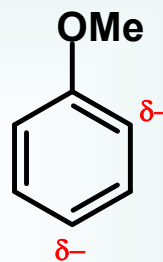
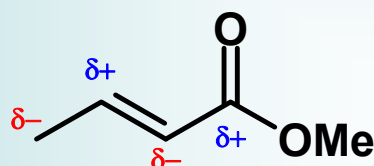


Organometallics in Organic Synthesis

1. So who cares (i.e., why?)

-Pattern of reactivity of organic compounds is imposed on molecule by existing functional groups



- By default, this limits what you can do with the compound
- Coordination of a metal fragment can change this completely
i.e., can render – an electrophilic species nucleophilic
 - a nucleophilic species electrophilic
 - can make a normally unstable molecule stable
 - can make a stable molecule reactive
 - can make impossible reactions possible

The (Very) Basics of Organometallics

-The 18 Electron Rule

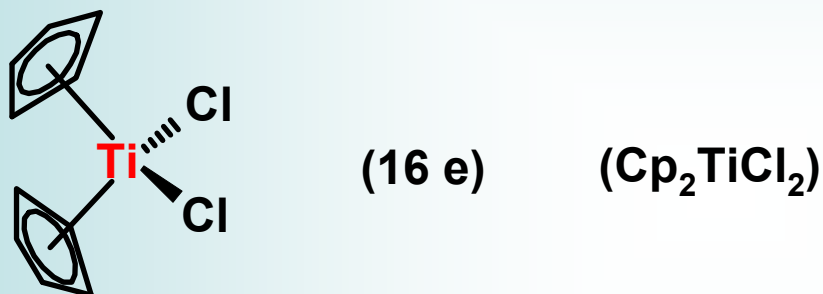
Most (middle) transition metal complexes prefer having
18 valence electrons ($2s + 6p + 10d$)

For transition metal complexes in the 0 oxidation state

4e	5e	6e	7e	8e	9e	10e
Ti	V	Cr	Mn	Fe	Co	Ni
Zr	Nb	Mo	Rc	Ru	Rh	Pd
Hf	Ta	W	Re	Os	Ir	Pt

-The 18 e rule is followed most closely in complexes of middle transition metals (Cr to Co)

-As for early transition metal complexes, it's usually too difficult to get enough ligands around the metal to get it to 18 e (i.e., Ti)



- As for late transition metal complexes (Ni, Pd, Pt), particularly the square planar $\text{M}^{\text{II}}\text{L}_4$ complexes

- tend to be very stable as 16 e⁻ complexes

- energy gap to 9th orbital is quite big; molecule is quite willing not to fill that orbital

To count to 18 (or 16), need e⁻'s from ligands

- I'll adopt a 'radical approach' – not only valid one

A) Inorganic Ligands

1e⁻

-X

-H

-R

2e⁻

R₃P:

(RO)₃P:

R-C≡N:

R-N≡C:

R₃N:

R₂S:

R₂O:

3e⁻

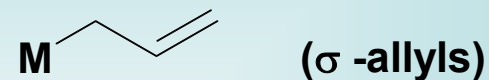
NO (usually) nitrosyl complexes

Organic Ligands - Part 1

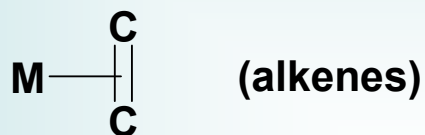
$\eta^1 (1 e^-)$

-R (alkyls)

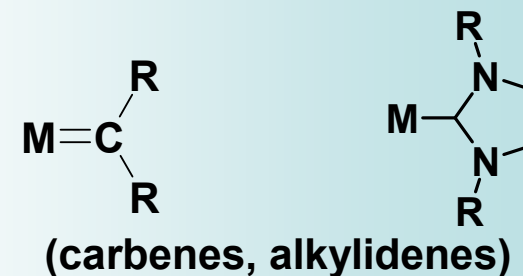
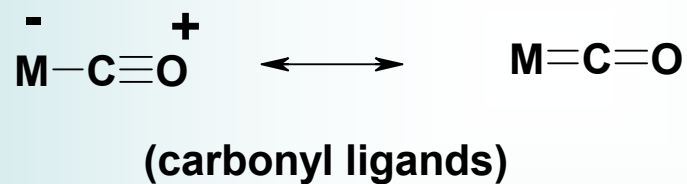
-Ph (aryls)



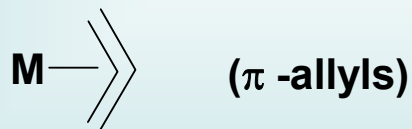
$\eta^2 (2 e^-)$



$\eta^1 (2e^-)$



$\eta^3 (3e^-)$

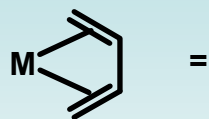


$\eta^1 (3e^-)$



Organic Ligands, Cont'd.

η^4 ($4e^-$)



=

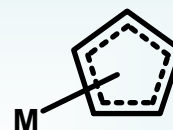


(trimethylenemethanes)
(TMM)

η^5 ($5e^-$)

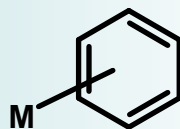


(dienyls)



(cyclopentadienyls)

η^6 ($6e^-$)

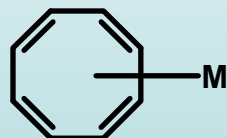


(arenes, trienes)

η^7 ($7e^-$)

(trienyls)

η^8 ($8e^-$)



(cyclooctatetraenes) - rarely, usually η^4

So.....

