

# Oxidative Addition & Reductive Elimination

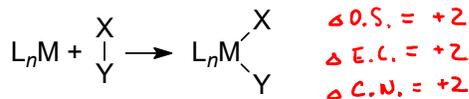
Robert H. Crabtree: Pages 159 – 182 and 235 - 266

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## Oxidative Addition

- Oxidative addition is a key step in many transition-metal catalyzed reactions

- Basic reaction:



- The new M-X and M-Y bonds are formed using the electron pair of the X-Y bond and one metal-centered lone pair
- The metal goes up in oxidation state (+2), X-Y formally gets reduced to X<sup>-</sup>, Y<sup>-</sup>
- The ease of addition (or elimination) can be tuned by the electronic and steric properties of the ancillary ligands
  - OA favored by strongly e-donating L**
- The most common applications involve:
  - Late transition metals (platinum metals: Ru, Rh, Pd, Ir, Pt) - not too sensitive to O<sub>2</sub> and H<sub>2</sub>O; routinely used in organic synthesis
  - C-Halogen, H-H or Si-H bonds
- Common for transition metals, rare for main-group metals

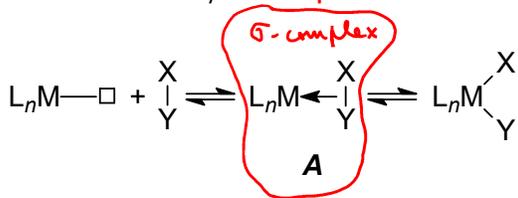
but: Grignard reagents!  $MeBr + Mg \longrightarrow MeMgBr$

Change in configuration	Example	Group
d <sup>10</sup> → d <sup>8</sup>	Cu <sup>I</sup> → Cu <sup>III</sup> Pd <sup>0</sup> → Pd <sup>II</sup> Pt <sup>0</sup> → Pt <sup>II</sup>	11 10 10
d <sup>8</sup> → d <sup>6</sup>	Pd <sup>II</sup> → Pd <sup>IV</sup> Pt <sup>II</sup> → Pt <sup>IV</sup> Ir <sup>I</sup> → Ir <sup>III</sup> Rh <sup>I</sup> → Rh <sup>III</sup>	10 10 9 9
d <sup>6</sup> → d <sup>4</sup>	Re <sup>I</sup> → Re <sup>III</sup> Mo <sup>0</sup> → Mo <sup>II</sup>	7 6
d <sup>4</sup> → d <sup>2</sup>	Mo <sup>II</sup> → Mo <sup>IV</sup>	6
d <sup>7</sup> → d <sup>6</sup>	2Co <sup>II</sup> → 2Co <sup>III</sup>	9
d <sup>4</sup> → d <sup>3</sup>	2Cr <sup>II</sup> → 2Cr <sup>III</sup>	6

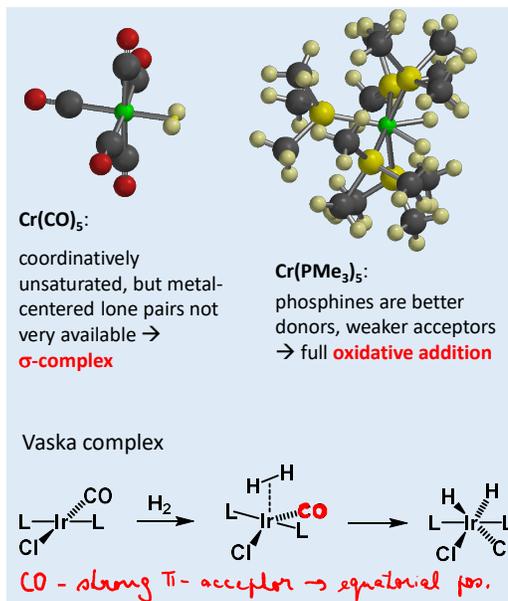
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## Oxidative addition – concerted mechanism

**Concerted addition** - mostly with **non-polar** X-Y bonds

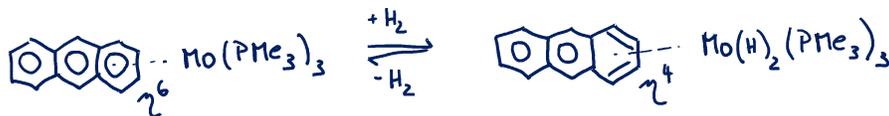


- H<sub>2</sub>, silanes, alkanes, ...
- Arene C-H bonds more reactive than alkane C-H bonds
- H-H, C-H strong bond, but M-H and M-C bonds can be stronger
- Reaction may stop here if back-donation from metal to the σ\* orbital of the X-Y is weak
- Final product expected to have *cis* X,Y groups
- C-C OA rare – can be driven by ring strain



