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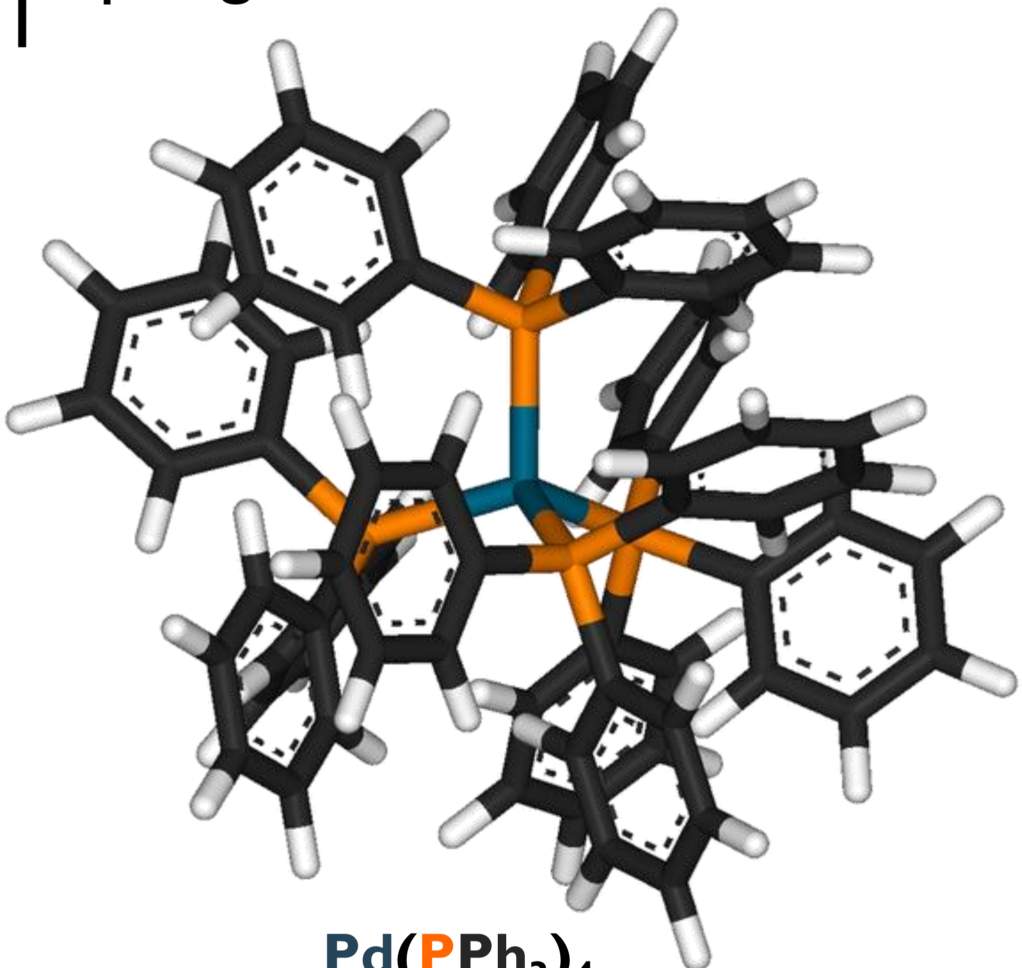


$Pd(PPh_3)_4$

Organometallic chemistry and catalysis

http://en.wikipedia.org/wiki/Tetrakis(triphenylphosphine)palladium(0)

Summary of previous lecture

Organometallic chemistry

- the chemistry of compounds containing a C-M bond
- intersection of organic and inorganic chemistry
- allows "impossible" organic reactions to occur

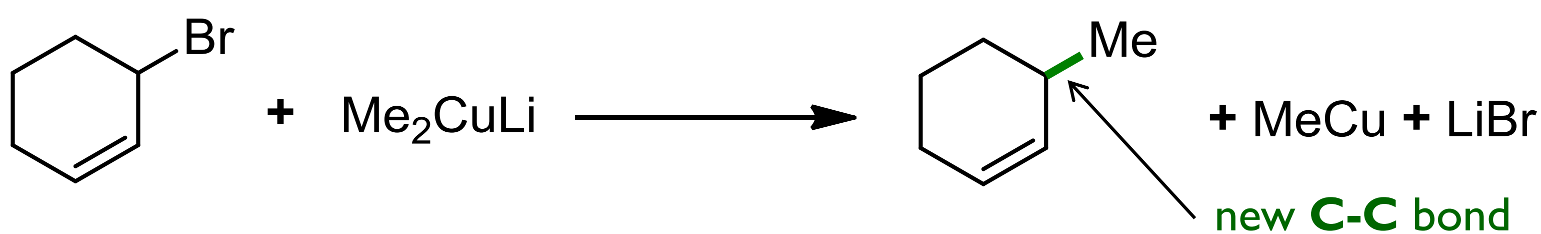
Organolithium and Grignard reagents

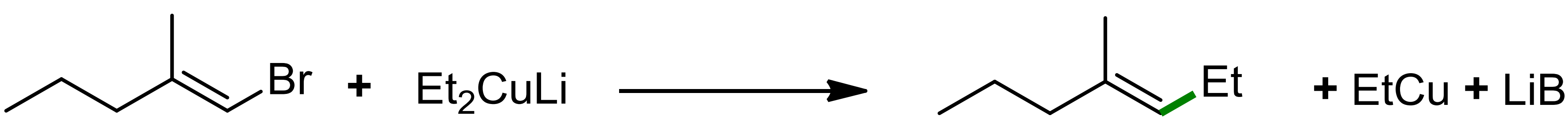
- Polar C-M bonds
- nucleophilic carbon atom, carbanion character
- strongly basic
- reactive toward water/oxygen/acidic protons
- reactivity toward carbonyl groups for C-C bond forming reactions
- used in **stoichiometric amounts** (i.e. 1:1 or greater)