The number of electrons on the free metal

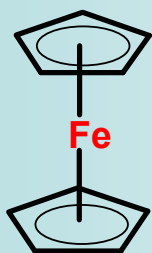
+ sum of the η number of the hydrocarbon ligands + sum of the electrons donated by other ligands

+ any negative charge on the complex

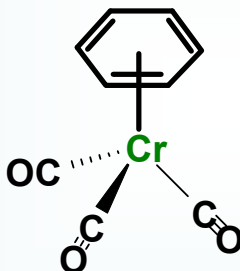
- positive charge on the complex

Should = 18 normally

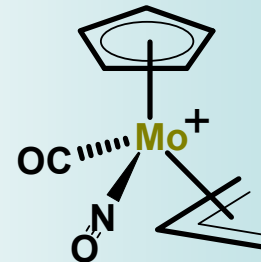
Many exceptions with early or late transition metals ; works best with middle transition metals



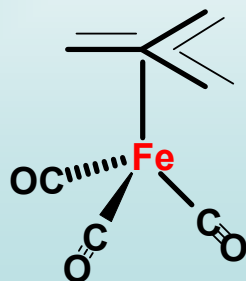
$$8 (\text{Fe}) + (2 \times 5) = 18e^-$$



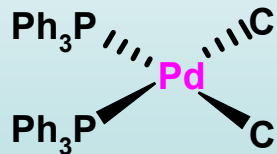
$$6 (\text{Cr}) + 6 (\text{Ph}) + (3 \times 2) = 18 e^-$$



$$6 (\text{Mo}) + 5 (\text{Cp}) + 2 + 3 + 3 - 1 = 18 e^-$$



$$8 + 4 (\text{TMM}) + (3 \times 2) = 18 e^-$$



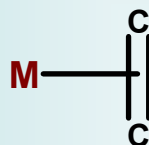
$$10 (\text{Pd}) + (2 \times 2) + (2 \times 1) = \underline{16} e^-$$

Bonding of Hydrocarbon Ligands

- In its simplest form, bonding of the π - system to a transition metal fragment is based on the

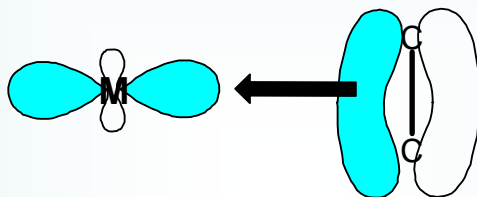
Dewar-Chatt-Duncanson Model

Consider



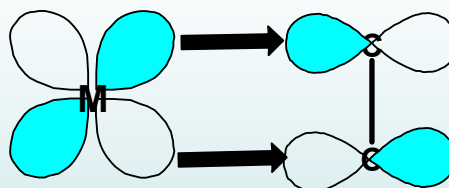
- There are two contributions to bonding

1) Ligand to Metal Donation



Note: this is not a π - bond, but rather a σ - bond

2) Metal to Ligand Back Donation



Note: this is a π - bond

Dewar, M. J. S. *Bull. Chim. Soc. Fr.* **1951**, C71.

Chatt, J.; Duncanson, L. A. *J. Chem. Soc.* **1953**, 2939.

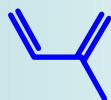
For higher level descriptions:

η^3 , η^4 , η^5 - see Yamamoto, A., p. 58-72

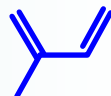
η^6 - see Collman, Hegedus, Norton, Finke p. 43-47⁸

Consequences of Bonding of Hydrocarbon Ligands

- 1) - In the alkene, the C=C bond is made weaker by complexation
- 2) - The ligand may be made more or less electron rich by complexation
-depends on case
- 3) - The organic fragment often loses its only plane of symmetry
-for example

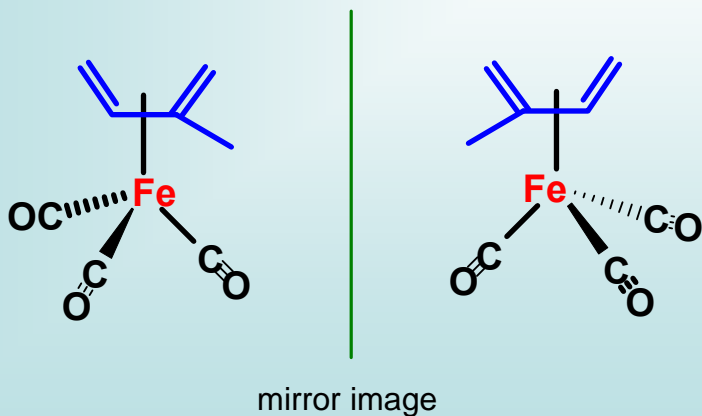


and



are the same compound

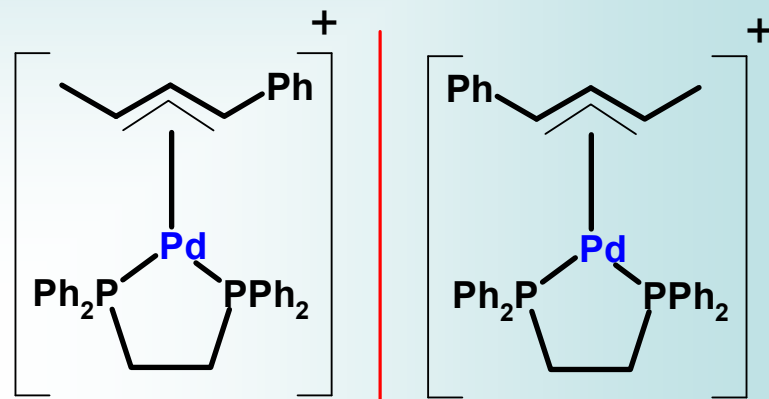
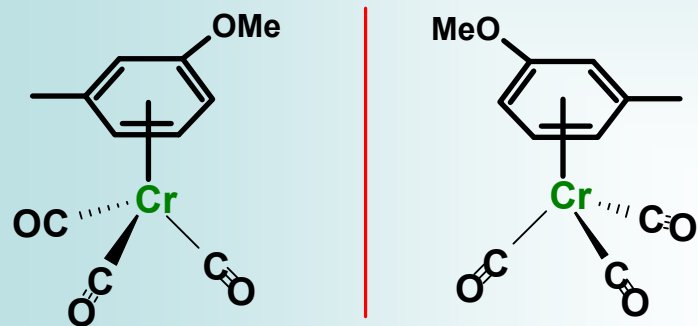
But.....



