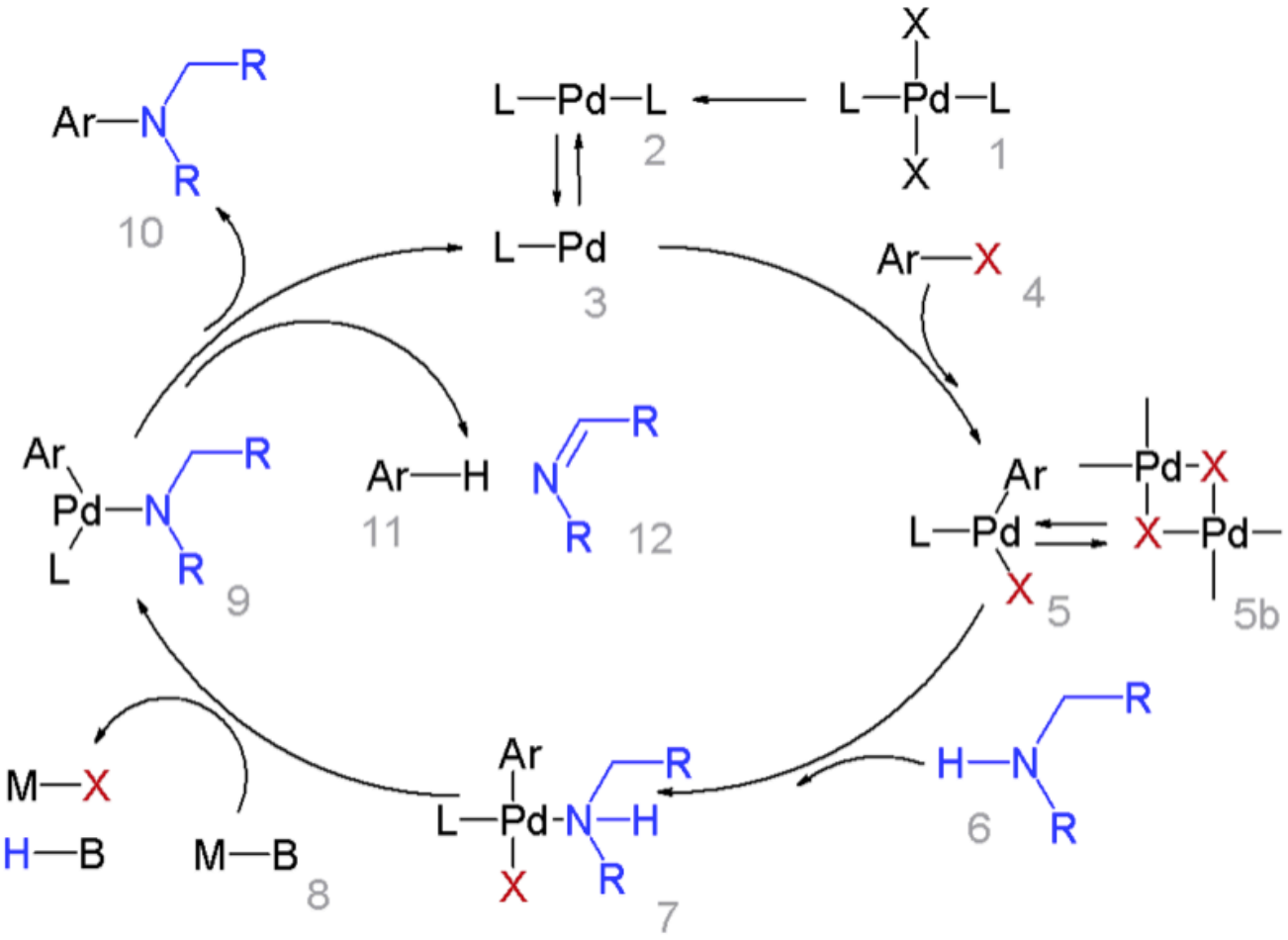
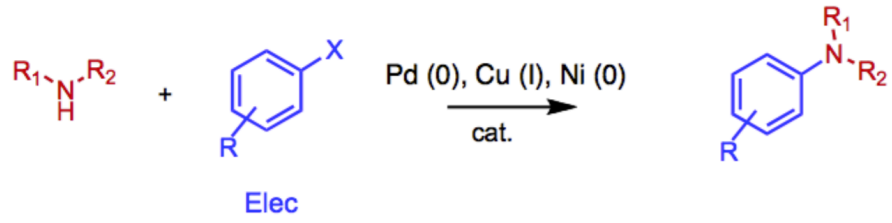
Buchwald-Hartwig Amination



Formation de liaisons C-N catalysée par le Pd, Cu, Ni



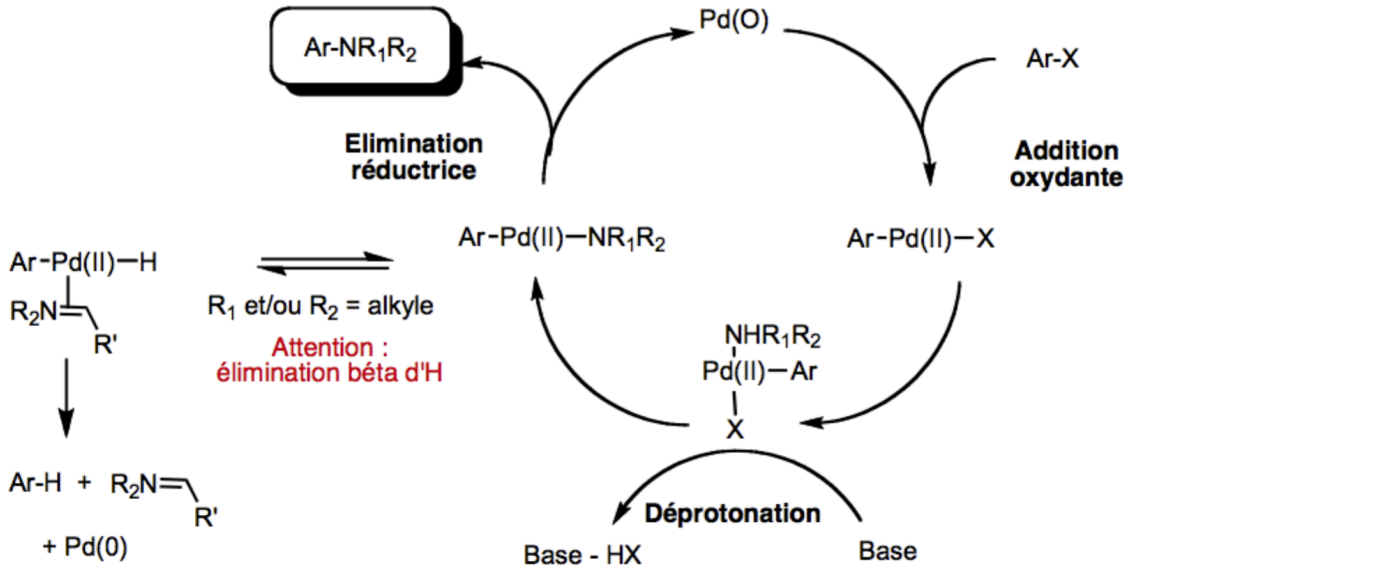
X = I, Br, Cl, OTf, etc.