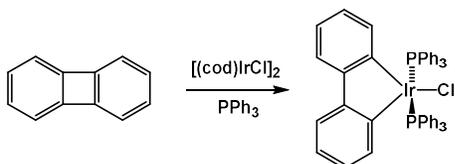
## Examples of less common OA reaction

- 18e complexes – either a ligand loss or a change of ligand coordination

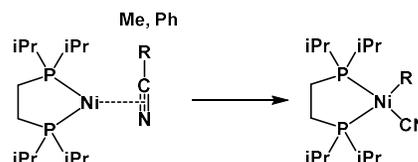


### Insertion into to a C-C bond

Driven by ring strain:

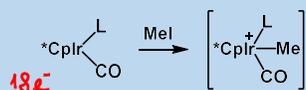
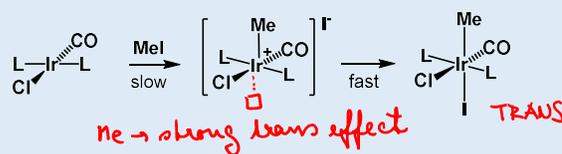
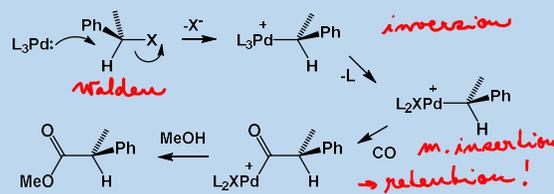
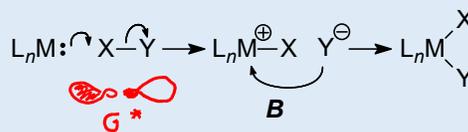


Driven by formation of a strong M-CN bond:



## Oxidative Addition – S<sub>N</sub>2 mechanism

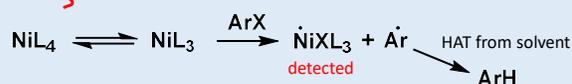
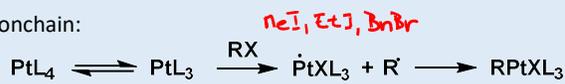
- **Stepwise addition** - with **polar** X-Y bonds
  - HX, R<sub>3</sub>SnX, acyl and allyl halides, ...
  - low-valent, electron-rich metal fragment (Ir<sup>I</sup>, Pd<sup>0</sup>, ...)
- Metal initially acts as **nucleophile** – metal electron pair attacks σ\* orbital of the X-Y at the less electronegative atom (C in alkyl halides)
- Ionic intermediate (**B**); accelerated by polar solvents
- Final geometry (*cis* or *trans*) not easy to predict
- The first step does not change the electron count – hence allowed to 18 e complexes. Only the association with the anion changes the electron count and thus requires ligand exchange.
- **B** sometimes stable: **electrophilic addition** to the metal
- The more nucleophilic M, the greater reactivity in S<sub>N</sub>2 additions
- Ni(PR<sub>3</sub>)<sub>4</sub> > Ni(PAr<sub>3</sub>)<sub>4</sub> > Ni(PR<sub>3</sub>)<sub>3</sub>(alkene) > Ni(PAr<sub>3</sub>)<sub>3</sub>(alkene) > Ni(cod)<sub>2</sub>
- Sterics: MeI > EtI > iPrI
- Leaving group: ROTs > RI > RBr > RCl



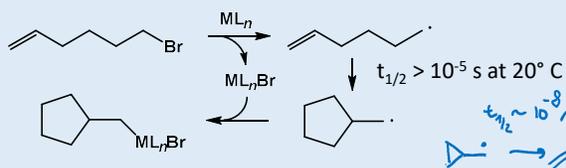
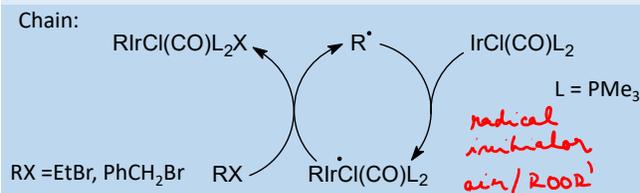
## Oxidative Addition – Radical Mechanism

- **Radical addition** has been observed but is relatively rare
- 1-electron transfer from M to the σ\* orbital of the X-Y
- Rates
  - Faster for electron-rich metals
  - RI > RBr > RCl >> ROTs
  - 3° > 2° > 1° > Me *more stable radicals*
- Tests:
  - Formation R-R
  - Spectroscopy
  - Radical clocks

