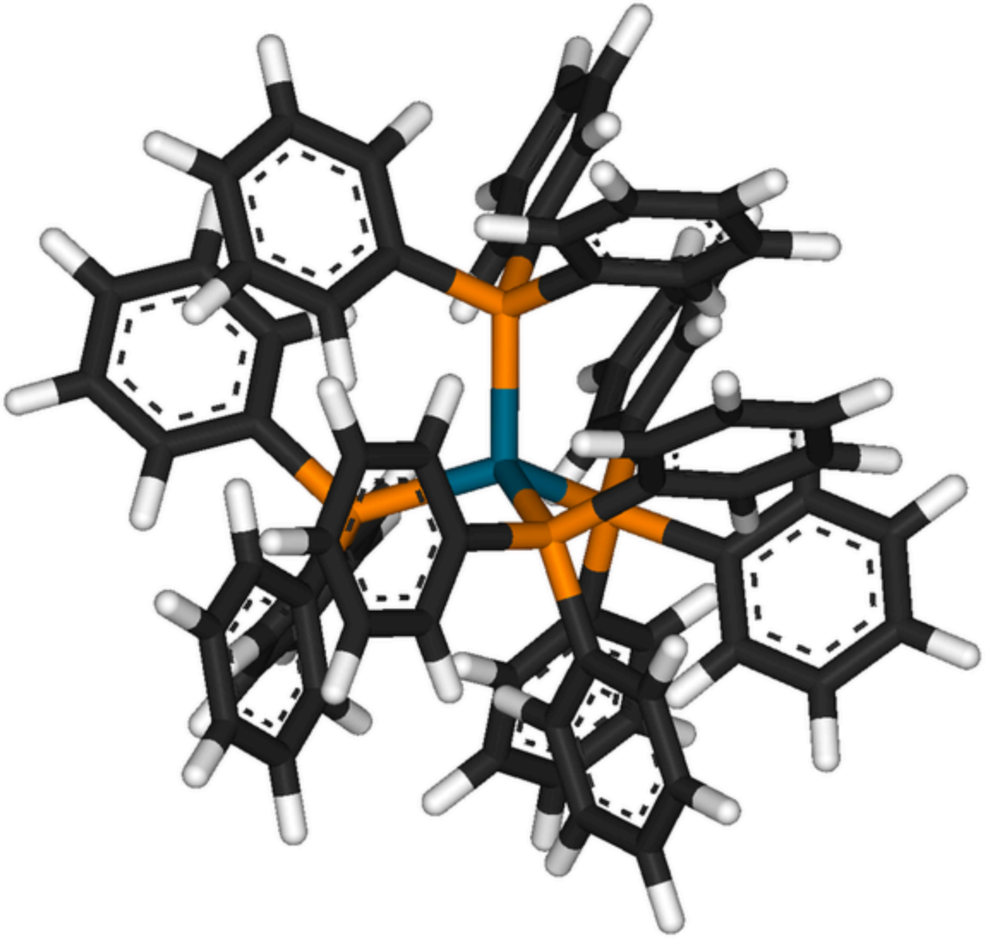
344 | Organic Chemistry Laboratory
Summer 2013



Lecture 6 Transition metal organometallic chemistry and catalysis
July 30 2013

Summary of Grignard lecture

Organometallic chemistry

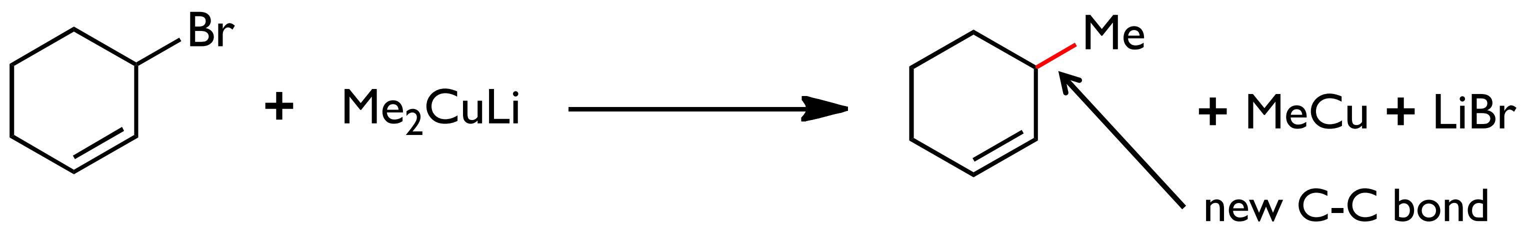
- the chemistry of compounds containing a C-M bond
- intersection of organic and inorganic chemistry
- allows "impossible" organic reactions to occur

