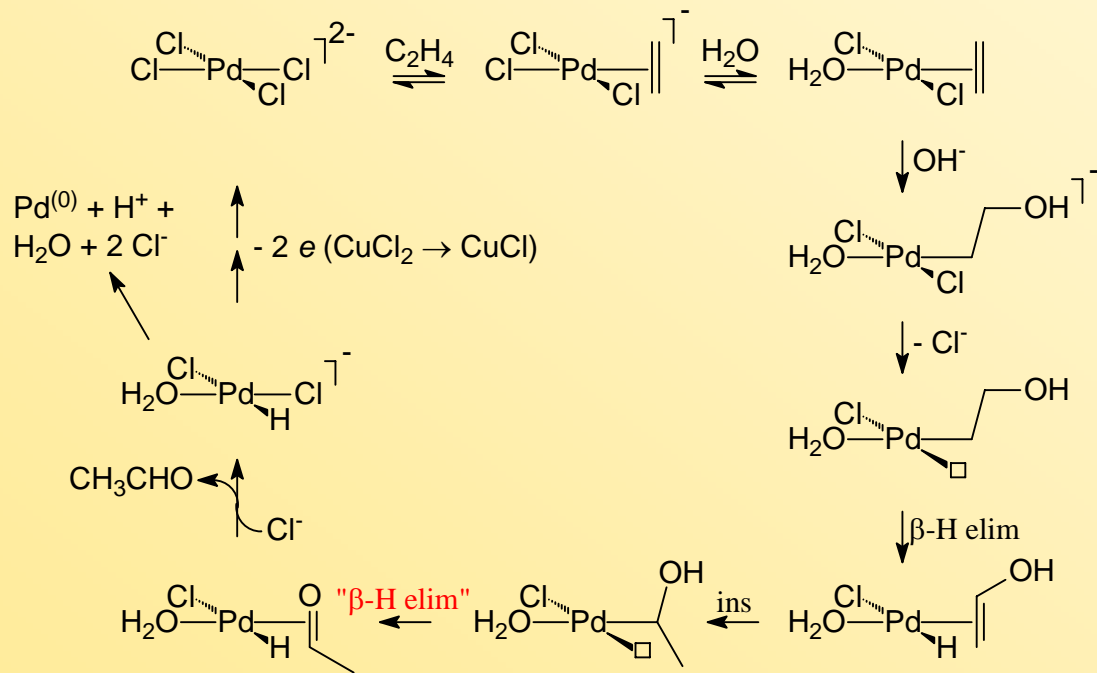


Ligand Substitution

Reactivity of Coordinated Ligands



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OF MANITOBA

Why care about substitution ?

Basic premise about metal-catalyzed reactions:

- Reactions happen in the coordination sphere of the metal
- Reactants (substrates) come in, react, and leave again
- Binding or dissociation of a ligand is often the slow, rate-determining step

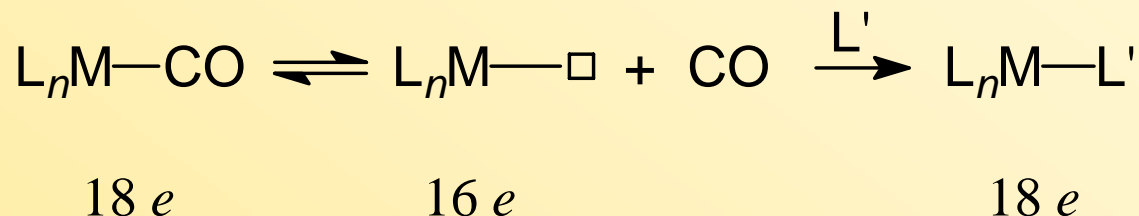
This premise is not always correct, but it applies in the **vast majority** of cases.

Notable exceptions:

- Electron-transfer reactions
- Activation of a single substrate for external attack
 - peroxy-acids for olefin epoxidation
 - CO and olefins for nucleophilic attack

Dissociative ligand substitution

Example:

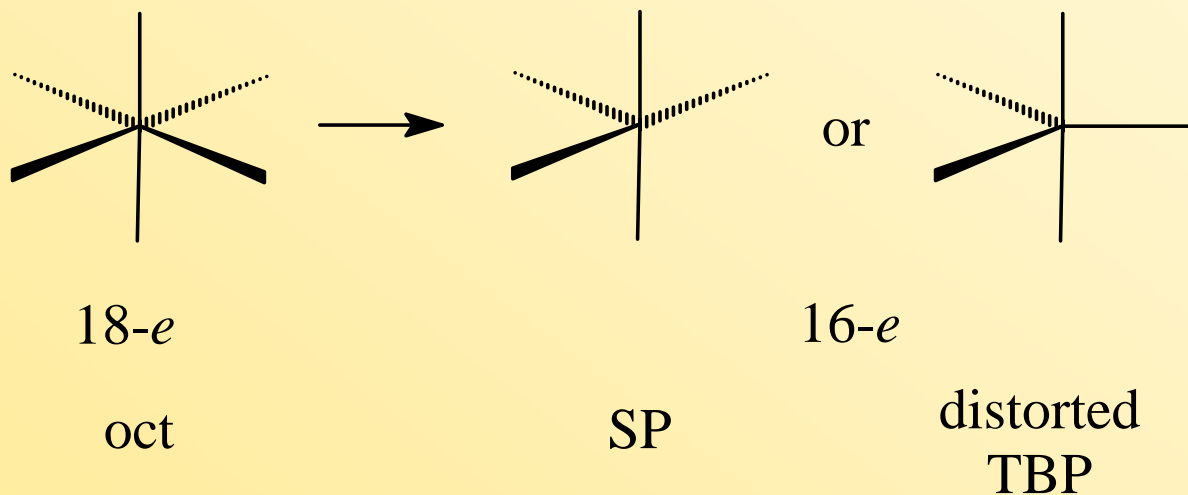


Factors influencing ease of dissociation:

- 1st row < 2nd row > 3rd row
- $d^8\text{-ML}_5 > d^{10}\text{-ML}_4 > d^6\text{-ML}_6$
- stable ligands (CO, olefins, Cl⁻) dissociate easily (as opposed to e.g. CH₃, Cp).

Dissociative substitution in ML_6

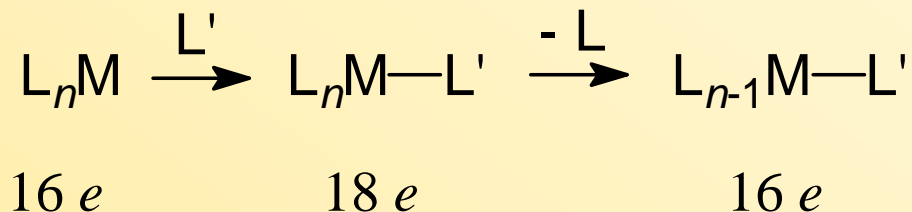
16-e ML_5 complexes are usually *fluxional*;
the reaction proceeds with partial inversion, partial retention of stereochemistry.