Nonchain:



Chain:



## Reductive elimination

- For metals in higher oxidation state (OS drops by 2 in RE)
- Can be stimulated by oxidation or photoexcitation
- Rate depends strongly on types of groups to be eliminated

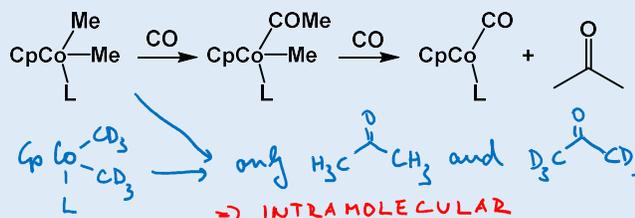
Usually easy for:

- H + alkyl / aryl / acyl  $\rightarrow$  cis-M(R)(H) rare because of rapid RE
- H 1s orbital shape, *c.f.* insertion
- alkyl + acyl
- SiR<sub>3</sub> + alkyl etc.

- Intramolecular mechanism  
 $\rightarrow$  confirmed in cross-experiments with labelled complexes

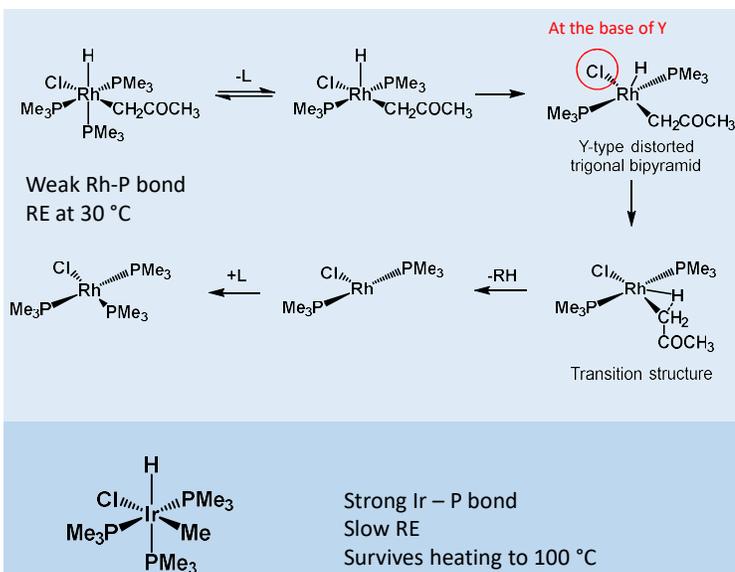
Change in configuration	Example	Group
d <sup>8</sup> $\rightarrow$ d <sup>10</sup>	Au <sup>III</sup> $\rightarrow$ Au <sup>I</sup>	11
	Pd <sup>II</sup> $\rightarrow$ Pd <sup>0</sup>	10
	Ni <sup>II</sup> $\rightarrow$ Ni <sup>0</sup>	10
d <sup>6</sup> $\rightarrow$ d <sup>8</sup>	Pd <sup>IV</sup> $\rightarrow$ Pd <sup>II</sup>	10
	Pt <sup>IV</sup> $\rightarrow$ Pt <sup>II</sup>	10
	Ir <sup>III</sup> $\rightarrow$ Ir <sup>I</sup>	9
	Rh <sup>III</sup> $\rightarrow$ Rh <sup>I</sup>	9

RE involving acyl groups is easier than for alkyls:

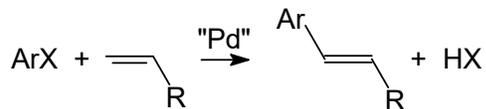


## Reductive elimination

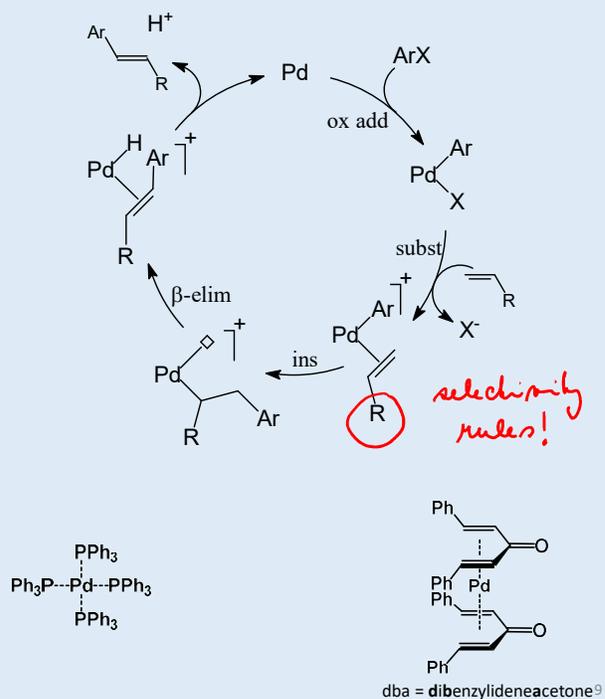
- Mechanisms  
 opposite of oxidative addition
- Octahedral complexes  
 Pt(IV), Pd(IV), Ir(III), Rh(III)  
 Often first – a ligand loss  
 RE from six coordinated complex – slow
- RE of C-Hal, C-O, C-N: high kinetic barrier  
 F, OR, NR<sub>2</sub> – at the base of the Y in the TS  
 $\rightarrow$  remote from the coupling partner  
 $\rightarrow$  C-N couplings exist –  
 chelating phosphine ligands



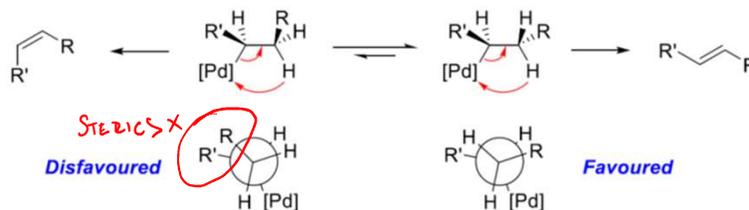
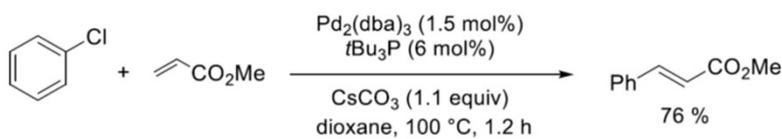
## The Heck reaction



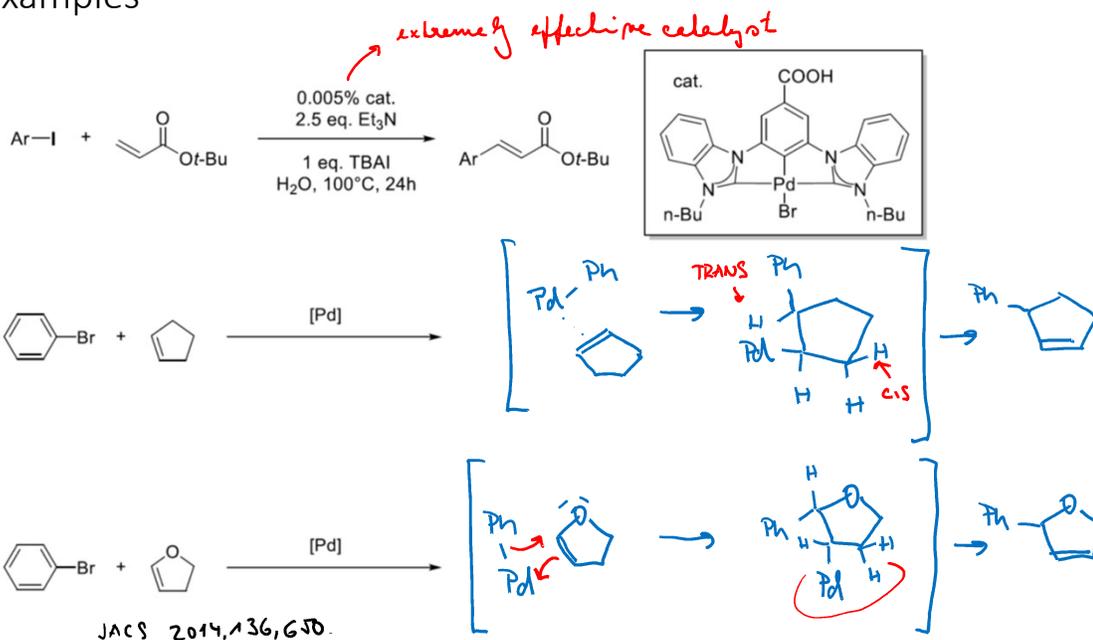
- Pd often added in the form of  $\text{Pd}_2(\text{dba})_3$ , usually with phosphine ligands
- Typical **catalyst loading**: 1-5%  
But examples of turnovers of  $10^6$  or more  
[TON = mol(product)/mol(catalyst)]
- Intermediates:
  - Coordination environment of Pd during catalysis mostly unknown
  - Dramatic effects of ligand variation show that **at least one ligand** is bound to Pd for **at least part of** the cycle.
- ArI, ArBr react well, ArCl react slow, ArOAc does not react