These are not the same compound
- the plane of symmetry is destroyed

No non-superimposable mirror images
Enantiomers

Other examples



Same situation: Each pair is enantiomeric

Basic Organometallic Reactions

There are several additional fundamental types of reactions in organometallic chemistry

The more complex reactions are normally some combination of these fundamental ones

1) Lewis Acid Dissociation

- many transition metal compounds, especially hydrides, can lose as Lewis acid (i.e., deprotonate)

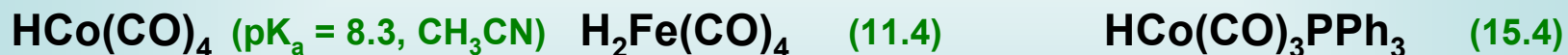


change in number of metal valence e-'s 0

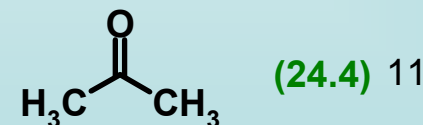
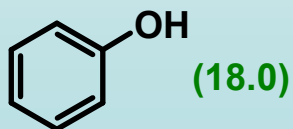
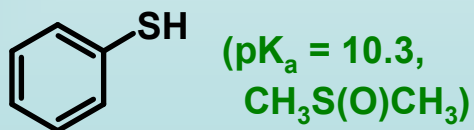
change in formal metal oxidation state **-2**

change in coordination number at the metal **-1**

**This may be a surprise, but many transition metal hydrides are quite acidic
-notice that making the metal more electron rich decreases acidity**

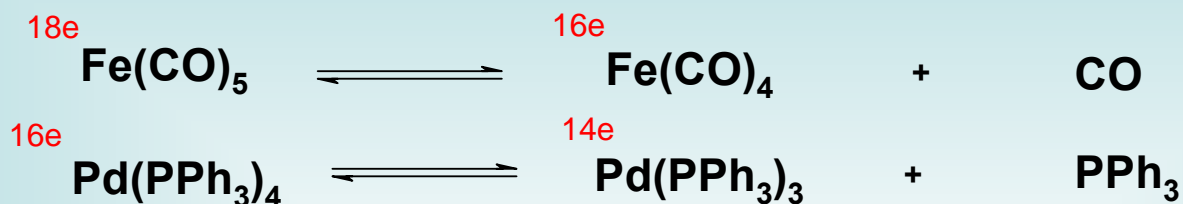


Winkler, J. R. et al (Gray, H. B.) *J. Am. Chem Soc.* **1986**, 108, 2263.



2) Lewis Base Dissociation

Very, very, very.....common process



change in number of metal valence e-'s -2

change in formal metal oxidation state 0

change in coordination number at the metal -1

-Reverse reaction: Lewis base Association

Obvious application are in ligand substitution processes,
which may be dissociative ('S_N1 like')