The 5-coordinate intermediates are normally too reactive to be observed unless one uses *matrix isolation* techniques.

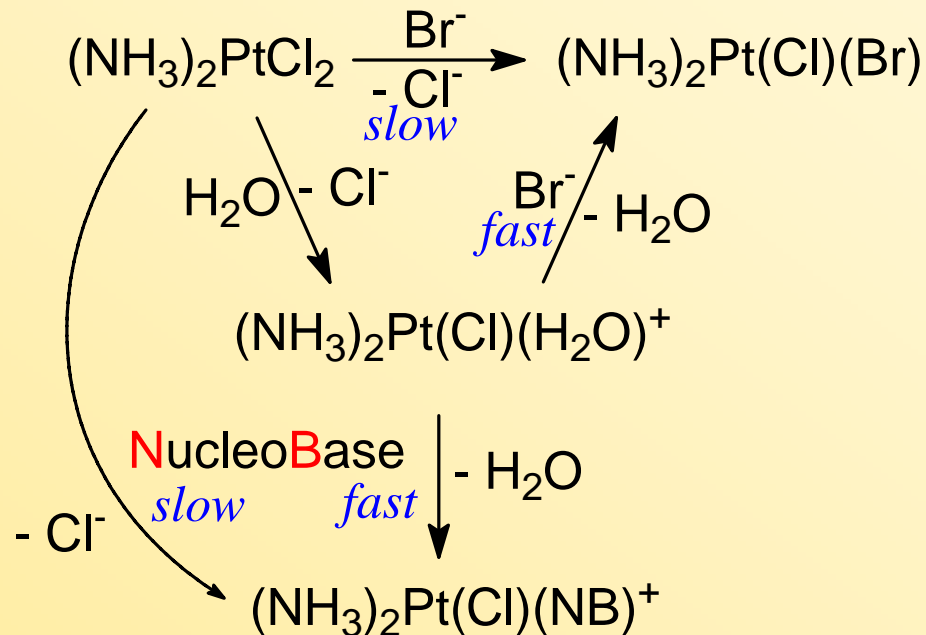
Associative ligand substitution

Example:



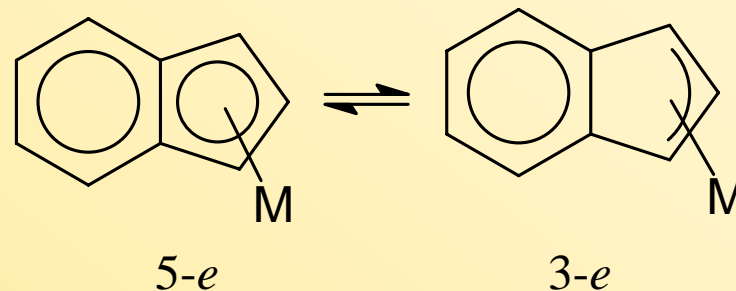
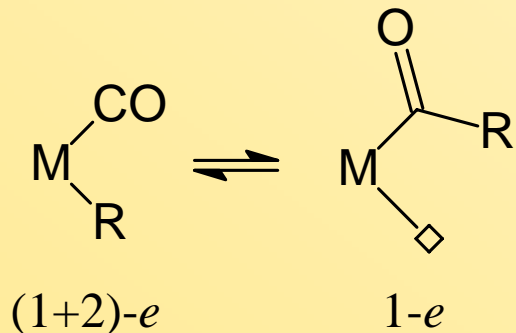
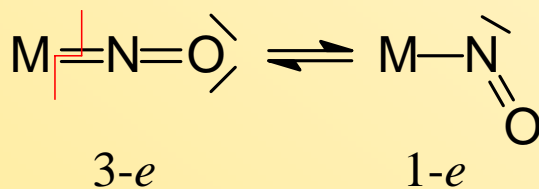
Sometimes the solvent is involved.

Reactivity of *cis*-platin:



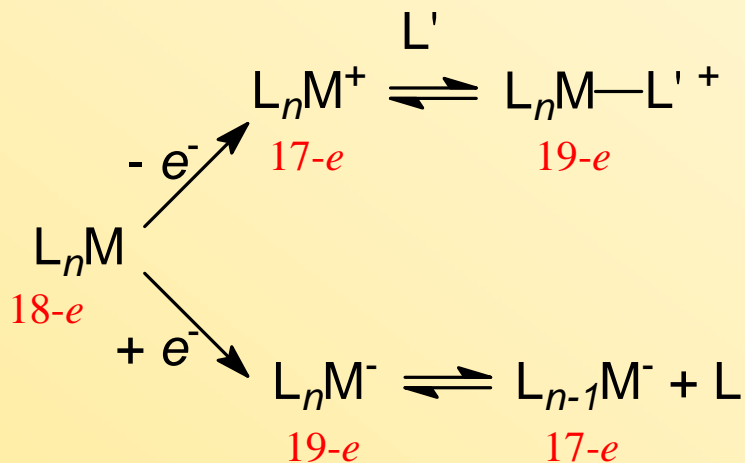
Ligand rearrangement

Several ligands can switch between $n-e$ and $(n-2)-e$ situations, thus enabling associative reactions of an apparently saturated complex:



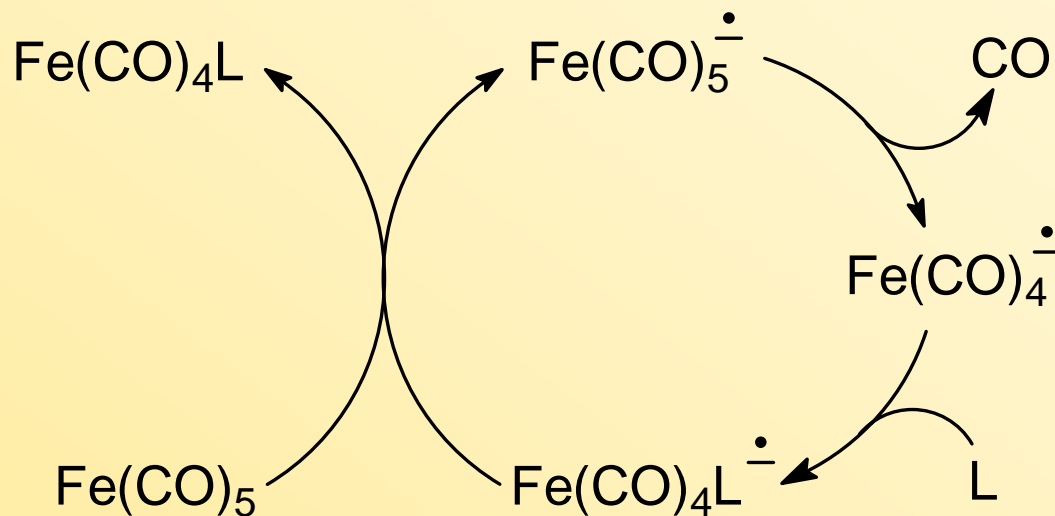
Redox-induced ligand substitution

Unlike 18-e complexes, 17-e and 19-e complexes are **labile**.
Oxidation and reduction can induce rapid ligand substitution.