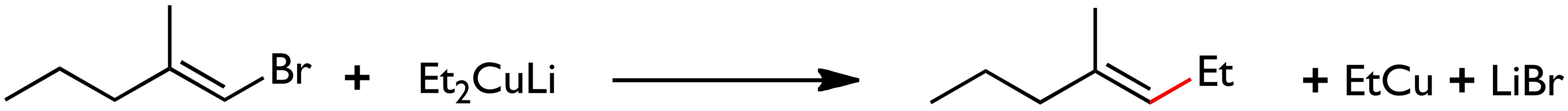
Organolithium and Grignard reagents

- 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



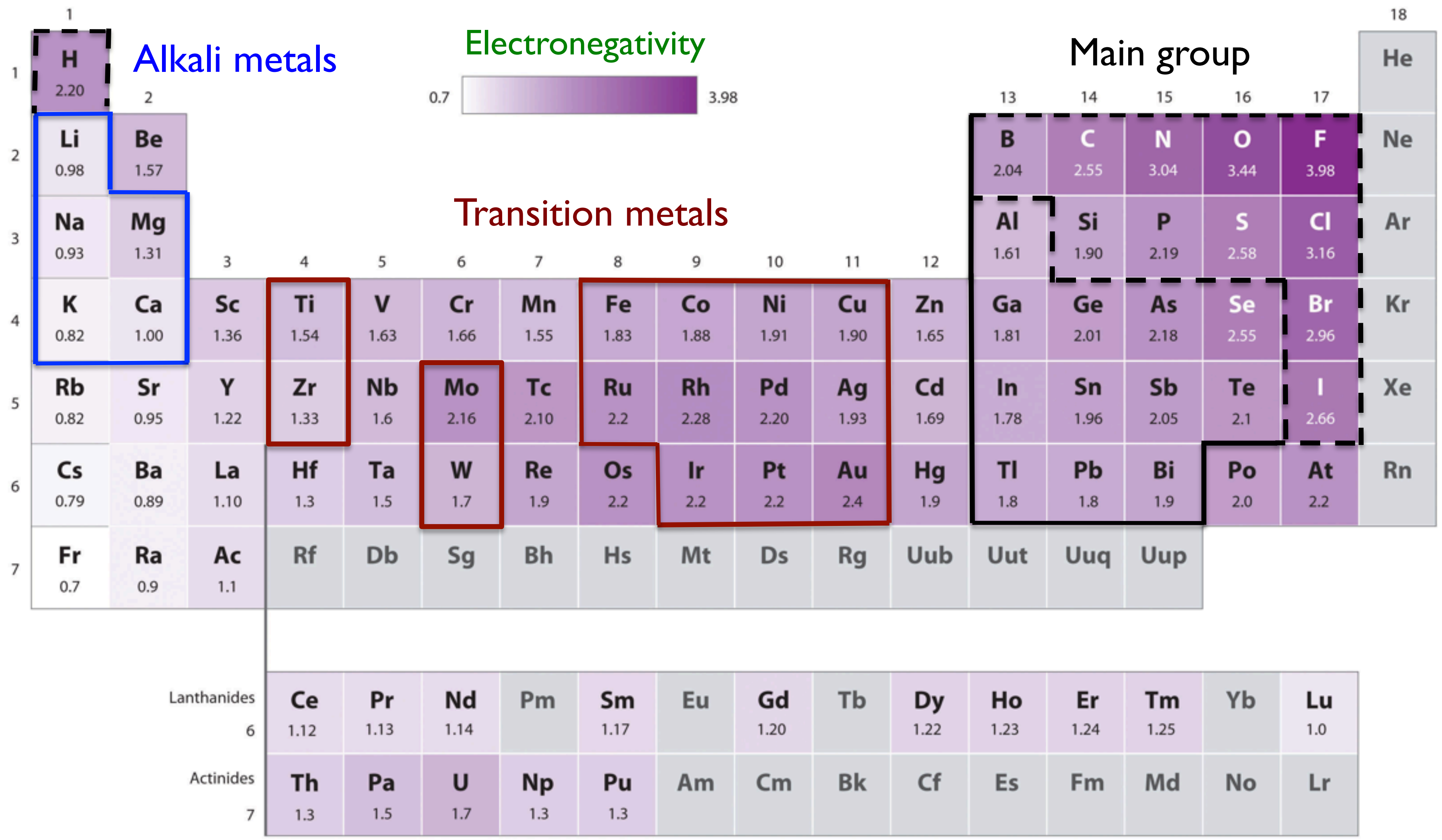


Pro: joins (“couples”) 2 different R groups to form a new C-C bond

Con: requires a **stoichiometric** amount of reagent

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

Periodic Table – common organometallics



Alkali metals

Electronegativity

0.7 ▨ 3.98

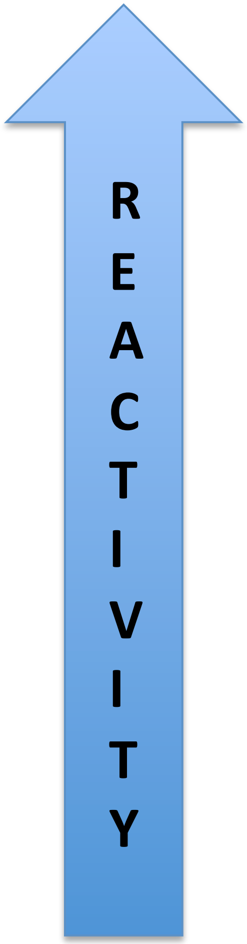
Transition metals

Main group

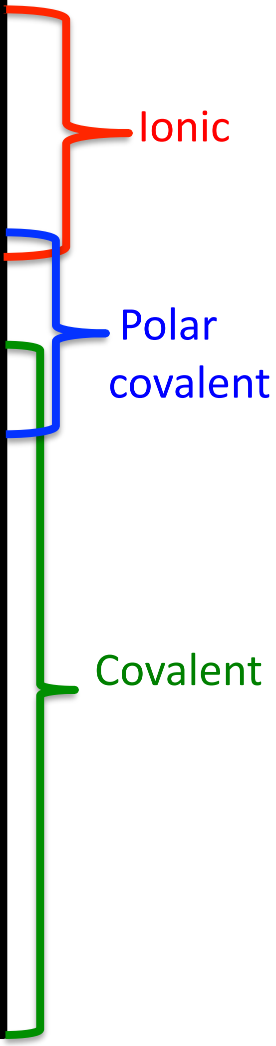
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	H 2.20																	He
2	Li 0.98	Be 1.57											B 2.04	C 2.55	N 3.04	O 3.44	F 3.98	Ne
3	Na 0.93	Mg 1.31											Al 1.61	Si 1.90	P 2.19	S 2.58	Cl 3.16	Ar
4	K 0.82	Ca 1.00	Sc 1.36	Ti 1.54	V 1.63	Cr 1.66	Mn 1.55	Fe 1.83	Co 1.88	Ni 1.91	Cu 1.90	Zn 1.65	Ga 1.81	Ge 2.01	As 2.18	Se 2.55	Br 2.96	Kr
5	Rb 0.82	Sr 0.95	Y 1.22	Zr 1.33	Nb 1.6	Mo 2.16	Tc 2.10	Ru 2.2	Rh 2.28	Pd 2.20	Ag 1.93	Cd 1.69	In 1.78	Sn 1.96	Sb 2.05	Te 2.1	I 2.66	Xe
6	Cs 0.79	Ba 0.89	La 1.10	Hf 1.3	Ta 1.5	W 1.7	Re 1.9	Os 2.2	Ir 2.2	Pt 2.2	Au 2.4	Hg 1.9	Tl 1.8	Pb 1.8	Bi 1.9	Po 2.0	At 2.2	Rn
7	Fr 0.7	Ra 0.9	Ac 1.1	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Uub	Uut	Uuq	Uup			

Lanthanides 6	Ce 1.12	Pr 1.13	Nd 1.14	Pm	Sm 1.17	Eu	Gd 1.20	Tb	Dy 1.22	Ho 1.23	Er 1.24	Tm 1.25	Yb	Lu 1.0
Actinides 7	Th 1.3	Pa 1.5	U 1.7	Np 1.3	Pu 1.3	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

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
C-Mg	2.55 – 1.31 = 1.24	48
C-Ti	2.55 – 1.54 = 1.01	40
C-Al	2.55 – 1.61 = 0.94	37
C-Cu	2.55 – 1.90 = 0.65	25
C-B	2.55 – 2.04 = 0.51	20
C-Cl	2.55 – 3.16 = - 0.61	24
C-Br	2.55 – 2.96 = - 0.41	16
C-H	2.55 – 2.20 = 0.35	14

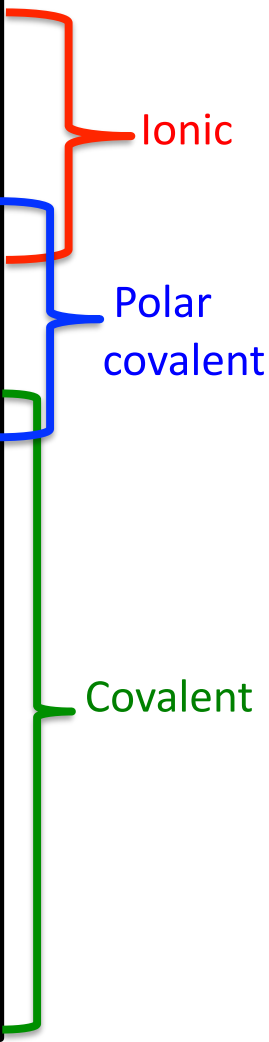


\# Pauling electronegativity, X

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

Carbon-Metal bond polarity

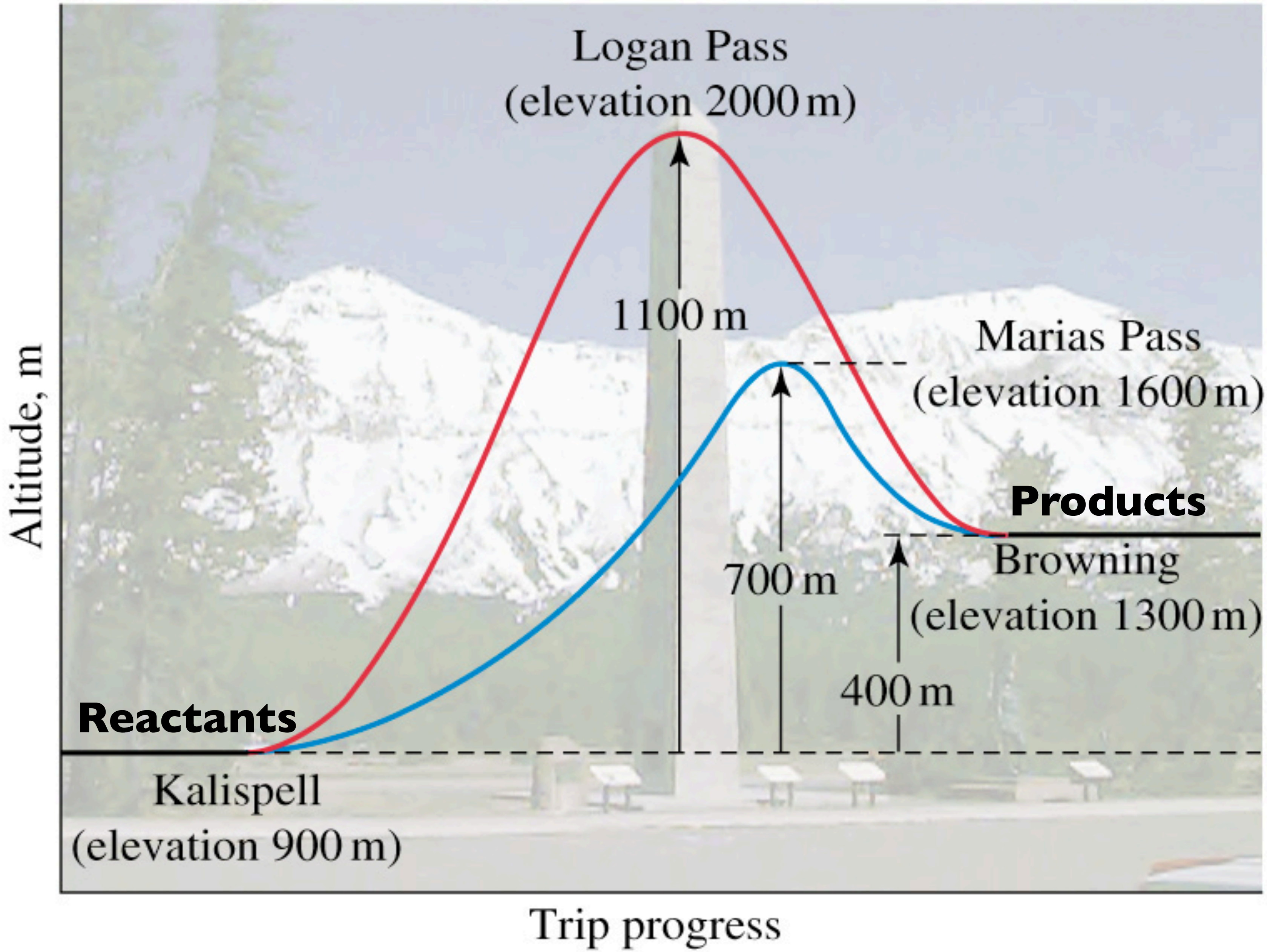
	C-M bond	**Δ Electronegativity[#]**	**% ionic character***
	C-K	2.55 – 0.82 = 1.73	68
	C-Na	2.55 – 0.93 = 1.62	63
	C-Li	2.55 – 0.98 = 1.57	61
Grignard	C-Mg	2.55 – 1.31 = 1.24	48
Ziegler-Natta	C-Ti	2.55 – 1.54 = 1.01	40
Gilman	C-Cu	2.55 – 1.90 = 0.65	25
Schrock	C-Mo	2.55 – 2.06 = 0.49	19
Grubbs	C-Ru	2.55 – 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?