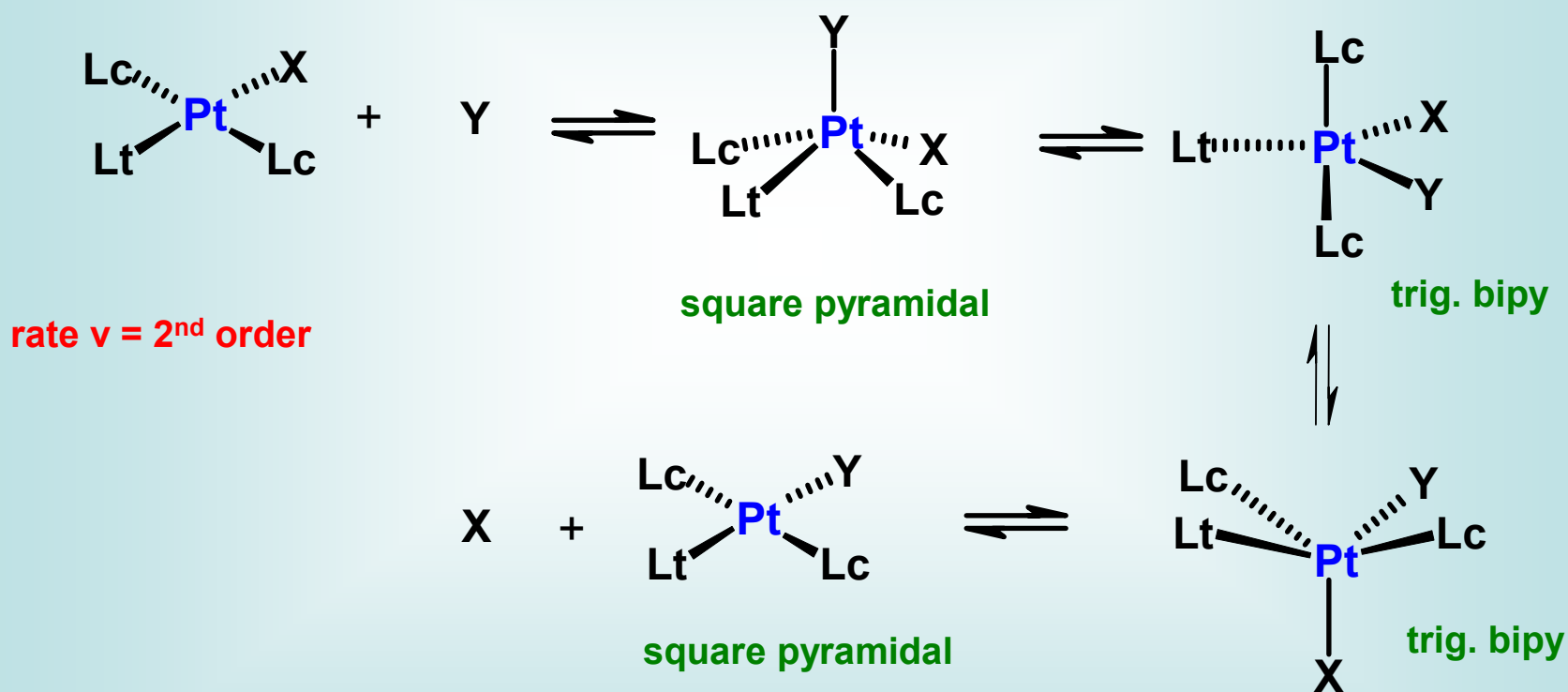


$$v = k [\text{Ni(CO)}_4] \quad \text{1st order}$$

Most common for 18 e⁻ systems

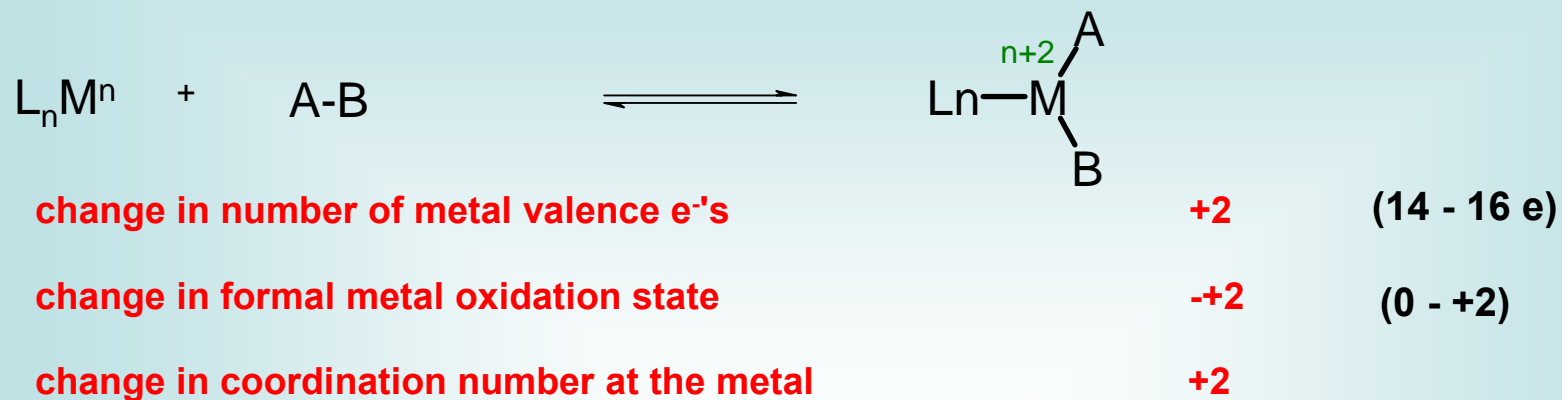
- Alternatively, this can be associative, i.e., "S_N2 like"

-more common for 16 e⁻, d⁸ square planar complexes (i.e., Ni^{II}, Pd^{II}, Pt^{II}, Rh^I, Ir^I)



3) Oxidative Addition

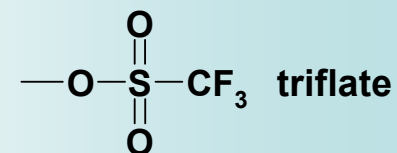
- represented by



for more details, see: R Yamamoto pp. 222-239
R Collman & Hegedus pp. 279-321

-Overall reaction is cleavage of the A-B bond with bonding to the metal

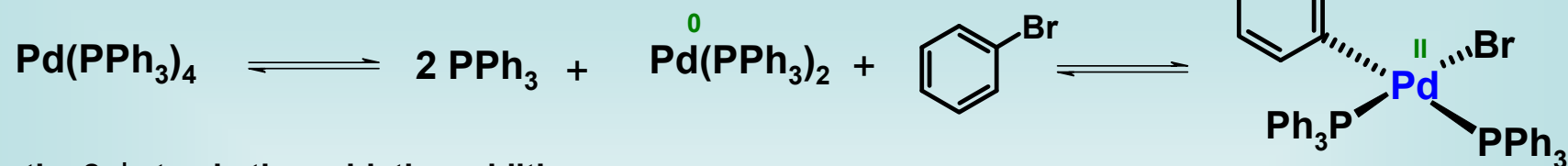
- Most common A-B is R_3C-X X = halogen or pseudohalogen



-Classic 'organic' example is Grignard reagent formation



- Most common example in this course will be of the following type:



- the 2nd step is the oxidative addition

Therefore, system needs: a) 2 available oxidation states i.e., Pd⁰/Pd^{II}, Fe⁰/Fe^{II}, Ir^I/Ir^{III}

