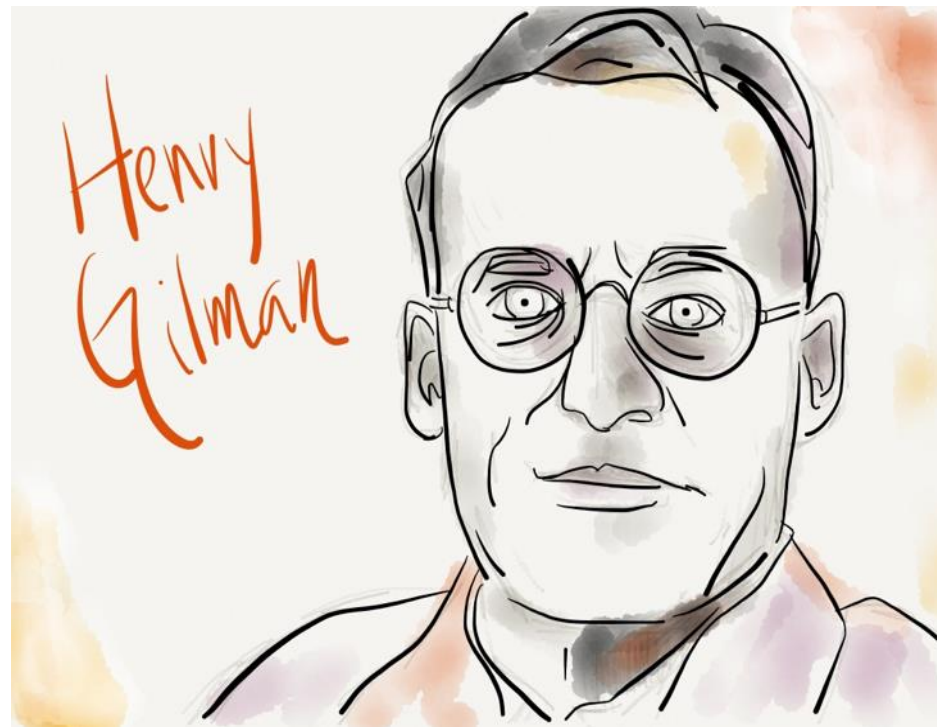
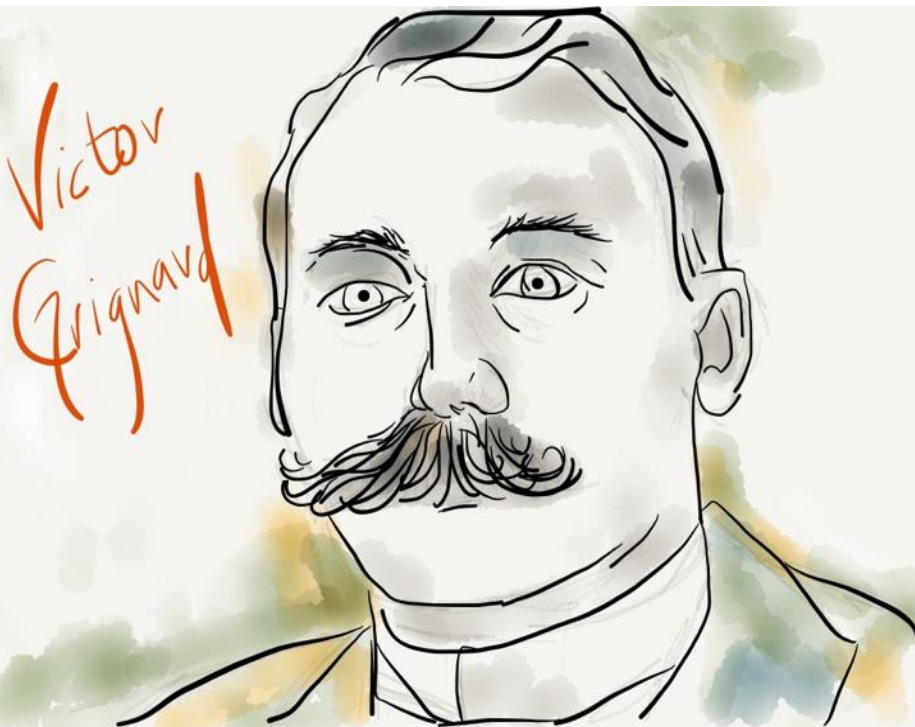


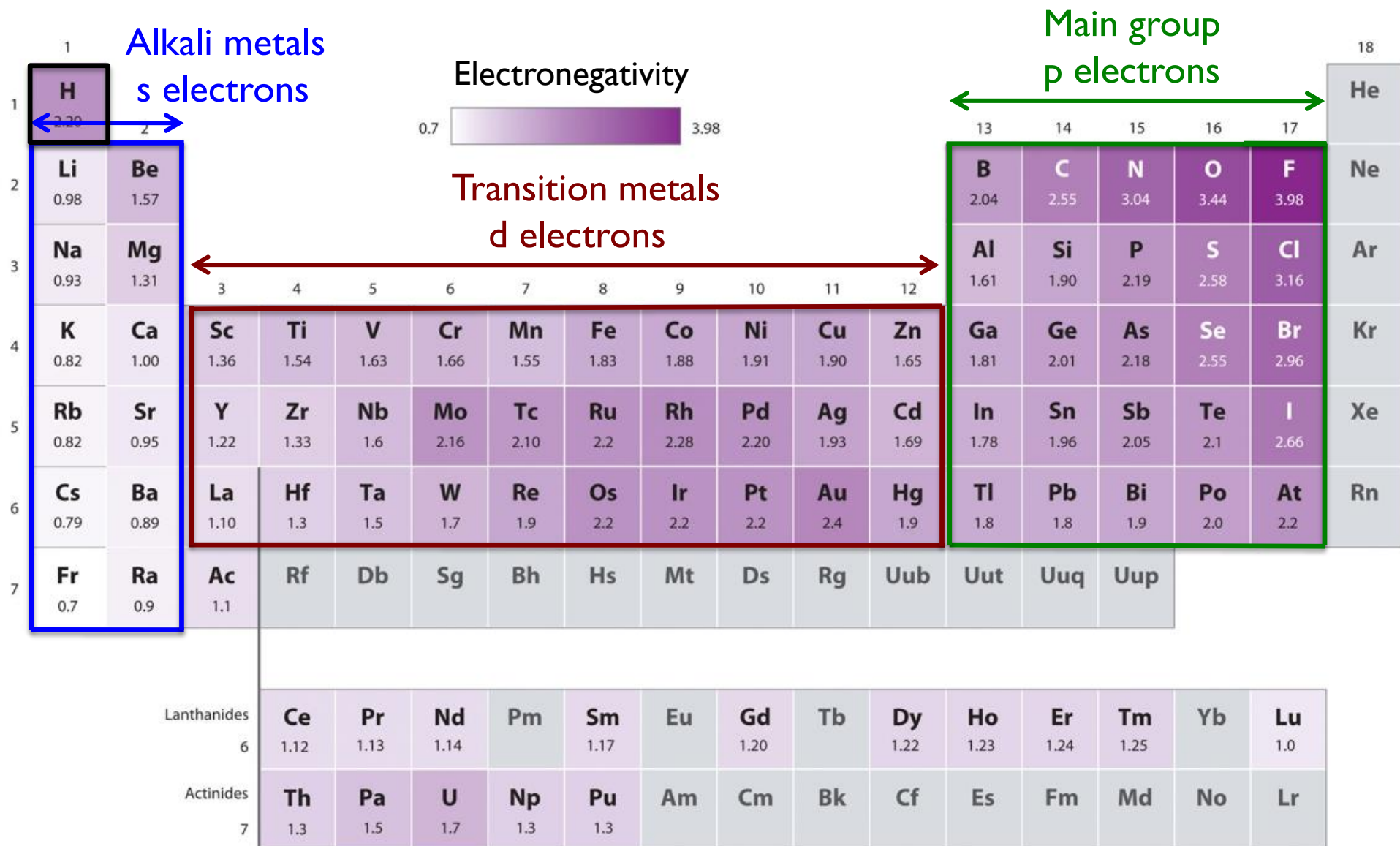
344

Organic Chemistry Laboratory

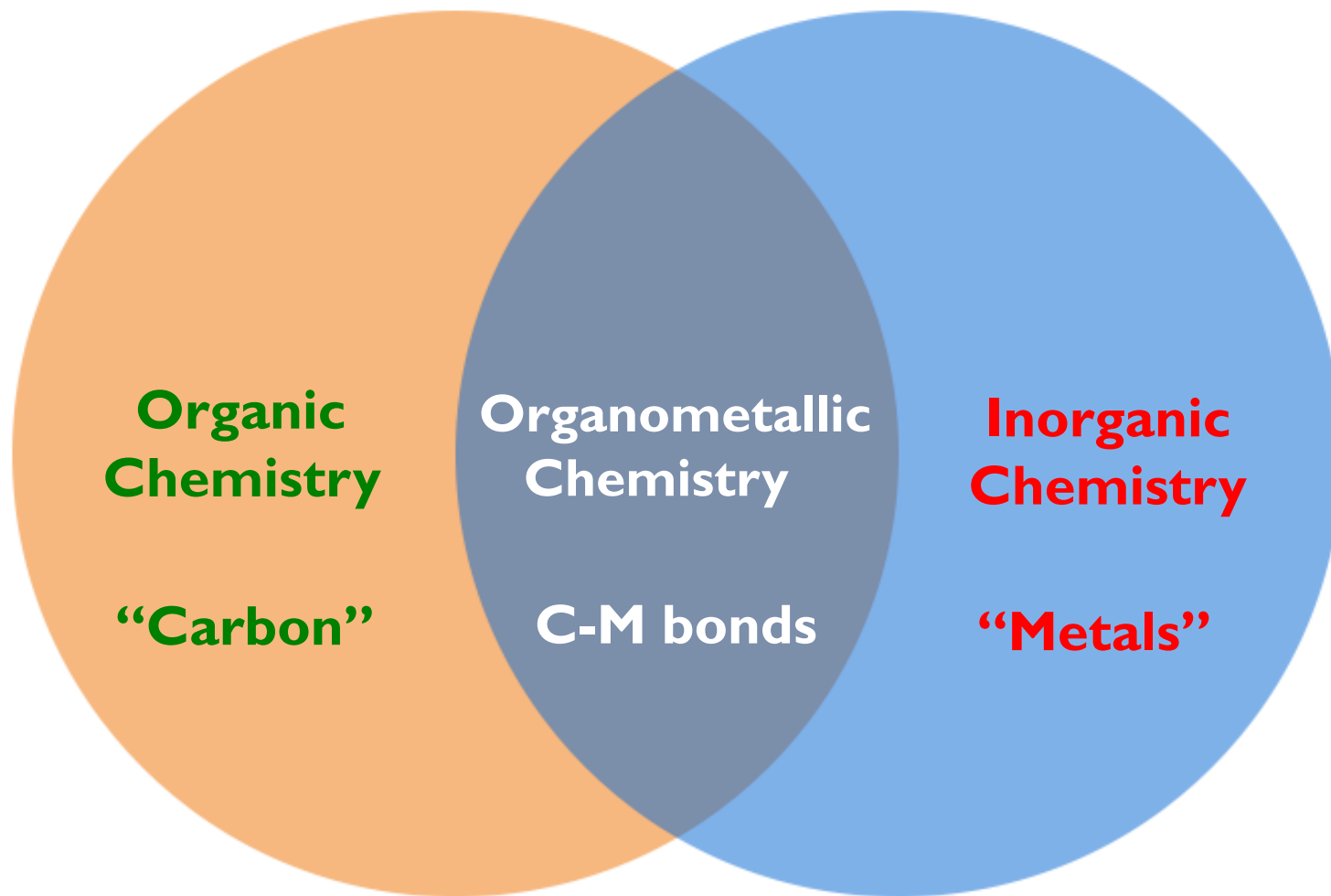
Introduction to organometallic chemistry