Ligand = 1,2 et 3 ème générations

R_1, R_2 = Alkyle, aryle, H

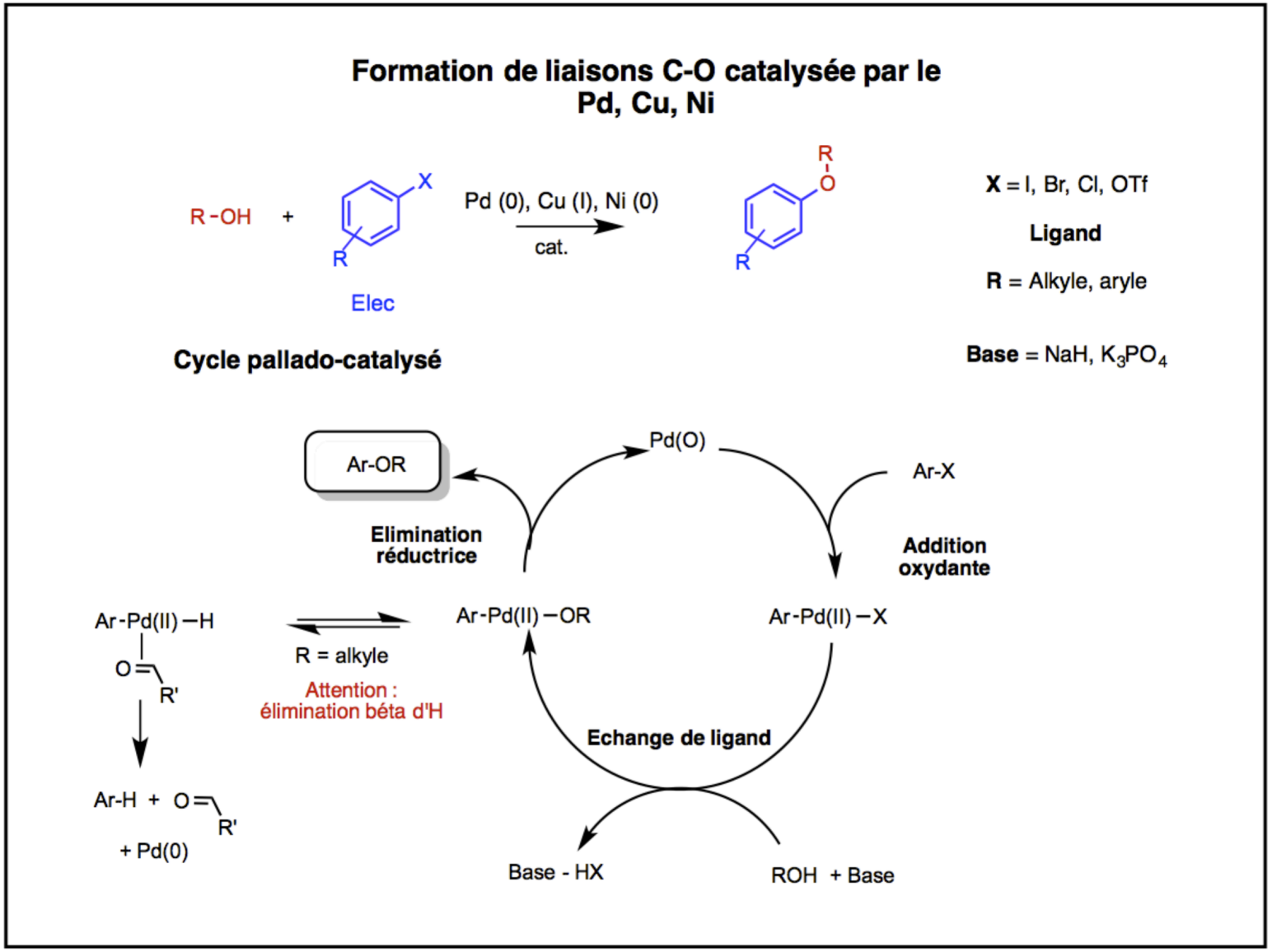
Base = *t*BuONa, Cs_2CO_3

Cycle pallado-catalysé

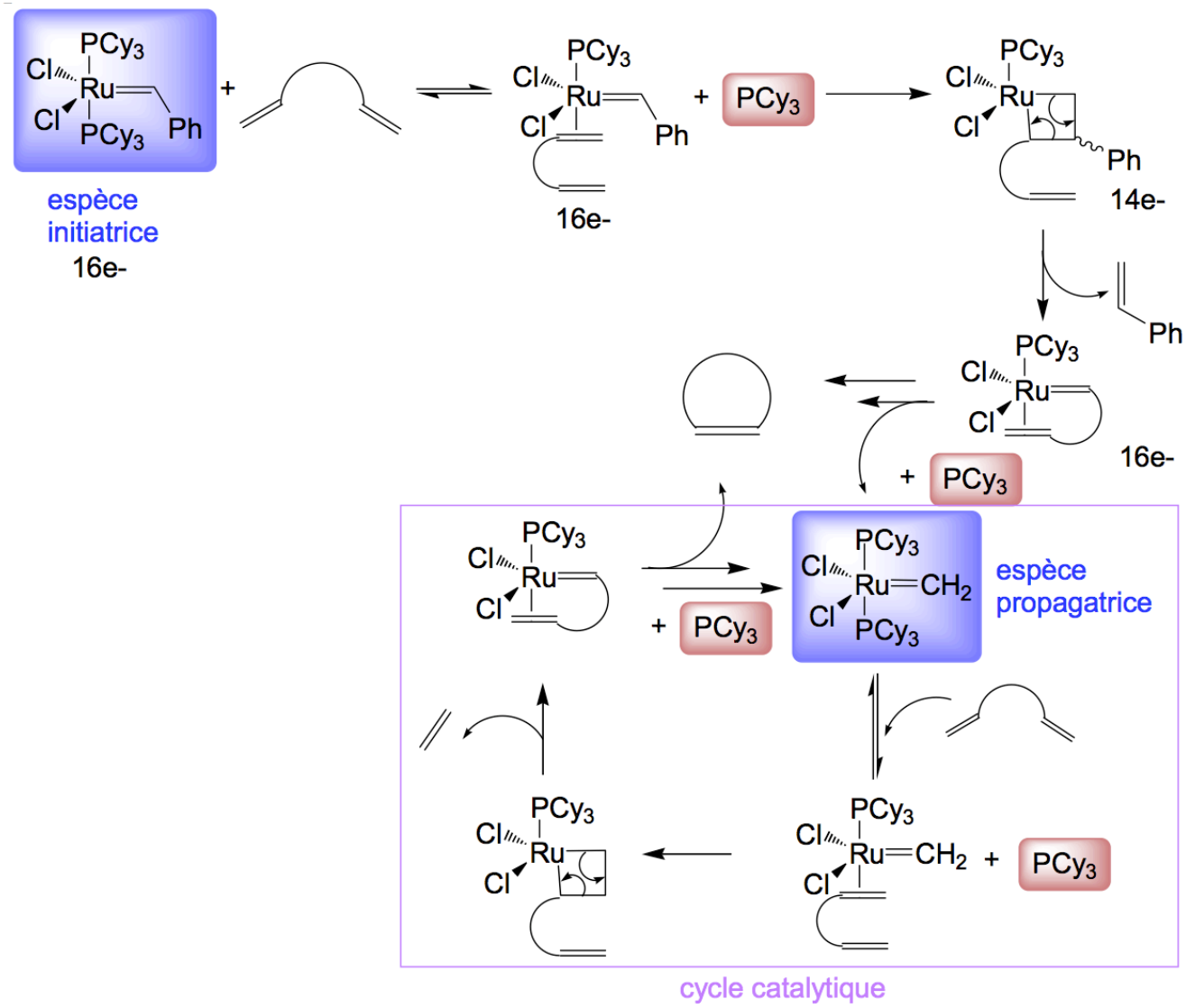


Ligand biphosphine limite l'élimination béta

Buchwald-Hartwig Alkoxylation (C-O coupling)

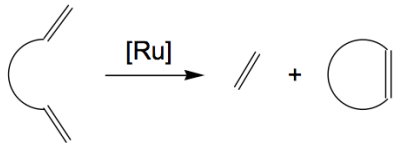


RCM

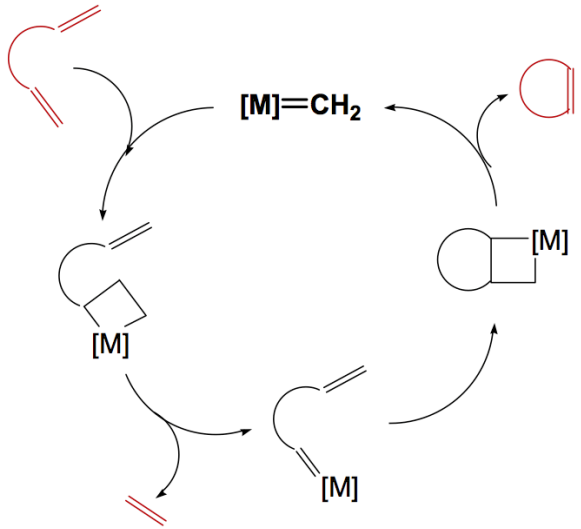

PCy3
Cl
Ru
Ph
espèce
initiatrice
16e-
16e-
14e-
espèce
propagatrice
CH2
cycle catalytique

ROM

Assez souvent la réaction se fait au reflux du dichlorométhane. Lors de la réaction il y a dégagement d'éthylène. Certains auteurs utilisent le benzène comme solvant.

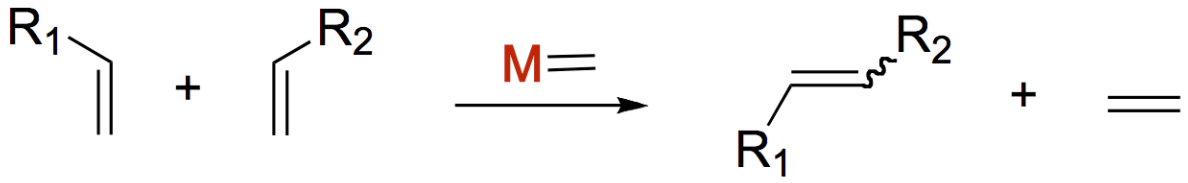


Mécanisme de la réaction :

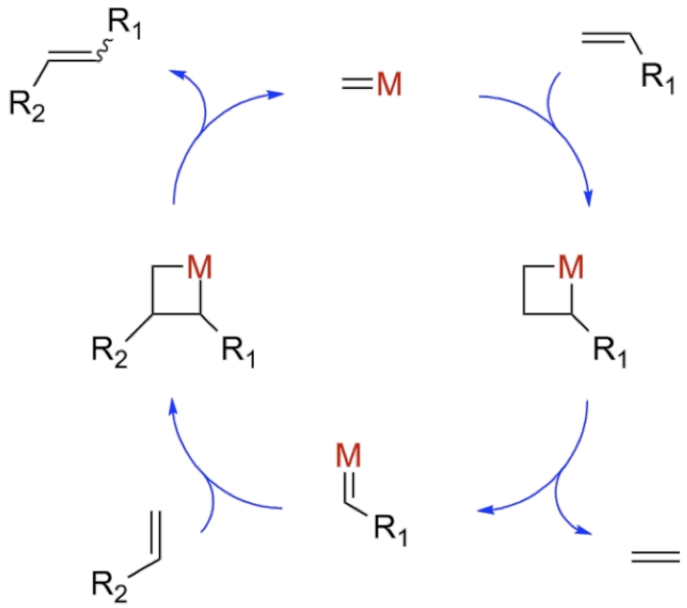


Cross Metathesis

Mécanisme : Chauvin (Nobel 2005)



Cycle catalytique



Features of Silicon Chemistry

I) GENERALITES

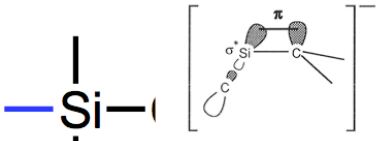
Structure électronique:
[Ne] $3s^2 3p^2 3d^0$