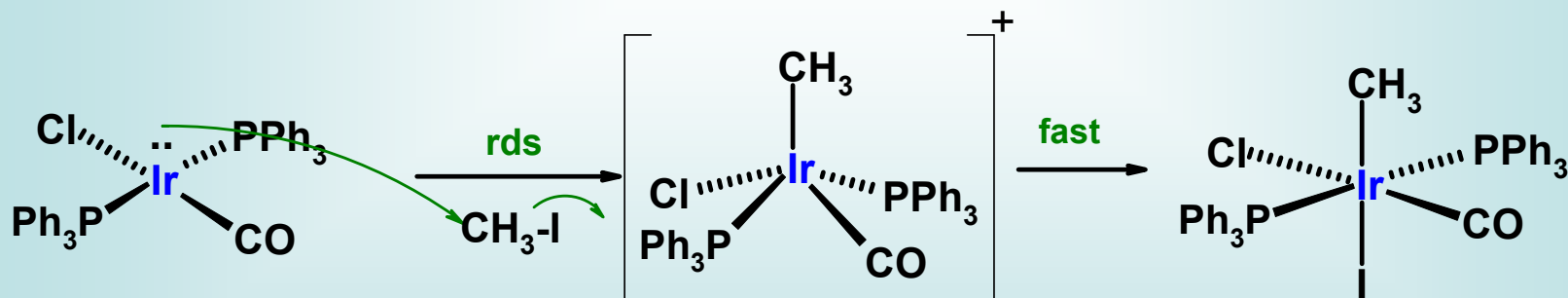
b) open coordination site

- Reverse reaction: Reductive Elimination

Mechanism

- Most is known about late transition metals (such as Ir, Ni groups)

A) If the R of R-X is alkyl (especially 1° or 2°), the reaction is believed to (usually) occur via an S_N2 substitution

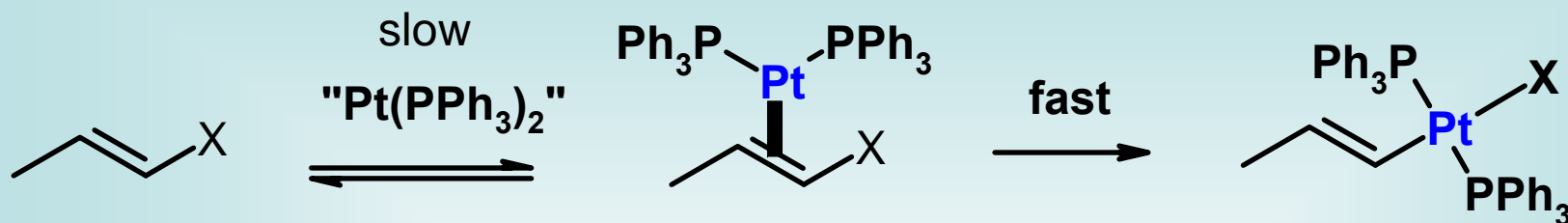


- *Inversion* at alkyl carbon *has* been observed

- Kinetics are overall 2nd order

$$v = k [\text{Ir}^I] [\text{CH}_3\text{I}]$$

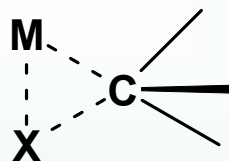
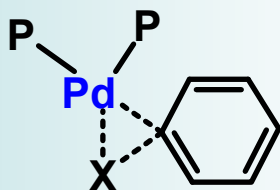
B) Vinyl (and perhaps aryl) halides go via π - complex formation, with ultimate direct insertion



- Goes with retention of configuration of C=C configuration
- Also believed to be mechanism for addition of H_2

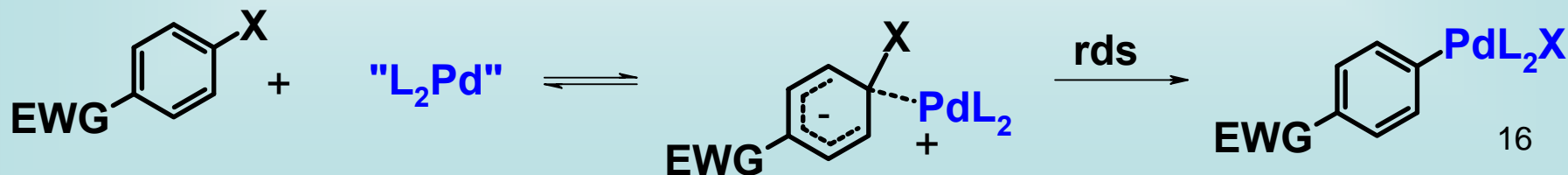
B') Aryl halides go via direct insertion into C-X bond (*clearly related to B*)

i.e.,

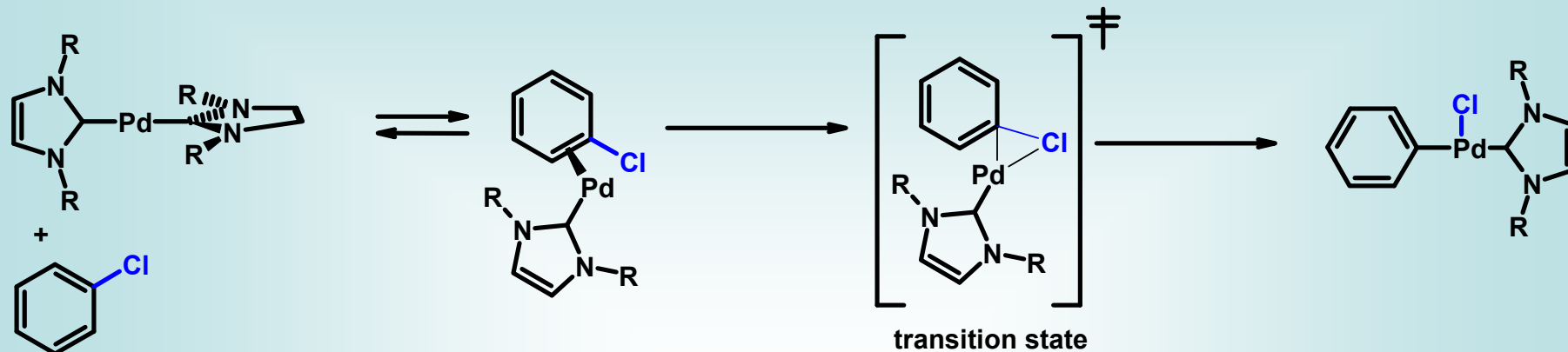


Could result in retention of configuration in some cases

C) - Now defrocked - Nucleophilic Aromatic Substitution - was an old proposal for aryl cases, to rationalized that cases with electron withdrawing groups "always" go faster