Periodic Table



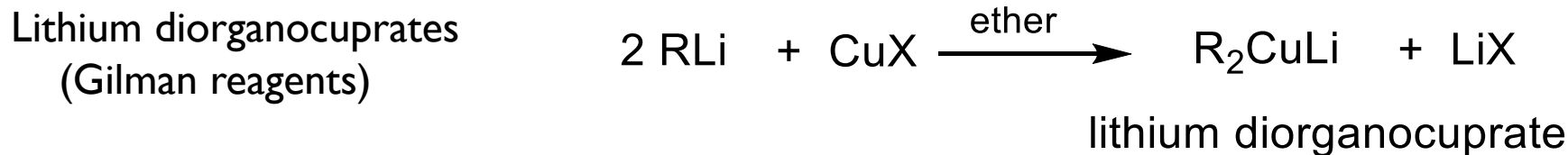
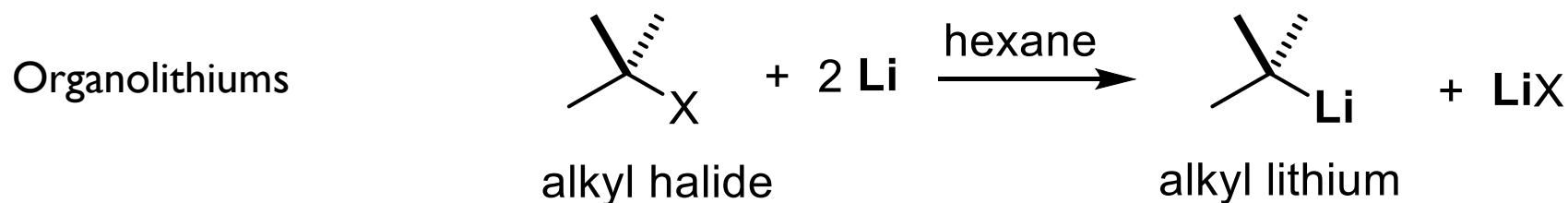
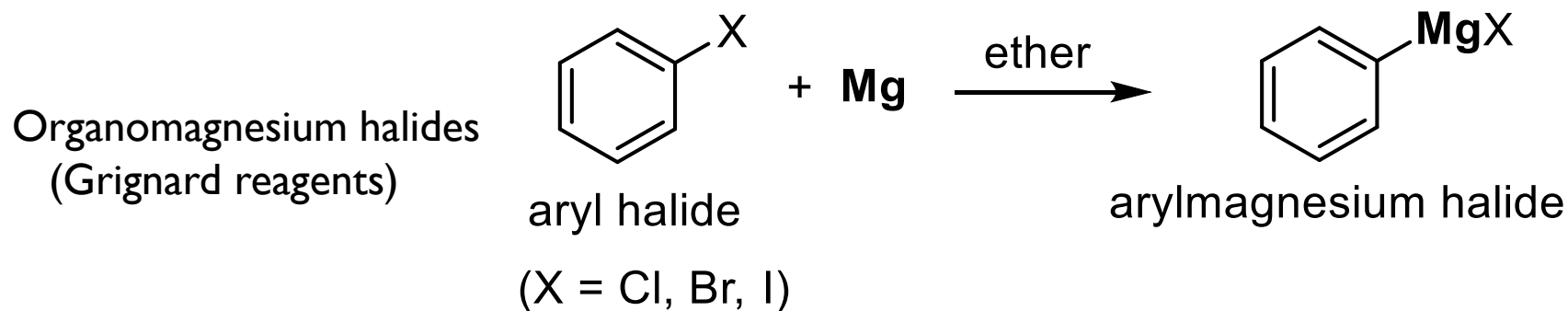
What is organometallic chemistry?



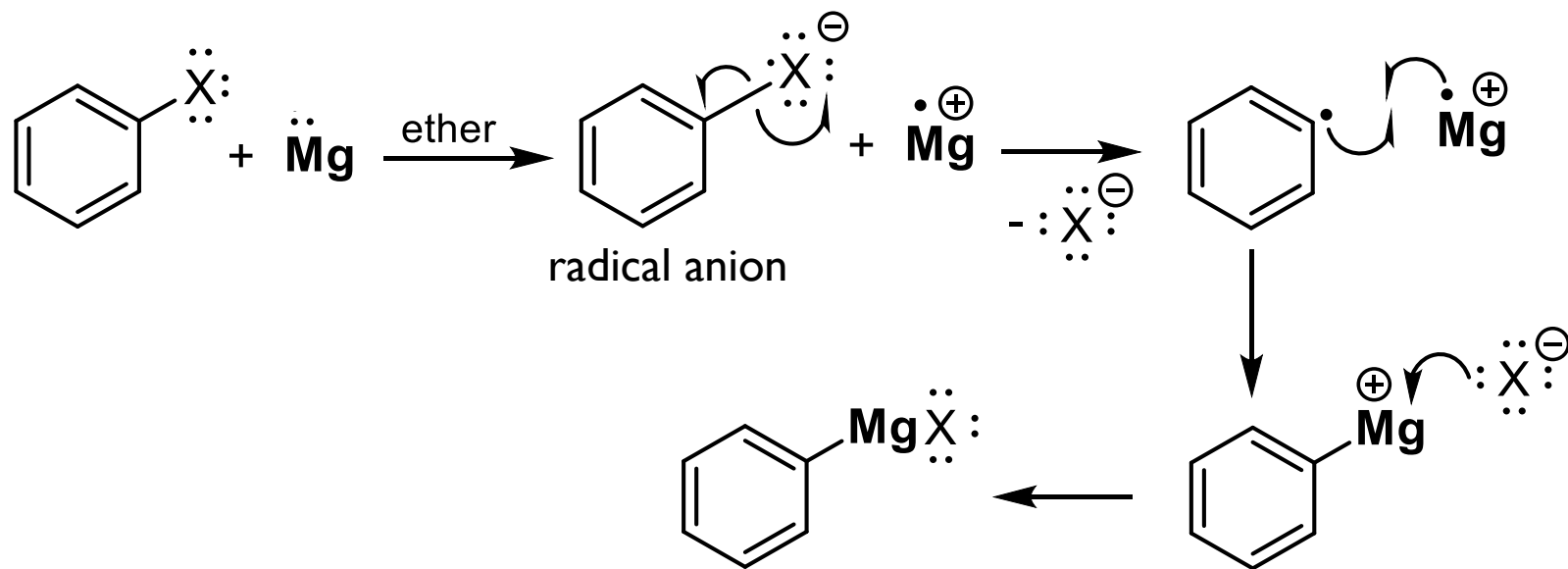
Organometallic chemistry = Study of compounds containing a Carbon-Metal bond

Organometallic chemistry = Organic synthesis using metals

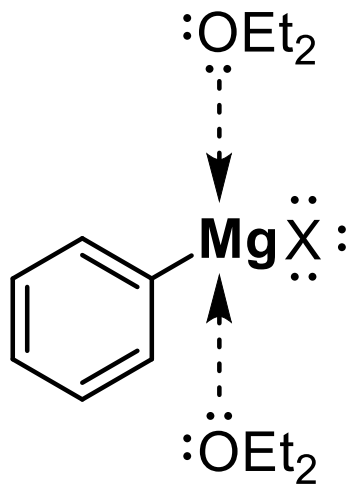
Organometallics – s-block compounds



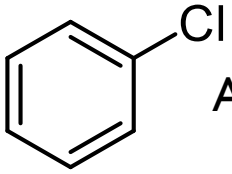
Formation of Grignard reagents



Why use diethyl ether as the solvent?