Gilman reagents: C-C bond formation

Lithium diorganocuprates are useful for C-C bond forming reactions

$$2\ EtLi + CuI \xrightarrow{\text{ether}} Et_2CuLi + LiI$$



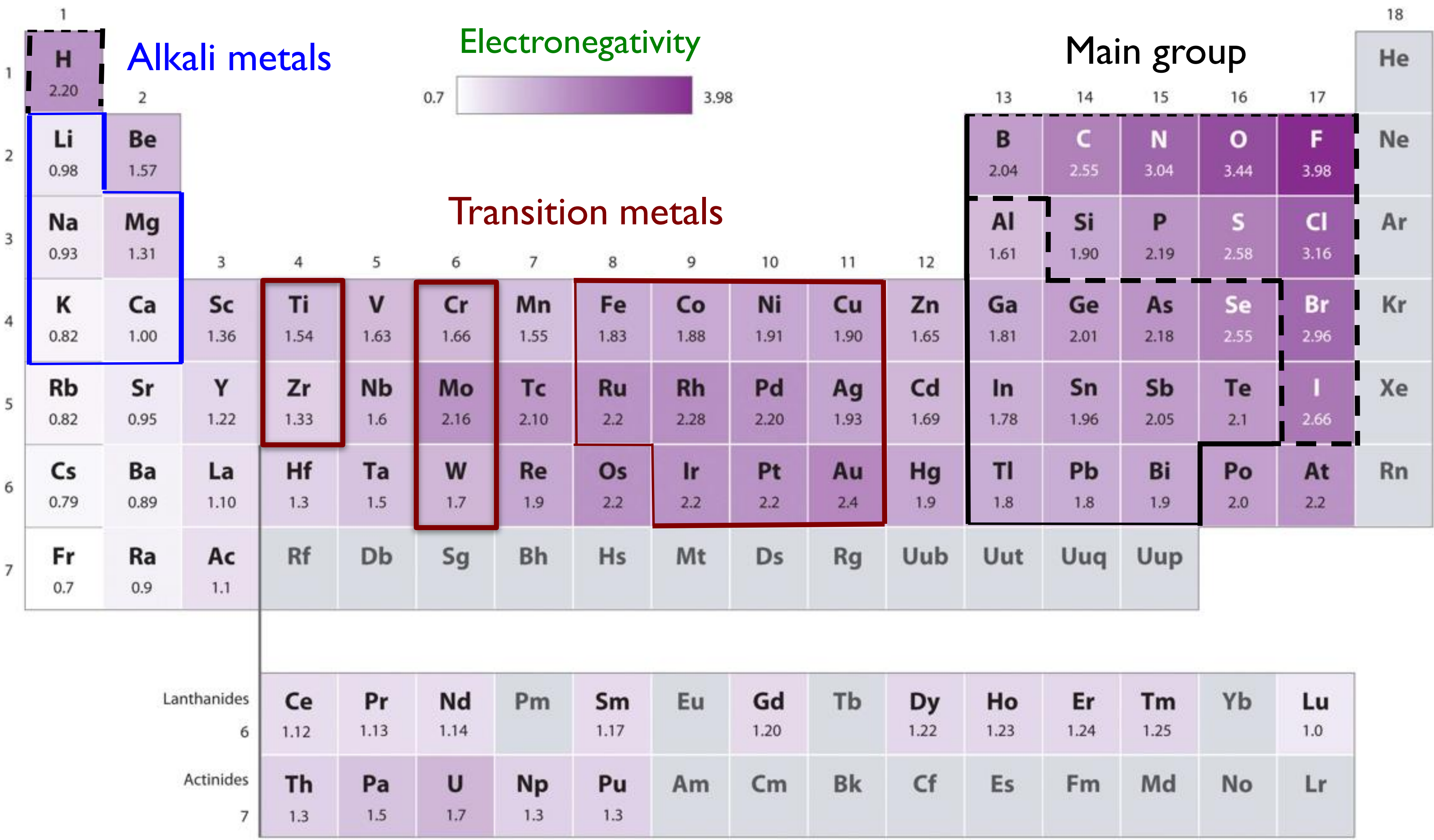


Good: joins (“couples”) 2 different R groups to form a new **C-C** bond

Not so good: requires a **stoichiometric** amount of organometallic reagent

Ideal: a **coupling reaction** using a sub-stoichiometric (“**catalytic**”) amount of reagent

Periodic Table – common organometallics



Carbon-Metal bond polarity

	C-M bond	Δ Electronegativity#	% ionic character*
	C-K	2.55 – 0.82 = 1.73	68
	C-Na	2.55 – 0.93 = 1.62	63
	C-Li	2.55 – 0.98 = 1.57	61
Grignard	C-Mg	2.55 – 1.31 = 1.24	48
Ziegler-Natta	C-Ti	2.55 – 1.54 = 1.01	40
Gilman	C-Cu	2.55 – 1.90 = 0.65	25
Schrock	C-Mo	2.55 – 2.06 = 0.49	19
Grubbs	C-Ru	2.55 – 2.20 = 0.35	14
	C-H	**2.55 – 2.20 = 0.35**	**14**
Pd-coupling	C-Pd	2.55 – 2.20 = 0.35	14
Wilkinson	C-Rh	2.55 – 2.28 = 0.27	11

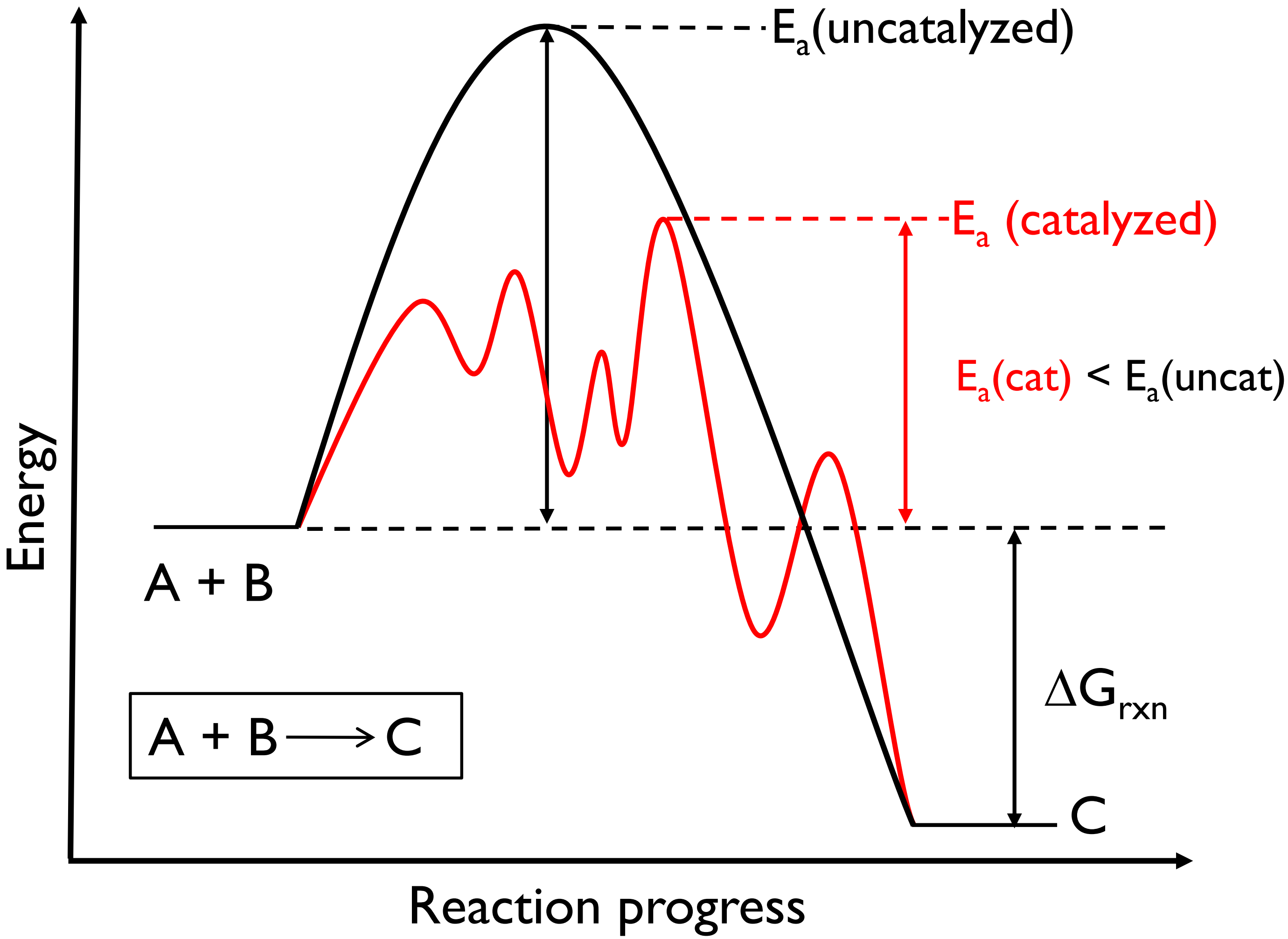
Pauling electronegativity, X

* % ionic character = $[(X_C - X_M) \div X_C]$

What is a catalyst?

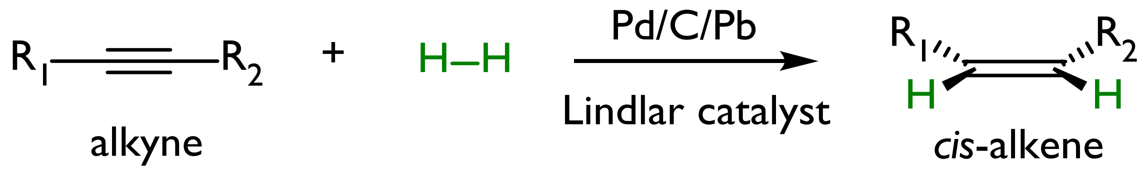
A catalyst **increases the rate of a reaction** by lowering the activation energy (E_a)

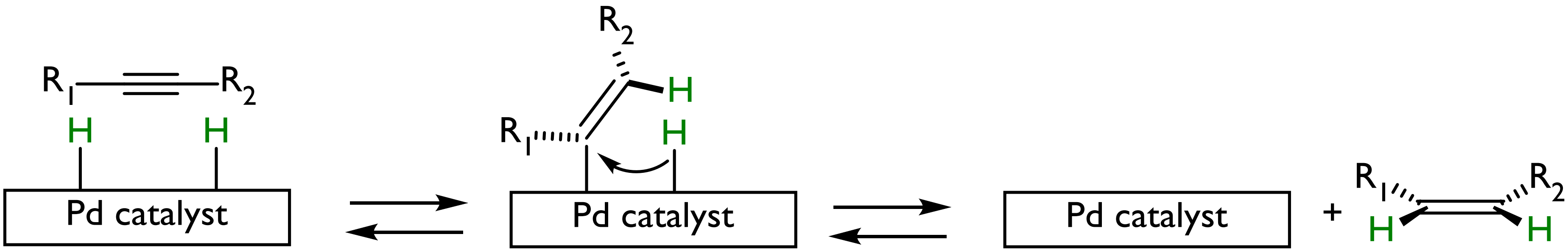
A catalyst does not change the energy of the starting materials or products



Heterogeneous vs. Homogeneous catalysis

Catalytic hydrogenation of an alkyne





The catalyst (Pd metal) and reactants (alkyne and H_2 gas) are in <u>different phases</u>

THIS IS A **HETEROGENEOUS** CATALYST SYSTEM

A **HOMOGENOUS** catalyst is in the <u>same phase</u> as the reactants (usually solution)

But metals are insoluble in organic solvents……and chemistry happens in solution

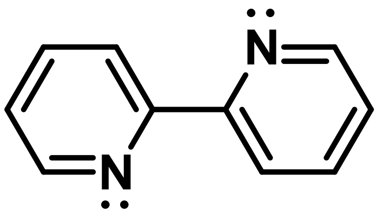
How can we make a homogeneous metal catalyst system?

Need **ligands……**

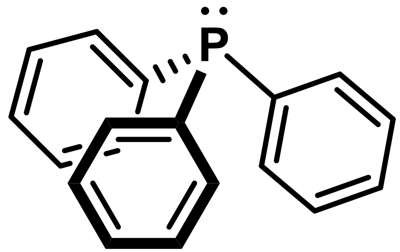
Ligands

Ligands are molecules bonded to a transition metal via donor atoms such as P, N, C, O etc.

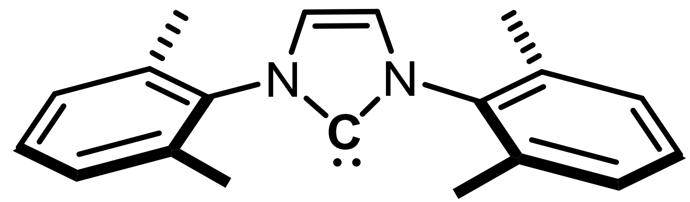
Ligands act as Lewis bases (i.e. sigma-electron donors) toward the transition metal



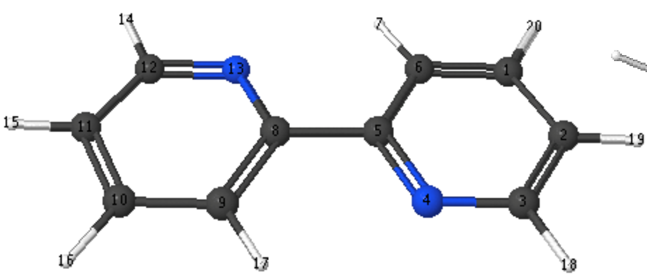
2,2'-Bipyridine (bpy)

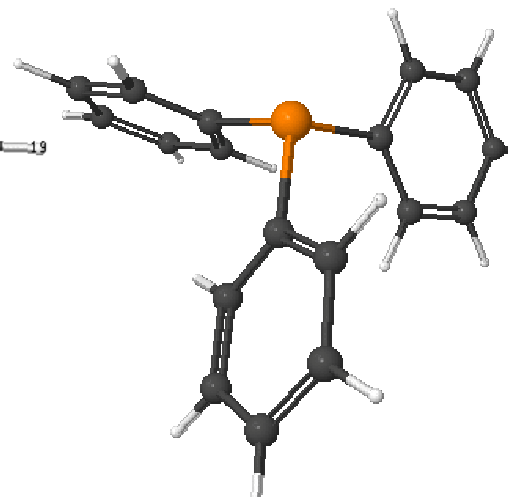


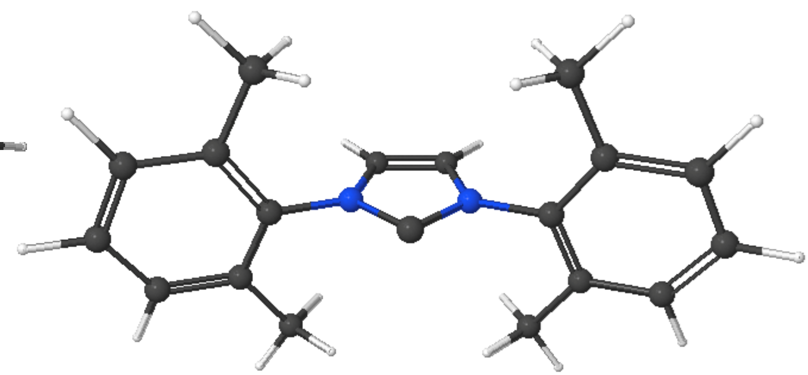
Triphenyl phosphine (PPh_3)



N-heterocyclic carbene





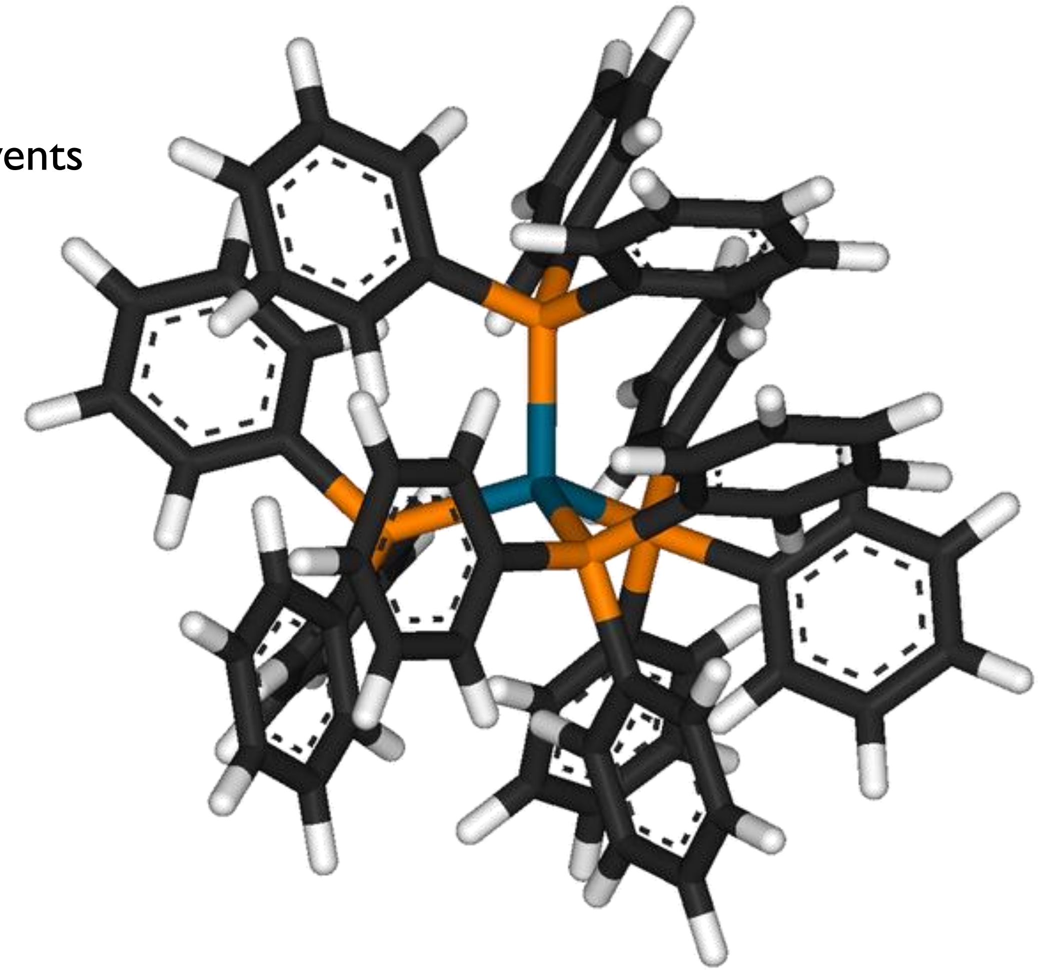


Metal-ligand compounds are called **coordination complexes**

A coordination complex of palladium

$PdCl_2 + 2\ PPh_3 \longrightarrow PdCl_2(PPh_3)_2 \quad + 2\ PPh_3 \longrightarrow Pd(PPh_3)_4$

Metal complexes are <u>soluble</u> in organic solvents



$Pd(PPh_3)_4$

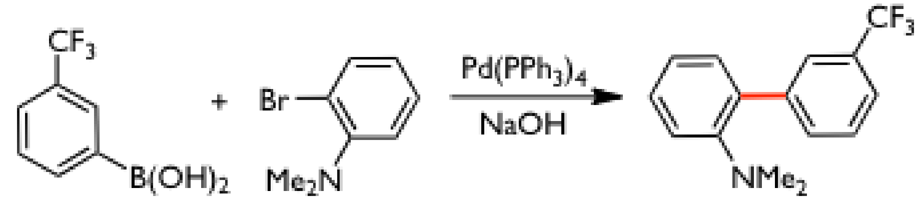
Tetrakis(triphenylphosphine)palladium

http://en.wikipedia.org/wiki/Tetrakis(triphenylphosphine)palladium(0)

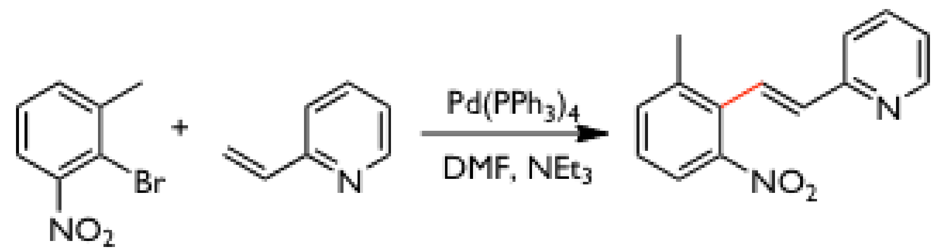
Palladium: One metal, many reactions

Pd-catalyzed C-C bond formation

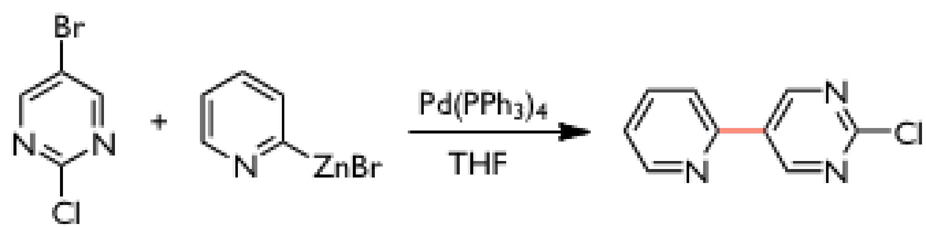
Suzuki-Miyaura



Mizoroki-Heck

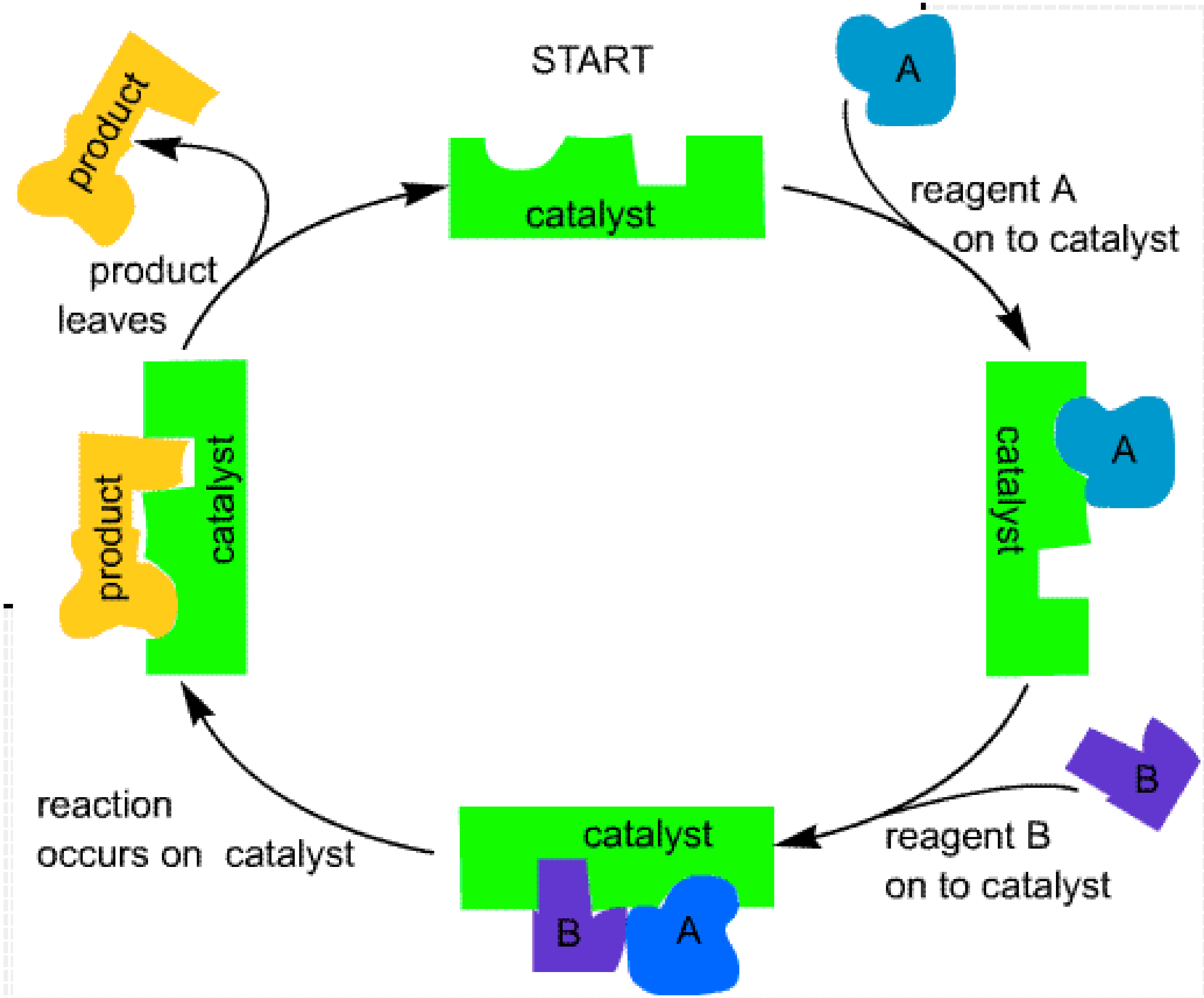


Negishi



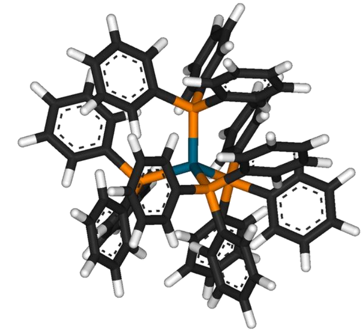
2010 Nobel Prize in Chemistry

Basics of catalytic cycle – generalized view



Understanding the catalytic cycle

Most Pd-catalyzed coupling reactions proceed via a common catalytic cycle



$$\mathrm{A{-}X} + \mathrm{M{-}R} \xrightarrow[\text{"conditions"}]{Pd(PPh_3)_4} \mathrm{A{-}R} + \mathrm{M{-}X}$$

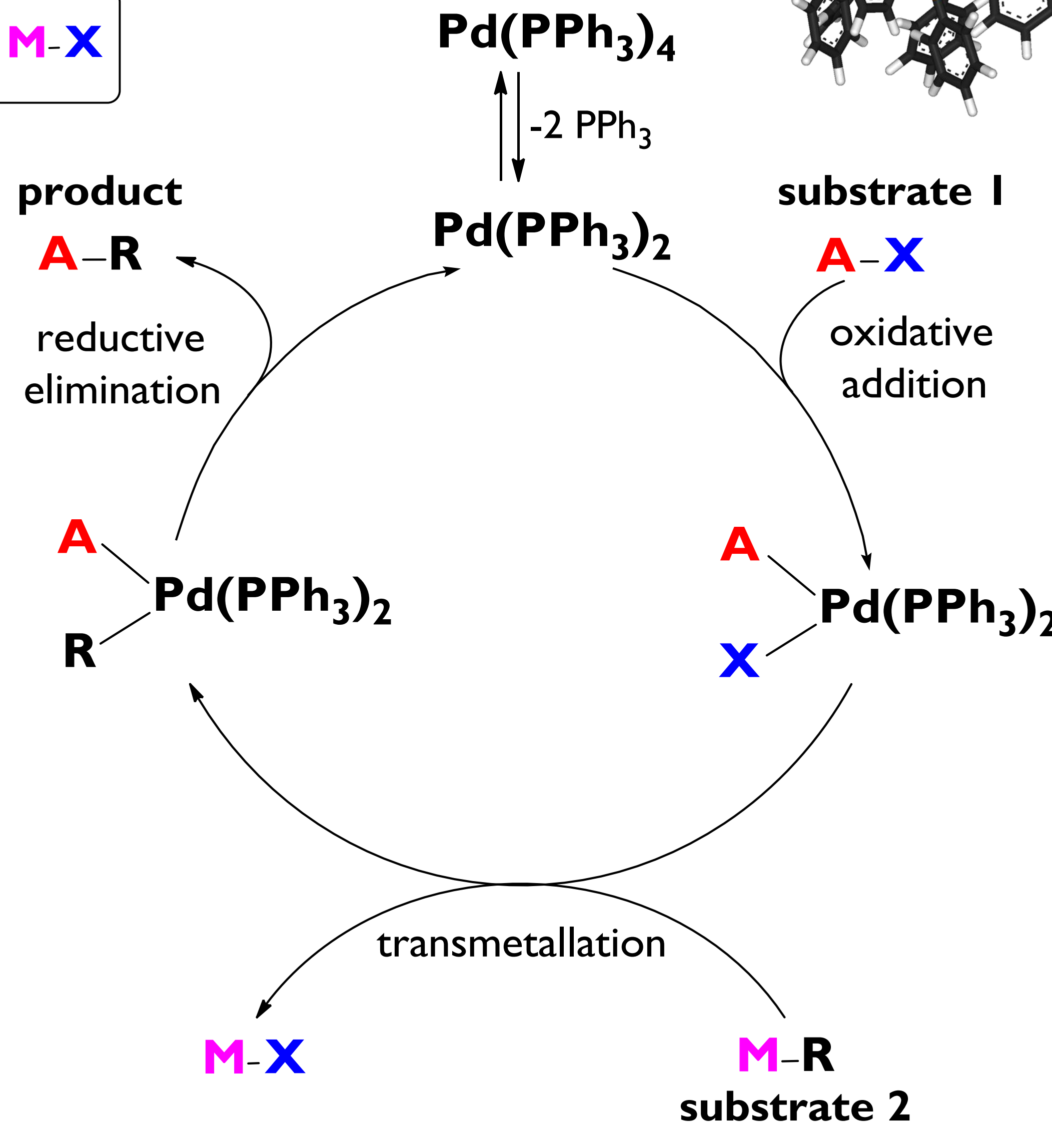
A = organic fragment 1

R = organic fragment 2

X = halide or other counter ion

M = metal atom

3 key steps



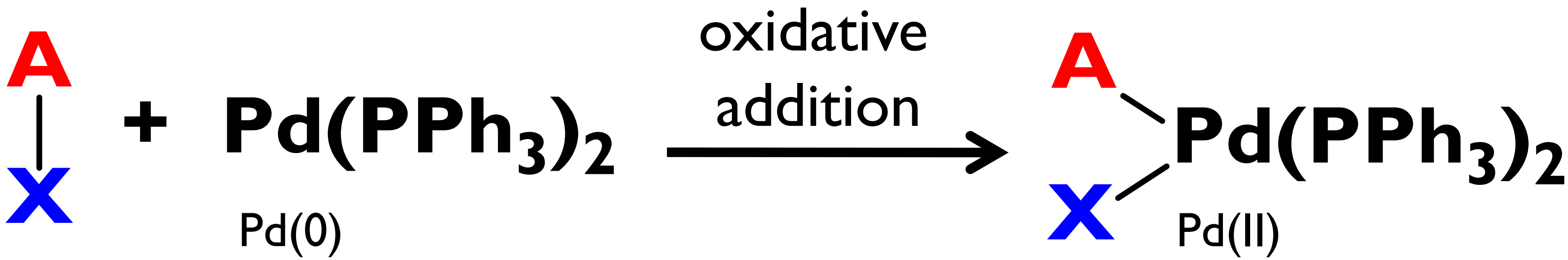
Key steps of the cycle – oxidative addition

$$A{-}X + M{-}R \xrightarrow[\text{"conditions"}]{Pd(PPh_3)_4} A{-}R + M{-}X$$

First step of typical C-C coupling catalytic cycle

Addition of a reagent (**A**-**X**) to $Pd(PPh_3)_2$ species

A-**X** is typically an **aryl, alkenyl,** or **alkynyl halide**



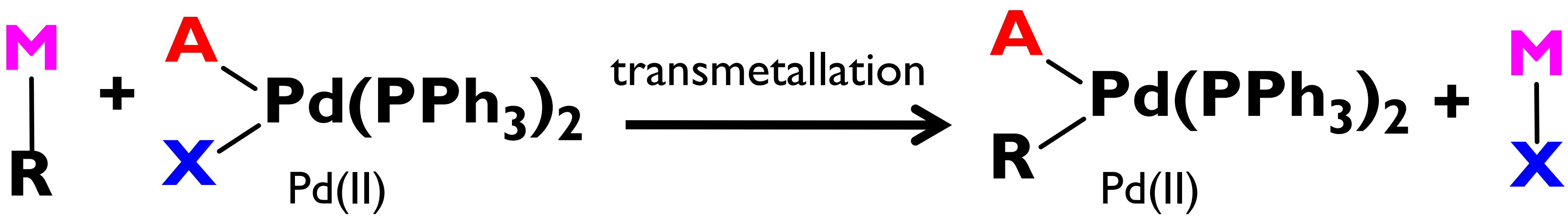
Key steps of the cycle – transmetallation

Middle step of typical C-C coupling catalytic cycle

$$A{-}X + M{-}R \xrightarrow[\text{"conditions"}]{Pd(PPh_3)_4} A{-}R + M{-}X$$

Exchange reaction between **MR** and Pd(II) species

R = aryl, alkenyl, alkynyl group   **M** = B (Suzuki), Sn (Stille), Mg (Kumada), Zn (Negishi)



Organic group (**R**) replaces **X** on Pd

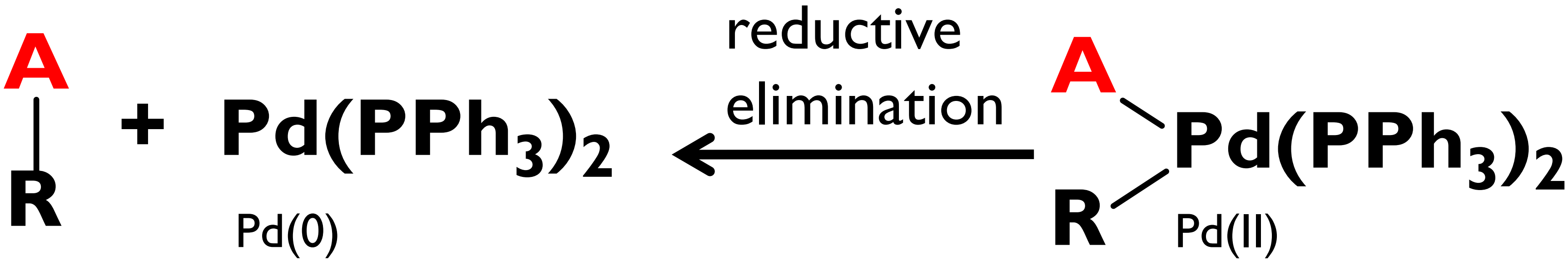
Drive toward less polar C-M bond in transmetallation product

Key steps of the cycle – reductive elimination

$$A{-}X + M{-}R \xrightarrow[\text{"conditions"}]{Pd(PPh_3)_4} A{-}R + M{-}X$$

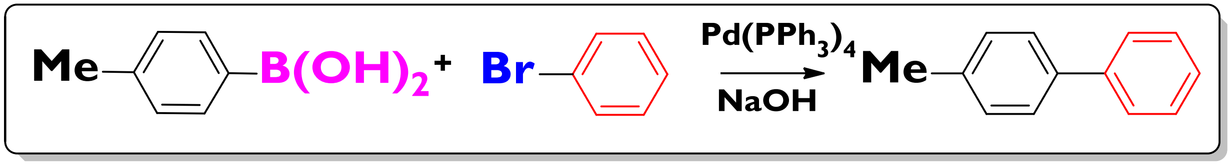
Final step of typical C-C coupling catalytic cycle

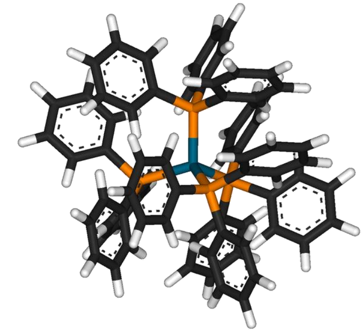
Elimination of product (**A**-**R**) from Pd atom



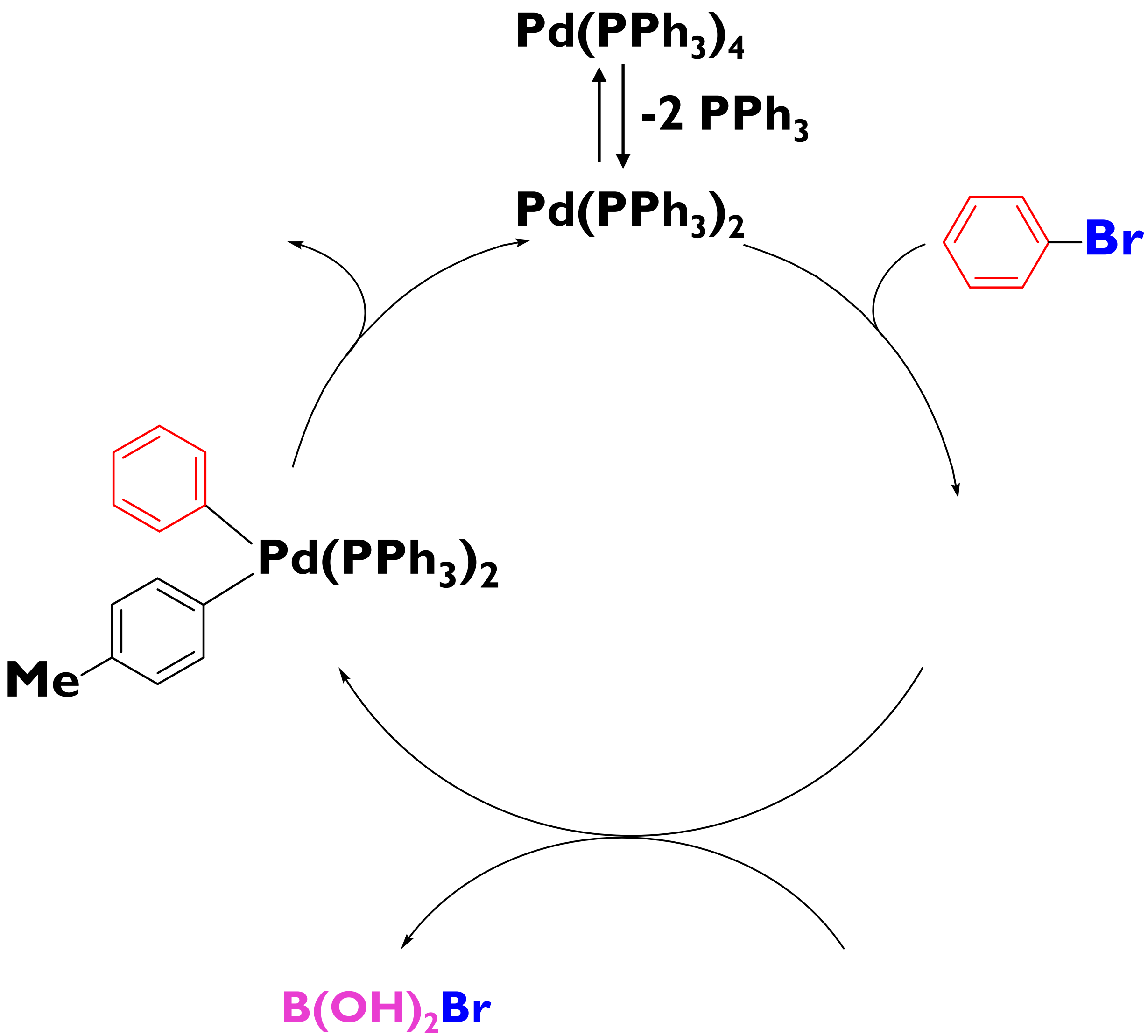
Coupling product **A**-**R** released, active catalyst $Pd(PPh_3)_2$ reformed

Suzuki coupling – the catalytic cycle





$Pd(PPh_3)_4$



Summary

Organometallic chemistry

- the chemistry of compounds containing a C-M bond
- enables "impossible" organic reactions to occur

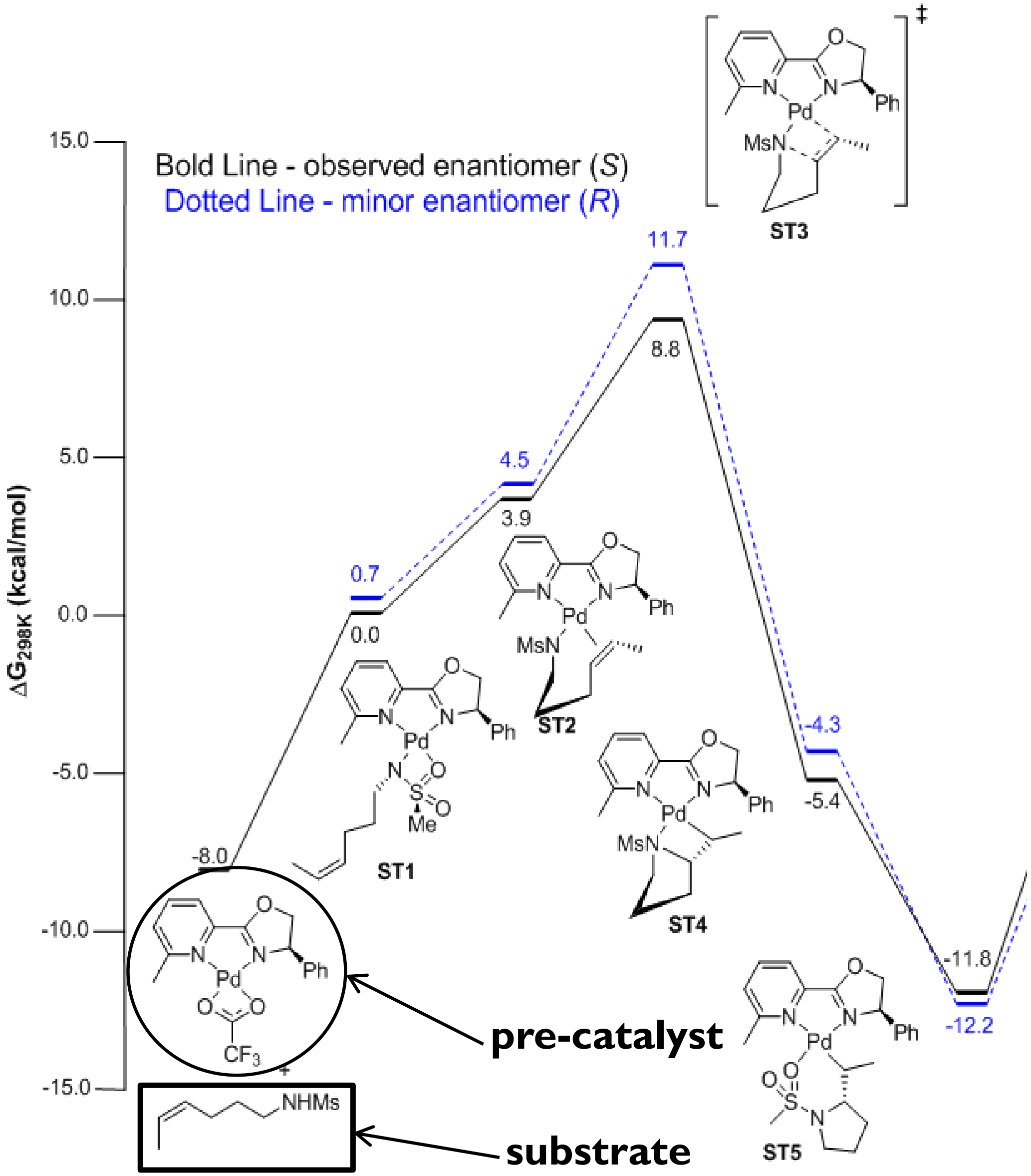
Organolithium and Grignard reagents

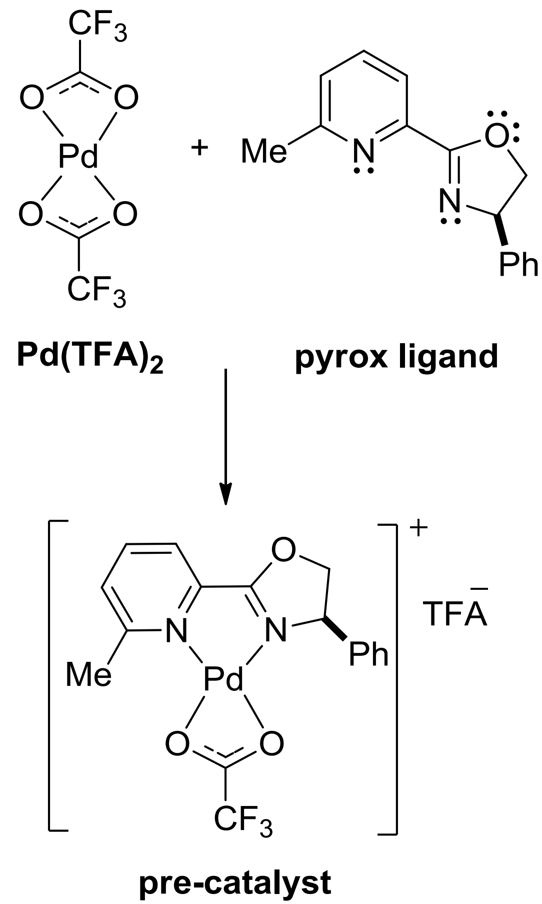
- polar C-M bond, carbanion character, strong bases, reactive toward carbonyl and acidic groups
- used in stoichiometric (1:1 or greater) amounts

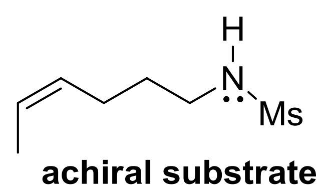
Transition metal-ligand complexes

- ligands coordinate to transition metal to form complex, soluble in organic solvents
- complexes serve as catalysts for organic reactions
- a catalyst lowers E_a of a reaction, is not consumed (turnover), sub-stoichiometric amount
- chemistry takes place on metal atom ("bind/react/release")
- catalytic coupling cycle: oxidative addition, transmetallation, reductive elimination
- Pd-catalyzed C-C bond forming reactions are hugely important in pharma and industry
- **Practice problem set!**

An example from current research
Pd-catalyzed amidation of alkenes







Ms = -SO_2Me

Stahl, S. S. *Org. Lett.* **2011**, *13*, 2830-2833.

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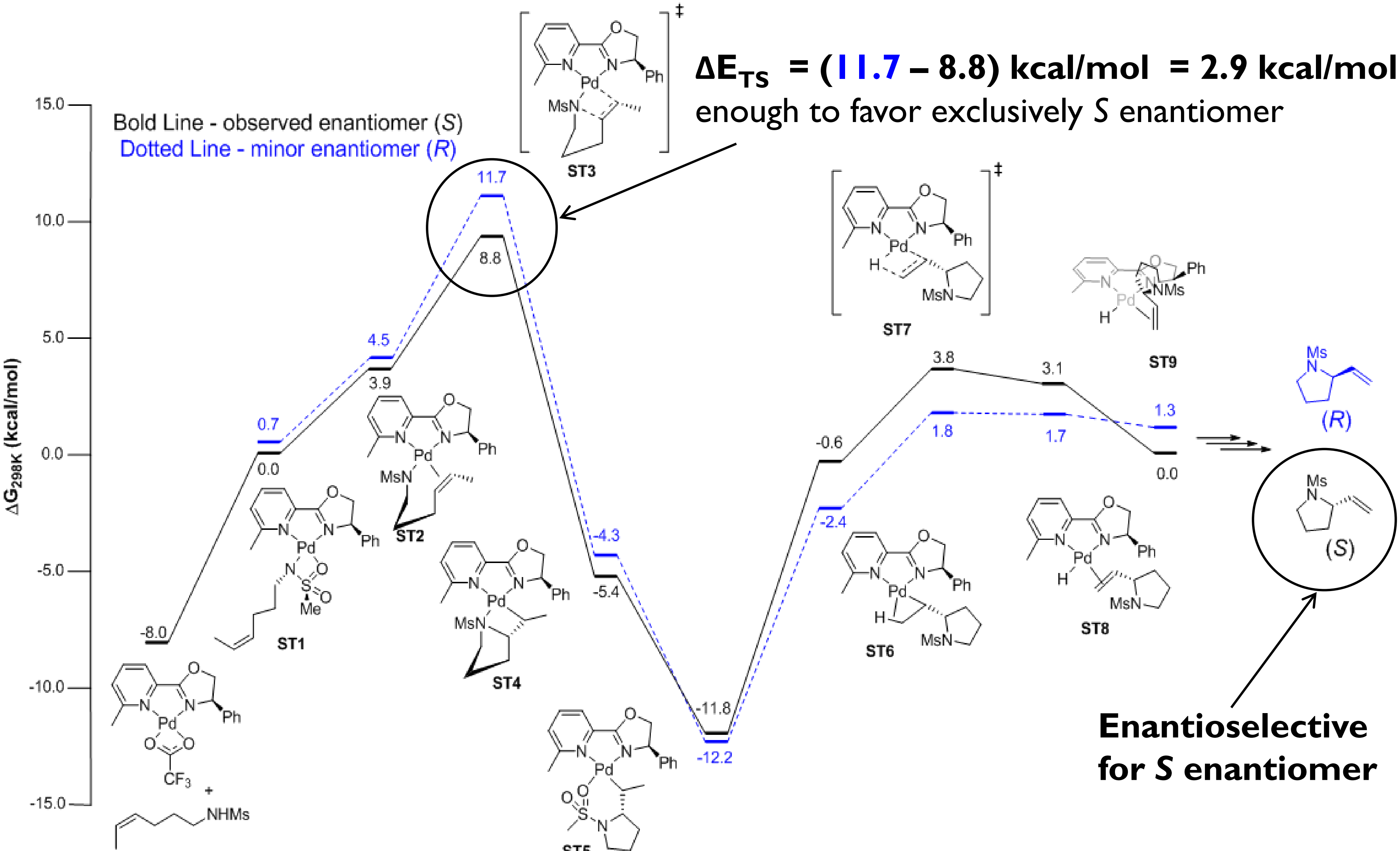
Pd-catalyzed amidation of alkenes



ΔE_{TS} = (11.7 – 8.8) kcal/mol = 2.9 kcal/mol

enough to favor exclusively *S* enantiomer

Enantioselective for *S* enantiomer

Stahl, S. S. *Org. Lett.* **2011**, *13*, 2830-2833.