- Reduction promotes dissociative substitution.
- Oxidation promotes associative substitution.
- In favourable cases, the product oxidizes/reduces the starting material \Rightarrow **redox catalysis**.

Redox-induced ligand substitution

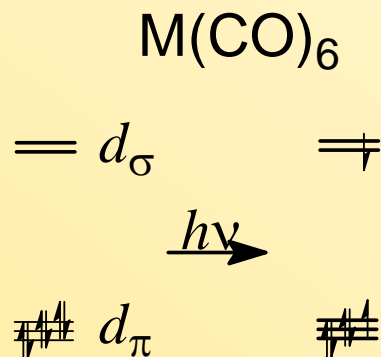


Initiation by added reductant.

Sometimes, radical abstraction produces a 17-e species (see C103).

Photochemical ligand substitution

Visible light can excite an electron from an M-L bonding orbital to an M-L antibonding orbital (**L**igand **F**ield transition, LF). This often results in fast ligand dissociation.

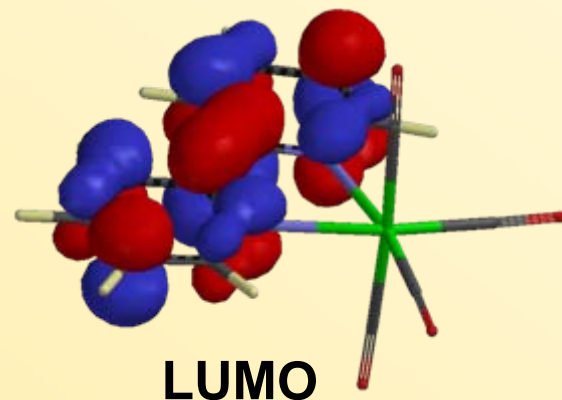
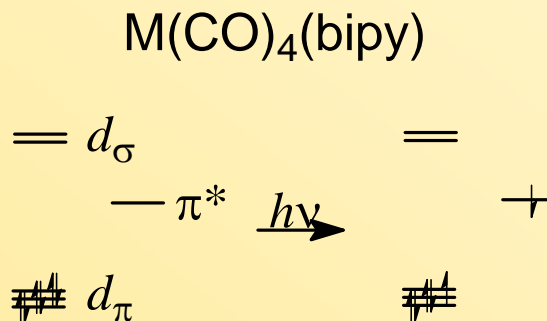
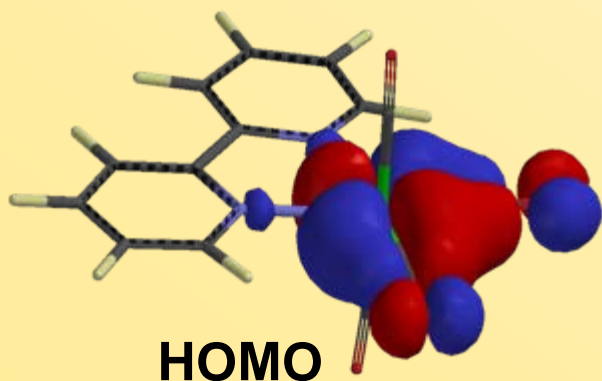


Requirement: the complex must absorb, so it must have a colour!
or use UV if the complex absorbs there

Photochemical ligand substitution

Some ligands have a low-lying π^* orbital and undergo **Metal-to-Ligand Charge Transfer (MLCT)** excitation. This leads to easy associative substitution.

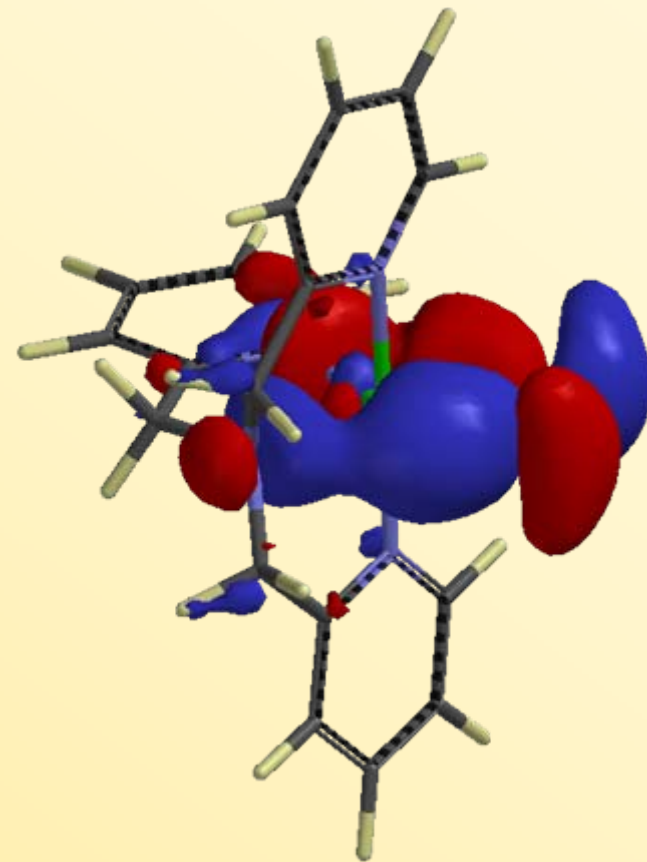
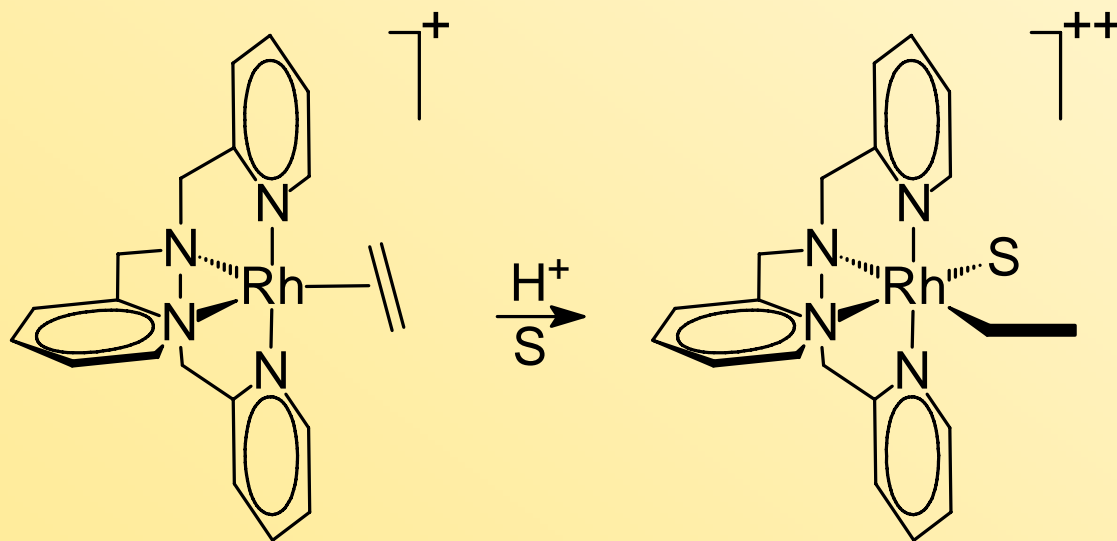
- The excited state is formally (n-1)-e !
- Similar to oxidation-induced substitution