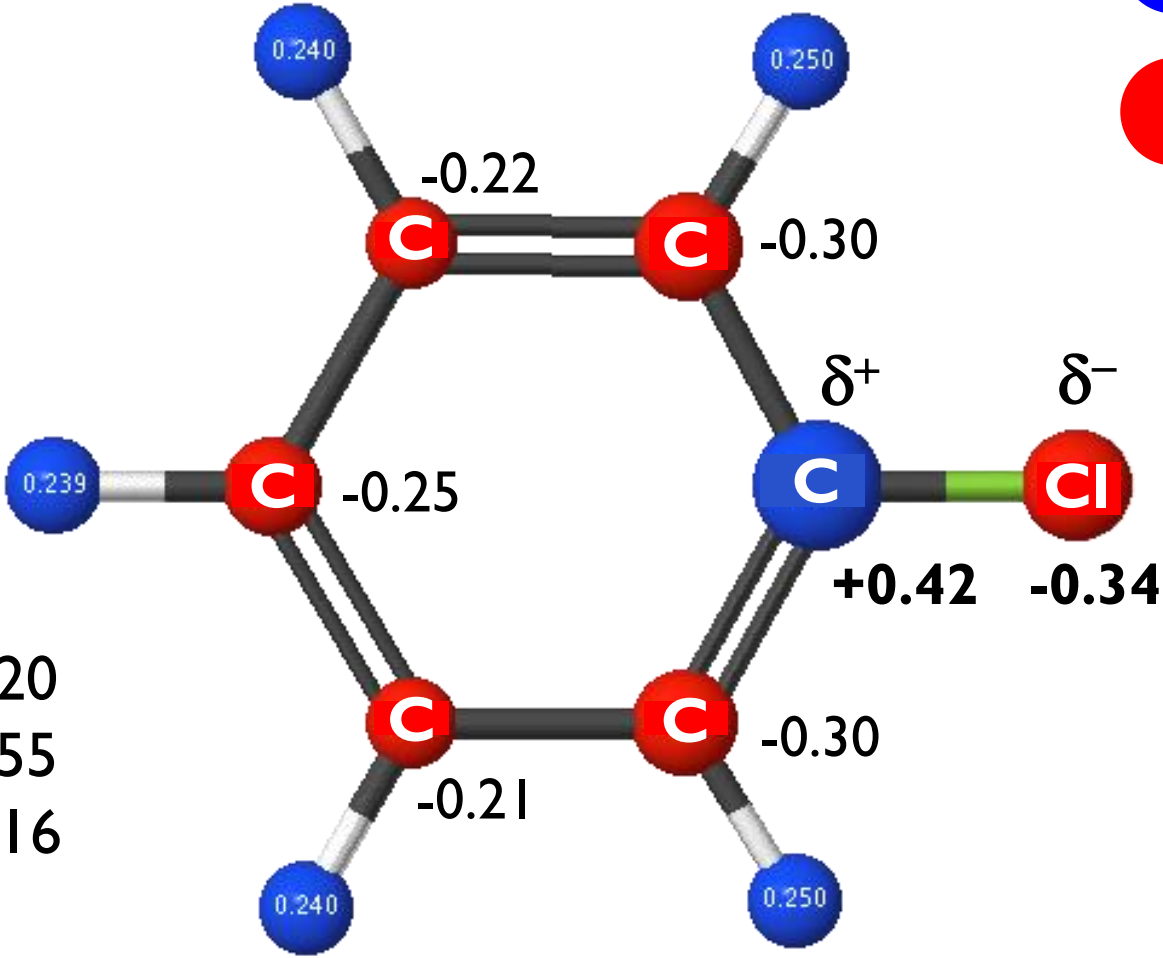
Charge distribution – Chlorobenzene



A typical organic compound

 = positively charged

 = negatively charged

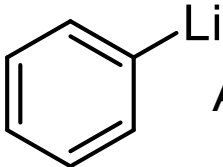


$X_H = 2.20$
 $X_C = 2.55$
 $X_{Cl} = 3.16$

X = Pauling electronegativity

NPA charges, B3LYP/6-31G(d)

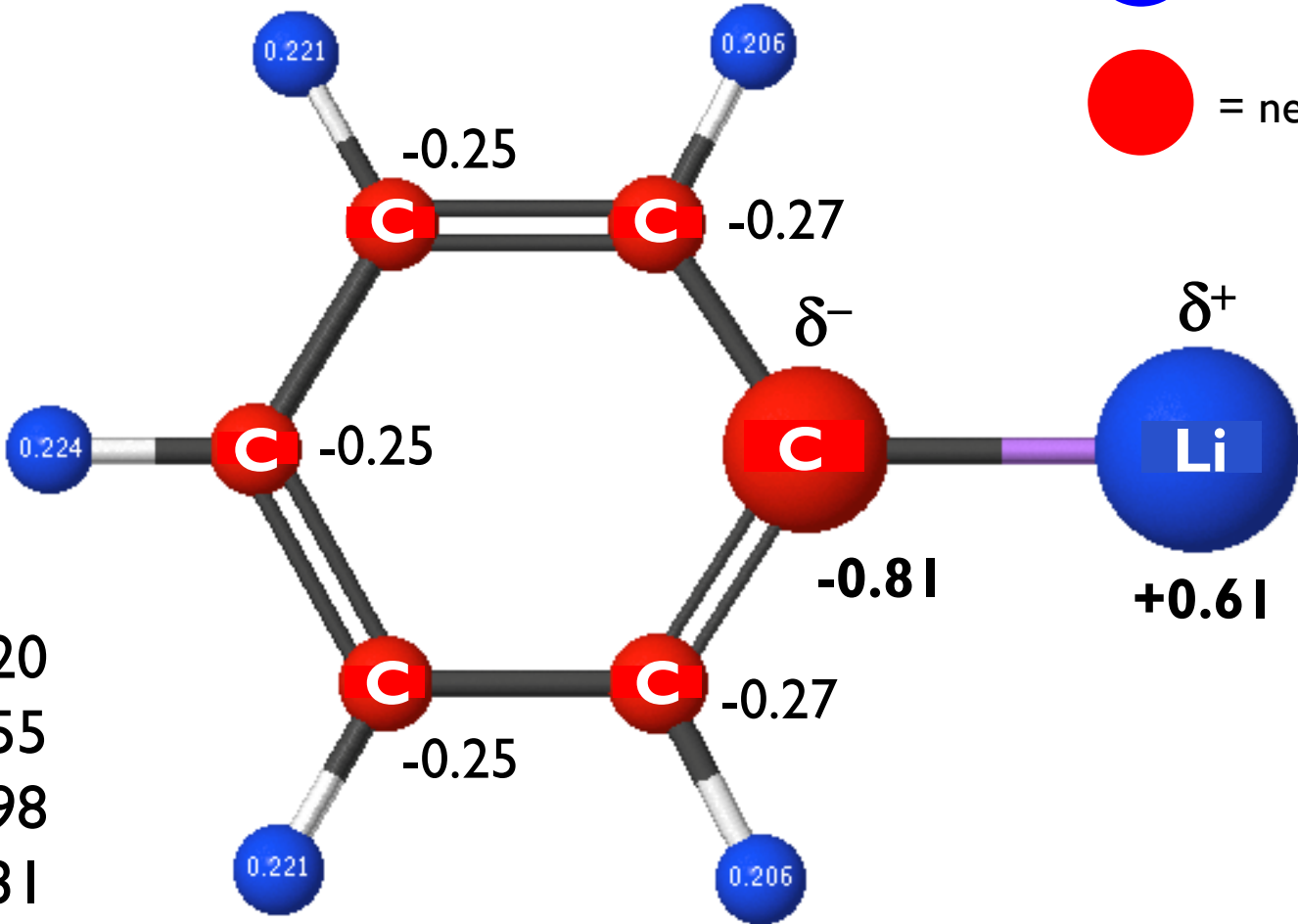
Charge distribution – Phenyl lithium



An organometallic compound

● = positively charged

● = negatively charged



$X_H = 2.20$
 $X_C = 2.55$
 $X_{Li} = 0.98$
 $X_{Mg} = 1.31$

X = Pauling electronegativity

NPA charges, B3LYP/6-31G(d)

Carbon-Metal bond polarity drives reactivity

**R
E
A
C
T
I
V
I
T
Y**

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-O	$2.55 - 3.44 = -0.89$	35
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

Ionic

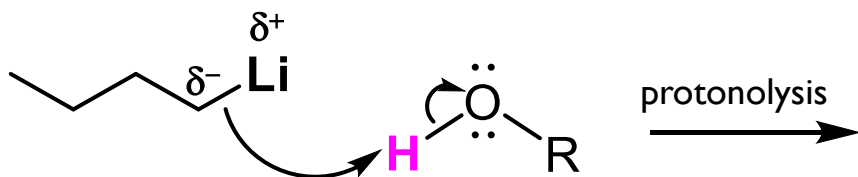
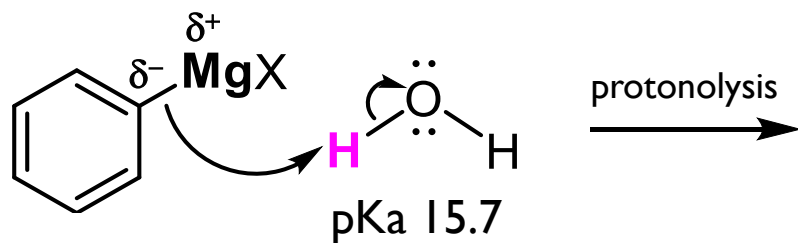
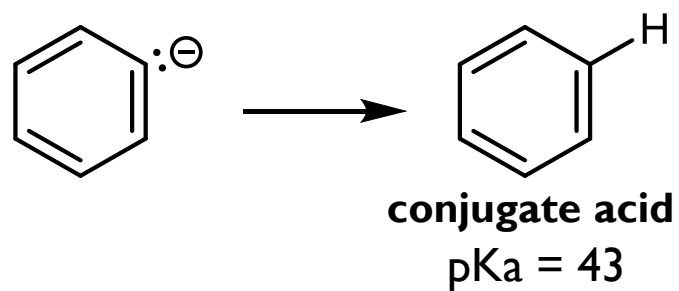
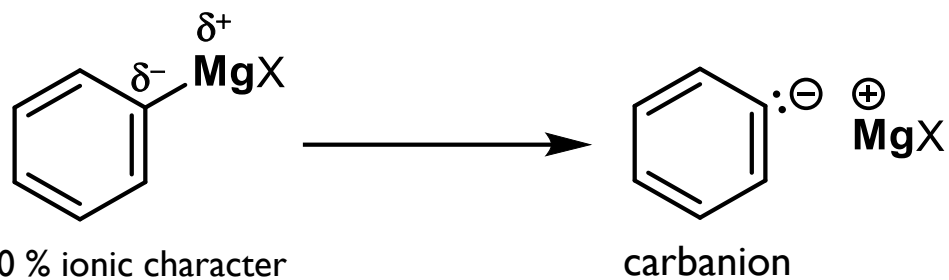
Polar covalent

Covalent

[#] Pauling electronegativity, X

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

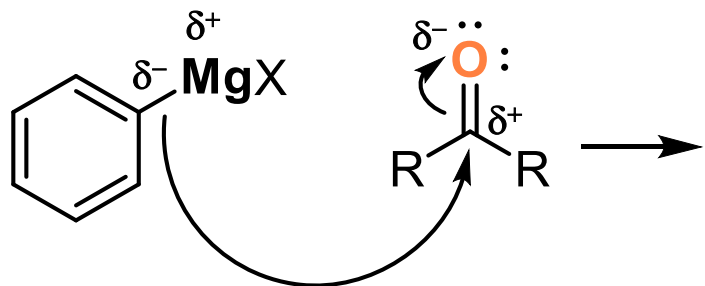
Reactivity of Grignard reagents



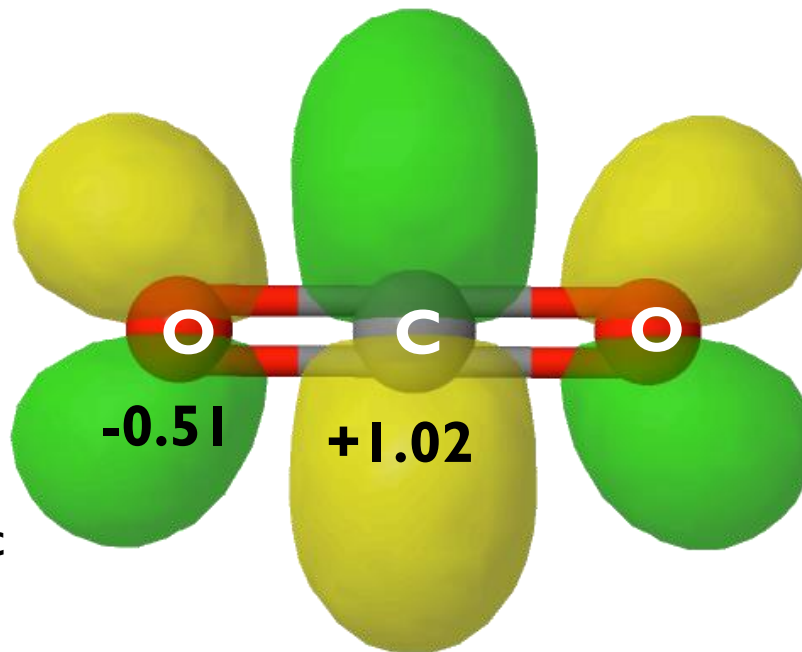
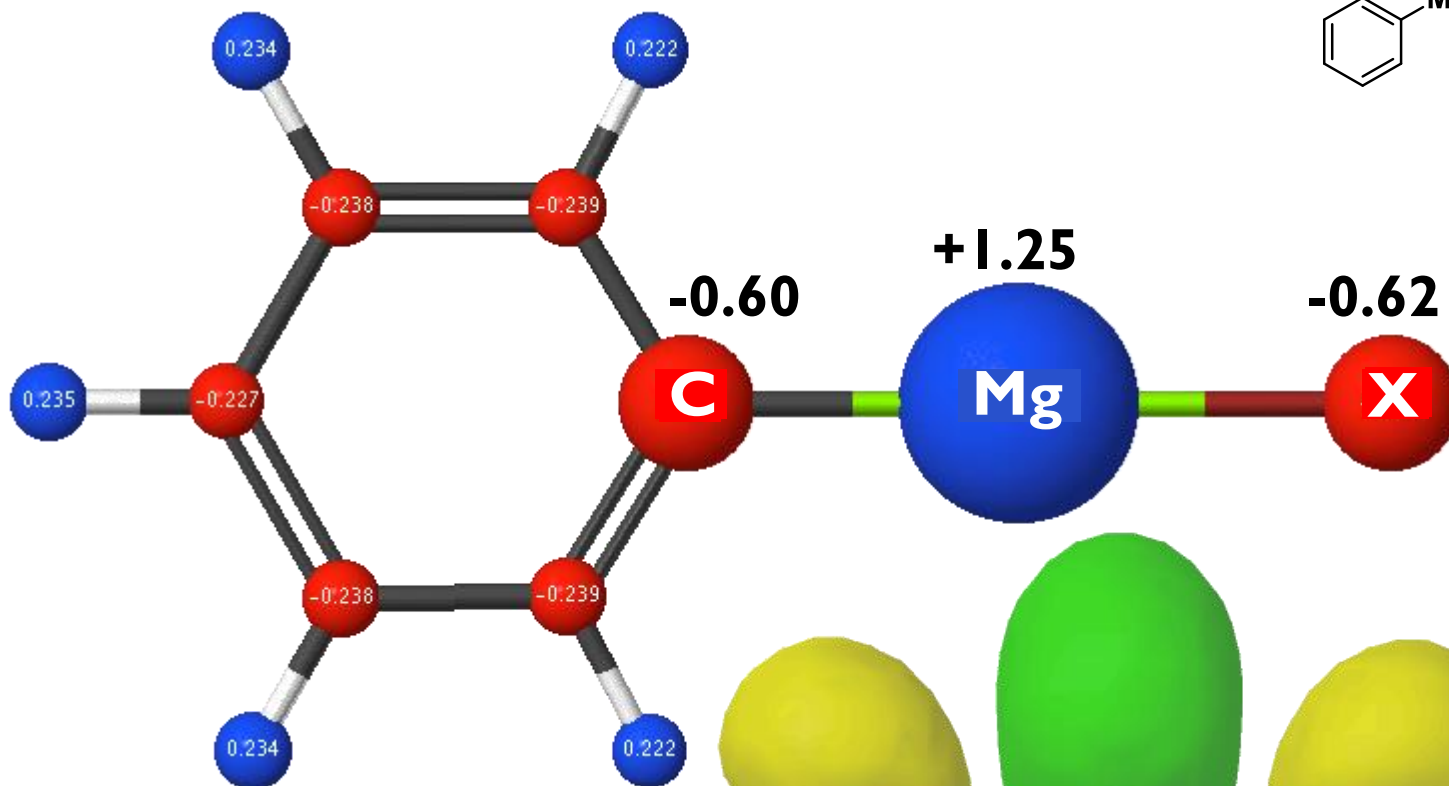
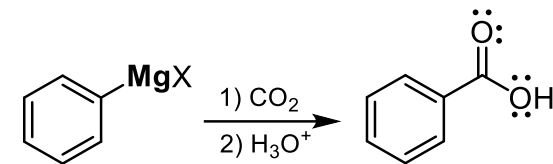
Reactivity of Grignard reagents

C-atom bonded to metal in RMgX has carbanion character, reacts as a **nucleophile**

The C-atom in a “typical” organic compound is **electrophilic** ($\text{C}=\text{O}$, $\text{C}-\text{O}$, $\text{C}-\text{N}$, $\text{C}-\text{Cl}$)



Reactivity of Grignard reagents



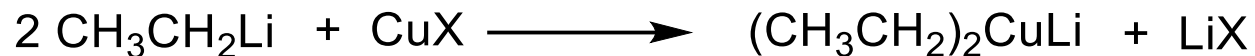
C-atom of PhMgBr is **nucleophilic**

C-atom of CO₂ is **electrophilic**

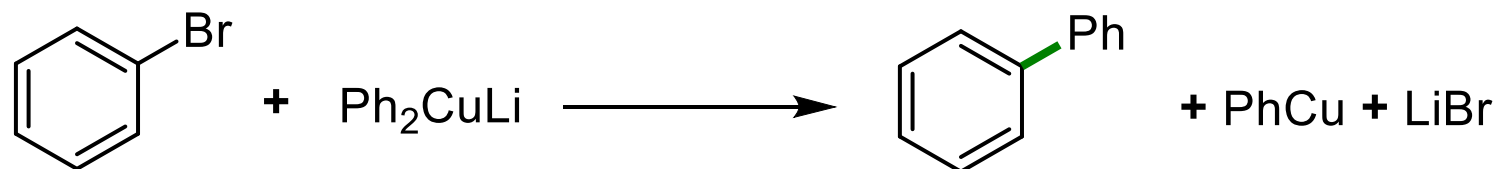
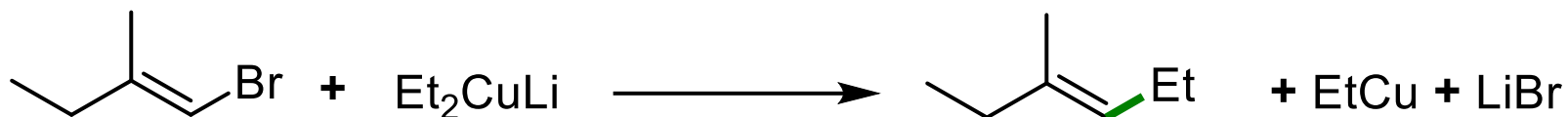
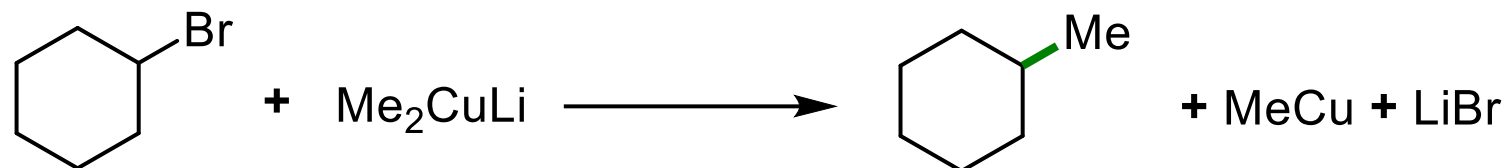
LUMO of CO₂

Metal exchange and coupling reactions

Metal exchange (transmetalation) between RLi and CuX to form lithium diorganocuprate



Lithium diorganocuprates are useful for C-C bond forming reactions



Good:

Not so good:

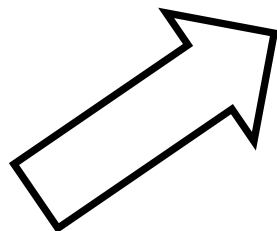
Ideal:

Palladium: One metal, many reactions

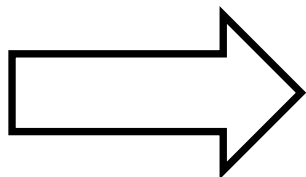
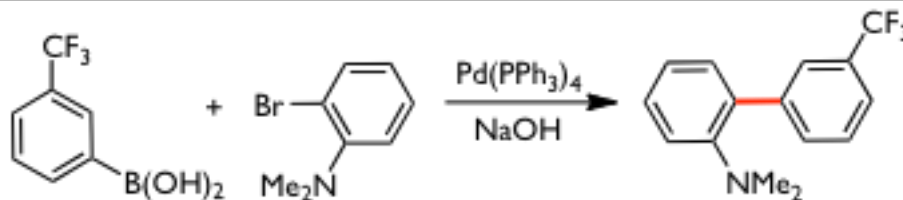
Pd-catalyzed
C-C bond
formation



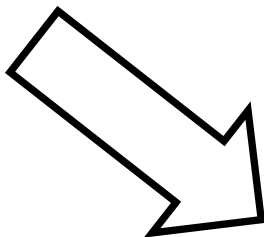
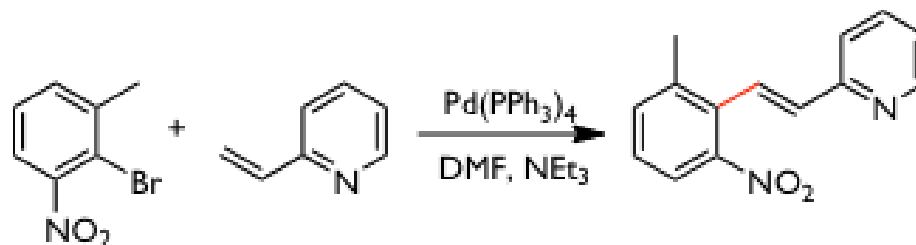
2010 Nobel Prize in Chemistry



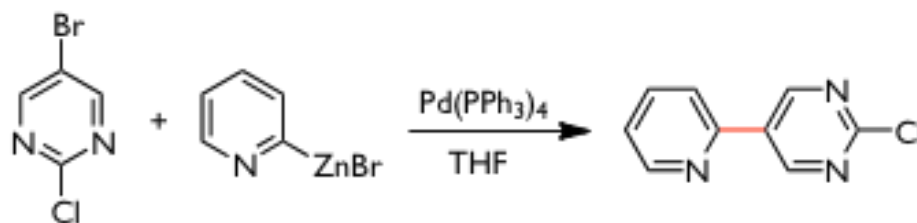
Suzuki-Miyaura



Mizoroki-Heck

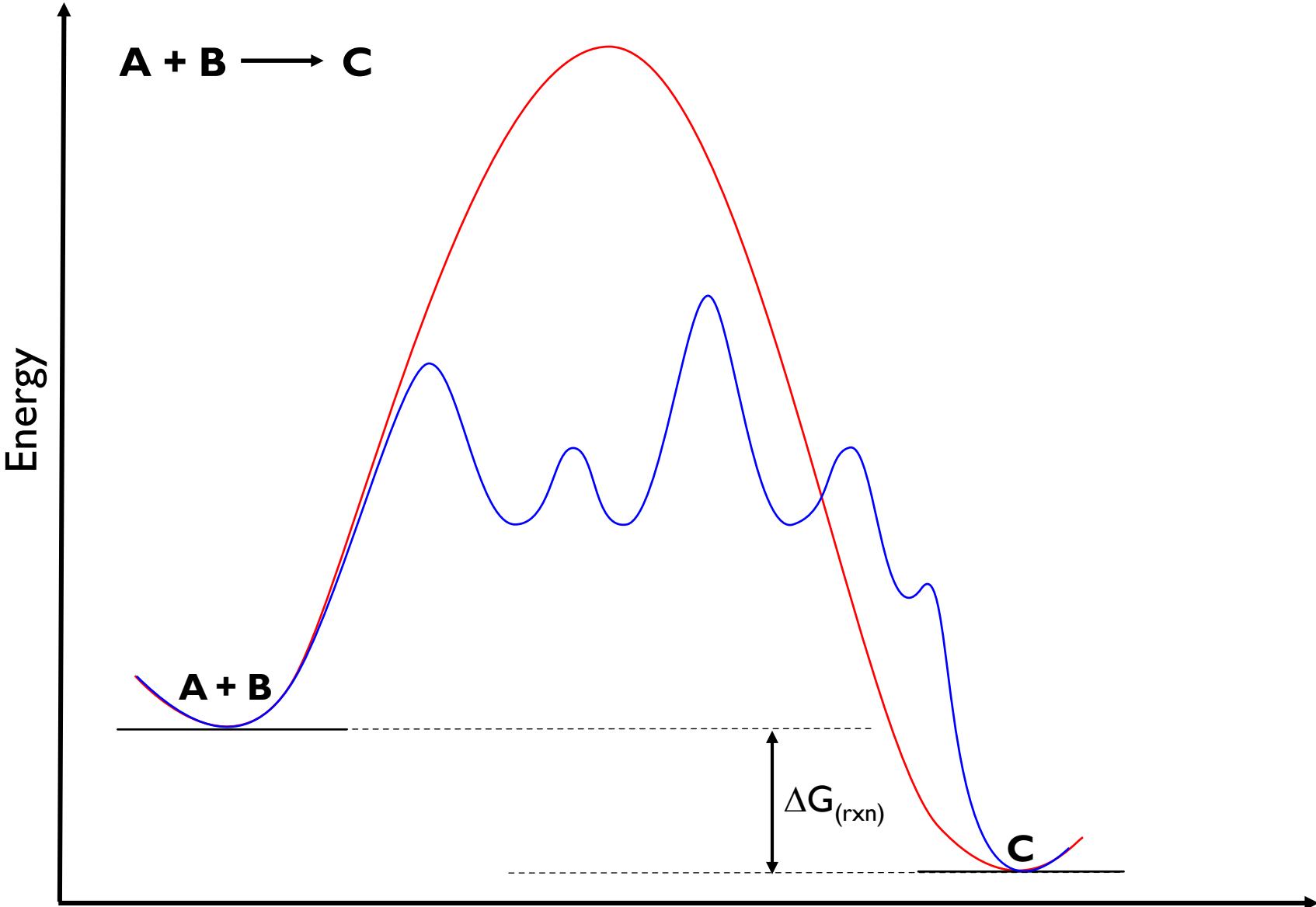


Negishi

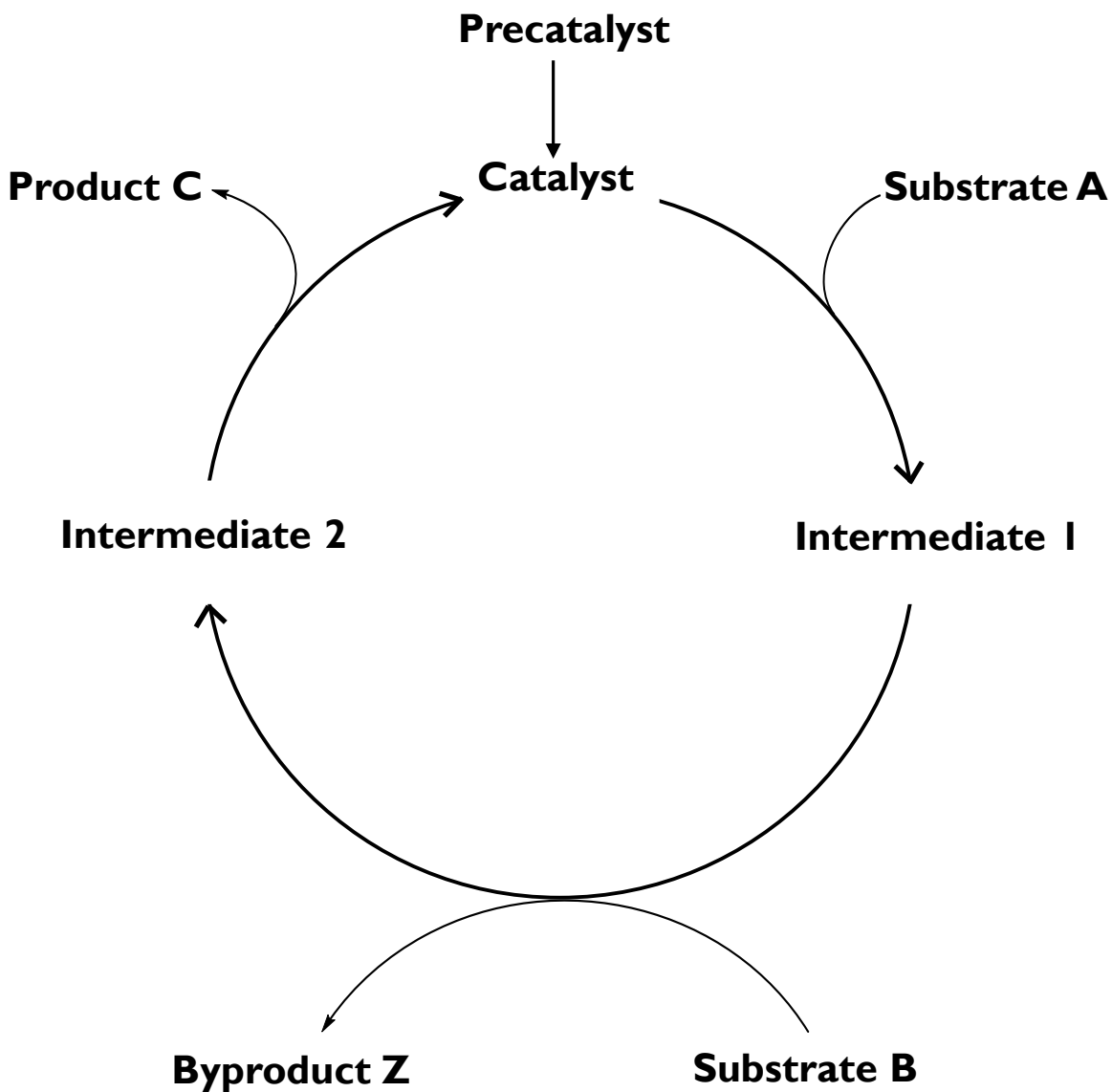
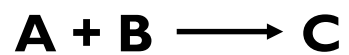


Catalysis

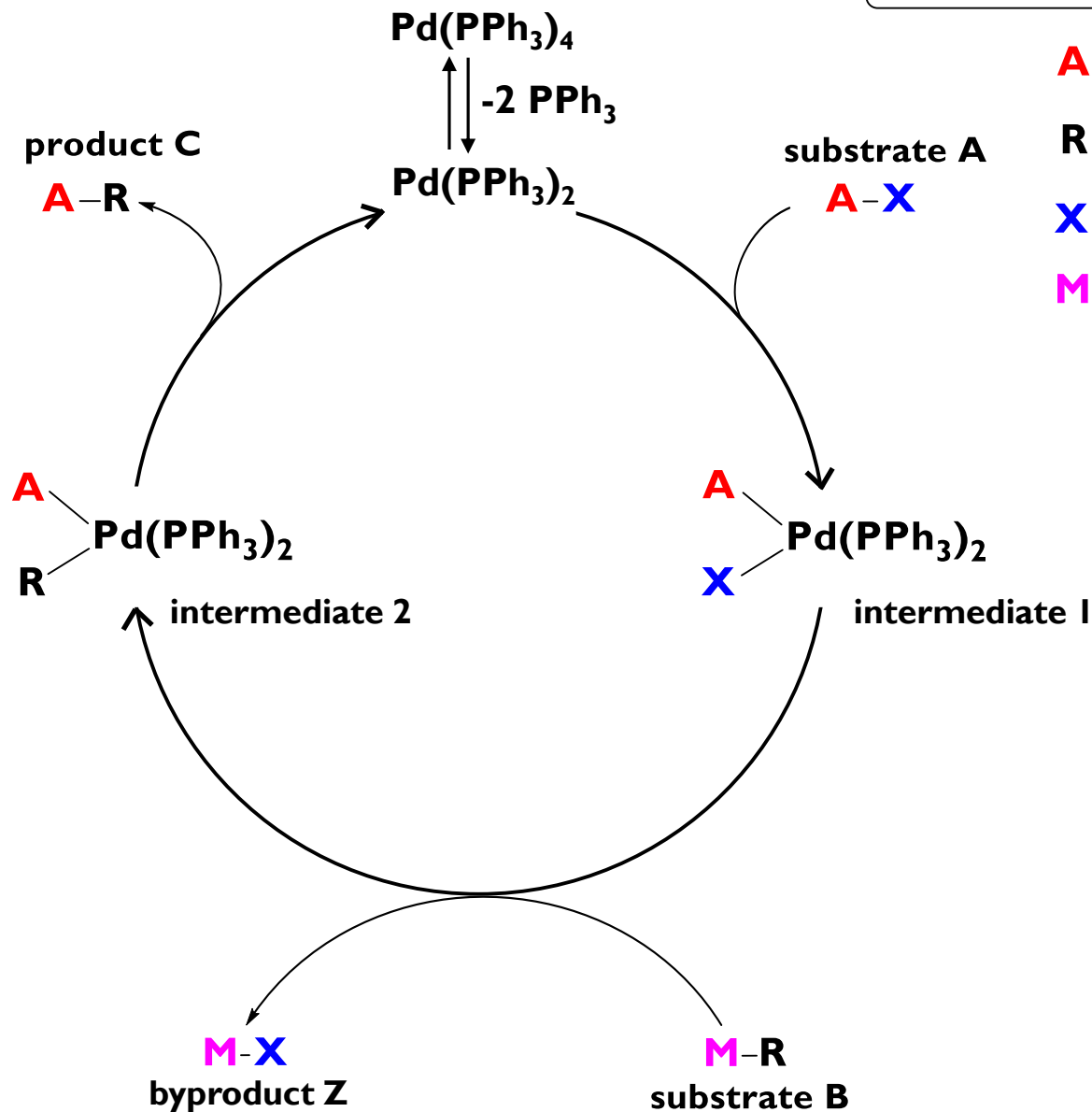
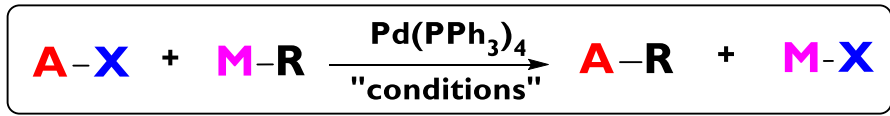
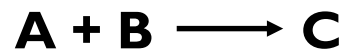
Many reactions are favorable thermodynamically but proceed slowly at room temp/pressure



Understanding the catalytic cycle



Understanding the catalytic cycle



A = organic fragment 1

R = organic fragment 2

X = halide or other counter ion

M = metal atom

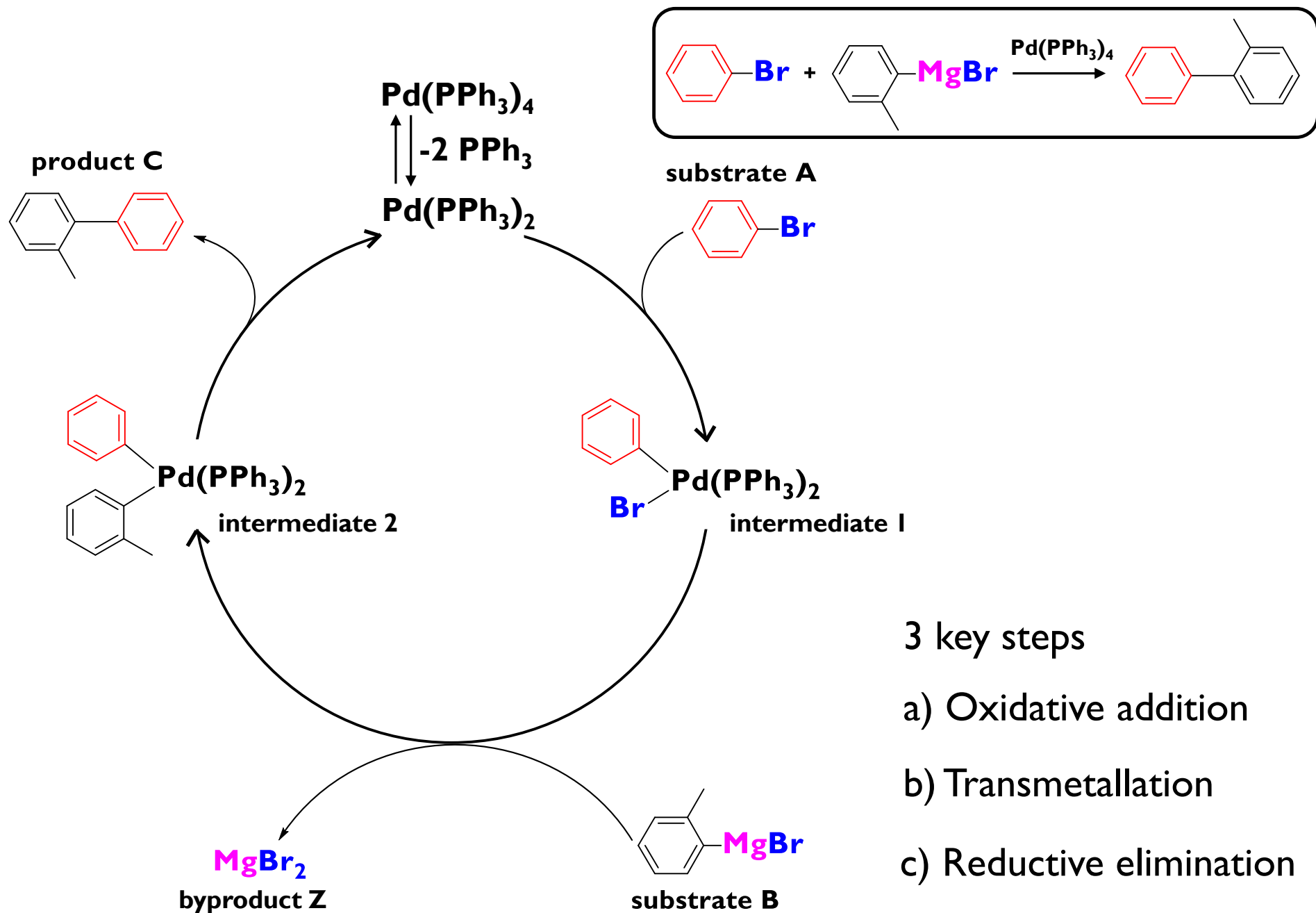
3 key steps

a) Oxidative addition

b) Transmetalation

c) Reductive elimination

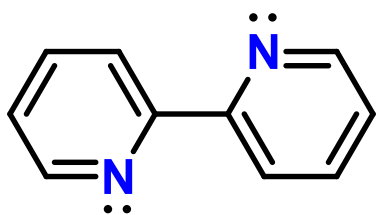
Kumada coupling – the catalytic cycle



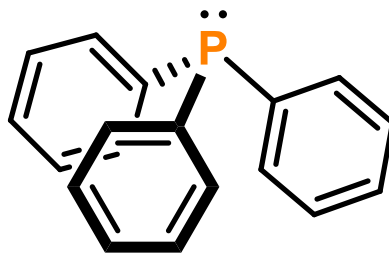
Ligands

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

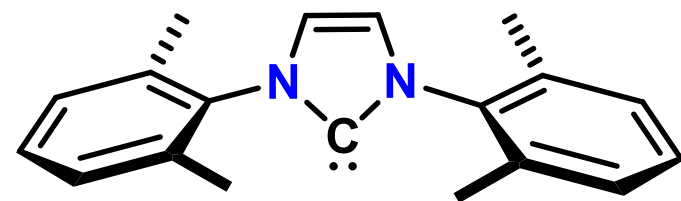
Ligands act as Lewis bases (i.e. electron donors) toward the transition metal



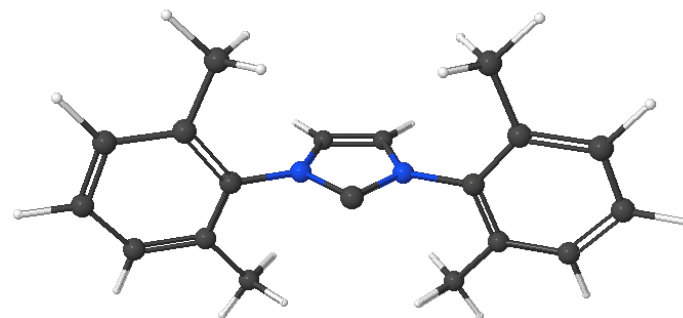
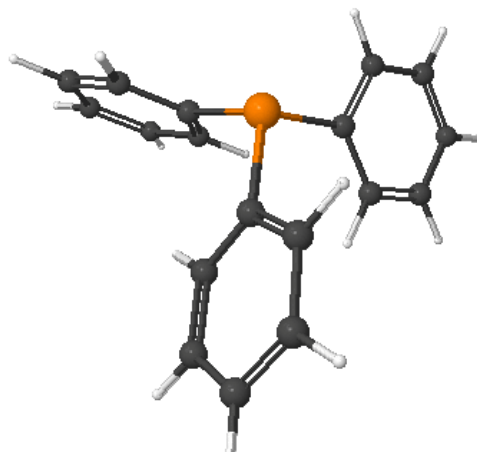
2,2'-Bipyridine (bpy)



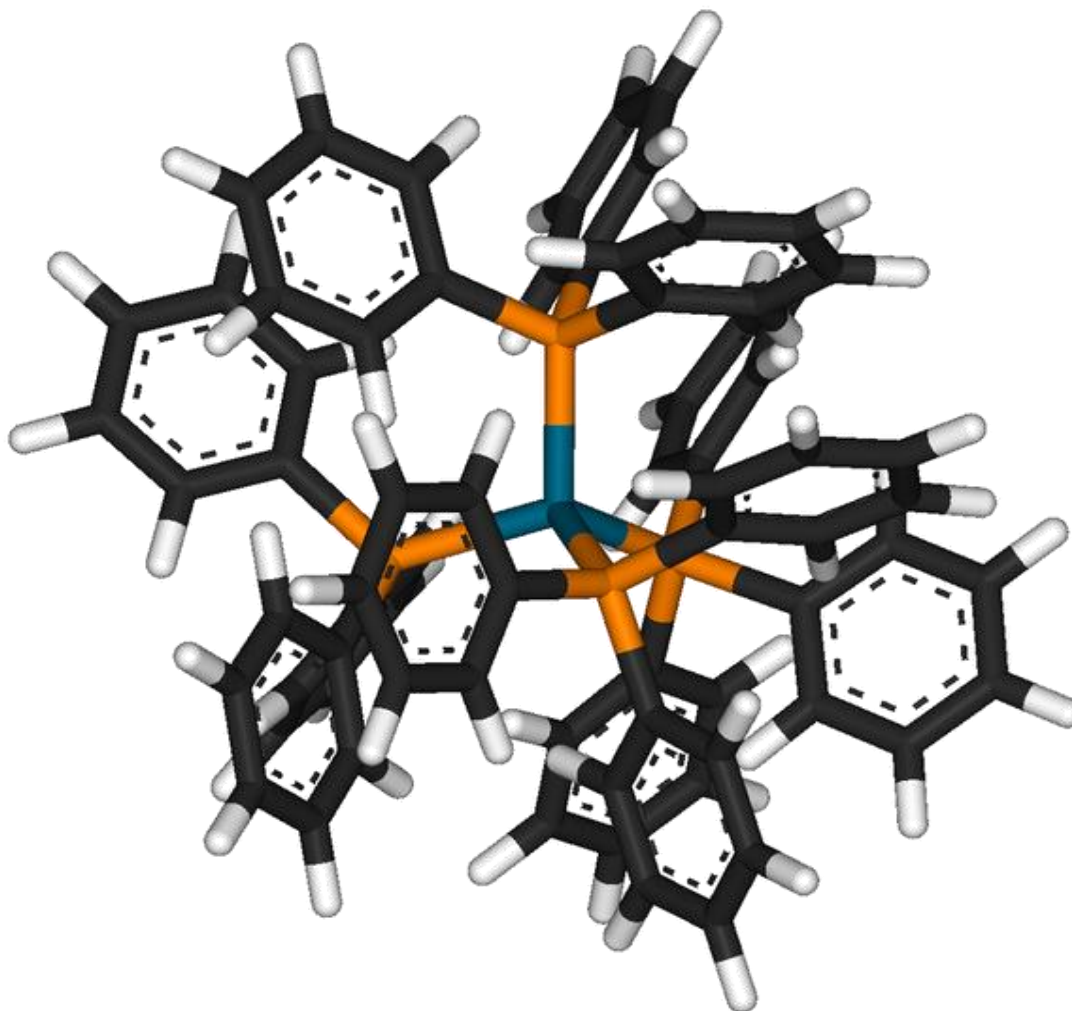
Triphenyl phosphine (PPh₃)



N-heterocyclic carbene (NHC)

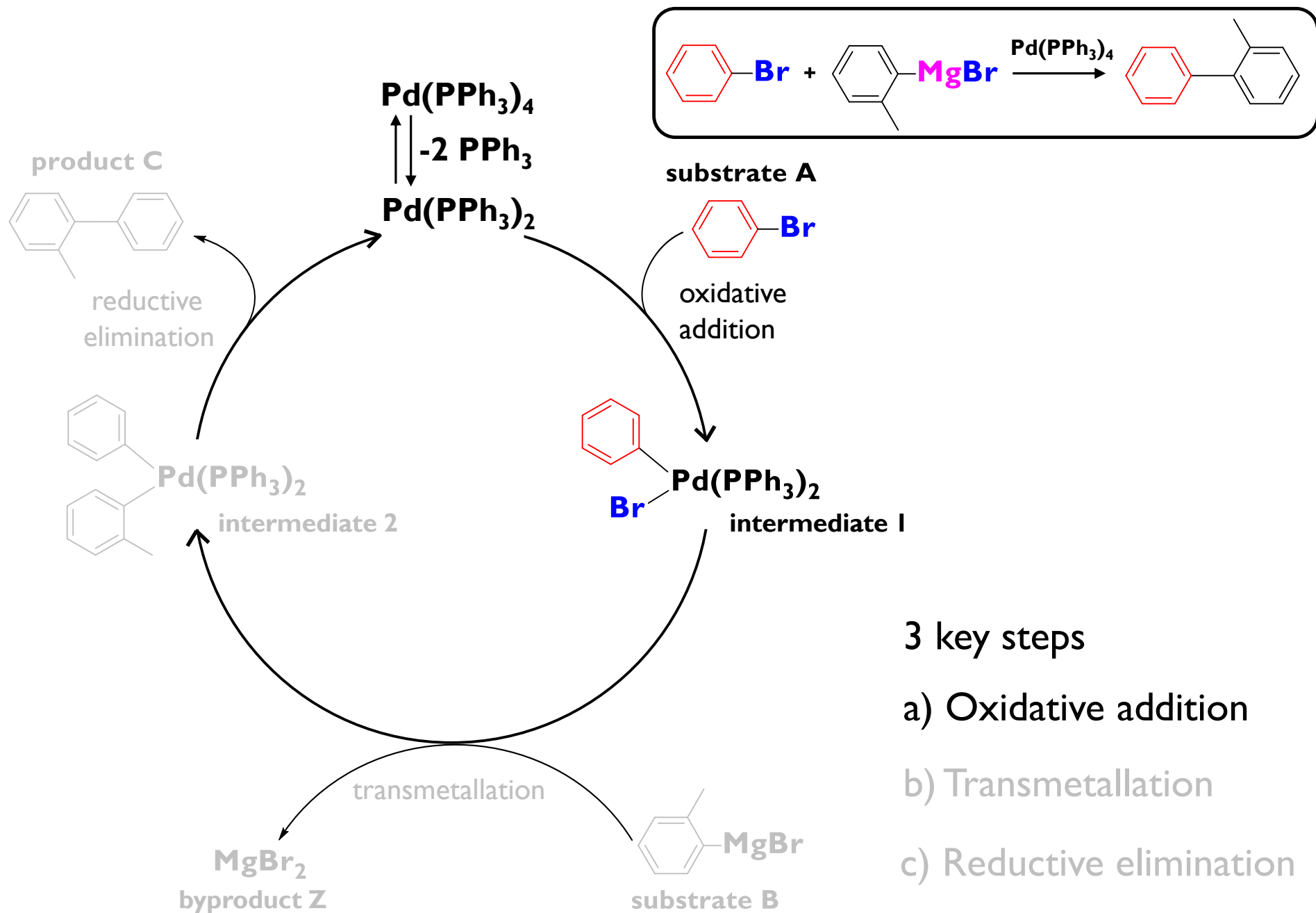


Metal-ligand compounds are called coordination complexes - serve as **precatalysts**



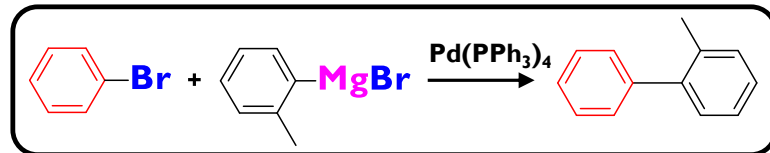
Tetrakis(triphenylphosphine)palladium

Kumada coupling – the catalytic cycle



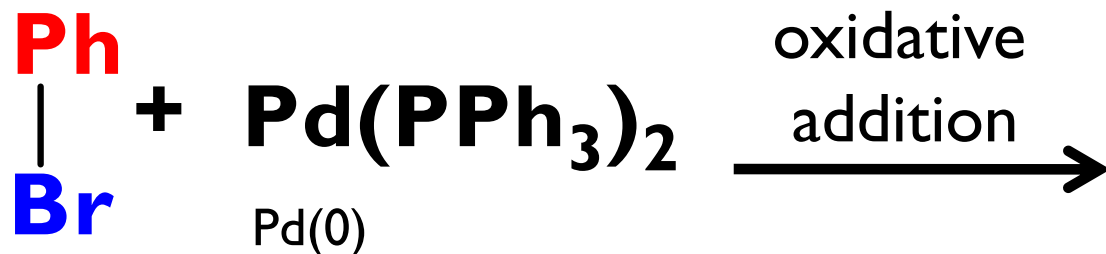
Key steps of the cycle – oxidative addition

First step of typical C-C coupling catalytic cycle



Addition of organic substrate (**Ph-Br**) to Pd(PPh₃)₂ species

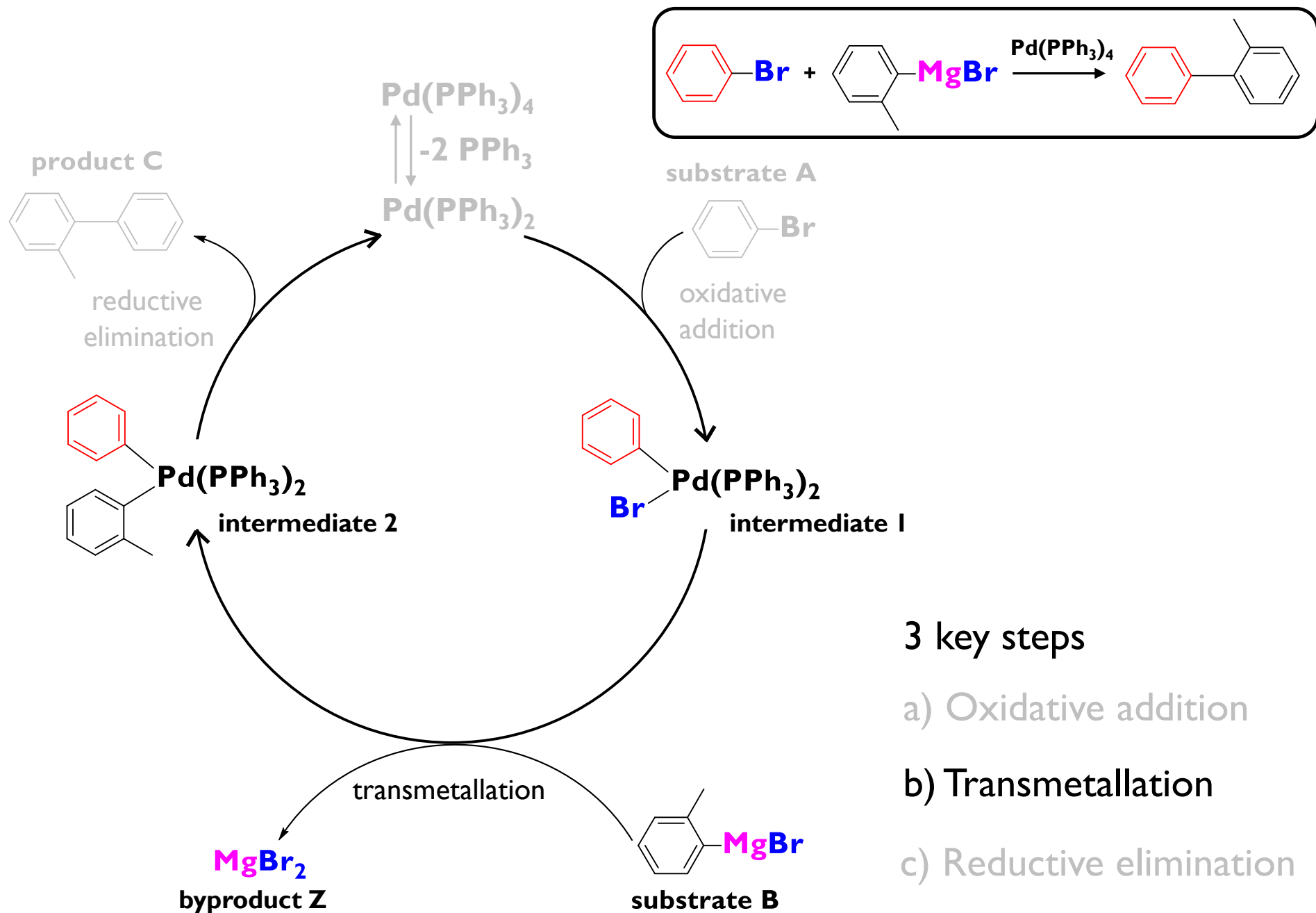
Substrate can be **aryl**, **alkenyl**, or **alkynyl halide**



Number of bonds to Pd increases by 2

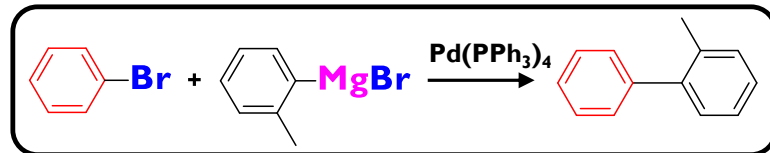
Pd oxidation state increases by 2 (Pd⁰ to Pd^{II})

Kumada coupling – the catalytic cycle



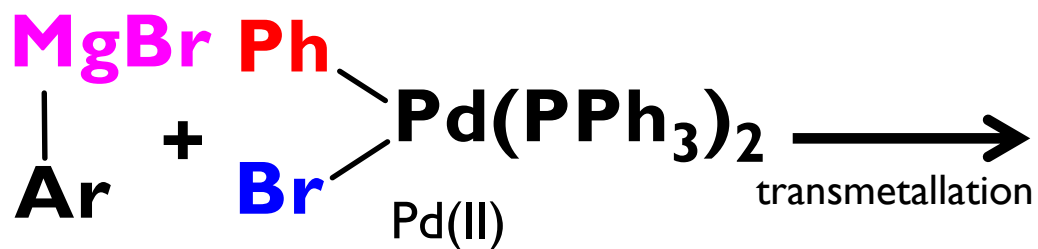
Key steps of the cycle – transmetallation

Middle step of typical C-C coupling catalytic cycle



Exchange reaction between **Ar-MgBr** and oxidative addition product

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

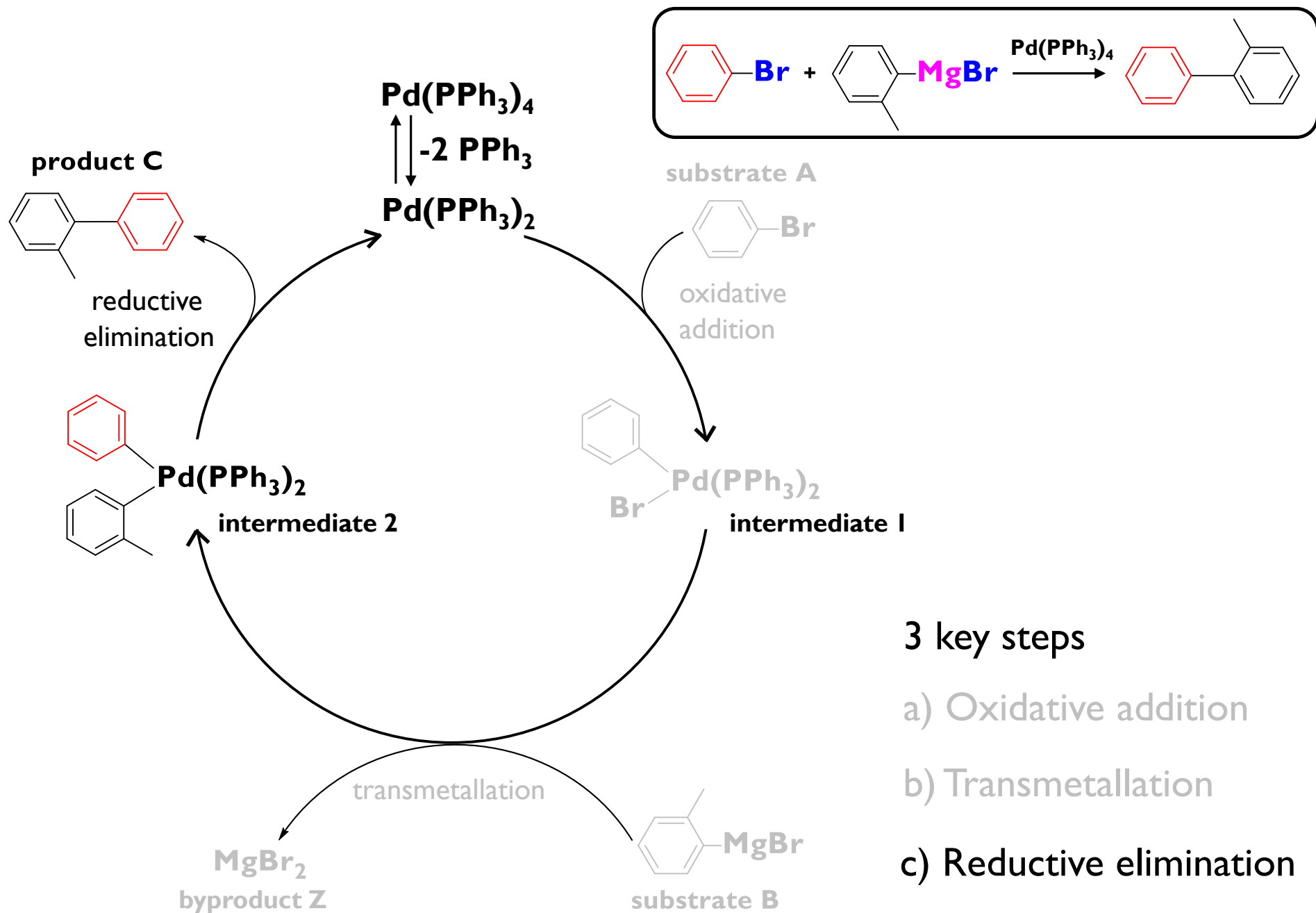


Organic group **Ar** replaces **Br** on Pd atom

Pd oxidation state and coordination number unchanged

Drive toward less polar C-M bond in transmetallation product

Kumada coupling – the catalytic cycle



3 key steps

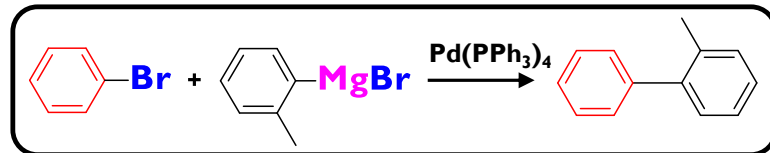
a) Oxidative addition

b) Transmetalation

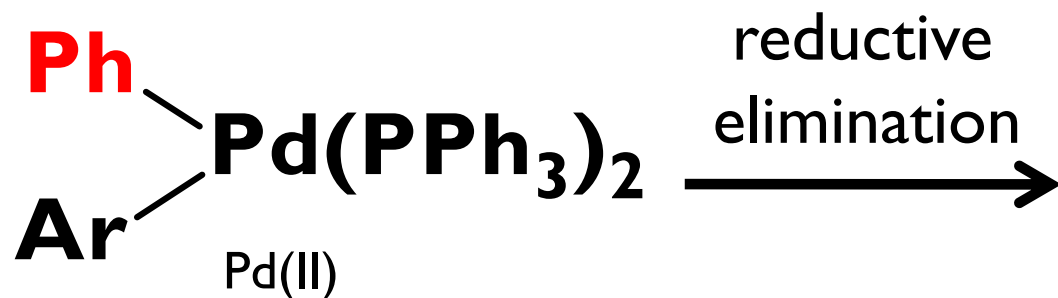
c) Reductive elimination

Key steps of the cycle – reductive elimination

Final step of typical C-C coupling catalytic cycle



Elimination of product (**Ph-Ar**) from transmetalation product



Coupling product **Ph-Ar** released, active catalyst $\text{Pd(PPh}_3)_2$ reformed

Pd oxidation state and coordination number decrease by 2

Summary

Organometallic chemistry

- the chemistry of compounds containing a C-M bond

Grignard and organolithium reagents

- polar C-M bond, carbanion character, strong bases, carbon nucleophiles, C-C bond forming
- used in stoichiometric (1:1 or greater) amounts

Pd-catalyzed coupling reactions

- a catalyst provides alternate, lower ΔG^\ddagger route to a product
- a catalyst is not consumed but can participate in many turnovers
- ligands coordinate to transition metal to form pre-catalyst complex
- metal-ligand complexes serve as catalysts for organic reactions
- bond forming/breaking takes place on metal atom
- 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!**