Une seule valence : 4

Spécificité de la chimie du Si

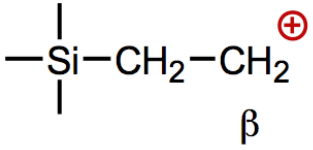
- Si est attaqué par des Nu
- Si-O est facilement formée mais aussi facilement rompue
- Si-F est extrêmement forte
- Si-H et Si-C sont fragiles (donneur potentiel de R^- et H^-
- longueur Si-Z > C-Z
- Stabilisation d'un carbanion en α

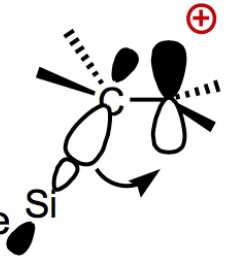
Liaison	Energie de la liaison (kJ/mol)	Longueur de liaison (Å)
Si-C	318	1,89
C-C	334	1,54
Si-O	531	1,63
C-O	340	1,41
Si-H	339	1,48
C-H	420	1,09
Si-F	807	1,55
C-F	452	1,4
Si-Cl	471	2,02
C-Cl	335	1,74



interaction σ* C-Si
(Orbitale d vacante)

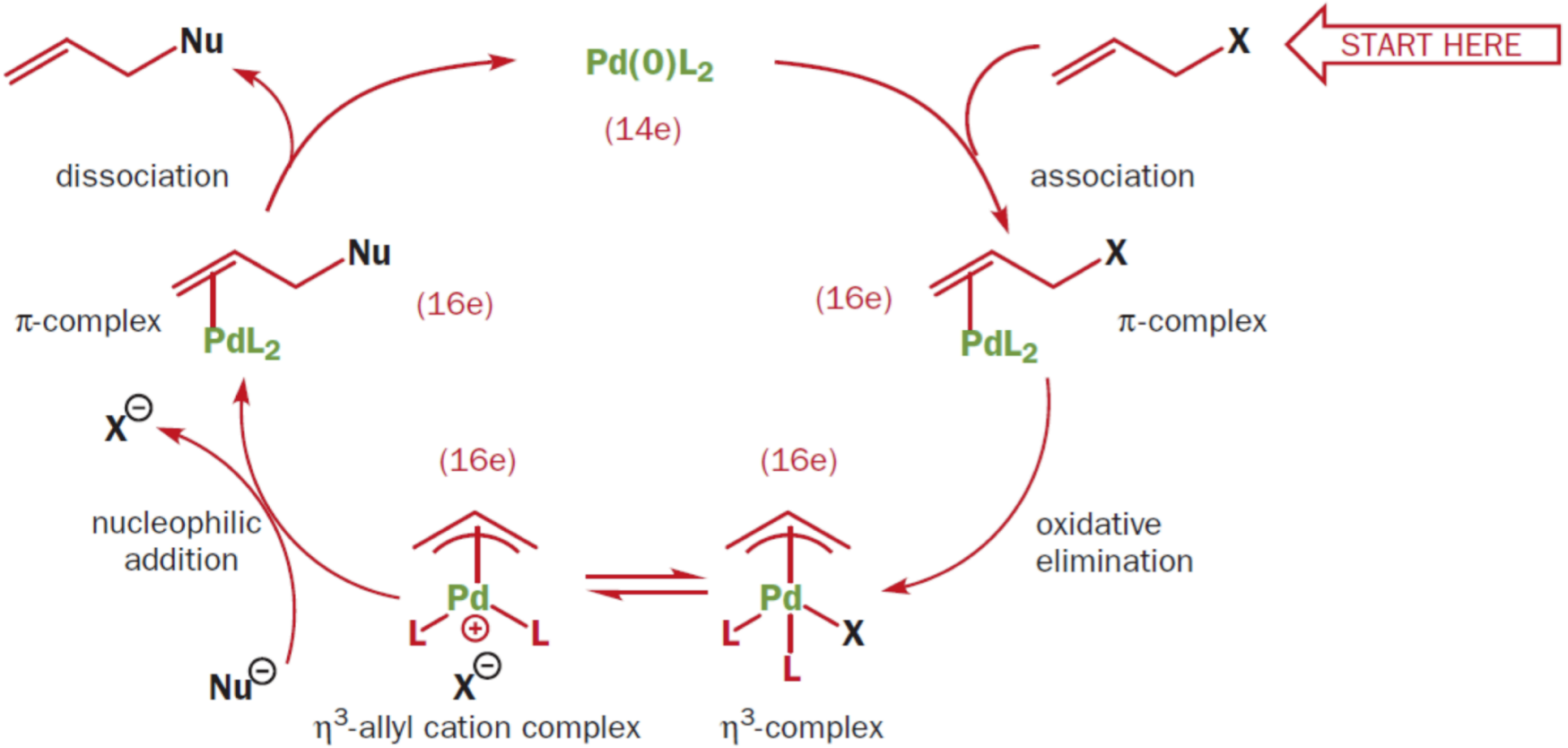
- Stabilisation d'un carbocation en β





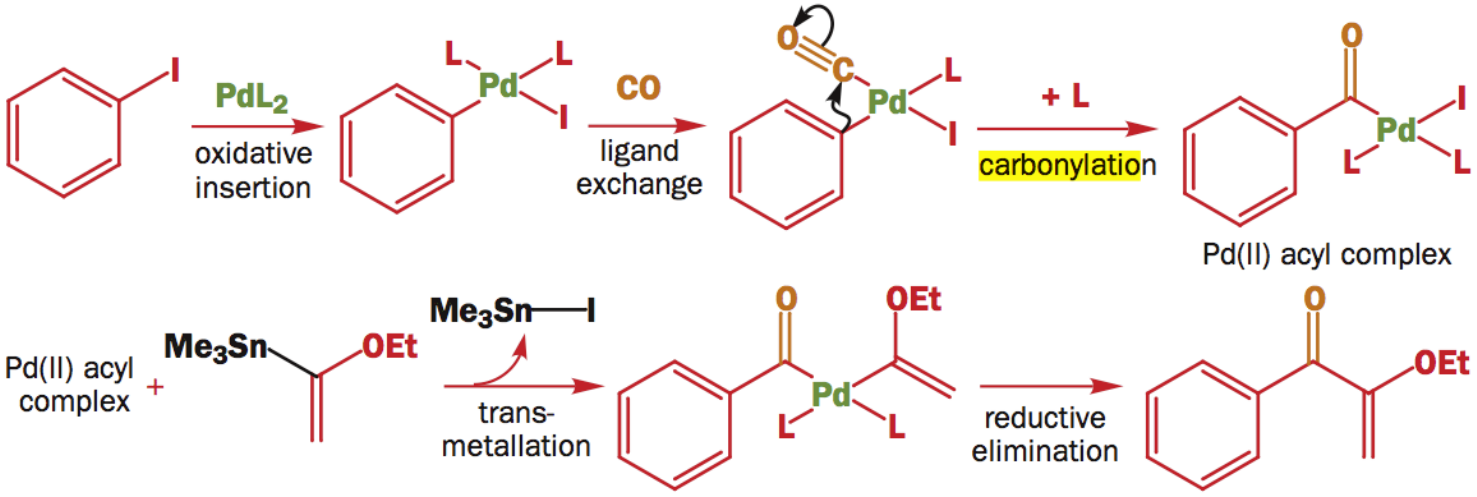
Interaction entre σ C-Si riche et la p vacante
$C^{\delta-}$-$Si^{\delta+}$: C = 2,50 Si = 1,74