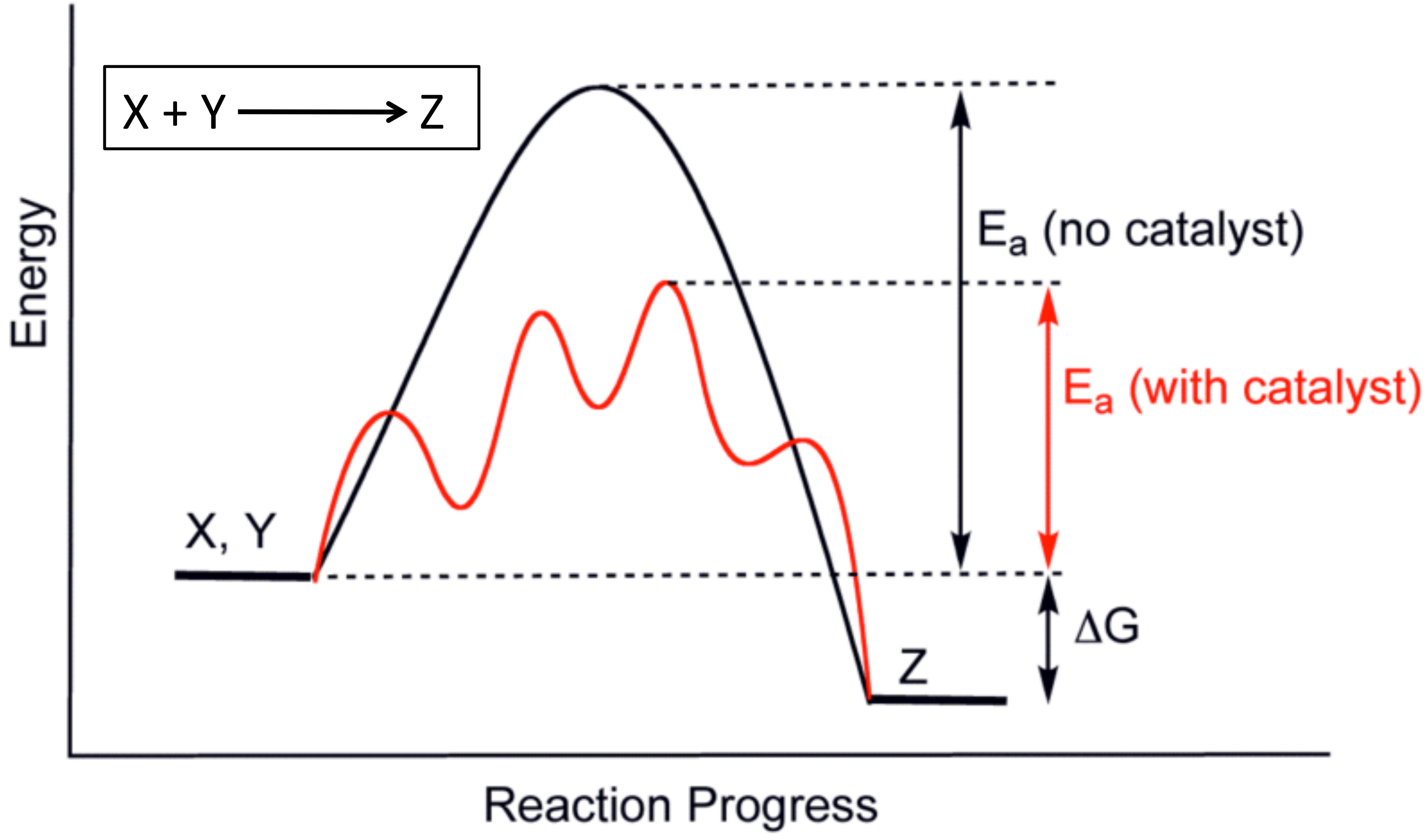


What is a catalyst?

Many reactions are favorable thermodynamically but proceed slowly at room temp/pressure

A catalyst **increases the rate of a reaction** by lowering the activation energy (Ea)
Changes the kinetics of a reaction

A catalyst does not change the energy of the starting materials, intermediates, or products
Does not change the thermodynamics of a reaction

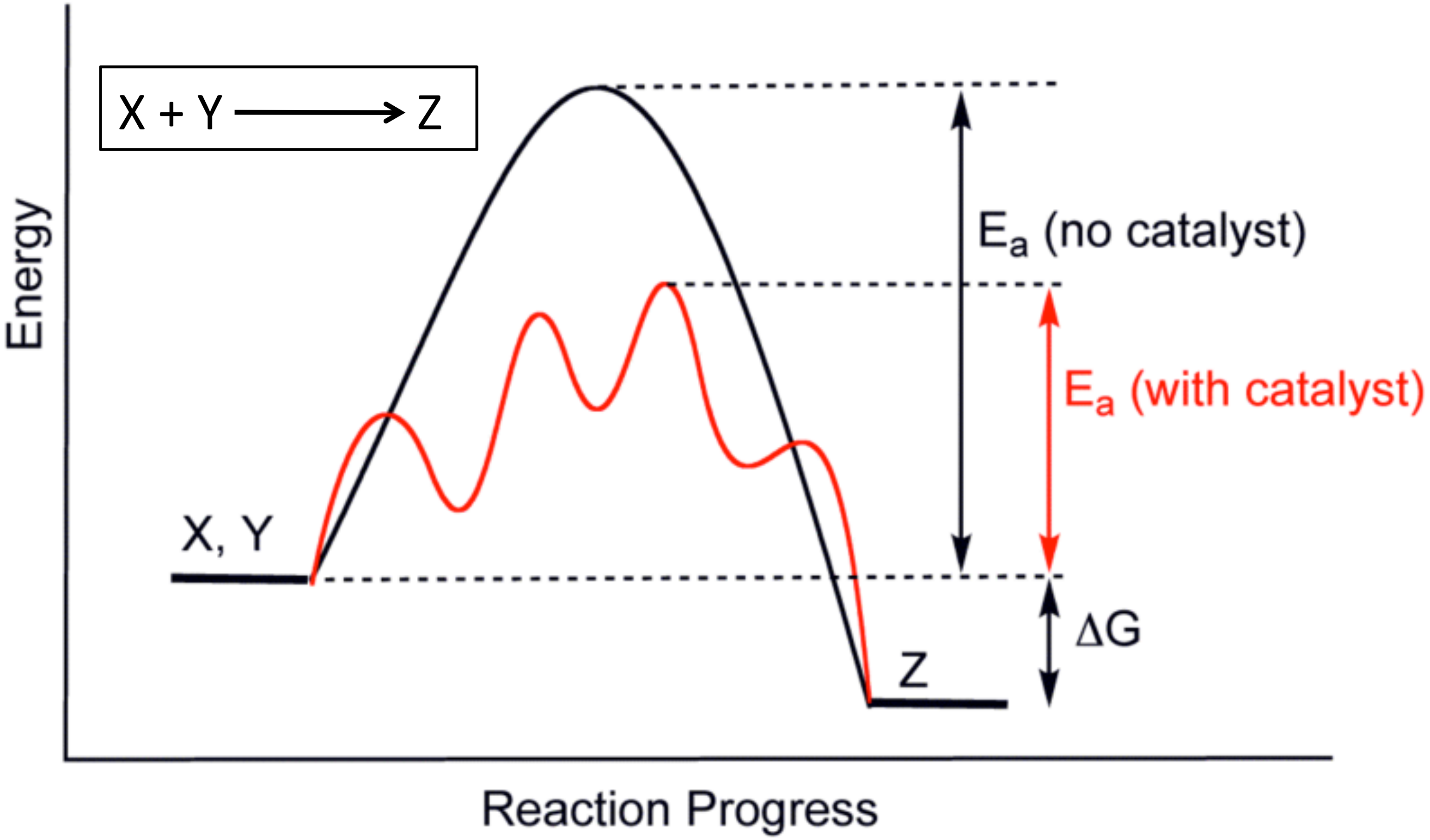


What is a catalyst?