M-M bonds dissociate easily (homolysis) on irradiation
 \Rightarrow (n-1)-e associative substitution

Electrophilic and nucleophilic attack on activated ligands

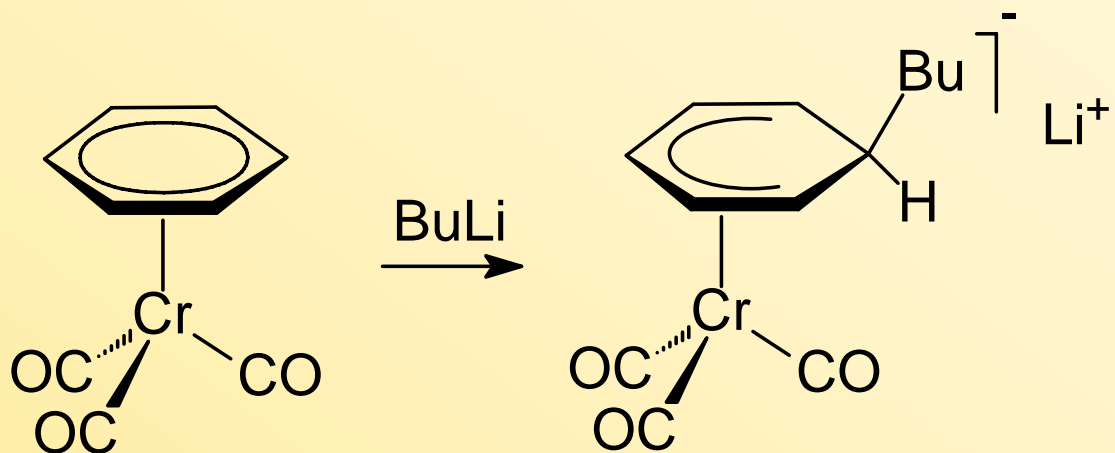
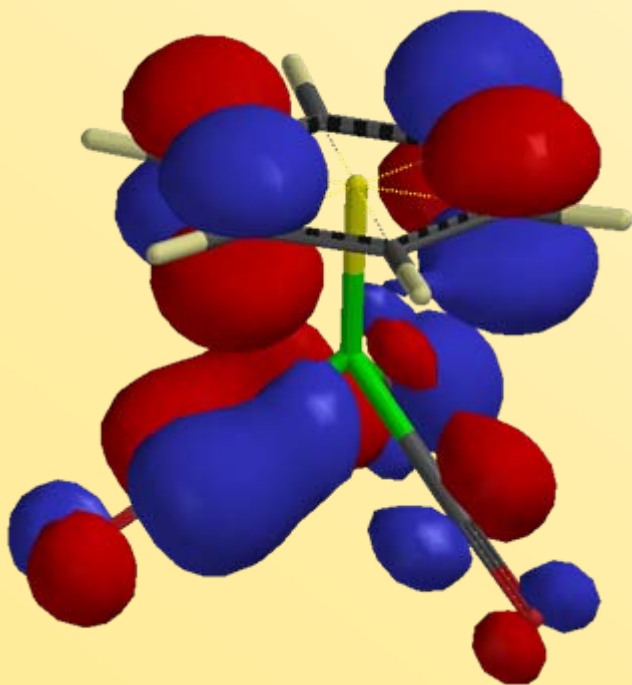
Electron-rich metal fragment:
ligands activated for **electrophilic** attack.



H_2O is acidic enough to protonate this coordinated ethene.
Without the metal, protonating ethene requires H_2SO_4 or similar.

Electrophilic and nucleophilic attack on activated ligands

Electron-poor metal fragment:
ligands activated for *nucleophilic* attack.

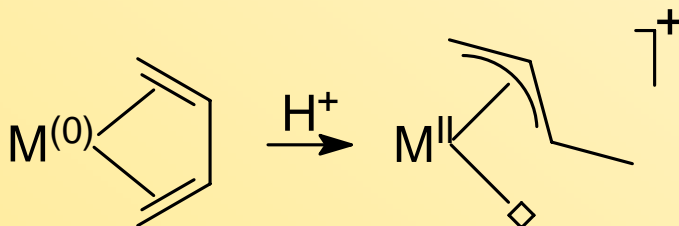
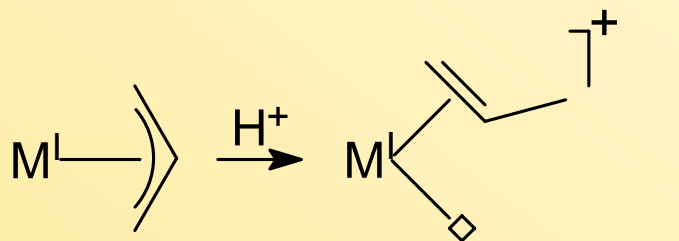


BuLi does not *add* to free benzene, it would at best *metallate* it (and even that is hard to do).