Tsuji-Trost Catalytic Cycle

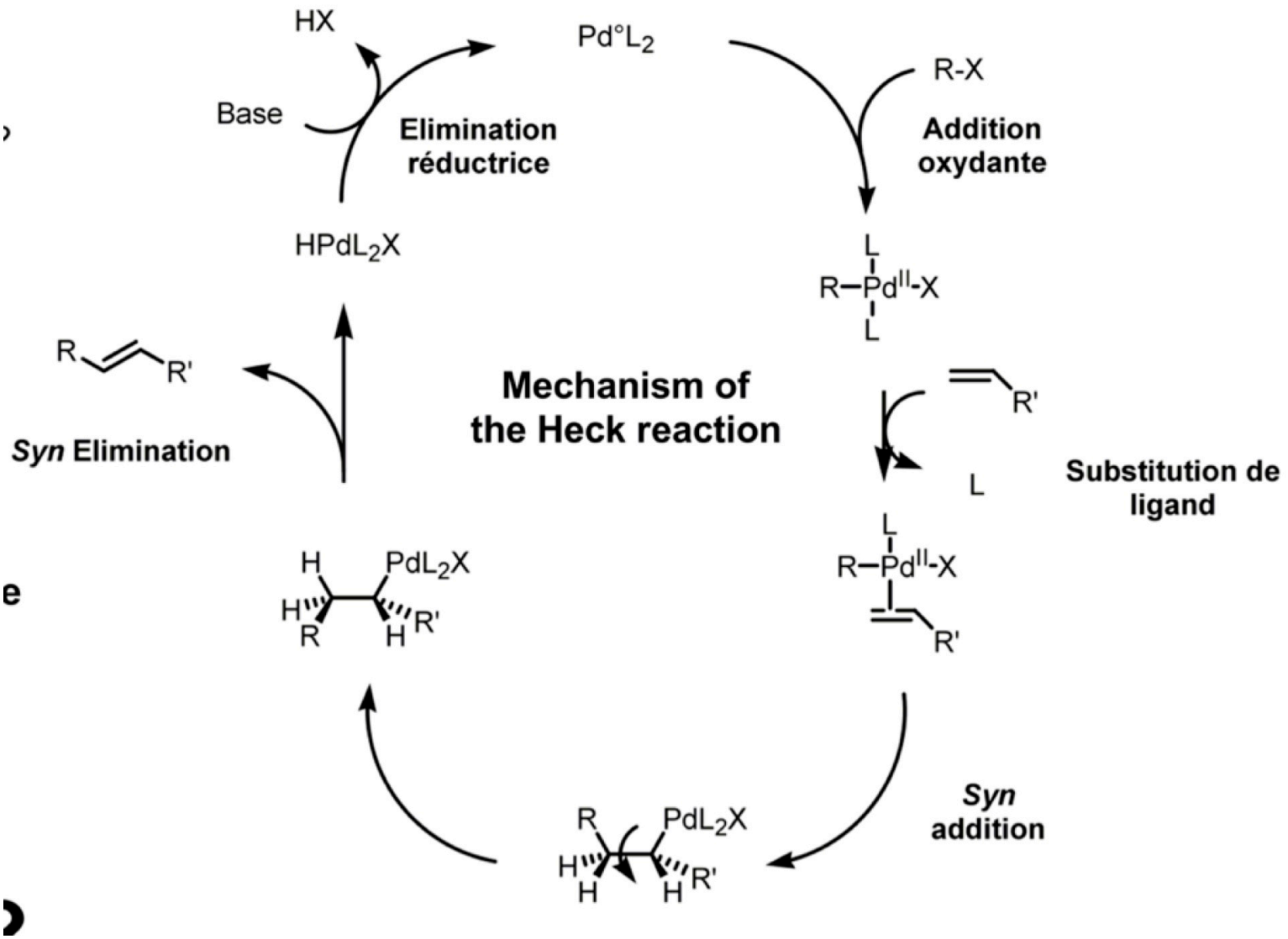


Carbonylative Stille Coupling

The mechanism is like that of a normal Stille coupling except that the carbon monoxide first exchanges for one of the phosphine ligands and then very rapidly inserts to produce an acyl palladium(II) complex. This then undergoes transmetallation with the vinyl stannane in the usual way forming trimethylstannyl iodide and the palladium complex with two carbon ligands. Reductive elimination gives the masked diketone and regenerates the palladium(0) catalyst. Transmetallation is the slow step in these coupling reactions so that there is time for the carbon monoxide insertion first. The final step—reductive elimination—releases the Pd(0) catalyst for the next cycle.

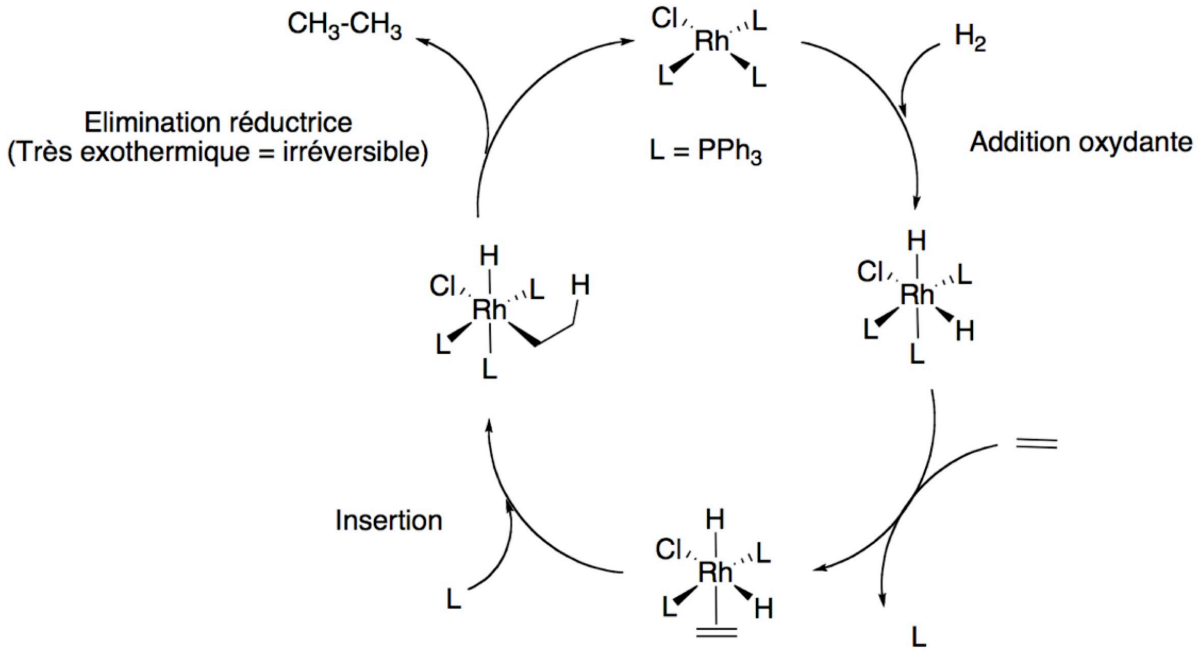


Heck Reaction

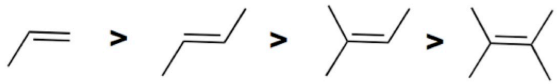


Selective Pd-catalyzed reduction of olefins

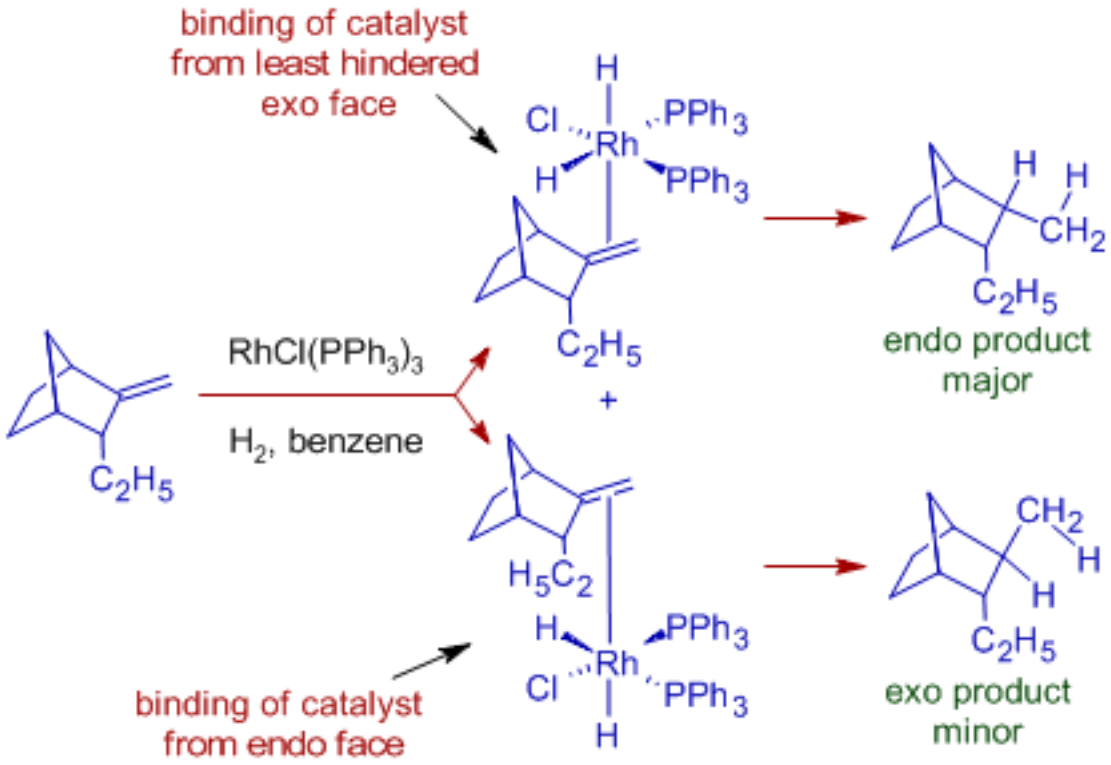
Hydrogénation catalytique des alcènes: addition oxydante
Exemple catalyseur de Wilkinson-Osborn (Rh)
Wilkinson - Prix Nobel en 1973