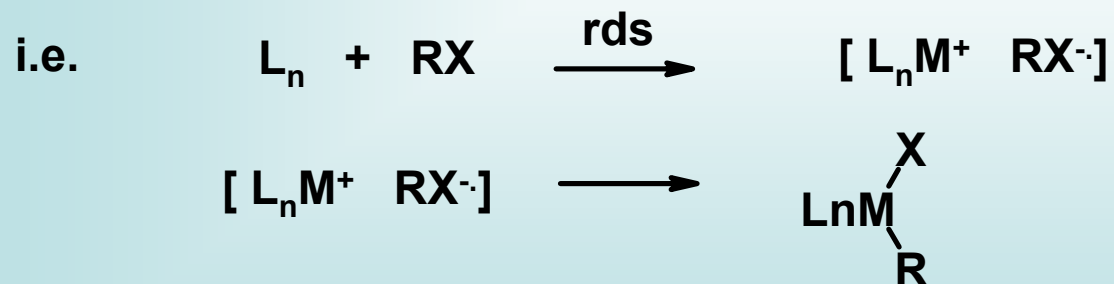


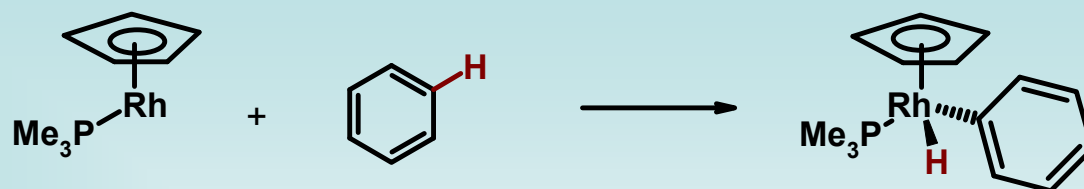
C)' - much more likely and often detected in calculations is initial formation of an η^2 -benzene complex



Green, J. C. J. Organomet. Chem. **2005**, 690, 6054.

D) - Electron transfer, radical mechanisms do exist (Ni, Mg)



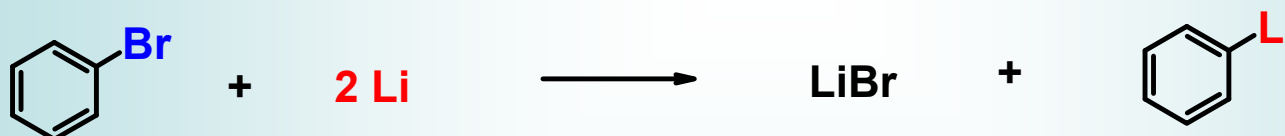


Bi, S. *Chem. Phys. Lett.* **2006**, 431, 385.

Aside: One electron oxidative additions also exist



Conventional organic example - Lithium-Halogen exchange



Many new opinions on these matters:

R Hartwig, J. F. *Synlett* **2006**, 1283.

R Espinet, P.; Echavarren, A. M. *Angew. Chem. Int. Ed. Engl.* **2004**, 43, 4704.

R Jutand, A. *Eur. J. Inorg. Chem.* **2003**, 2017.

Alcazar-Roman, L. M.; Luis, M.; Hartwig, J.F.; Rheingold, A. L.; Liabe-Sands, L. M.; Guzei, I. A. *J. Am. Chem. Soc.* **2000**, 122, 4618. (chelate PR_3)

Hartwig, J. F.; Paul, P. *J. Am. Chem. Soc.* **1995**, 117, 5373 (monodentate PR_3)

R Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, 33, 314.

Lersh, M.; Tilset, M. *J. Am. Chem. Soc.* **2005**, 127, 2471 (C-H activation).

4) Reductive Elimination - reverse of oxidative addition



change in number of metal valence e-'s

-2

(16e - 14e)