A catalyst alters the mechanism but the reaction is still faster because the catalyst lowers Ea

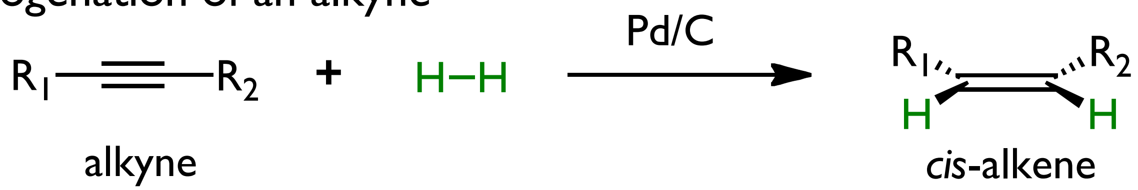
A catalyst is a species that is added to a reaction in order that the reaction takes place faster (i.e. at an increased rate) than it would in the absence of a catalyst

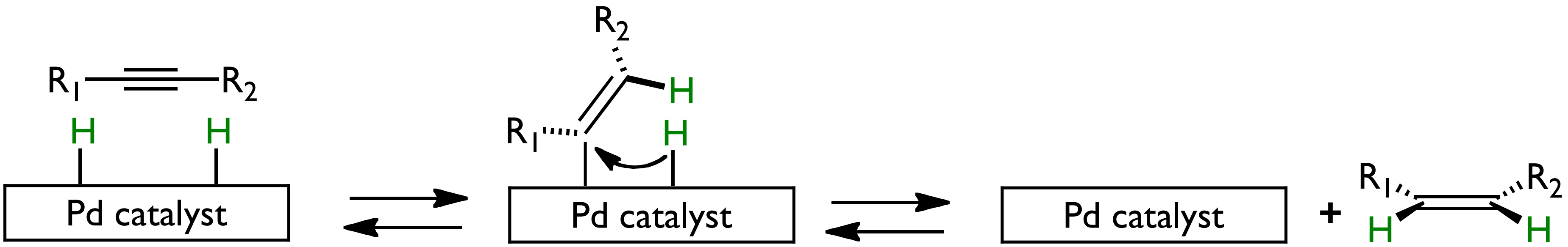
The C-C coupling reactions we highlight do not occur without a catalyst



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

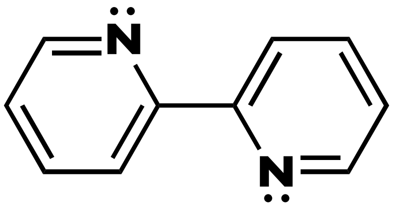
How can we make a homogeneous metal catalyst system?

Need **ligands……**

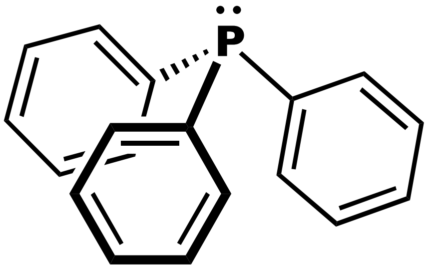
Ligands

Ligands are molecules bonded to a transition metal via “organic” elements such as C, N, O, P etc.

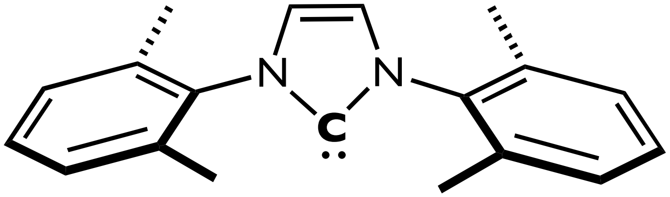
Ligands act as Lewis bases (i.e. sigma-electron donors) toward the transition metal



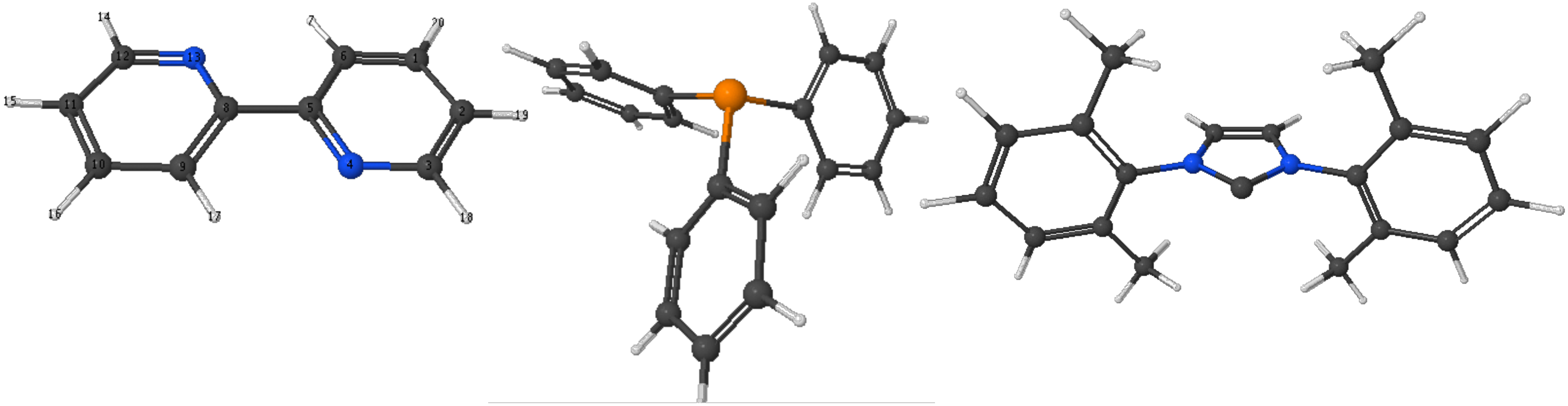
2,2’-Bipyridine (bpy)



Triphenyl phosphine (PPh_3)