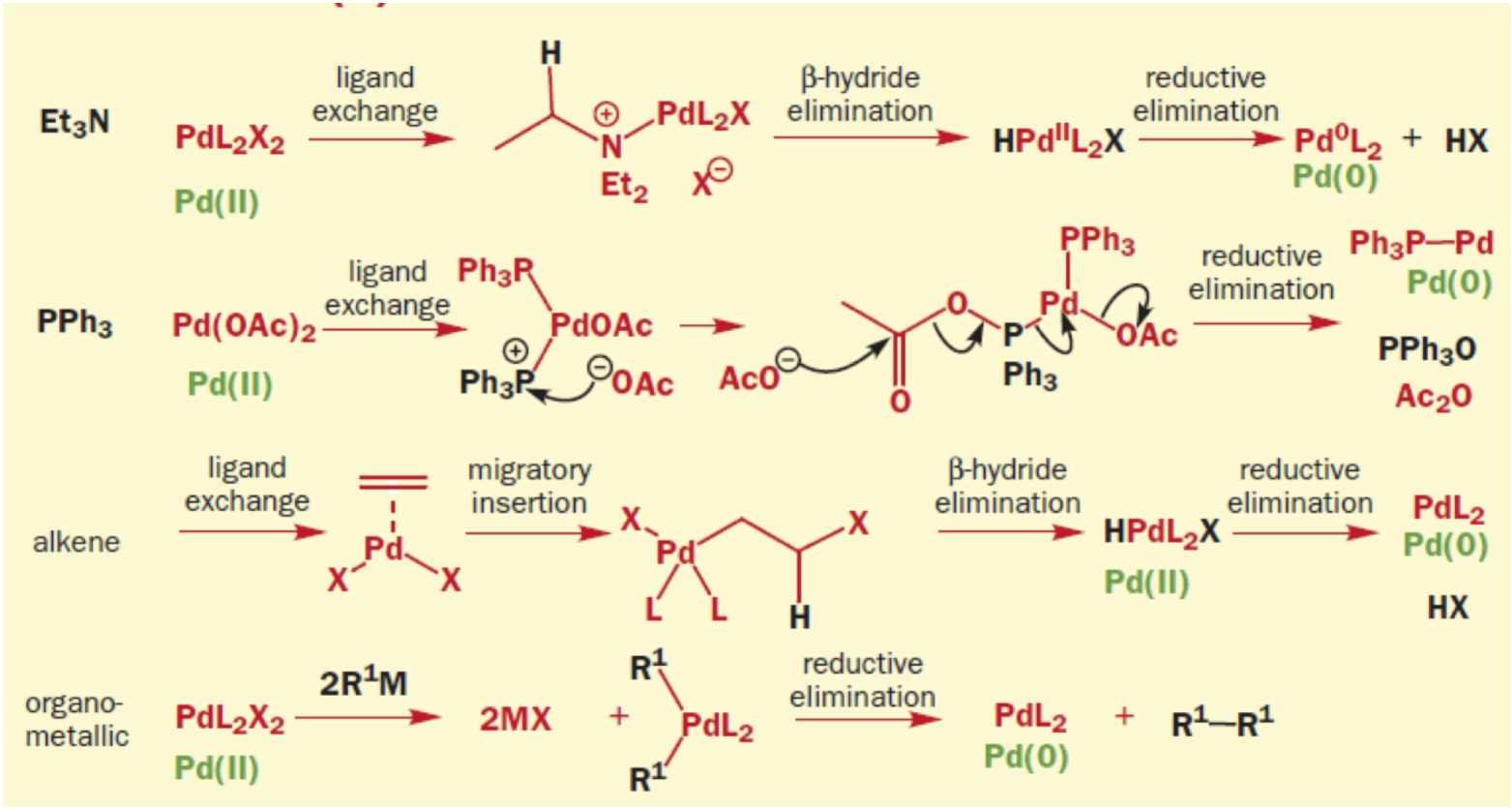
Sélectivité



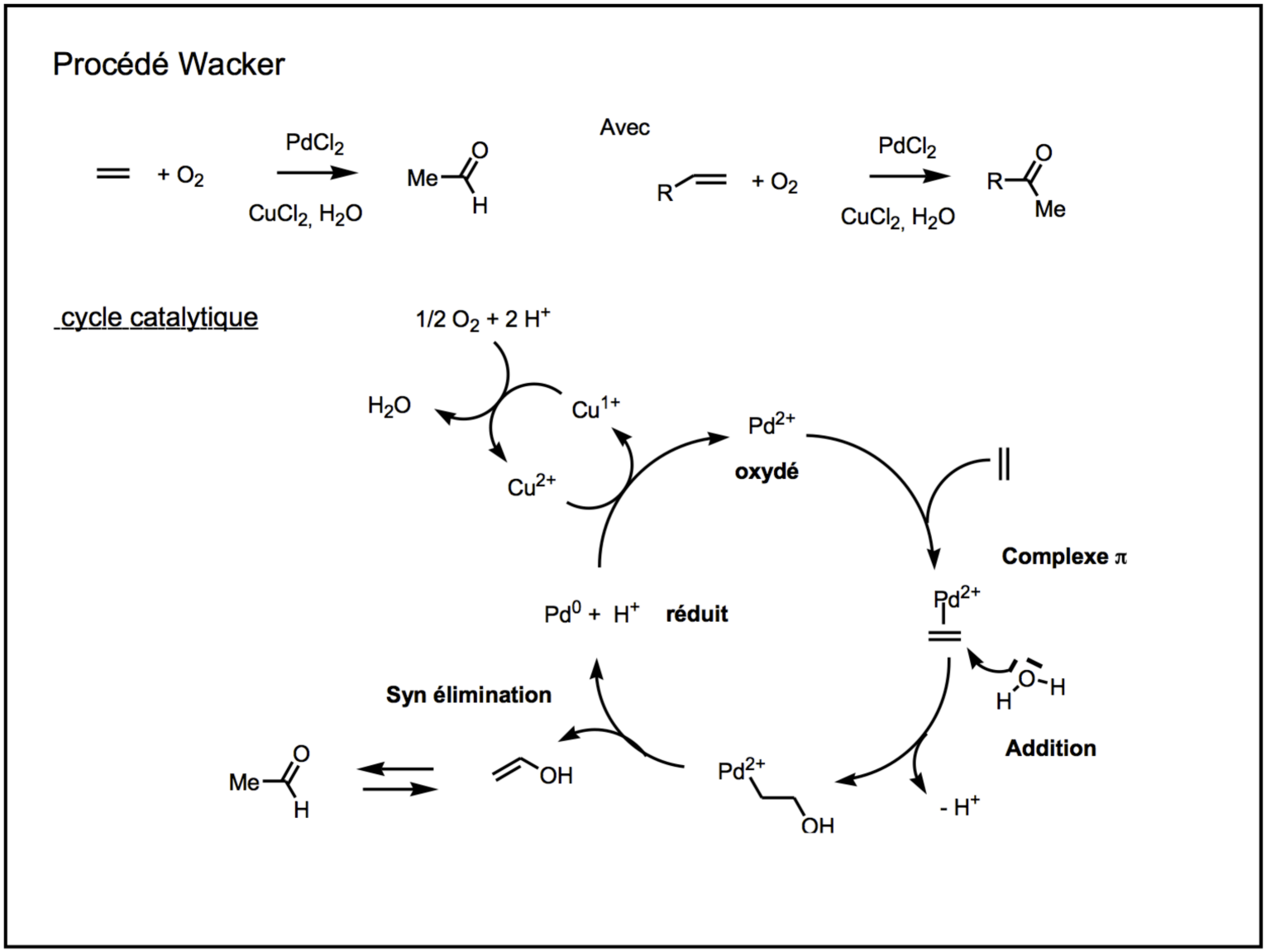
Example


binding of catalyst
from least hindered
exo face
RhCl(PPh3)3
H2, benzene
C2H5
H
Cl
Rh
PPh3
PPh3
H
C2H5
+
H5C2
H
Cl
Rh
PPh3
PPh3
H
binding of catalyst
from endo face
H
H
CH2
C2H5
endo product
major
CH2
H
H
C2H5
exo product
minor

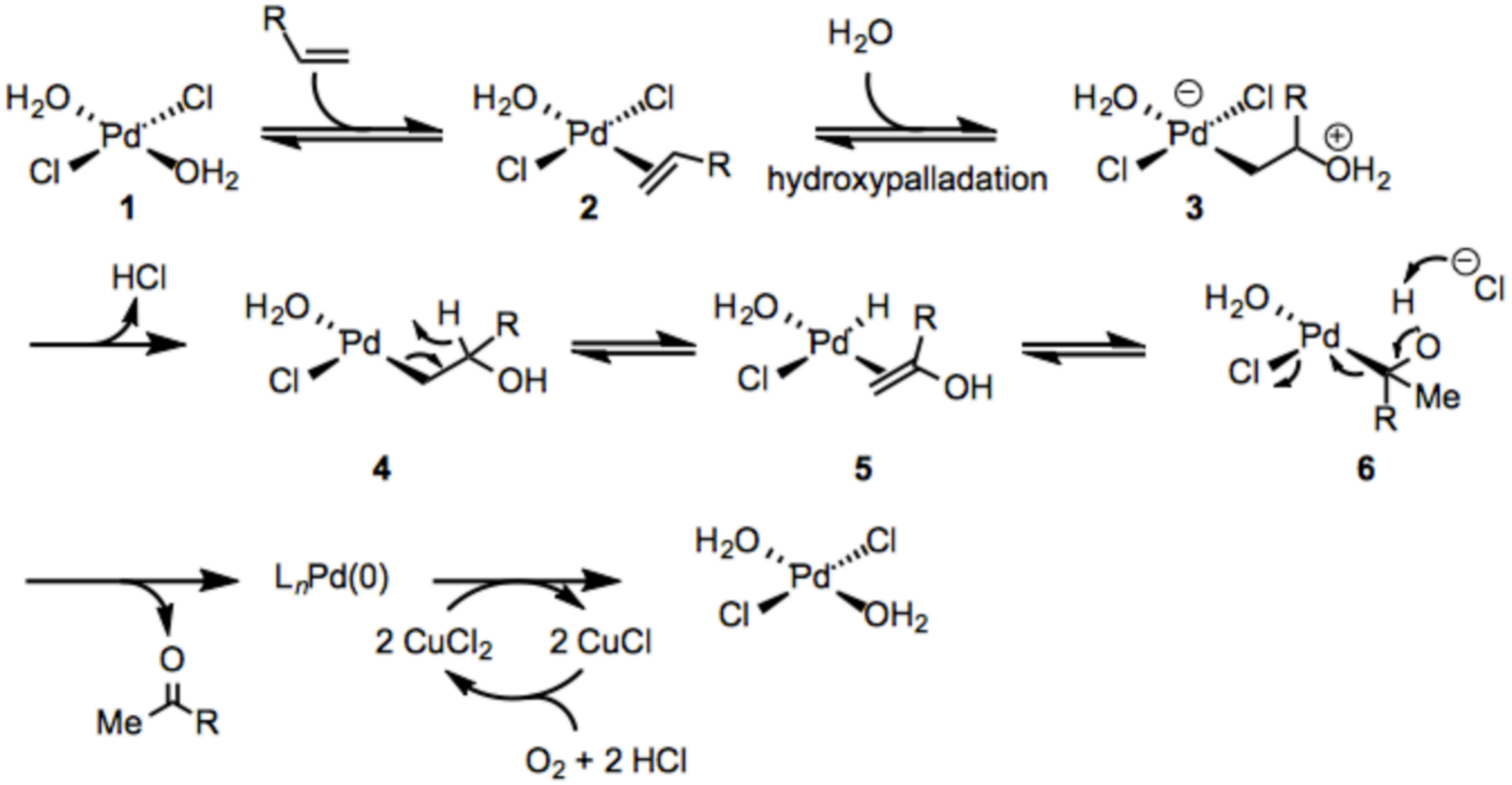
Pd(0) Generation



Wacker Process (simplified)