## Selectively trans-alkenes



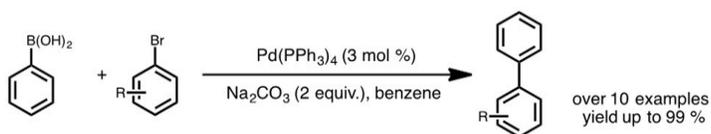
## Examples



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## Suzuki coupling

1981: Suzuki &amp; Miyaura



$\text{R}^1$  = aryl, alkene (vinyl), alkyne     $\text{R}^2$  = H (boronic acid), alkyl (boronic ester)     $\text{R}^3$  = aryl, alkene (vinyl), alkyne  
 $\text{X}$  = halide (I, Br, Cl\*) triflate (-OTf)    \*Cl requires special conditions for activation

- Many variations, mainly in the choice of electrophile
  - Instead of  $\text{B}(\text{OH})_2$  also  $\text{MgCl}$ ,  $\text{ZnBr}$ , etc.
- **Boronic acids:**
  - less toxic and safer for the environment than  $\text{R-Sn}$  and  $\text{R-Zn}$  compounds
  - It is easy to remove the inorganic by-products from the reaction mixture
  - Relatively cheap and easily prepared reagents
  - Reagents air-stable and water-stable

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## Suzuki coupling

*L* donor

$L-Pd-R_1$   
 $|$   
 $R_2$

*L* - electron donating  
→ supports OA,  
but dis-favors RE  
⇒ must be BULKY

The base activates the boronic acid

$Y-B(R_1)-Y + NaO^tBu \rightarrow Na^+ [Y-B(R_1)-O^tBu]^-$

**Rate:**  
 $R^{sp^2}-I > R^{sp^2}-OTf > R^{sp^2}-Br \gg R^{sp^2}-Cl$

**Catalyst:**  
Pd + phosphine ligands  
loading down up to 0.001 mol%

**Reaction requires a base** (NaO<sup>t</sup>Bu)

**SPhos** structure: COC1=CC=C(C=C1)C2=CC=C(C=C2)P(C)(C)C3=CC=CC=C3

- Mechanism of **transmetalation** is not well known  
"open" (3-center) mechanism or "closed" (4-center) mechanism
- Probably different for different electrophiles can react

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## Transmetalation

**Cyclic Mechanism**

$L-Pd^{II}-L + R^2-Sn(alkyl)_3 \rightarrow [L-Pd^{II}-R^2 + X-Sn(alkyl)_3] \xrightarrow{+L} L-Pd^{II}-R^2 + X-Sn(alkyl)_3$

**Open Mechanism**

$[L-Pd^{II}-L] + [R^1-C(Y)-Sn(alkyl)_3] \rightarrow [L-Pd^{II}-R^1 + L-C(Y)-Sn(alkyl)_3] \rightarrow L-Pd^{II}-R^2 + L-C(Y)-Sn(alkyl)_3$

(Y = L or solvent)

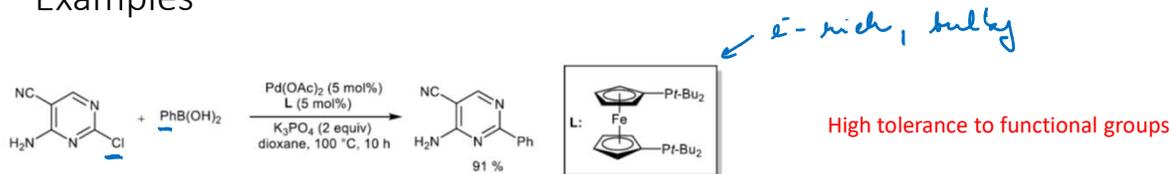
**SUZUKI:**

$Y-B-R_2 + R_1-O-Pd-L \rightarrow cis(O.A.)$

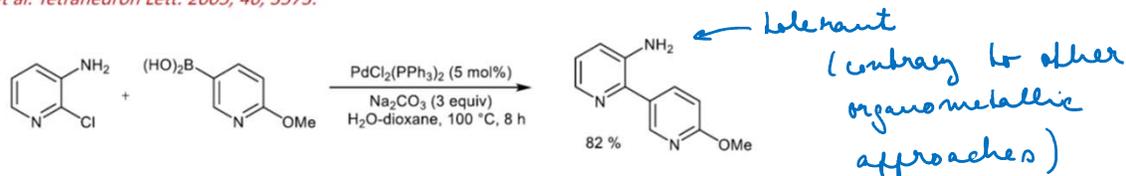
$OR^1-B(OR^2)-OR^3 + R_1-O-Pd-L \rightarrow cis(O.A.)$