N-heterocyclic carbene



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

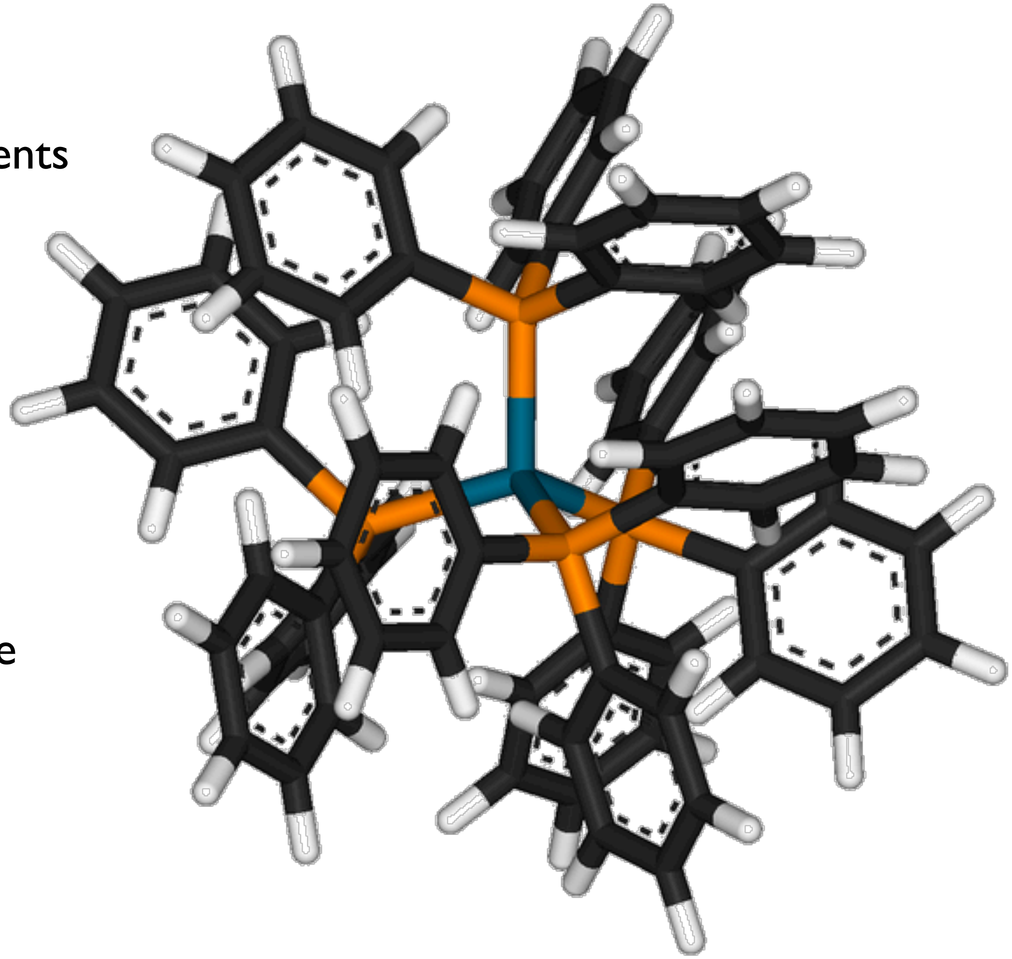
A coordination complex of palladium

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

Metal complexes are soluble in organic solvents

Ligands are vital because they……

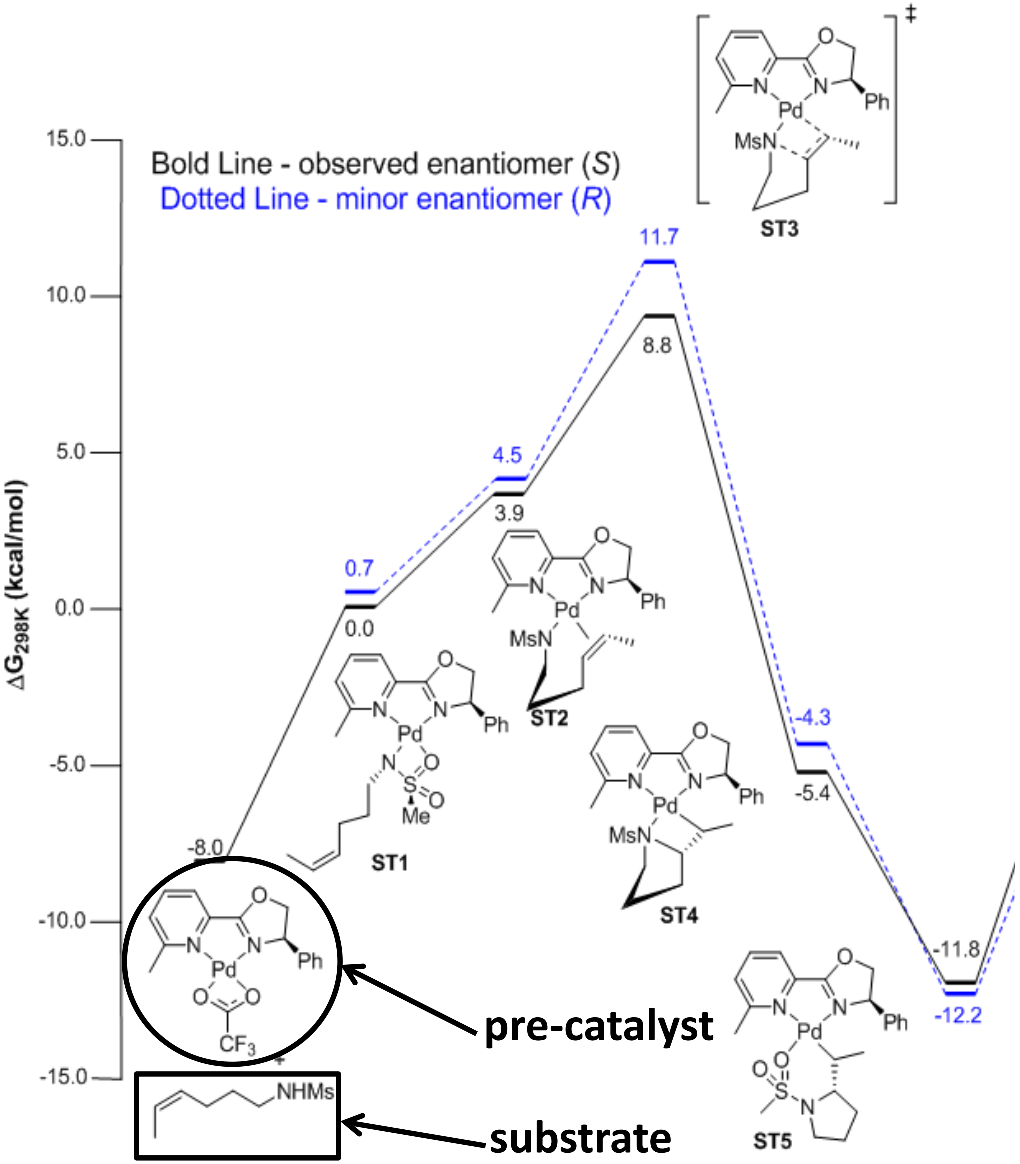
- bind to metal "just right"
- dissociate from metal to open an active site
- control size and shape of active site

