \longrightarrow [L_mM^{n+2}(R)]^+ + X^- \longrightarrow L_mM^{n+2}(R)(X)$$



$$L_mM^n + \underset{(H^+)}{R^+}X^- \longrightarrow [L_mM^n(X)]^- + R^+ \longrightarrow L_mM^{n+2}(X)(R)$$

Observed with R-X that tend to dissociate in solution, most notably with acids, H-X.

The most common variant involves first protonation of M, followed by coordination of X. M <u>must consequently be electron-rich and possess a high energy electron doublet</u>.



$$[Pt(PPh_3)_4] + H^+ + Cl^- \xrightarrow{-\,PPh_3} [HPt(PPh_3)_3]^+ + Cl^- \xrightarrow{-\,PPh_3} [HPtCl(PPh_3)_2]$$

Oxidative addition - radicalic mechanism

$$L_mM^n + R\bullet \longrightarrow L_mM^{n+1}(R)$$

$$L_mM^{n+1}(R) + X\text{-}R \longrightarrow L_mM^{n+2}(R)(X) + R\bullet$$

Characterized by poorly reproducible reaction rates and by the strong effect on the rate of initiator/inhibitors of radical reaction (light, dioxygen, organic peroxides…).

Both chain and non-chain reaction mechanisms possible.

More common with first row TM and for complexes with odd e^-. Faster with R-X that easily undergo homolysis of the R-X bond producing stable radicals. Consequently:

R-I > R-Br > R-Cl

Tertiary R > secondary R > primary R

Reductive elimination

Reverse of the oxidative addition reaction. Much less studied than the latter, since few complexes that give this reaction are stable enough to be investigated.

The metal centre reduces its oxidation number and its coordination number by 1 or 2 units. Electron-poor metals with not too low coordination numbers are needed. The reaction is more facile with metals of the first transition series and with complexes with odd coordination numbers (3, 5).

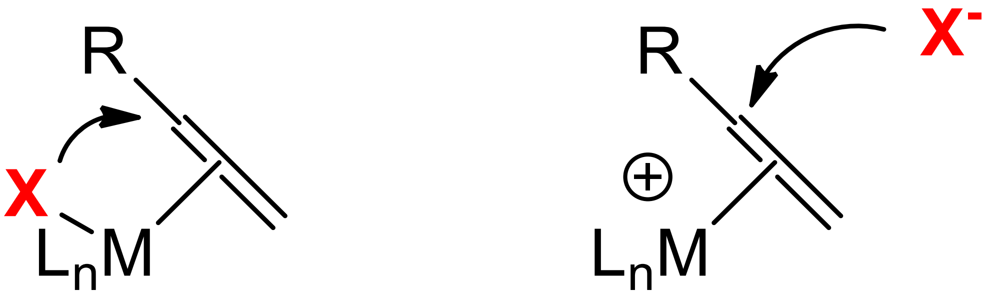
Most commonly the mechanism is concerted, and the groups that are eliminated must be mutually cis in the metal coordination sphere (three-center transition state, retention of configuration on R). Other mechanisms (S_N2, bimolecular…) are possible.

Elimination of acyls is faster than elimination of alkyls.

External nucleophilic/electrophilic attack to coordinated ligands

These attacks change the characteristics of the ligands in the complex <u>and also of the metal centre (which can be formally oxidized/reduced)</u>.

These reactions can be related with some of the previous reactions (insertions, oxidative additions, reductive eliminations) but take place <u>without precoordination</u> of the nucleophile/electrophile, and consequently often exhibit different regio- and most notably stereoselectivities.



External nucleophilic attack to coordinated ligands

Upon external nucleophilic attack, L ligands are converted in X ligands which remain bound to M without variations in the complex parameters:

E.g. alkenes → alkyls; carbonyl → acyl.

X ligands are instead removed from the coordination sphere of M, which consequently reduces its oxidation state by 2 units (S_N2 reductive elimination) and its coordination number by 1.

E.g. η^3-allyl → alkene

The reaction is favoured by electronegative metal centers (elettronegative M, medium-high oxidation state, cationic complexes, π-accepting supporting ligands).

External electrophilic attack to coordinated ligands

Upon external electrophilic attack, L or X ligands are removed from the coordination sphere of M (the coordination number decreases by 1).
On the other hand, external electrophiles often attack C-H bonds α to coordinated multiple C-C bonds: in this case, the electrophile abstracts a hydride and M provides an additional electron doublet for bonding to C. M is formally oxidized by 2 units and increases its coordination number by 1.
E.g. [Fe(cyclohexadienil)$(CO)_3]^+$ from Fe(cyclohexadiene)$(CO)_3$.

The reaction is favoured by metal centres that strongly donate e^- towards multiple C-C bonds (low oxidation states, electron-donating supporting ligands, neutral or anionic complexes).