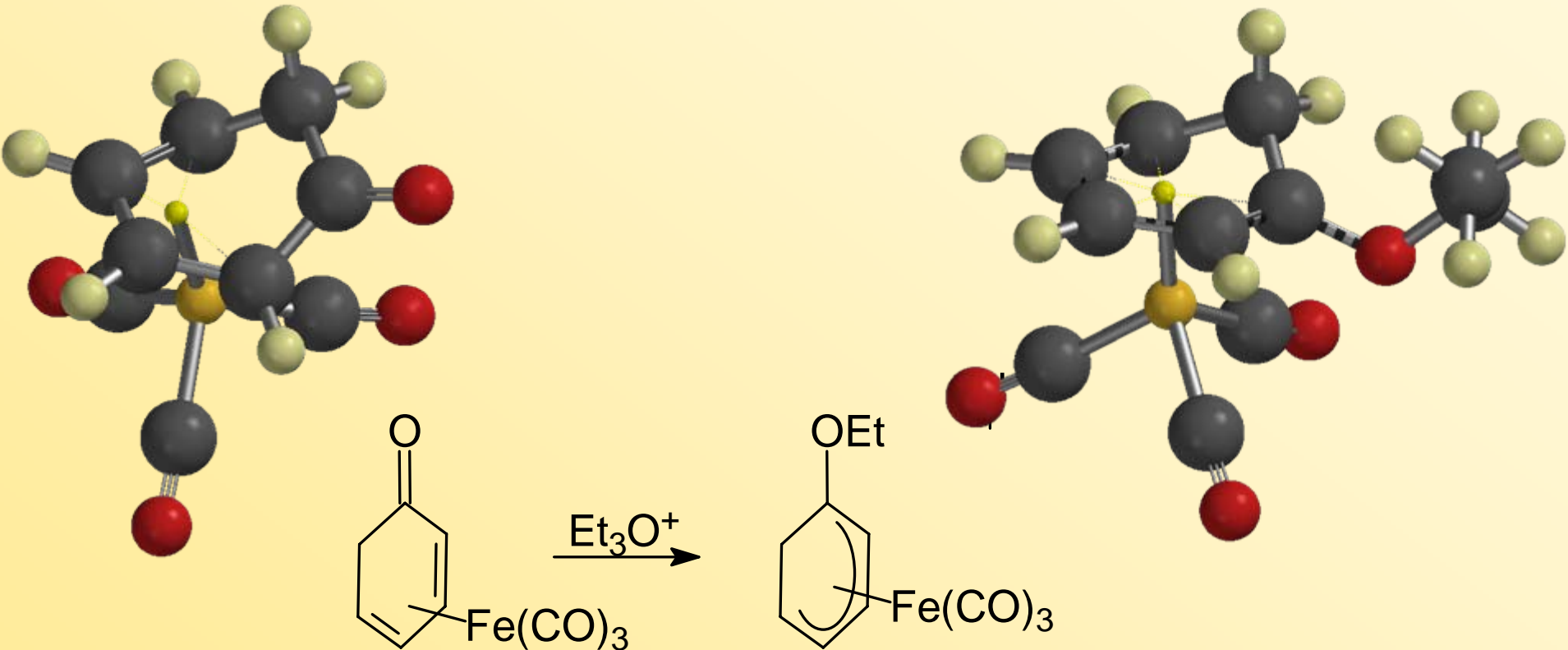
Electrophilic attack on ligand

Hapticity may increase or decrease.

Formal oxidation state of metal *may* increase.



Electrophilic addition

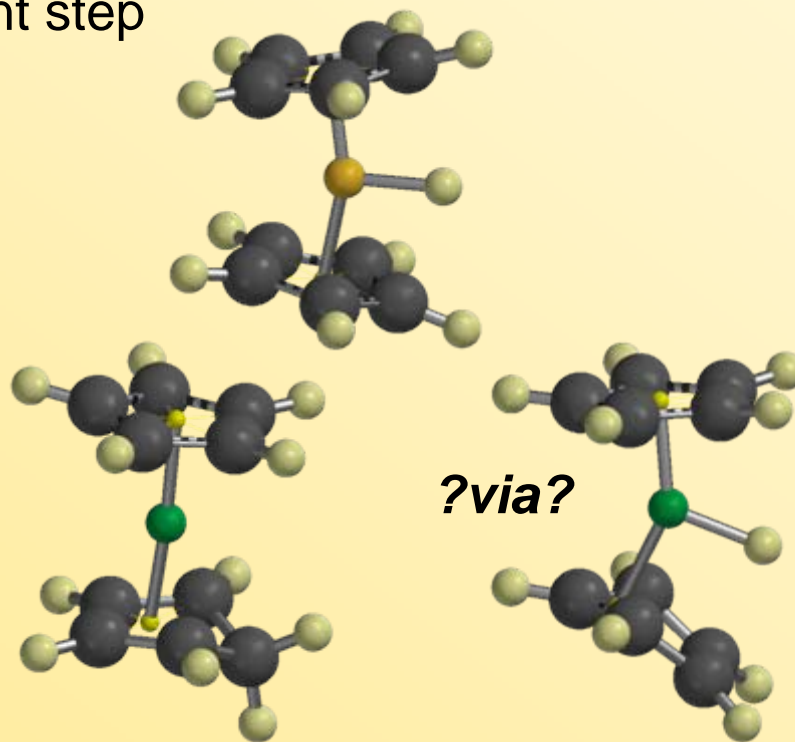
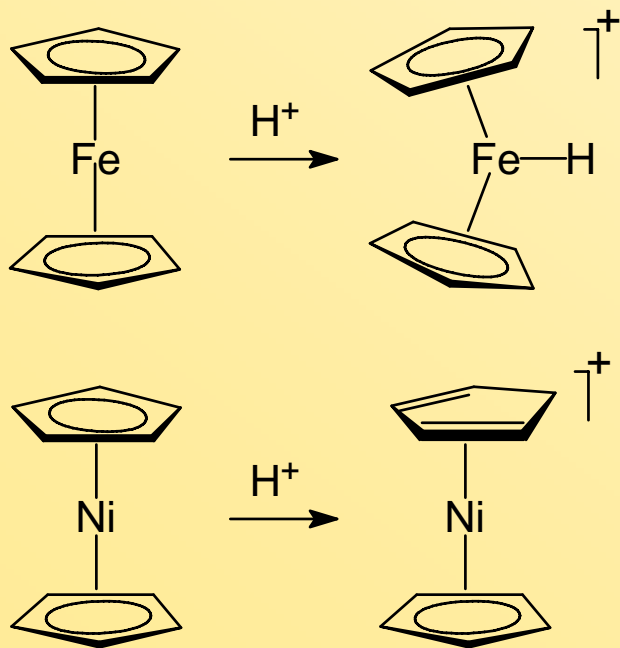


- Is formally oxidation of $\text{Fe}^{(0)}$ to Fe^{II} (the ligand becomes **anionic**).
- Ligand hapticity increases to compensate for loss of electron.