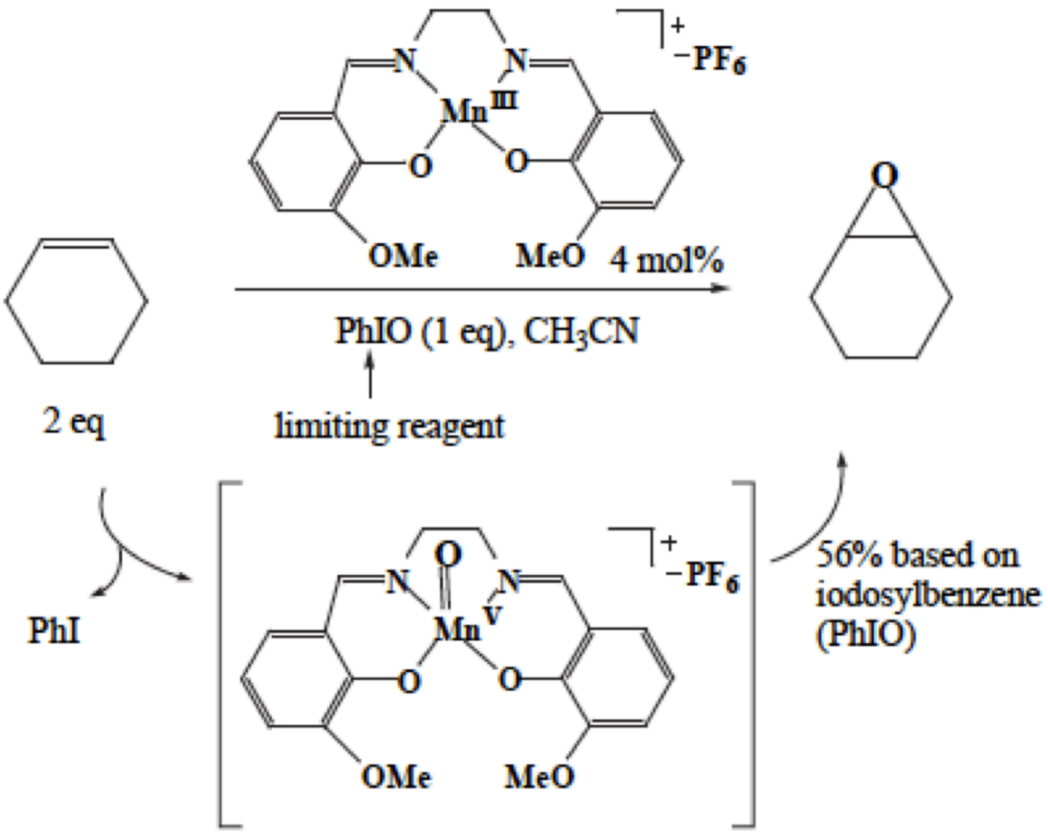
Wacker Process



Jacobsen Epoxidation

Epoxydation des oléfines
Jacobsen

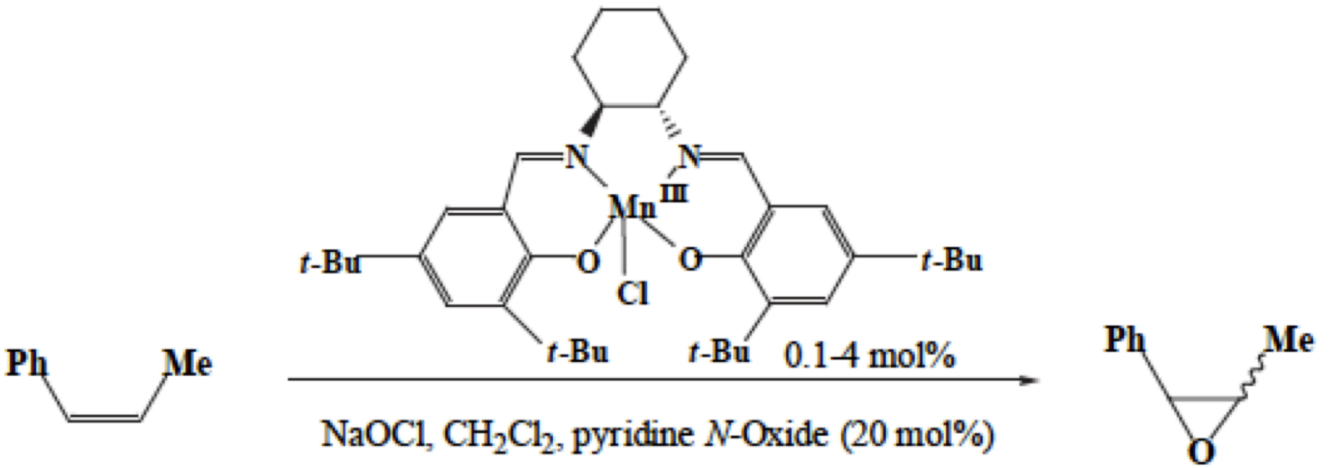
The first report of epoxidation activity:



Kochi *JACS* **1986** (108) 2309.

Application en synthèse asymétrique (difficulté isomérisation cis-trans- mécanisme radicalaire!)

The Jacobsen epoxidation



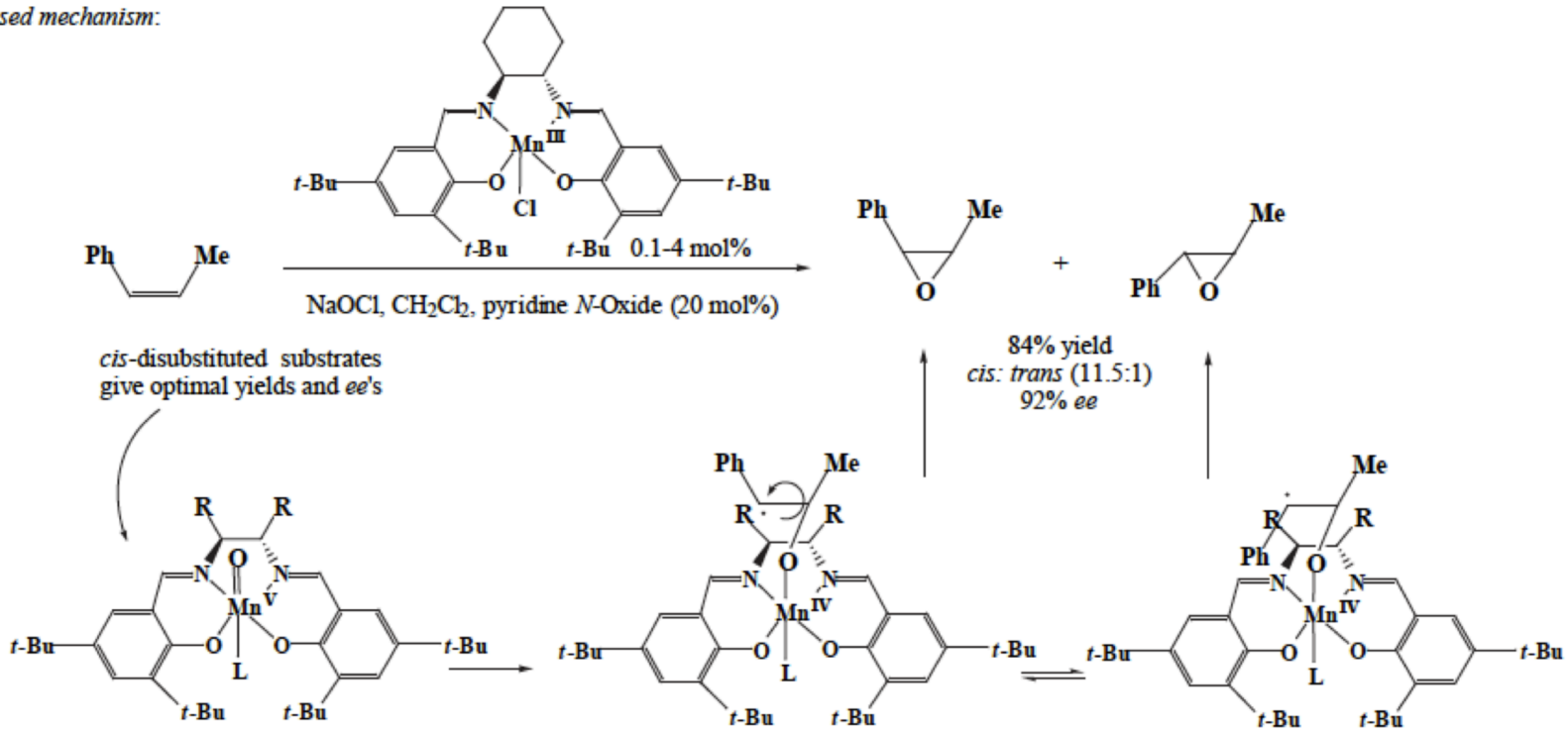
cis-disubstituted substrates
give optimal yields and *ee*'s

84% yield
cis: trans (11.5:1)
92% *ee*

Jacobsen *JACS* **1990** (112) 2801.
Jacobsen *JACS* **1991** (113) 6703.
Jacobsen *JOC* **1991** (56) 2296.
Jacobsen *TL* **1996** (37) 3271.