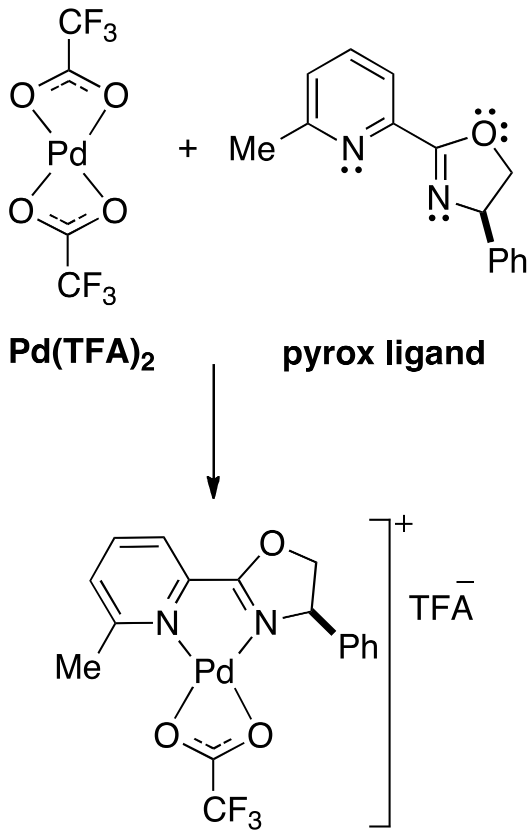


$Pd(PPh_3)_4$

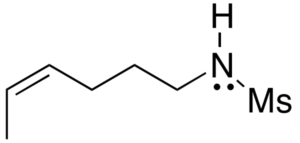
Tetrakis(triphenylphosphine)palladium

From WebMO lecture 2
Pd-catalyzed amidation of alkenes





pre-catalyst

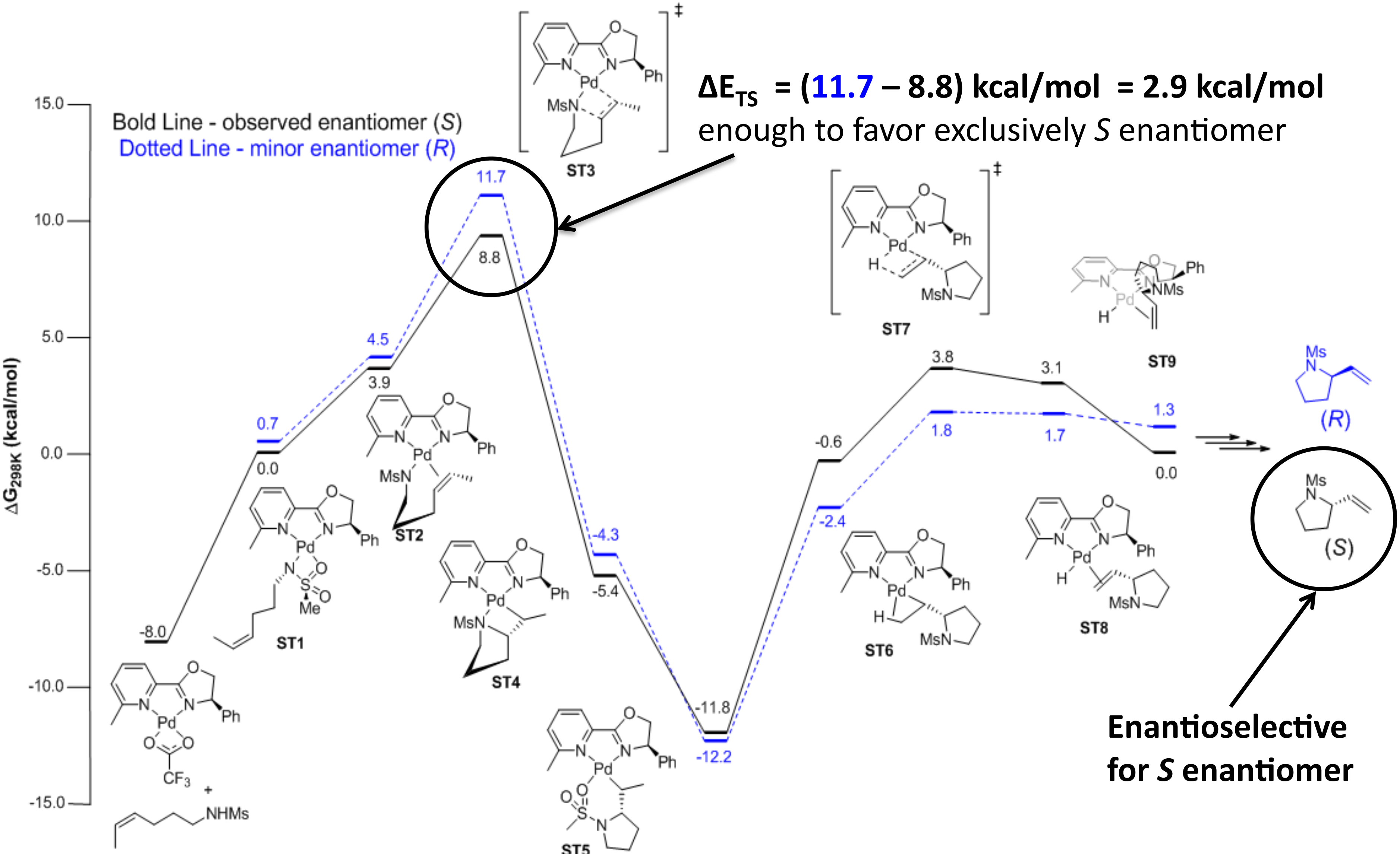


achiral substrate

Ms = $-SO_2Me$

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

From WebMO lecture 2
Pd-catalyzed amidation of alkenes



ΔE_{TS} = (11.7 – 8.8) kcal/mol = 2.9 kcal/mol
enough to favor exclusively *S* enantiomer