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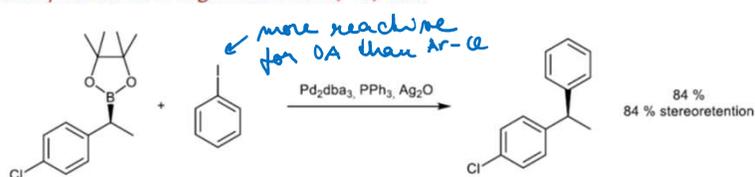
## Examples



*T. Heh et al. Tetrahedron Lett. 2005, 46, 3573.*



*A. E. Thompson et al. J. Org. Chem. 2005, 70, 388.*

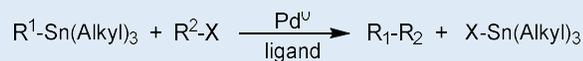


*C. M. Crudden et al. J. Am. Chem. Soc. 2009, 131, 5024.*

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## Other variants

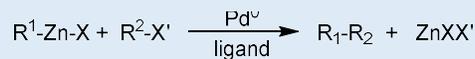
- Stille coupling



$\text{R}_1, \text{R}_2$ :  $\text{sp}^2$  hybridized C (allyl, alkenyl, aryl)  
 $\text{X}$ : halides (Cl, Br, I), pseudohalides (OTf)

Alkyl = Me, Bu  
 Me: very toxic  
 Bu: toxic

- Negishi coupling



$\text{R}_1$ :  $\text{sp}^2$  hybridized C (allyl, alkenyl, aryl), propargyl  
 $\text{R}_2$ :  $\text{sp}^2$  hybridized C (allyl, alkenyl, aryl)

also: alkyl, benzyl, homoallyl

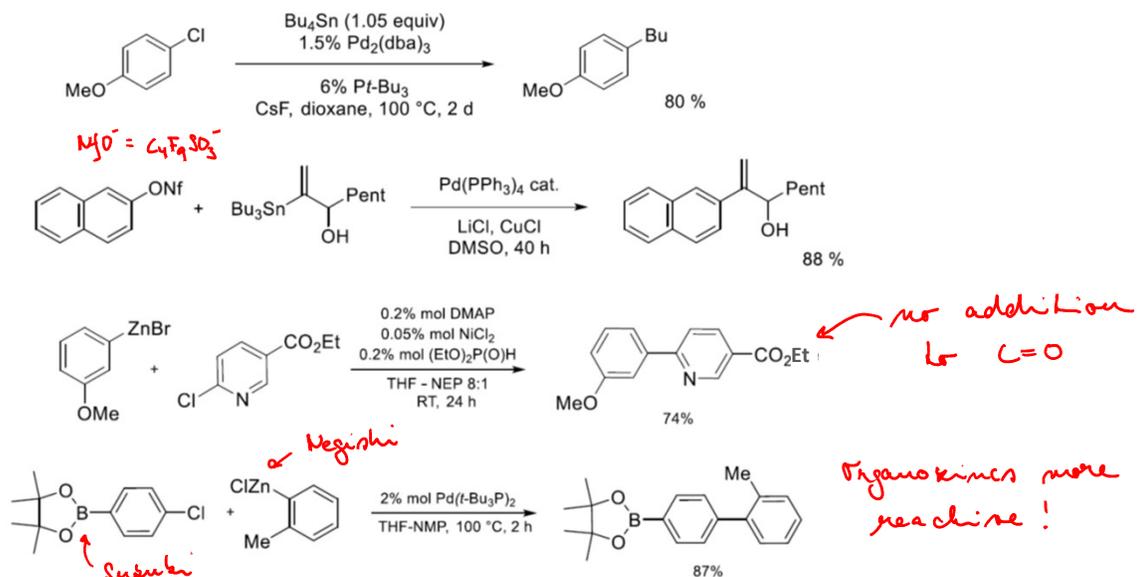
(Zn)X: Cl, Br, I

$\text{X}'$ : halides (Cl, Br, I), pseudohalides (OTf), AcO !