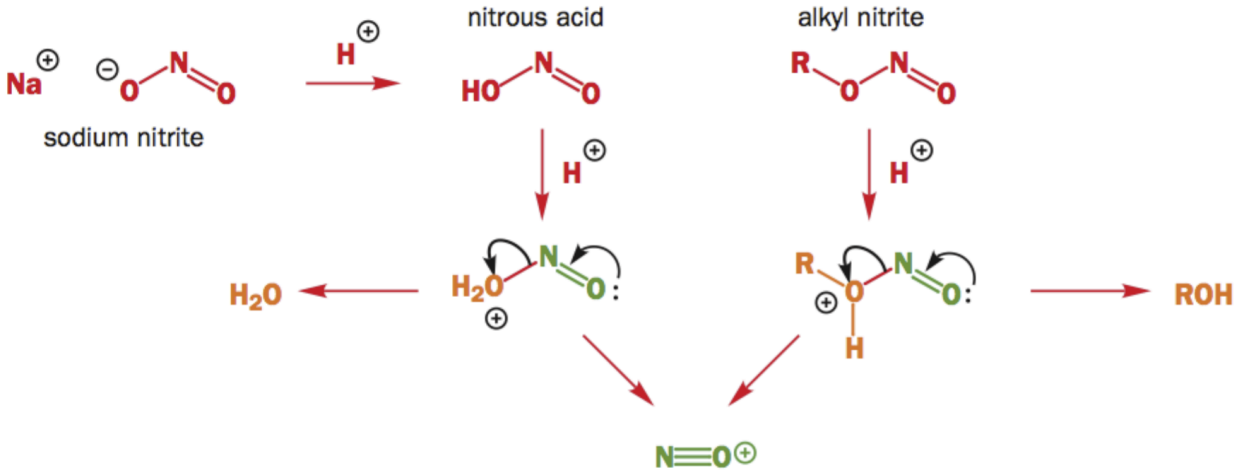
Mechanism

Proposed mechanism:

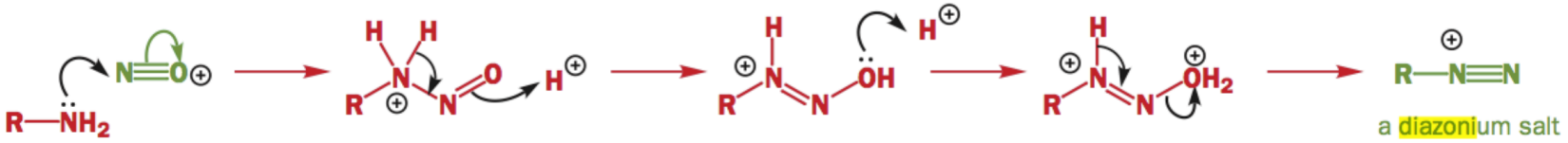


The S_N1 mechanism for nucleophilic aromatic substitution—diazonium compounds

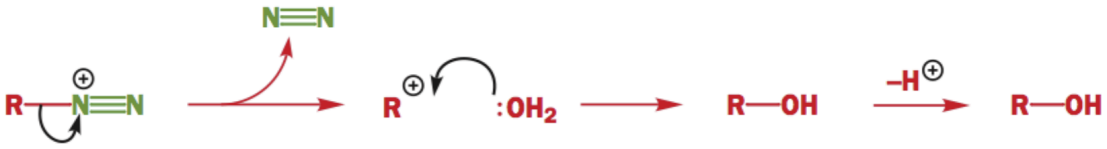
When primary amines are treated with nitrous acid (HONO), or more usually with a nitrite salt or an alkyl nitrite in acid solution, an unstable **diazonium salt** is formed. You met diazonium salts in Chapter 22 undergoing coupling reactions to give axo compounds, but they can do other things as well. First, a reminder of the mechanism of formation of these diazonium salts. The very first stage is the formation of the reactive species NO^+.



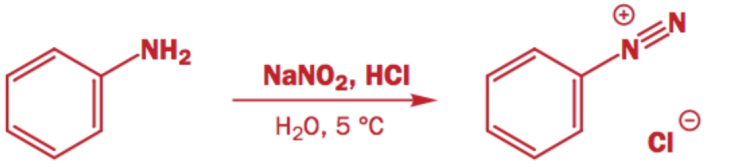
The NO^+ cation then attacks the lone pair of the amine and dehydration follows. The mechanism is quite simple—it just involves a lot of proton transfers! There is, of course, an anion associated with the nitrogen cation, and this will be the conjugate base (Cl^- usually) of the acid used to form NO^+.



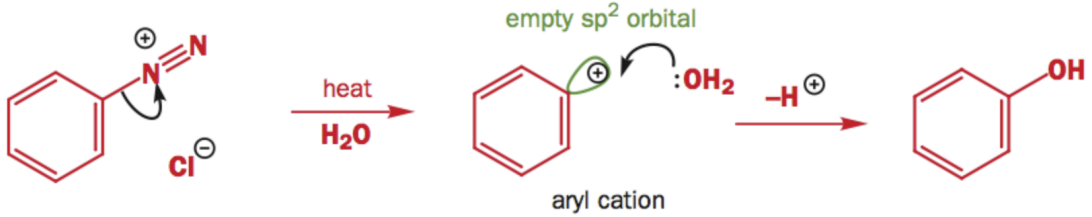
If R is an alkyl group, this diazonium salt is very unstable and immediately loses nitrogen gas to give a planar carbocation, which normally reacts with a nucleophile in an S_N1 process (Chapter 17) or loses a proton in an E1 process (Chapter 19). It may, for example, react with water to give an alcohol.



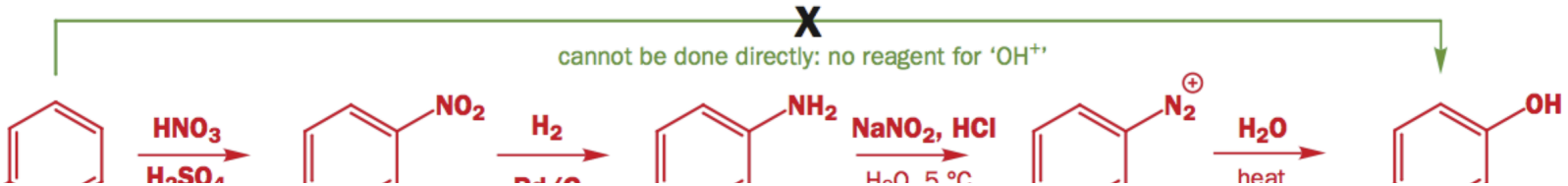
If R is an aryl group, the carbocation is much less stable (for the reasons we discussed earlier—chiefly that the empty orbital is an sp^2 rather than a p orbital) and that makes the loss of nitrogen slower. If the diazotization is done at lowish temperatures (just above 0 °C, classically at 5 °C), the diazonium salt is stable and can be reacted with various nucleophiles.



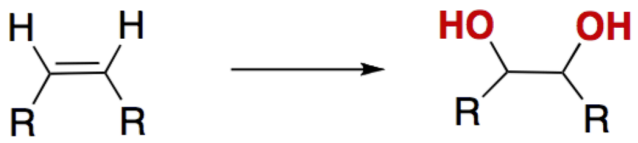
If the aqueous solution is heated, water again acts as the nucleophile and a phenol is formed from the amine. The aryl cation is an intermediate and this is an S_N1 reaction at an aromatic ring.



The point of this reaction is that it is rather difficult to add an oxygen atom to a benzene ring by the normal electrophilic substitution as there is no good reagent for 'OH^+'. A nitrogen atom can be added easily by nitration, and reduction and diazotization provide a way of replacing the nitro group by a hydroxyl group.