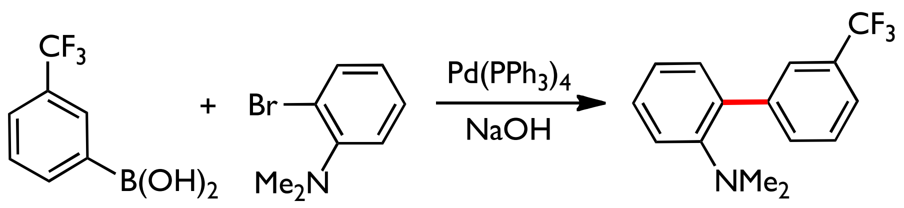
Enantioselective for *S* enantiomer

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

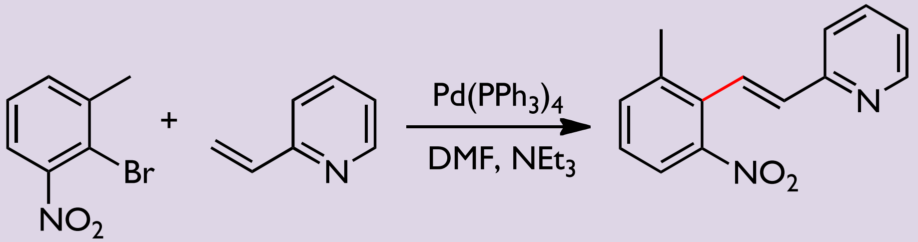
Palladium: One metal, many reactions

Pd-catalyzed C-C bond formation

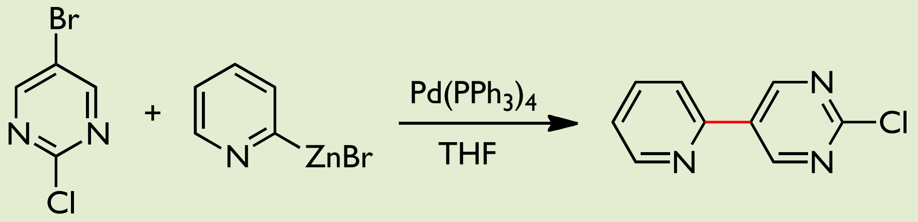
Suzuki



Heck

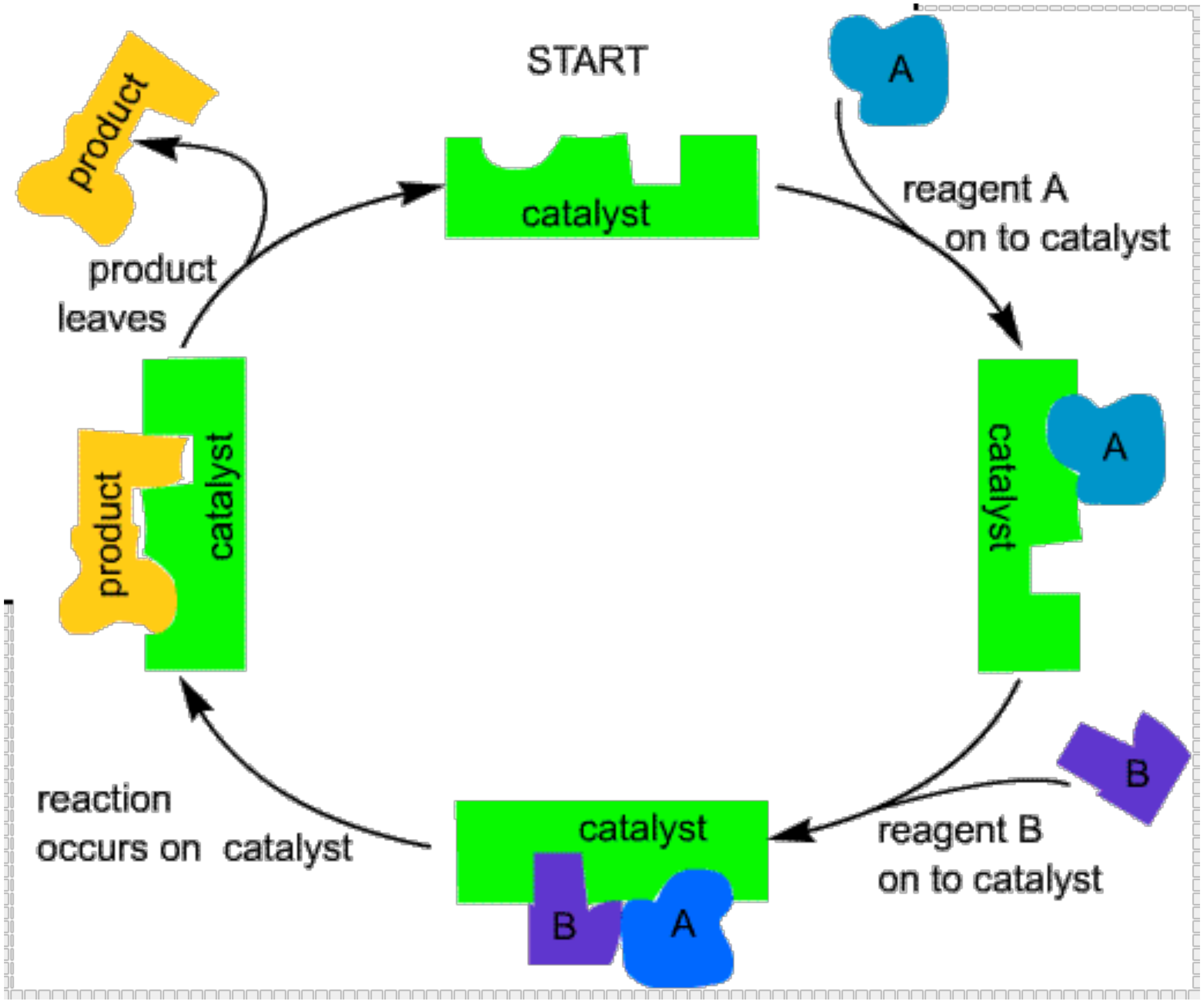


Negishi



2010 Nobel Prize in Chemistry

Basics of catalytic cycle

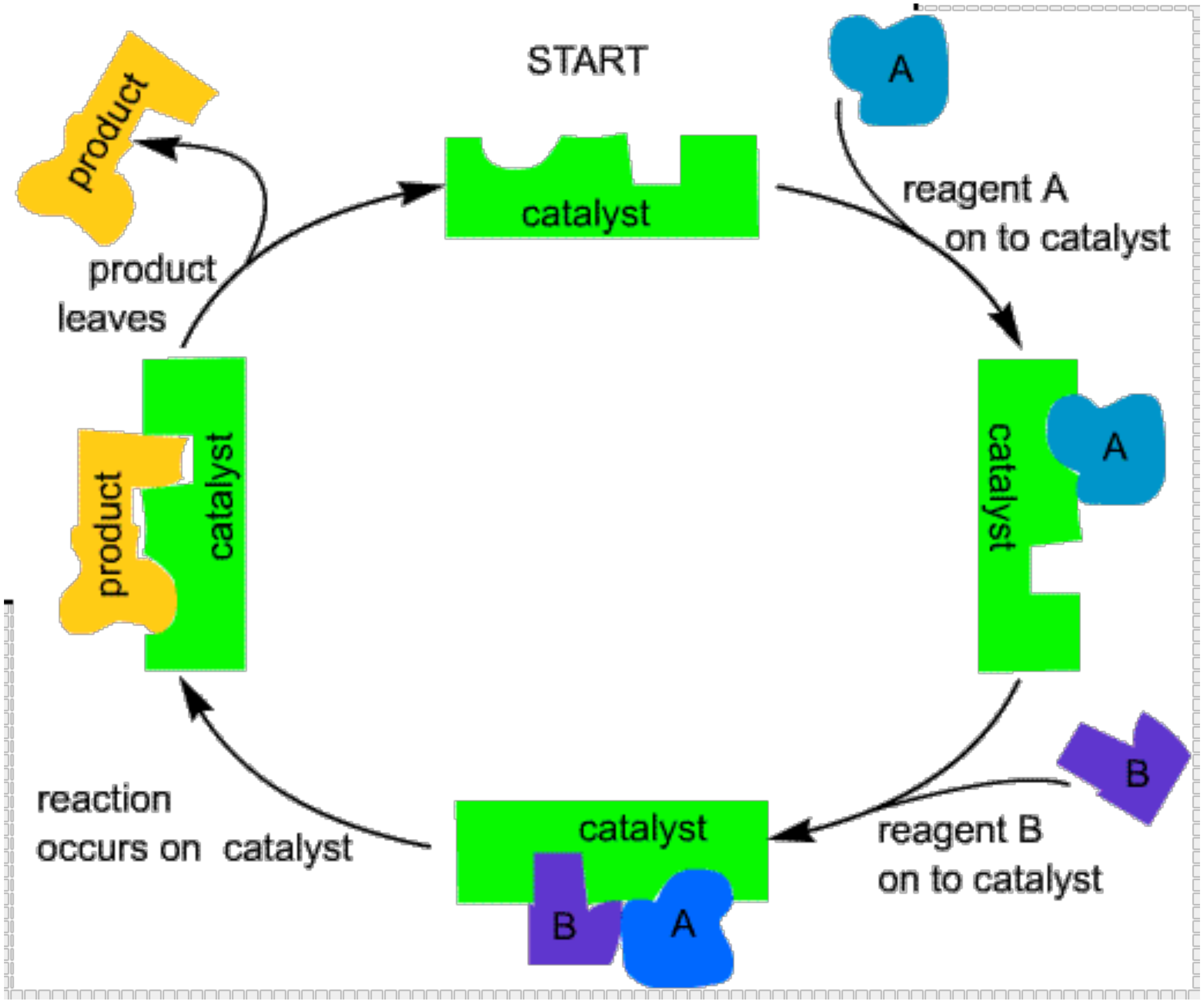


Reactions occur in the coordination sphere of the metal

Substrates (A and B) bind to the metal catalyst to undergo bond breaking and bond forming

Catalytically active species is reformed upon release of products

Basics of catalytic cycle



Each cycle produces one molecule of product

Catalyst is regenerated at the end of each cycle (a "turnover") **NOT CONSUMED**

Catalysts can undergo 10^3-10^6 (or more) turnovers before decomposing

Understanding the catalytic cycle

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

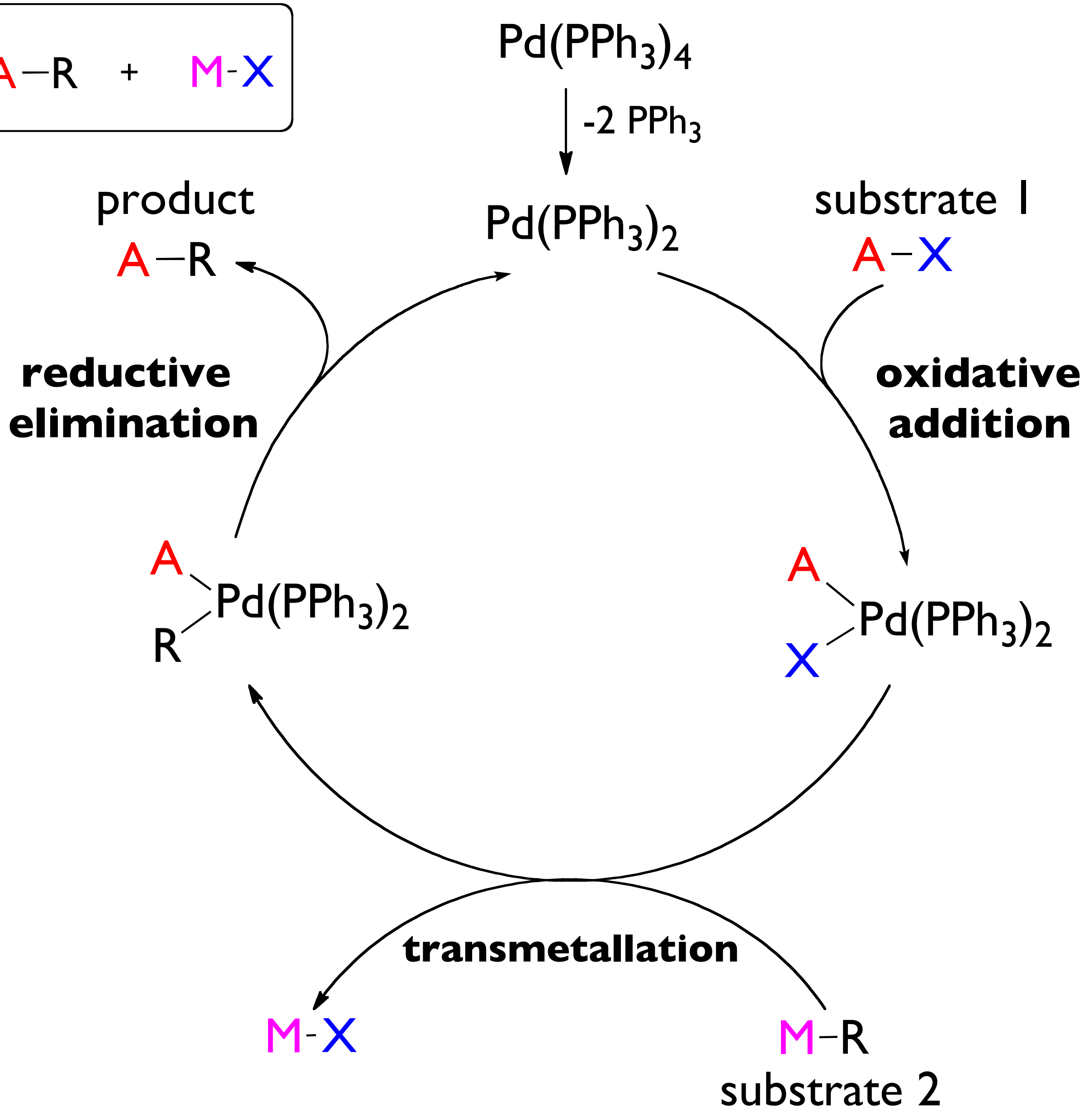
$$A{-}X \quad + \quad M{-}R \xrightarrow[\text{"conditions"}]{Pd(PPh_3)_4} A{-}R \quad + \quad M{-}X$$

3 key steps

a) Oxidative addition

b) Transmetallation

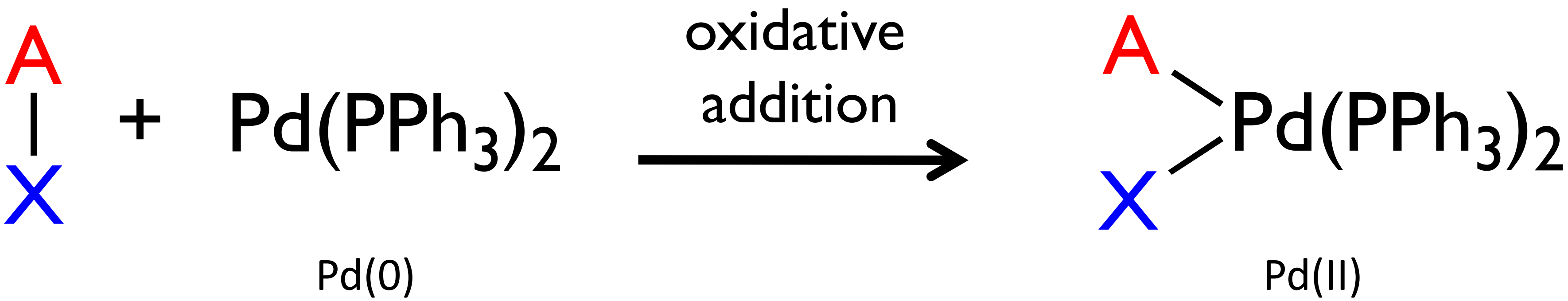
c) Reductive elimination



Key steps of the cycle – oxidative addition

First step of typical C-C coupling catalytic cycle

Addition of a reagent (A-X) to a metal atom



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

Pd oxidation state increases by 2 (Pd^0 to Pd^{II}) (oxidation potential = -0.92 V)