Similar scope as Suzuki coupling, but organostannanes are toxic  
organozincs are moisture and air sensitive

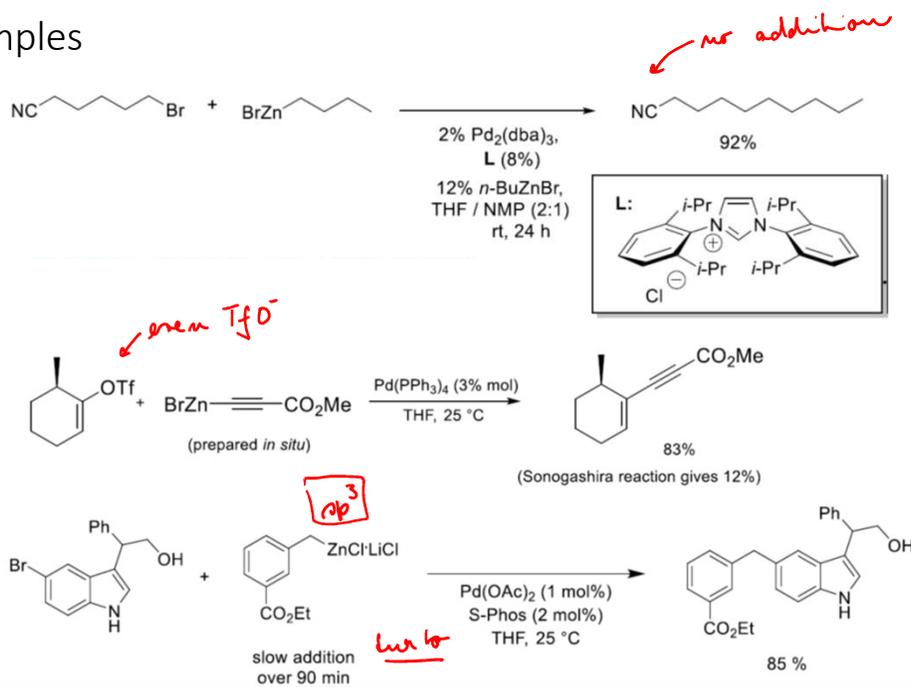
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## Examples



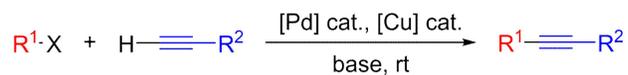
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## Examples

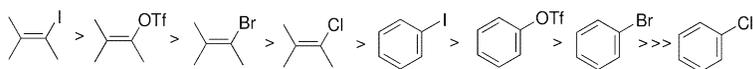


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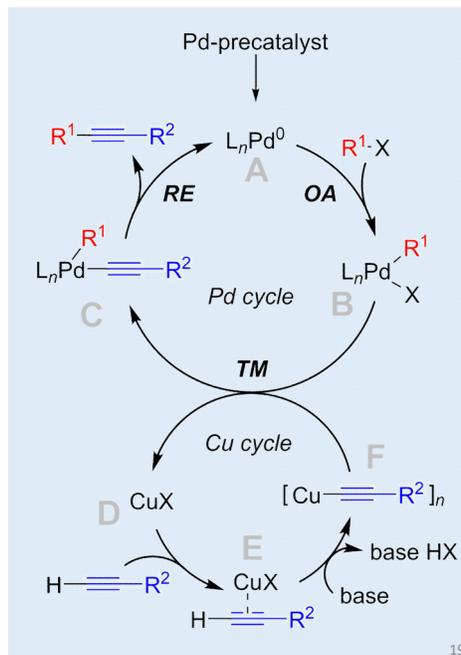
## Sonogashira coupling



R<sup>1</sup>: ~~Ar~~ <sup>Ar</sup>

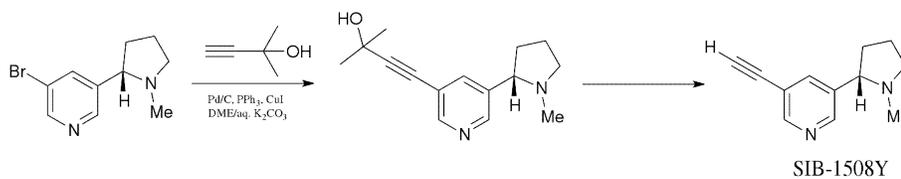
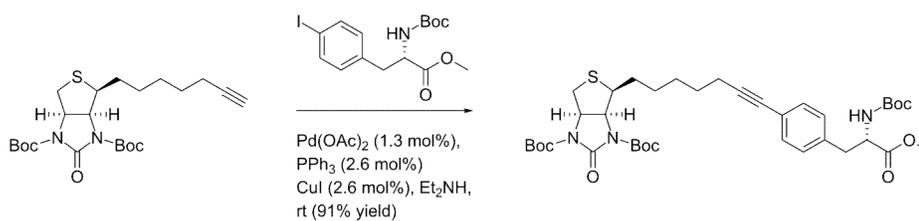