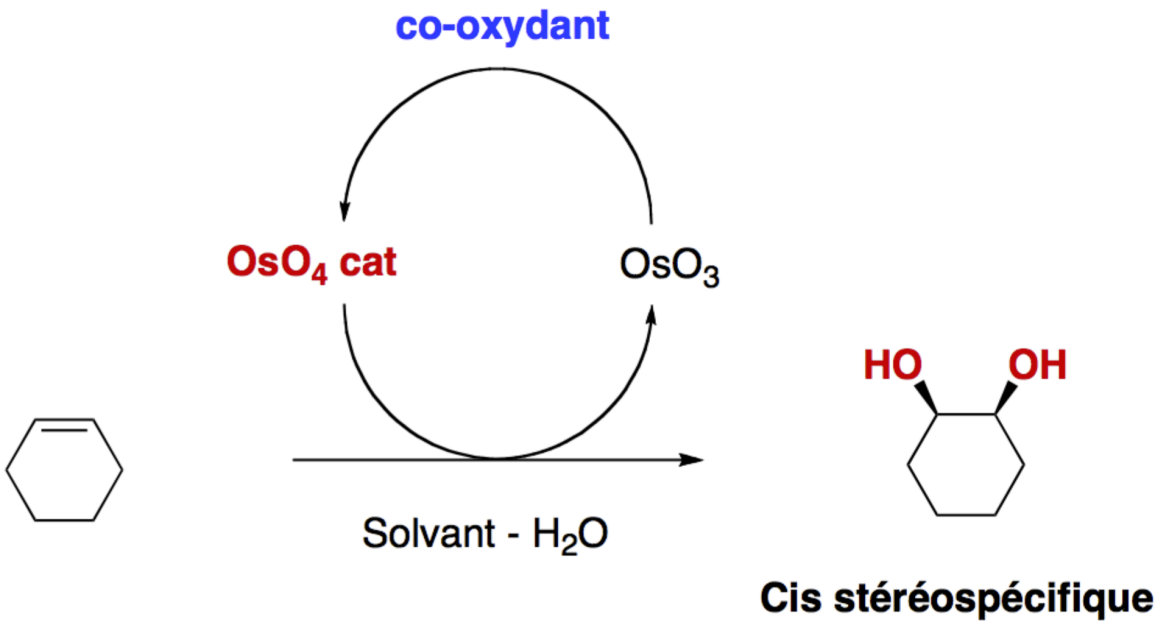


Dihydroxylation des alcènes

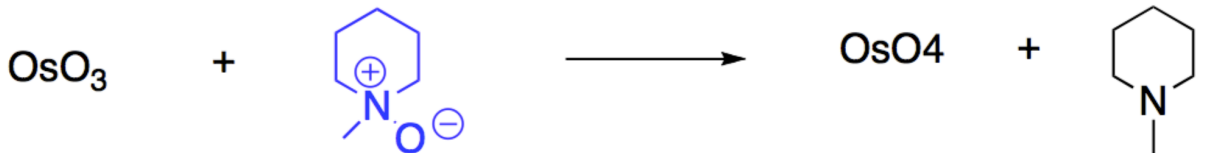


Oxydant : $KMnO_4$, OsO_4

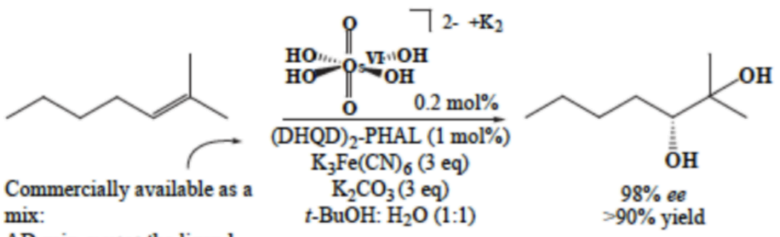
Exemple



Cis stéréospécifique



Cis dihydroxylation de Sharpless (synthèse asymétrique)



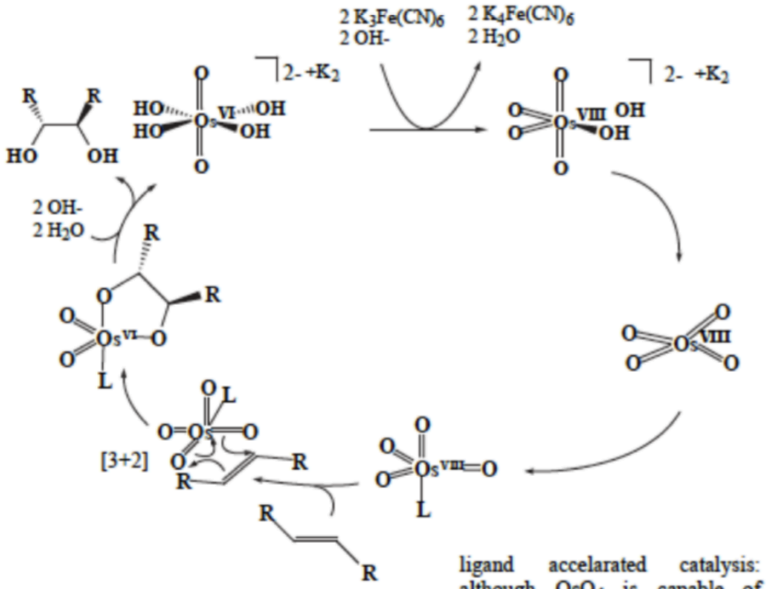
Commercially available as a mix:
AD-mix-α uses the ligand $(DHQ)_2$-PHAL
AD-mix-β uses the ligand $(DHQD)_2$-PHAL

98% *ee*
>90% yield

Works well for all olefin substitution patterns with the exception of *cis*-disubstituted and tetrasubstituted.

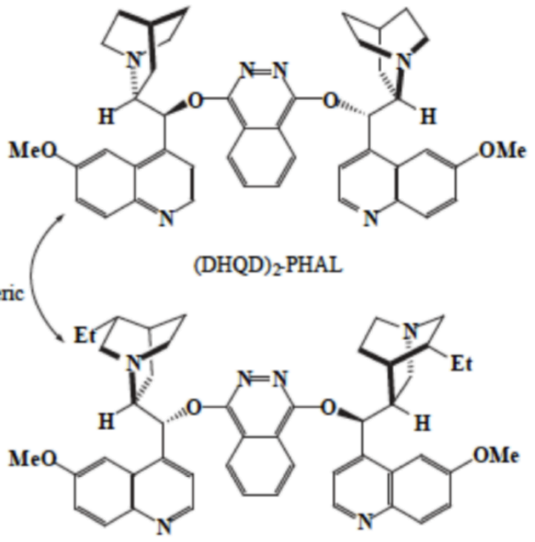
Sharpless *JOC* **1992** (57) 2768.

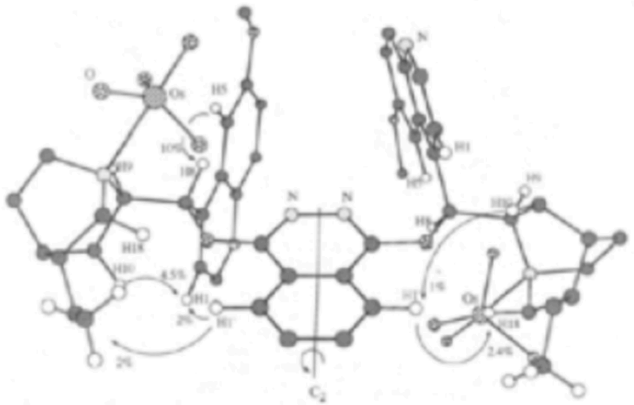
General mechanism: **Sharpless** *Chem. Rev.* **1994** (94) 2483.



Evidence favors the [3+2] mechanism *vs.* [2+2]:
Corey *TL* **1996** (28) 4899.
Houk, Sharpless, Singleton *JACS* **1997** (119) 9907.

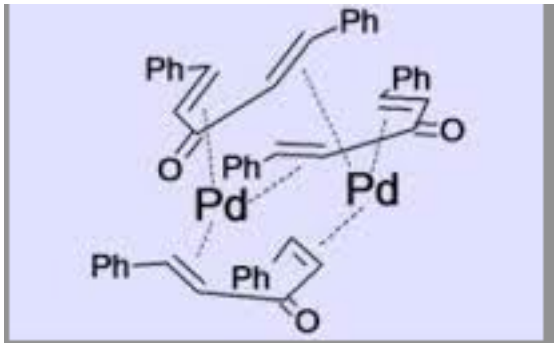
ligand accelarated catalysis: although OsO_4 is capable of dihydroxylating olefins, the ligand bound complex does so at a much greater rate.

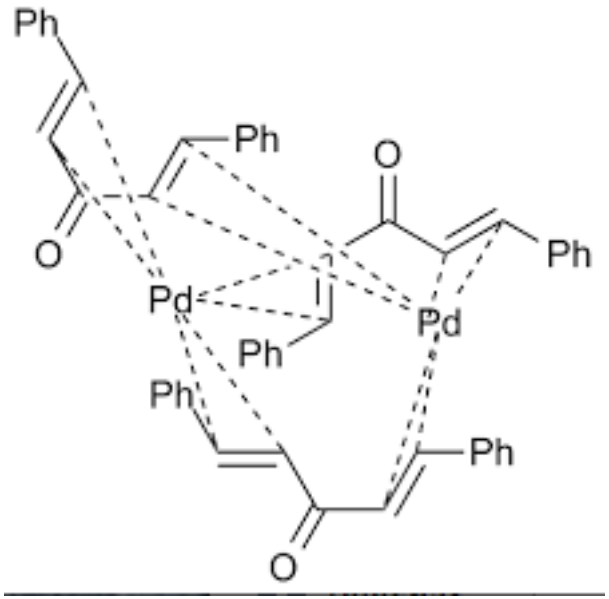
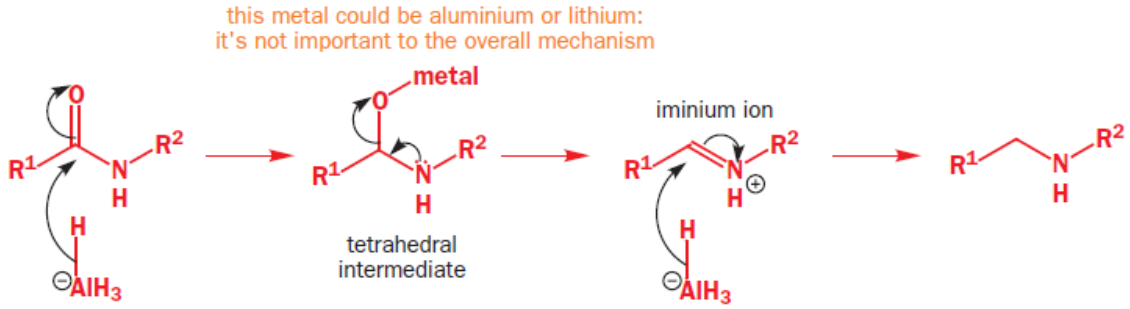




The enzyme-like binding cleft is especially well suited for π-stacking with aromatic substrates. Large rate accelarations are observed for aromatic substrates with the phalazine class of ligands.

Corey *JACS* **1993** (115) 2861, 12579.
Sharpless *JACS* **1994** (116) 1278.


Ph
Ph
Ph
O
Ph
O
Pd
Pd
Ph
Ph
O


Ph
Ph
O
O
Ph
Pd
Pd
Ph
Ph
Ph
O

Iminium ions can also be formed by reducing amides with lithium aluminium hydride. A tetrahedral intermediate is formed that collapses to the iminium ion.