Electrophilic attack at the metal

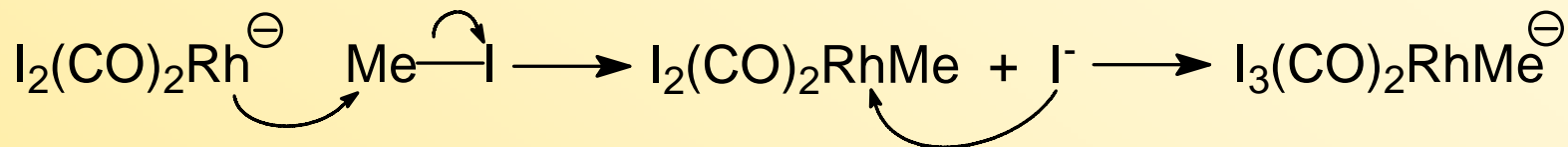
If the metal has lone pairs, it may compete with the ligand for electrophilic attack

Transfer of the electrophile to the ligand may then still occur in a separate subsequent step



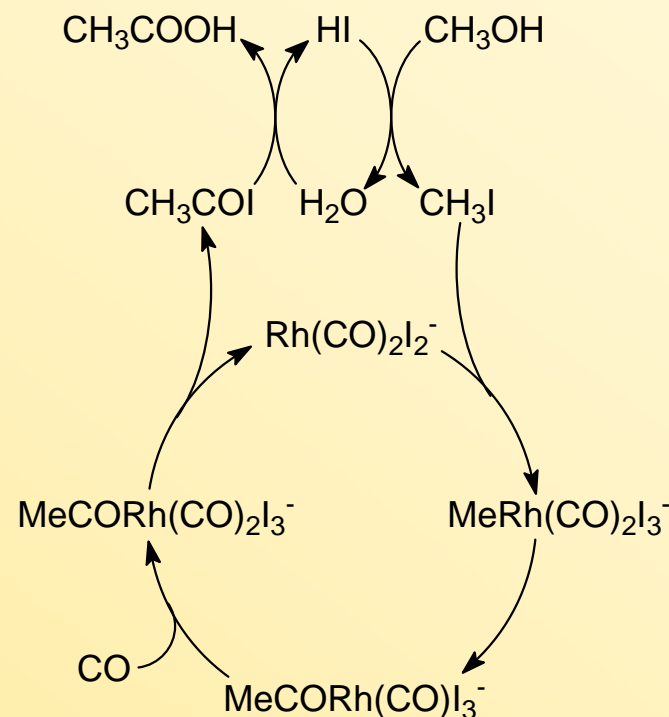
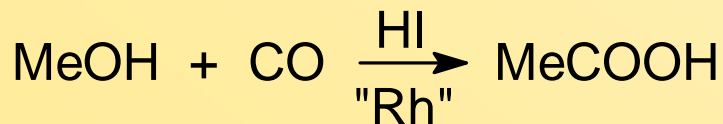
Electrophilic attack at the metal

Can be the start of oxidative addition



(although this could also happen via **concerted addition**)

Key reaction in the
Monsanto acetic acid process:



Nucleophilic attack on ligand

Nucleophile "substitutes" metal

⇒ hapticity usually decreases

Oxidation state mostly unchanged

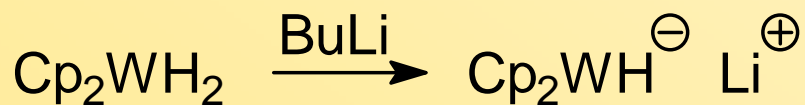
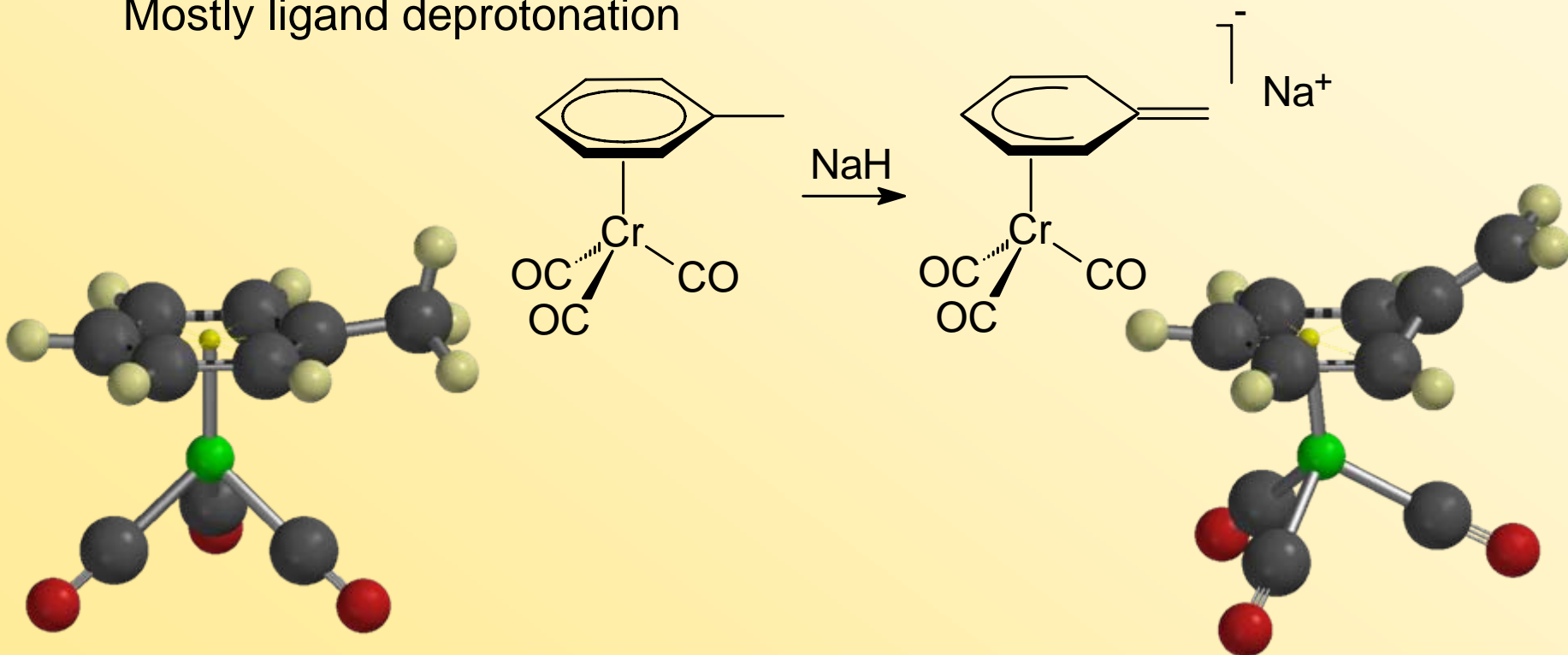
Competition: nucleophilic attack on metal