- Also copper-free variant, then acetylide bound directly to Pd<sup>II</sup>
- Also palladium-free variant – copper catalyzed
- Copper – side reaction – Glaser coupling (dimerization of alkynes)



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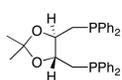
## Examples



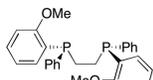
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## Catalytic olefin hydrogenation

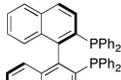
- Usually with platinum metals
  - e.g. Wilkinson's catalyst
- Many chiral variations available
  - enantioselectivity mechanism can be very subtle



(R,R)-DIOP

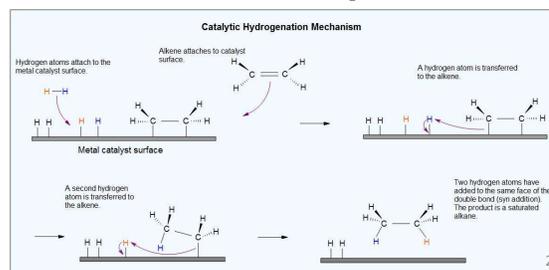
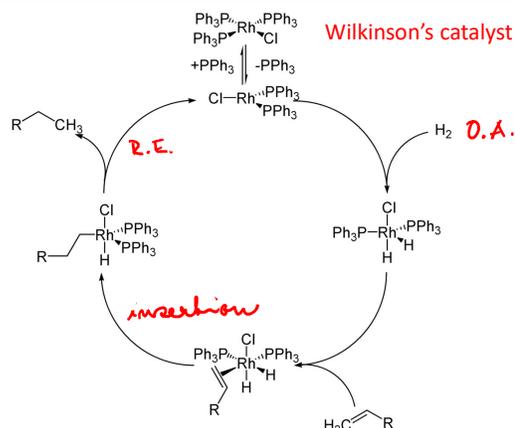


(R,R)-DIPAMP



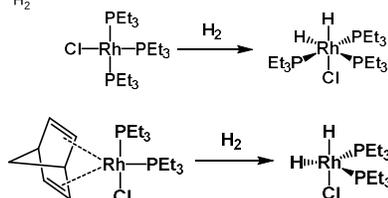
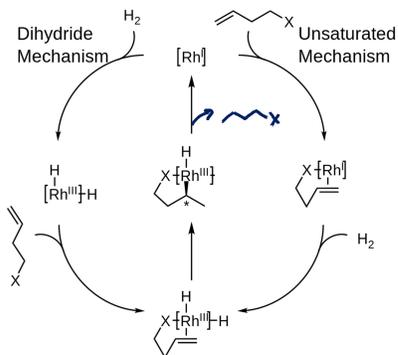
(R)-BINAP

- For achiral hydrogenation, heterogeneous catalysts ("Pd black") are often a good alternative
- Extremely high turnovers possible



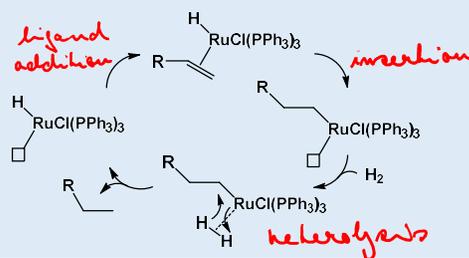
## Alternative mechanisms

- Unsaturated (olefin) mechanism:**
  - alkene adds first
  - Alternative mechanism for metals not forming a "stable" hydride.



Analog of the Wilkinson's catalyst  
 $\text{PEt}_3$  stronger bound to Rh than  $\text{PPh}_3 \rightarrow$  does not dissociate  
 $\text{H}_2$  OA  $\rightarrow$  stable complex – catalytically inactive  
 Catalytically active complex by hydrogenation of  $[(\text{nb}d)\text{RhCl}(\text{PEt}_3)_2]$   
 Similarly:  $[(\text{cod})\text{Rh}(\text{dpe})]\text{BF}_4$

- $\sigma$ -bond metathesis** instead of oxidative addition
  - early TM and metals that do not easily oxidize



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## What did you learn today?

- Oxidative addition
  - needs metal that can undergo a 2e oxidation and a 2e change in electron count
  - Mechanisms – concerted,  $S_N2$ , radical
- Reductive elimination – reverse of oxidative addition (decreases OS, EC and CN by 2)
- Heck reaction
- Suzuki reaction (Stille, Negishi)
- Sonogashira coupling
- Catalytic hydrogenation