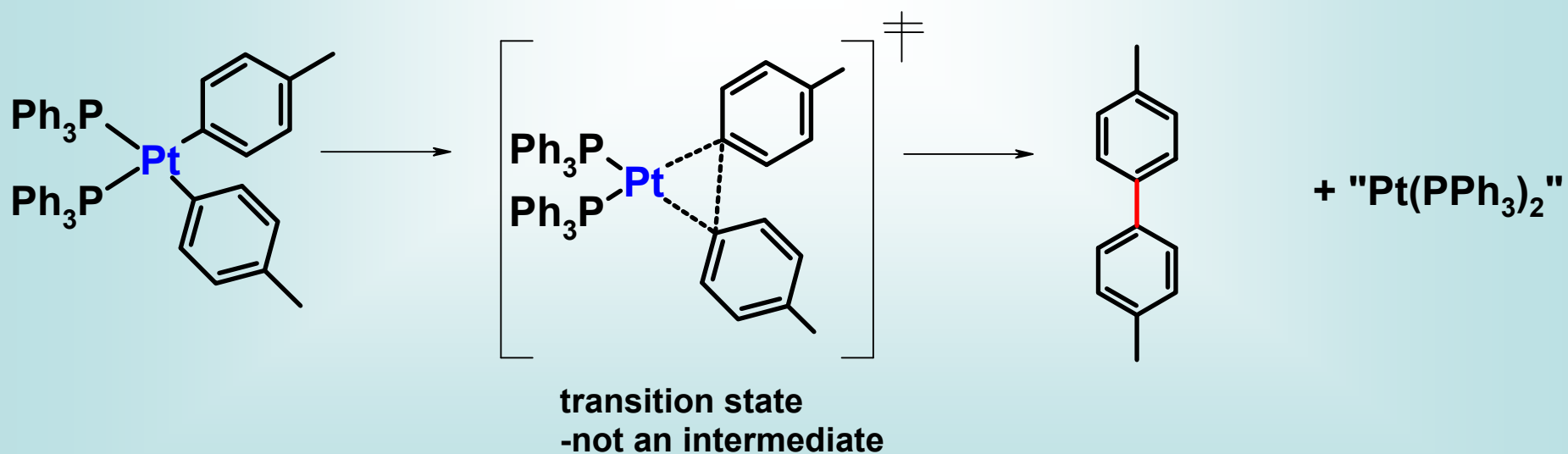
change in formal metal oxidation state

-2

(+2 - 0)

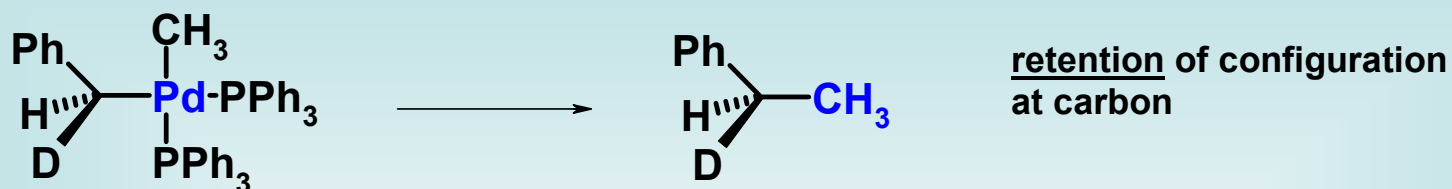
change in coordination number at the metal

-2



In 'normal' cases, the reaction goes by a concerted mechanism

-and, importantly for organic chemists.....



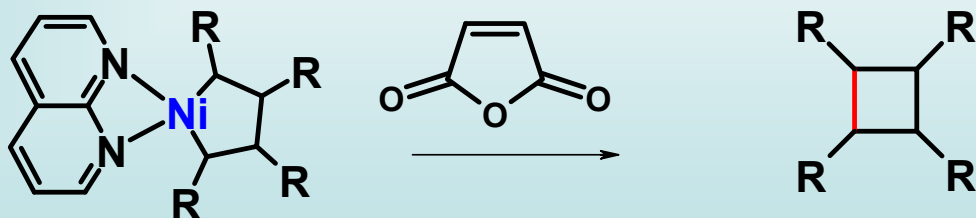
Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4981

Note: Whether the precursor is square planar or trigonal bipyramidal,
it's the *cis* groups which reductively eliminate

Other notes on reductive elimination:

- Again, need two accessible oxidation states
- Non 18 e⁻ situations must be accessible
- Ni group (Ni, Pd, Pt) are the usual synthetic choices

Since metal becomes more electron rich during the reaction,
the reaction is sometimes accelerated by addition of a ligand
which is electron withdrawing

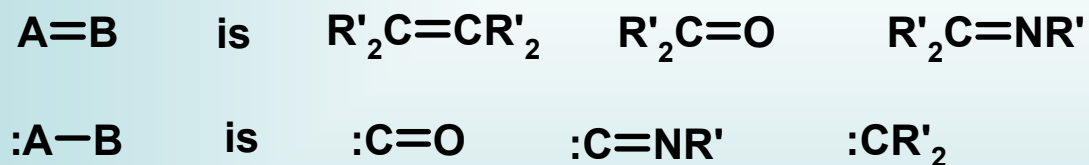
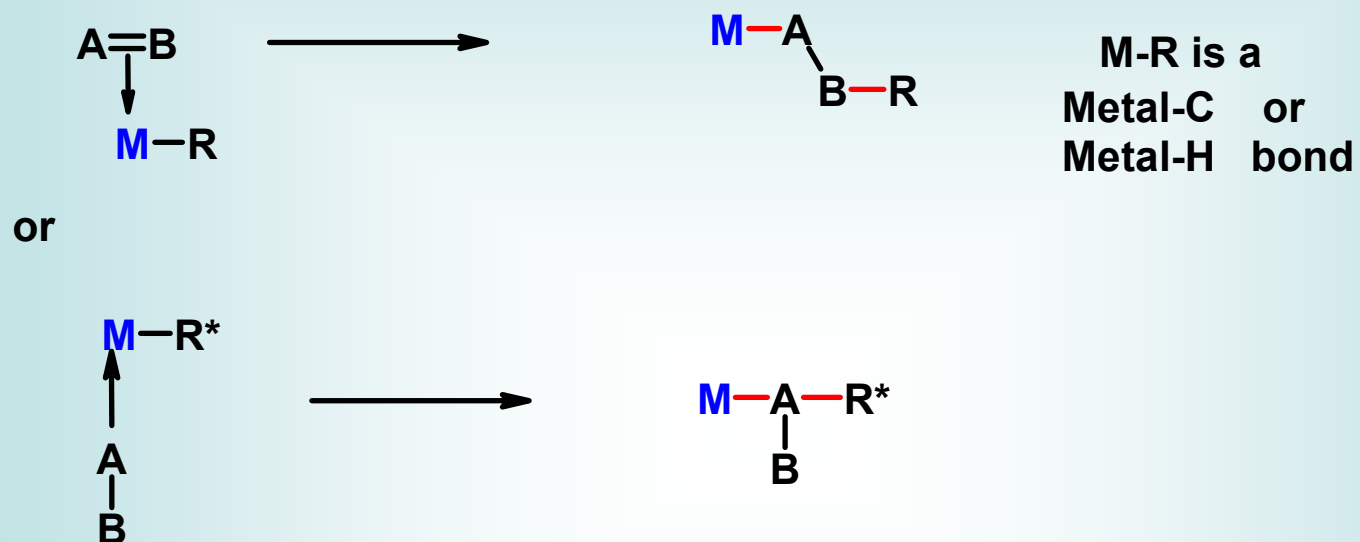