usually leads to ligand substitution

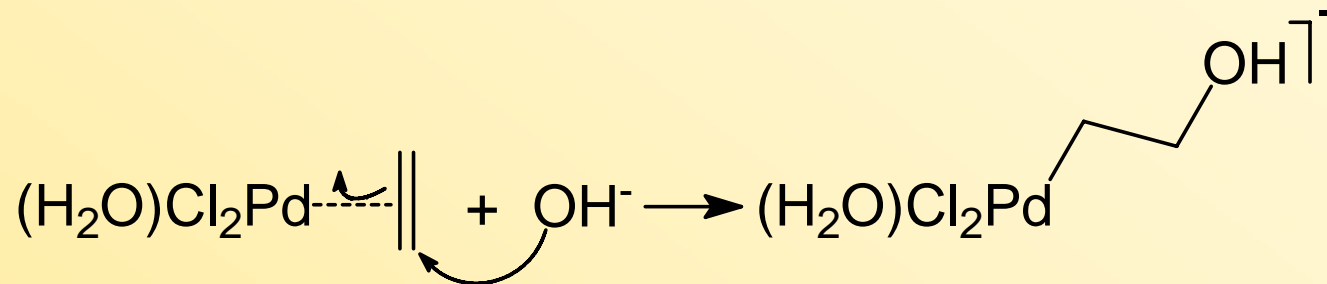


Nucleophilic abstraction

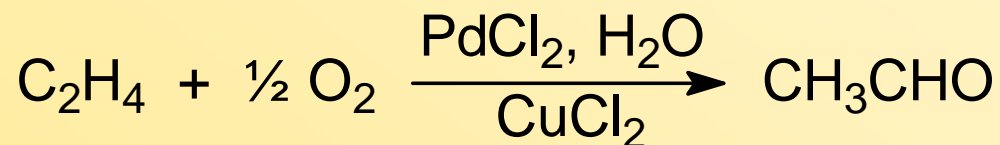
Mostly ligand deprotonation



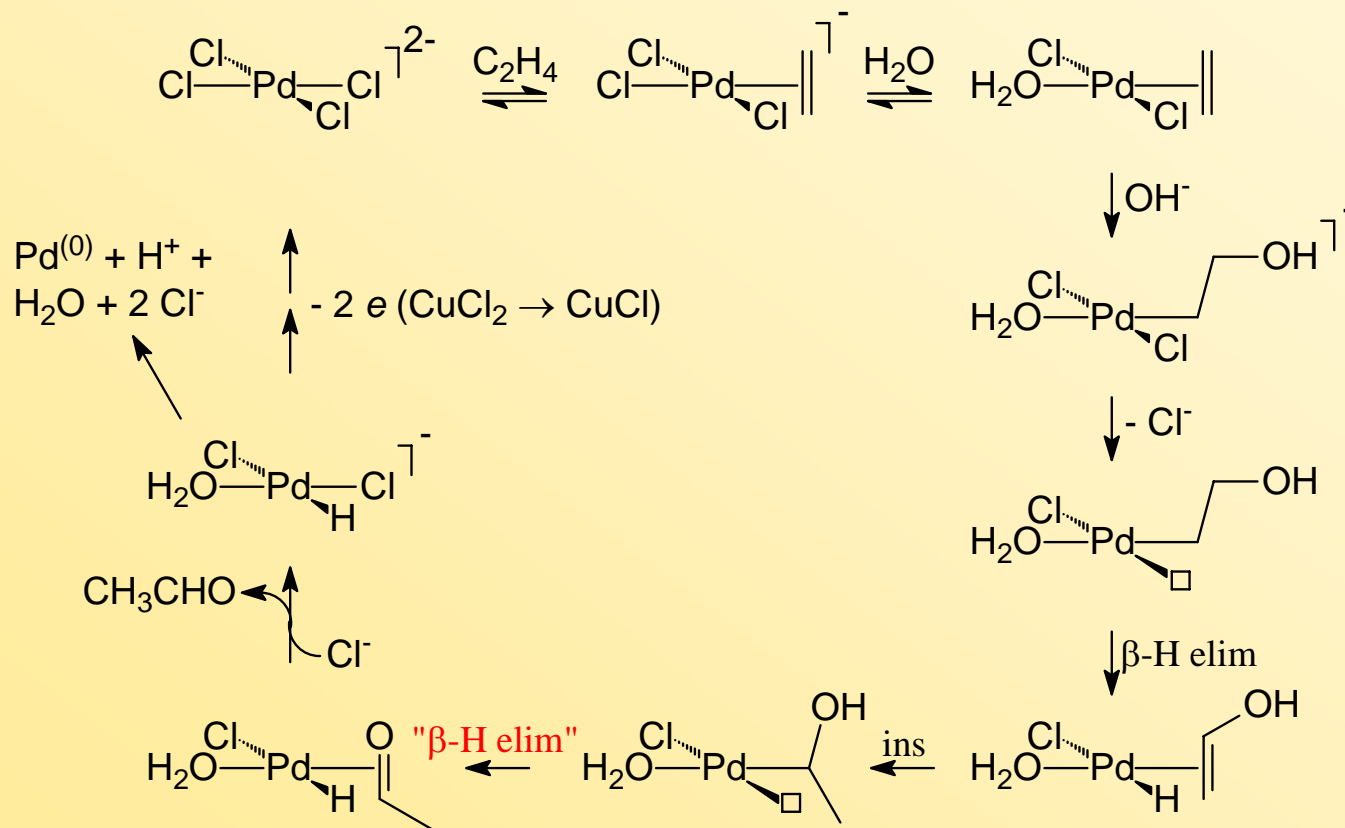
Nucleophilic addition



Key reaction of the Wacker process:



The Wacker process



The Wacker process

Characteristics of the Wacker process:

- The oxygen in the product derives from **water**, not directly from the oxygen used as oxidant
- higher olefins yield **ketones**, not aldehydes
- large amounts of halides required: corrosive
- side products resulting from nucleophilic attack of halide on olefin

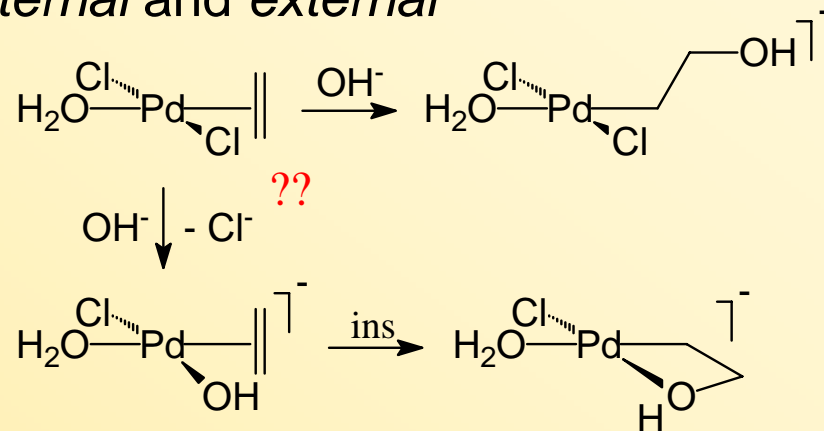
No longer important for acetic acid synthesis