Pd coordination number increase by 2

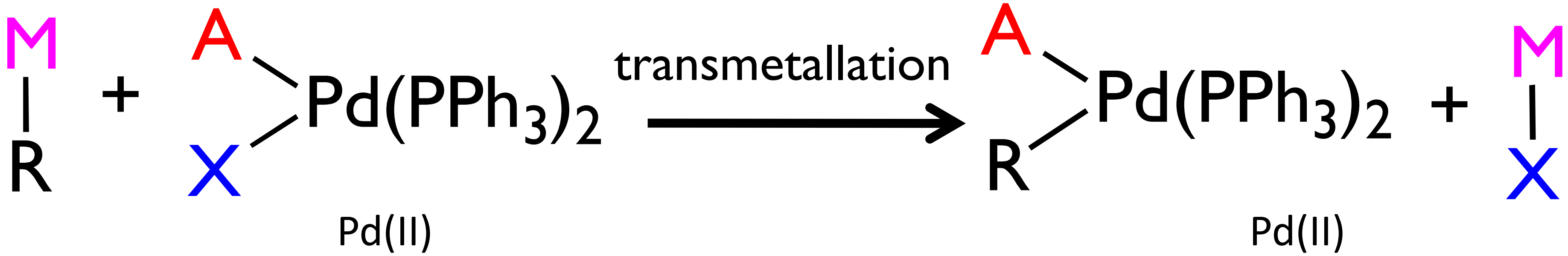
Recall – a very similar step occurs when making a Grignard reagent

Key steps of the cycle – transmetallation

Middle step of typical C-C coupling catalytic cycle

Exchange reaction between MR and Pd(II) species

Drive toward less polar C-M bond in product



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

Organic group (R) becomes bonded to Pd and MX is released

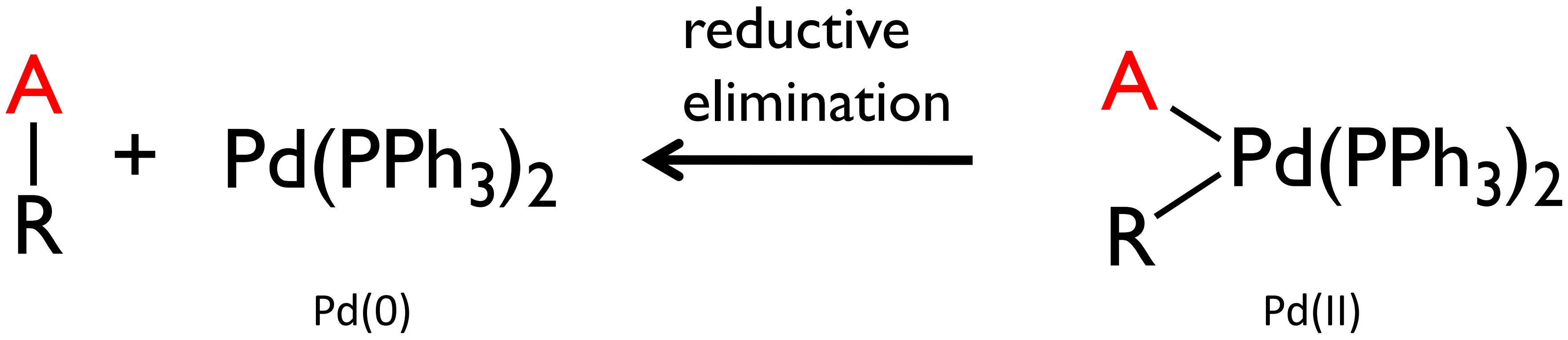
The two organic fragments to be coupled (A and R) are now on the Pd atom

Pd oxidation state and coordination number unchanged

Key steps of the cycle – reductive elimination

Last step of typical C-C coupling catalytic cycle

Elimination of product (A-R) from metal atom



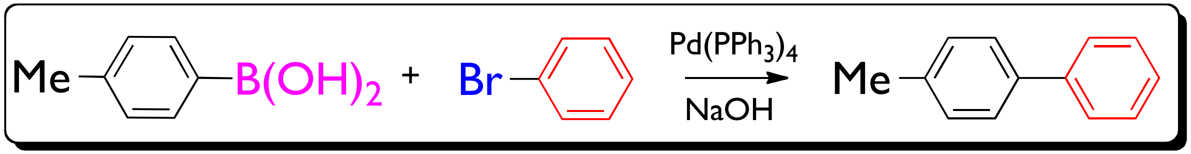
Coupling product A-R released, active catalyst reformed

Pd oxidation state decreases by 2 (Pd^{II} to Pd^{0}) (reduction potential = -0.92 V)

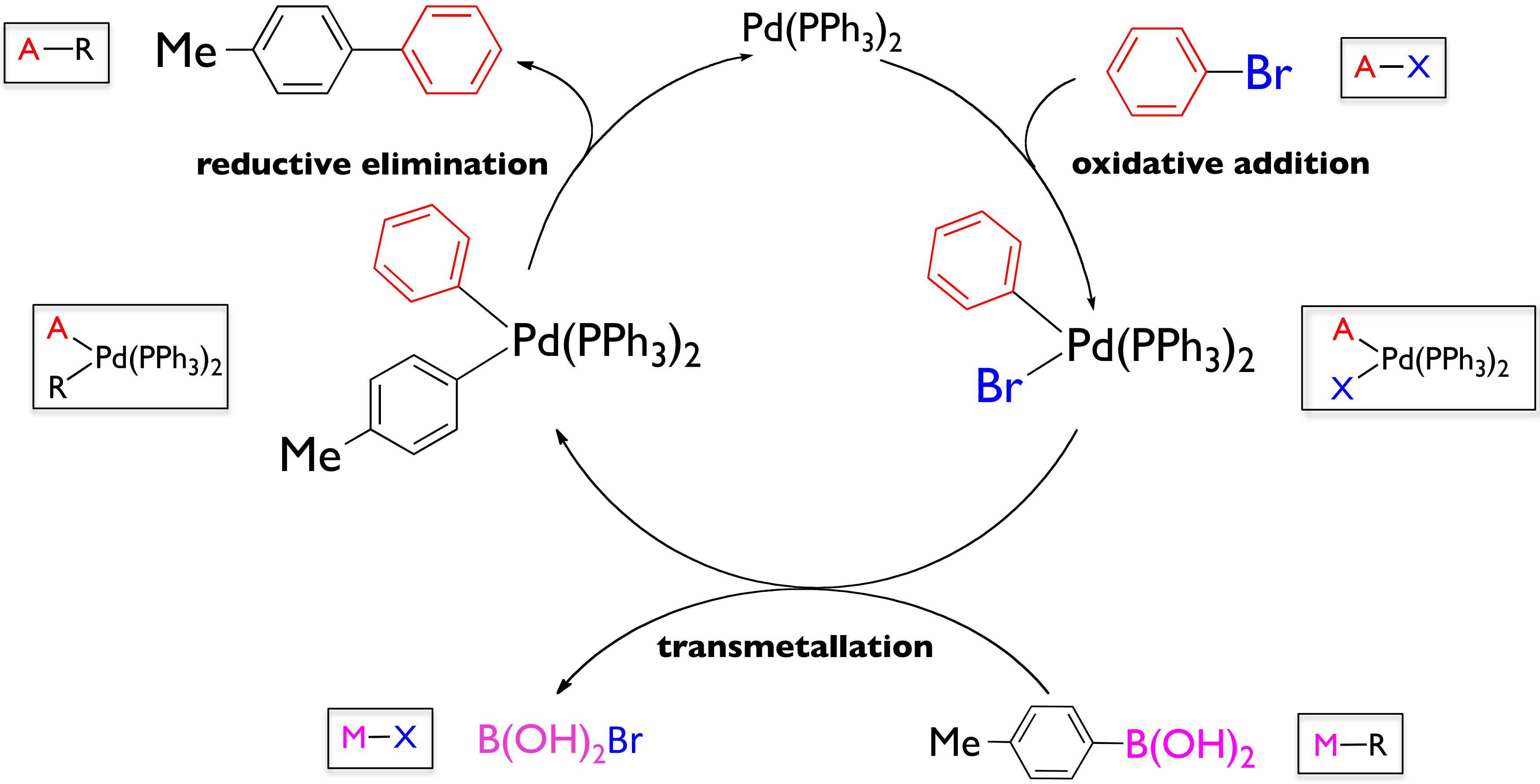
Pd coordination number decreases by 2

OxAdd and RedElim are the reverse of each other with respect to the metal

Suzuki coupling – the catalytic cycle



Coupling an arylboronic acid with an aryl bromide to give a biaryl compound



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 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