More details in general:

Yamamoto, pp. 240-5
Collman, Hegedus pp 322-33

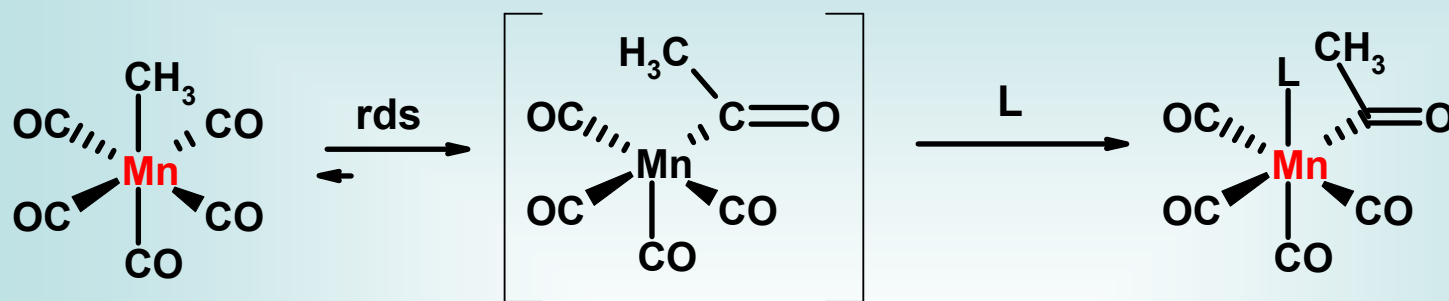
5) Insertion (Migration)

-There is more than one type possible



Most common $:\text{A}-\text{B}$ is CO

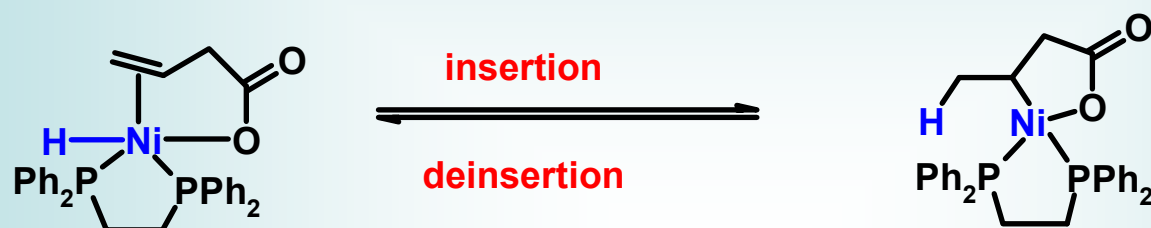
-The reaction is a concerted migration of R*, with retention of configuration at R* and the metal, if they are chiral



Change in # of valence electron at the metal	-2	(18 to 16e)
Change in metal oxidation state	0	(+1 to +1)
Change in coordination number	-1	(6 to 5)

Note: Reverse reaction is deinsertion

Most common A=B in this case are alkenes or alkynes
-for example, the intermediate step in hydrogenation



- The reverse reaction in this case (β-elimination) is one of the most common reactions of alkylmetals - main mode of decomposition

-again, if inserting group is alkyl, generally there is retention of configuration at R*

see R Cross, R. J., in "Chemistry of the Metal-Carbon Bond", Hartley and Patai, 1982, V.2

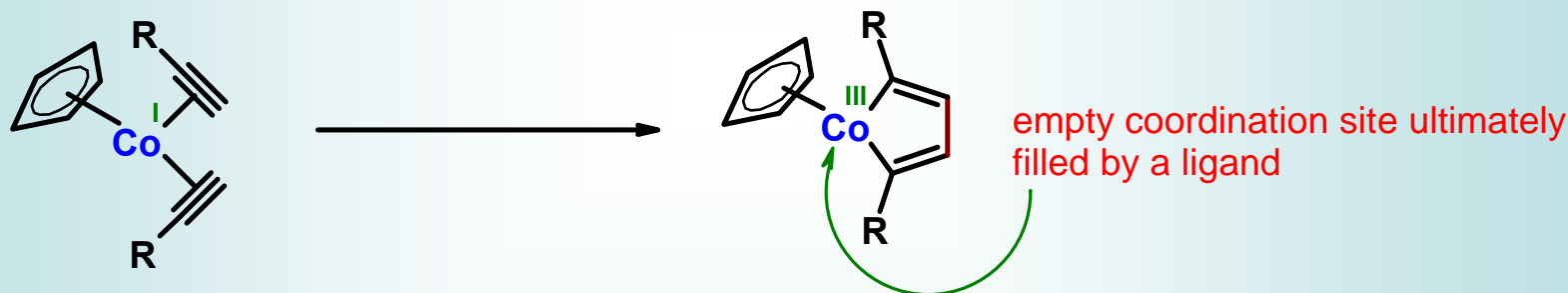
R Yamamoto, p. 246-272

6) Oxidative Coupling

Oxidative coupling occurs when two ' π -bound' ligands on the metal react with each other to form (usually) a C-C σ bond



One of the best known examples is....



-This has become increasingly important with a variety of metals and transformations

Change in number of valence electrons at metal -2 (18 to 16e)

Change in metal oxidation state +2 (+1 to +3)

Change in metal coordination number 0 ('3' to '3')