Several variations (with more complicated nucleophiles) used in organic synthesis

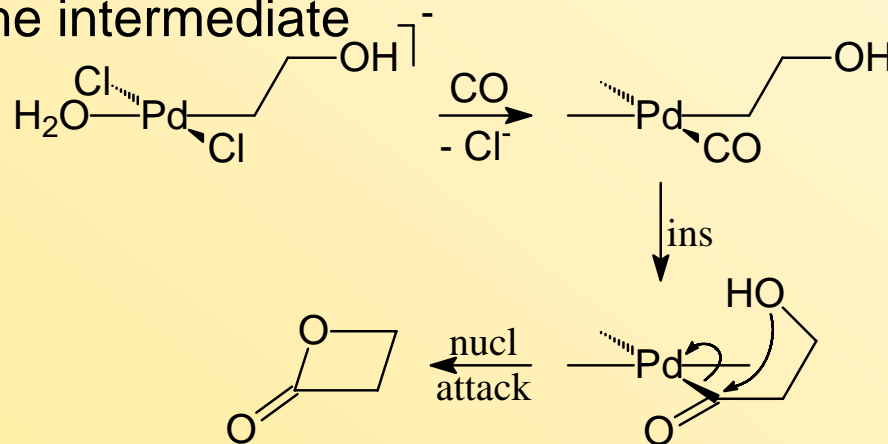


Nucleophilic attack on the ligand

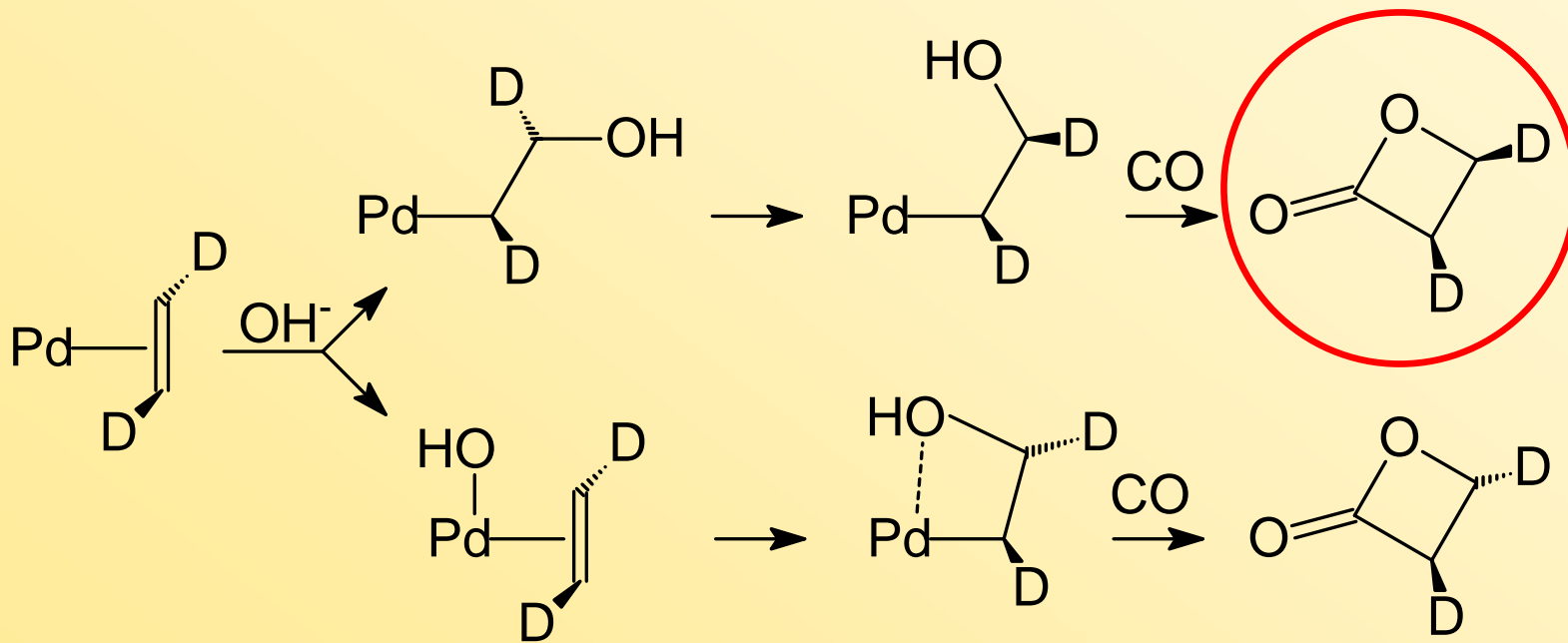
How can you distinguish between *internal* and *external* attack of OH⁻ ?



Use *trans*-CHD=CHD and trap the intermediate Pd-C-C-OH with CO:

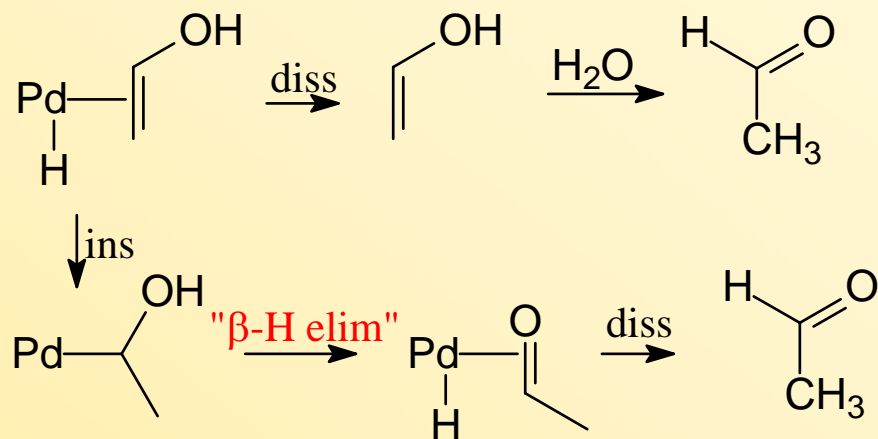


Using isotopic labelling to study mechanisms



Using isotopic labelling to study mechanisms

Could acetaldehyde be formed directly as vinyl alcohol ?



Perform reaction in D₂O:

