Organometallics in Homogeneous catalysis

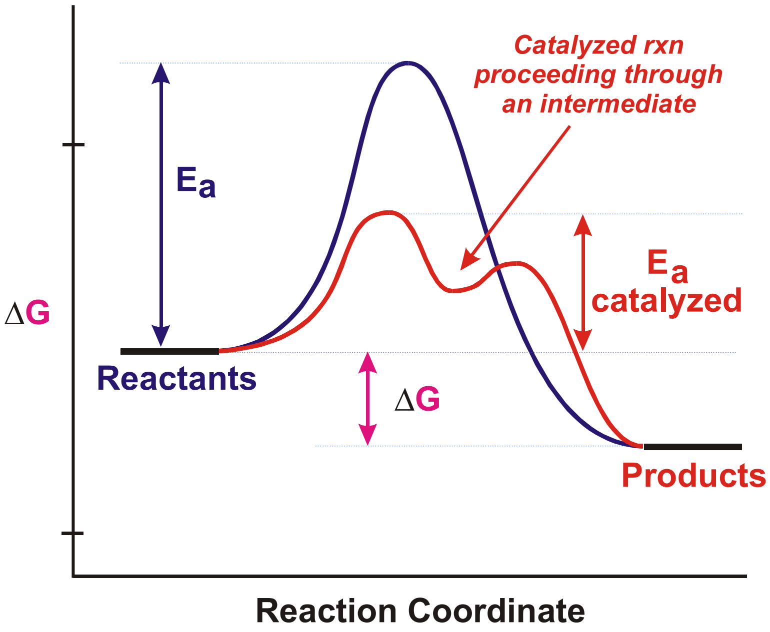
Definitions:

- Homogeneous catalysis: Catalyst and reaction substrates present in same phase (normally in solution).
- Heterogeneous catalysis: Catalyst and reaction substrates in different phase. Normally catalyst on solid support and substrates in solution or the gaseous phase.

Transition Metal Catalysis

$$A + B \xrightarrow{[\textit{catalyst}]} C$$

A catalyst is a substance that increases the rate of rxn without itself being consumed (but it is involved!) in the reaction. A catalyst speeds up the rate at which a chemical reaction reaches equilibrium. The overall thermodynamics of the rxn is *NOT* changed by the catalyst. Therefore, very endothermic (*non-spontaneous*) reactions are usually NOT suitable for catalytic applications.

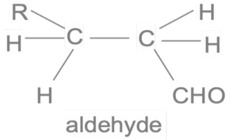


A catalyst provides an **alternate mechanism** (or pathway) for the **reactants** to be transformed into **products**. The catalyzed mechanism has an **activation energy** that is lower than the original uncatalyzed rxn. An excellent catalyst will lower the activation energy the most.

Evaluation of Homogeneous *vs.* Heterogeneous catalysis

Property	Homogeneous	Heterogeneous
Activity	All metal atoms active	Surface sites only
Product Selectivity	Controlled by ligand design	Difficult to control
Operating conditions	Relatively low temperature and pressure	High temperature and/or pressure
Product separation	Difficult eg distillation	Different phases - usually easy

Industrial Importance of Homogeneous processes with a transition metal complex catalyst

Process	Catalyst	Substrates	Product
Hydrogenation	$RhCl(PPh_3)_3$ (Wilkinson)	alkene	alkane
Monsanto Acetic Acid	$[RhI_2(CO)_2]^-$/HI	MeOH/CO	MeCOOH (acetic acid)
Hydroformylation (Oxo process)	$HCo(CO)_4$ $HRh(CO)(PPh_3)_3$	$H_2C{=}CHR/$ CO/H_2	
Alkene metathesis	Ru(carbene) Grubbs catalyst	$R_2C{=}CH_2$ $R'_2C{=}CH_2$	$R_2C{=}CR'_2$ $H_2C{=}CH_2$
Alkene polymerisation	Ziegler Natta (Ti) or metallocene (Zr)	alkenes	Polyethylene Polypropylene

Key properties of metal complexes for application as homogeneous catalysts

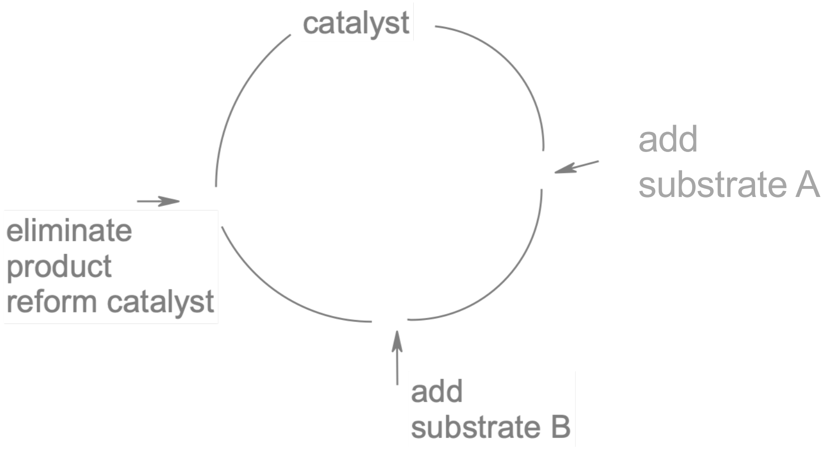
- Variable coordination number: allows coordination of basic feedstocks (CO, H_2, alkene) then elimination of product.

- Variable oxidation state: allows activation of substrates by oxidative addition then product removal by reductive elimination.

- Variable ligand set: Specificity for formation of a given product isomer (eg linear or branched chain) or enantiomer may be controlled via design of supporting ligands eg sterics of PPh_3.

Catalytic Cycles

- Most homogeneous processes proceed via catalytic cycles. A series of stoichiometric reactions form a closed loop.



- The 'catalyst' is regenerated at end of cycle.
- Individual steps include oxidative addition, reductive elimination, migratory insertion reactions. Most steps are reversible.
- Common substrates CO, H_2, alkenes.
- Steps proceed with alternating 16/18/16/18 electron systems.

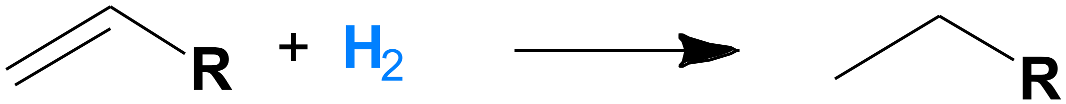
Some Catalysis Terminology

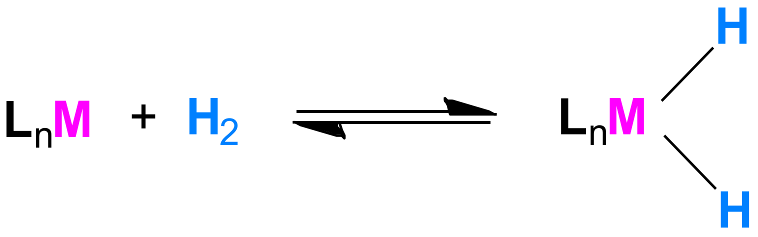
Turnover (TO) -- one loop through the catalyst cycle. Typically one equivalent of reactant is converted to one equivalent of product (per equivalent of catalyst).

Turnover Frequency (TOF) or Turnover Rate -- the number of passes through the catalytic cycle per unit time (typically sec, min or hrs). This number is usually determined by taking the # of moles of product produced, dividing that by the # of moles of catalyst used in the reaction, then dividing that by the time to produce the given amount of product.

1) # of turnovers performed – more is better
2) TOF (turnover frequency) – faster is better
3) Good selectivity for the product – this includes chemoselectivity, regioselectivity, and enantioselectivity (if applicable)
4) Reaction conditions – harsh? Mild? Unusual? Concentrations?

Hydrogenation





$$L_nM + H_2 \rightleftharpoons L_nM{<}^{H}_{H}$$

oxidative addition

$$L_nM\text{-}X + H_2 \rightleftharpoons L_nM\text{-}H + HX$$

hydrogenolysis

$$L_nM + H_2 + B: \rightleftharpoons [L_nM\text{-}H]^- + H^+:B$$

heterolytic cleavage

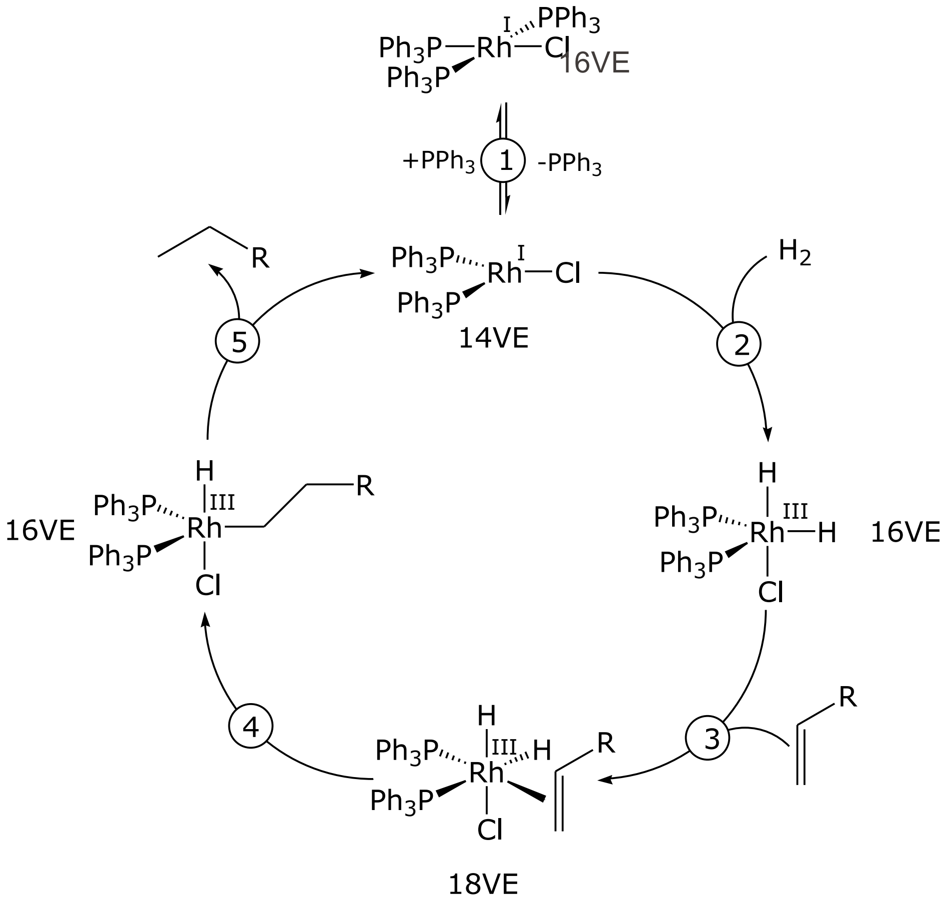
Selected catalytic cycles:

Hydrogenation of Alkenes:

The first practical catalyst was (Ph$_3$P)$_3$RhCl, known as Wilkinson’s catalyst, which enables the hydrogenation of terminal and internal alkenes at room temperature and standard pressure. Wilkinson shared the 1973 Nobel Prize in Chemistry with Fischer for this.

The key steps are:

1) Ligand dissociation.
2) Oxidative addition of H_2.
3) Coordination of alkene.
4) 1,2-Migratory insertion of the alkene.
5) Reductive elimination of alkane.

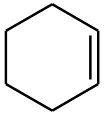
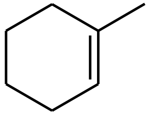
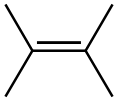
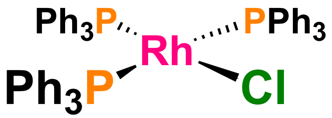
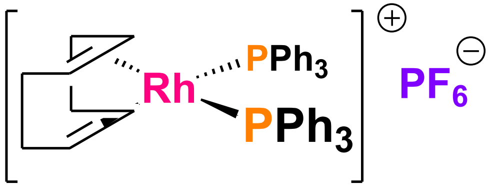
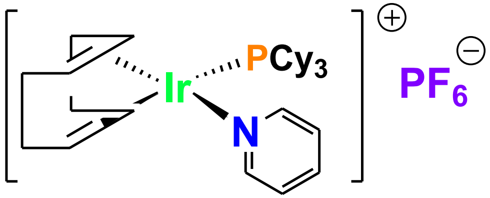


The “dissociative” pathway 1000 times faster than the pathway through the 18e- intermediate (RhCl(PPh$_3$)$_3$ (H)$_2$. although the 16e- RhCl(PPh$_3$)$_3$ complex is more electron-rich and should do an OA of H_2 faster than the 14e- RhCl(PPh$_3$)$_2$ species, a combination of steric effects and the higher reactivity of a 14e- species compensates.

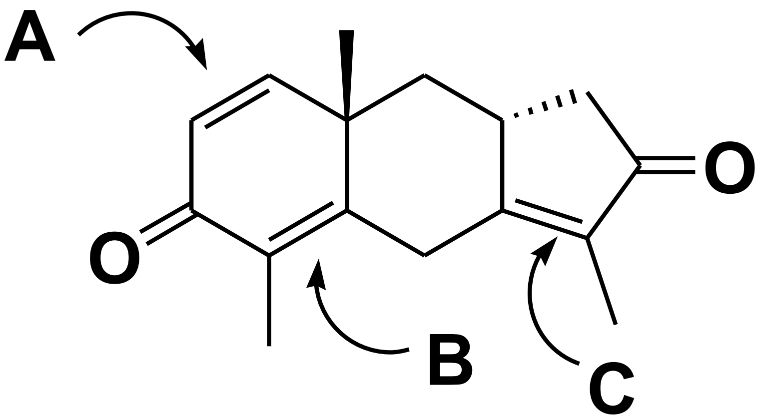
Activity:

Crabtree *Acc. Chem. Res.* **1979**, *12*, 331

TOF

				
 *Wilkinson's catalyst*	650	700	13	---
 *Schrock-Osborn catalyst*	4000	10	---	---
 *Crabtree's catalyst*	6400	4500	3800	4000

Problem: In the molecule below, which of the olefins (A, B, or C) would you expect to hydrogenation faster and why?

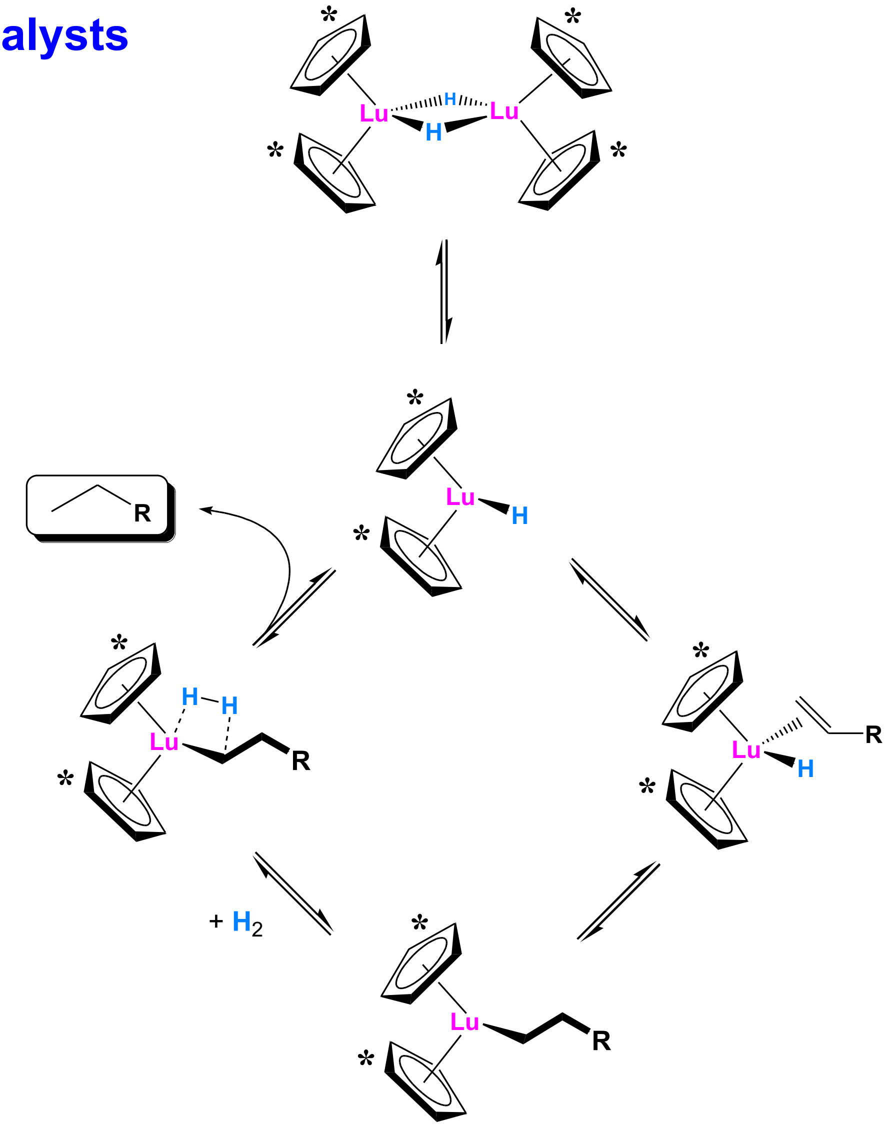


A will be the first double bond to be hydrogenated because it is the least sterically hindered (less substituted). Note that conjugated double bonds are generally less reactive than isolated double bonds. But all the double bonds in this molecule are conjugated, so steric effects dominate.

Lanthanide Hydrogenation Catalysts

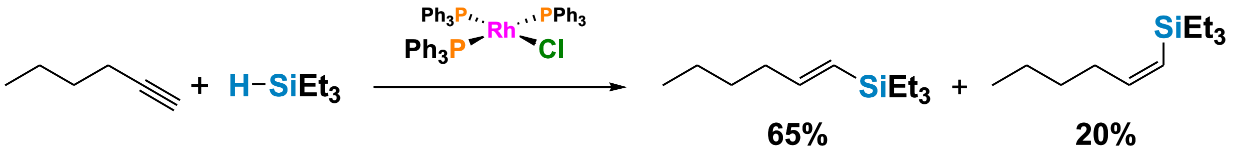
Tobin Marks reported the extraordinary activity of $(Cp^*_2LuH)_2$ for the hydrogenation of alkenes and alkynes. The monometallic complex catalyzes the hydrogenation of 1-hexene with a TOF = 120,000 hr^{-1} at 1 atm H_2, 25ºC!!

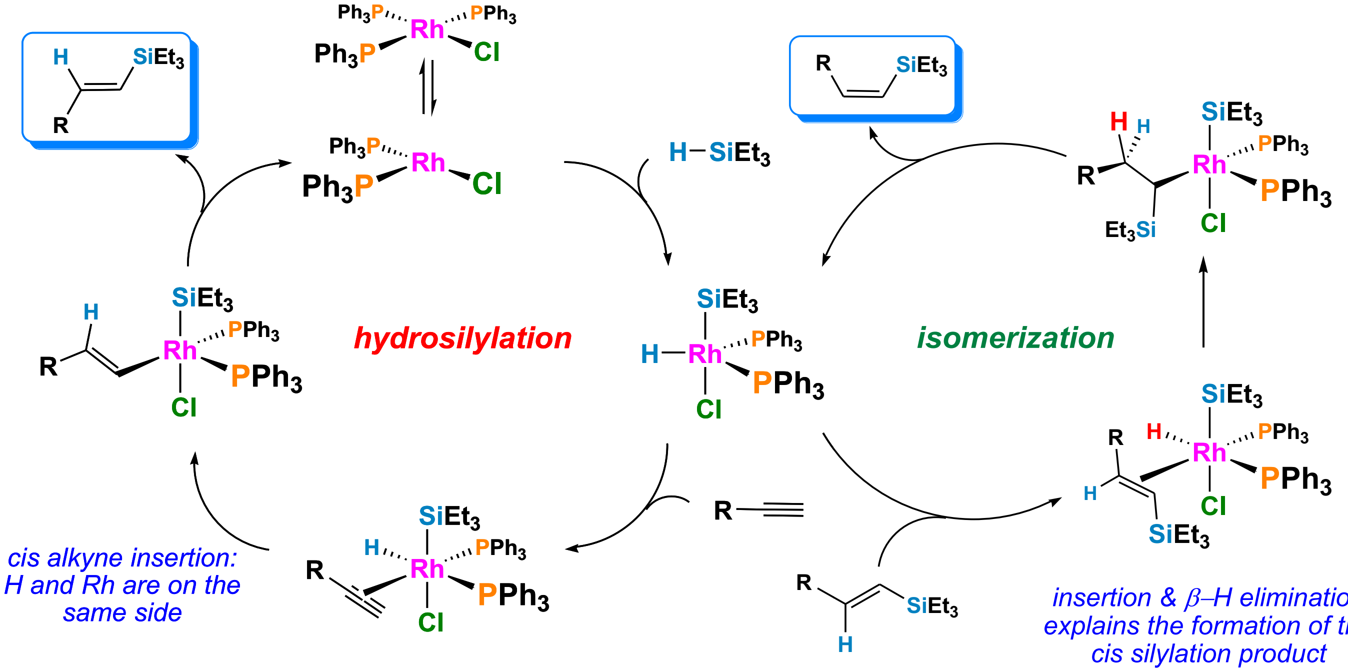
This is one of the most active hydrogenation catalysts known.



Other H-X additions: Hydrosilylation

Parish *JOMC* **1978**, *161*, 91

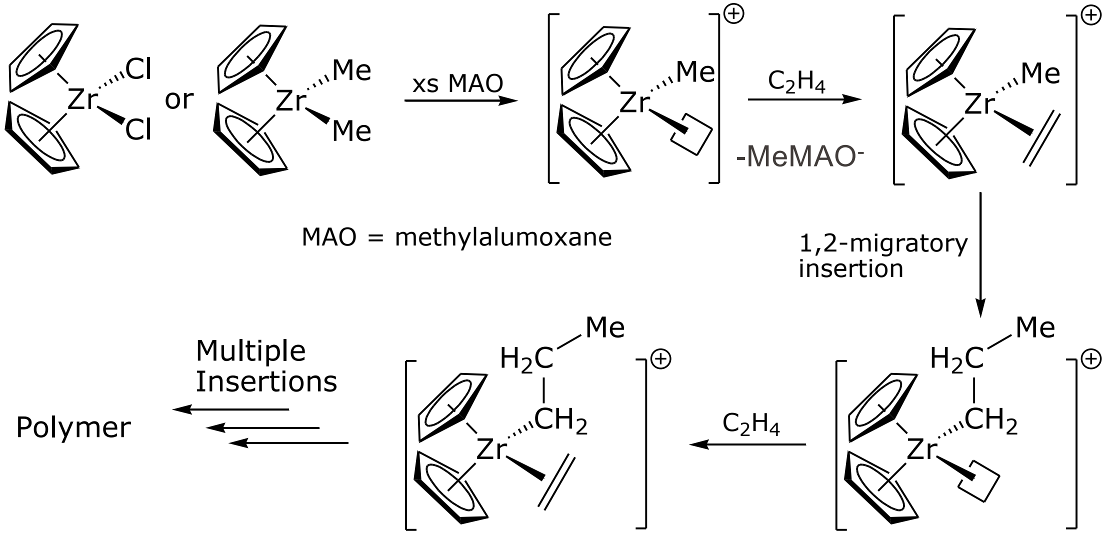




cis alkyne insertion:
H and Rh are on the
same side

insertion & β–H elimination
explains the formation of the
cis silylation product
(In fact, adding catalyst and HSiR$_3$
to the isolated trans product leads
to isomerization)

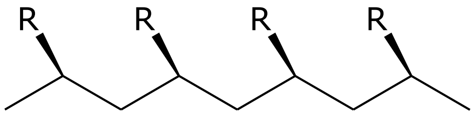
Alkene Polymerisation by Zirconocene Catalysts:



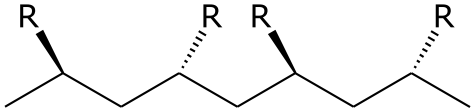
MAO = methylalumoxane

Different types of metallocene catalysts afford different types of tacticity in polymers derived from 1-substituted alkenes:

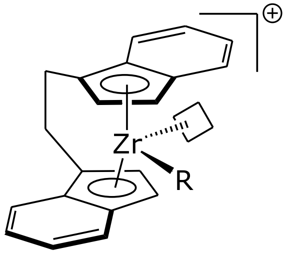
- isotactic:



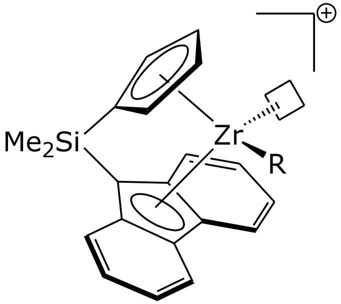
- syndiotactic:



- atactic: Random



produces
highly isotactic
polypropylene

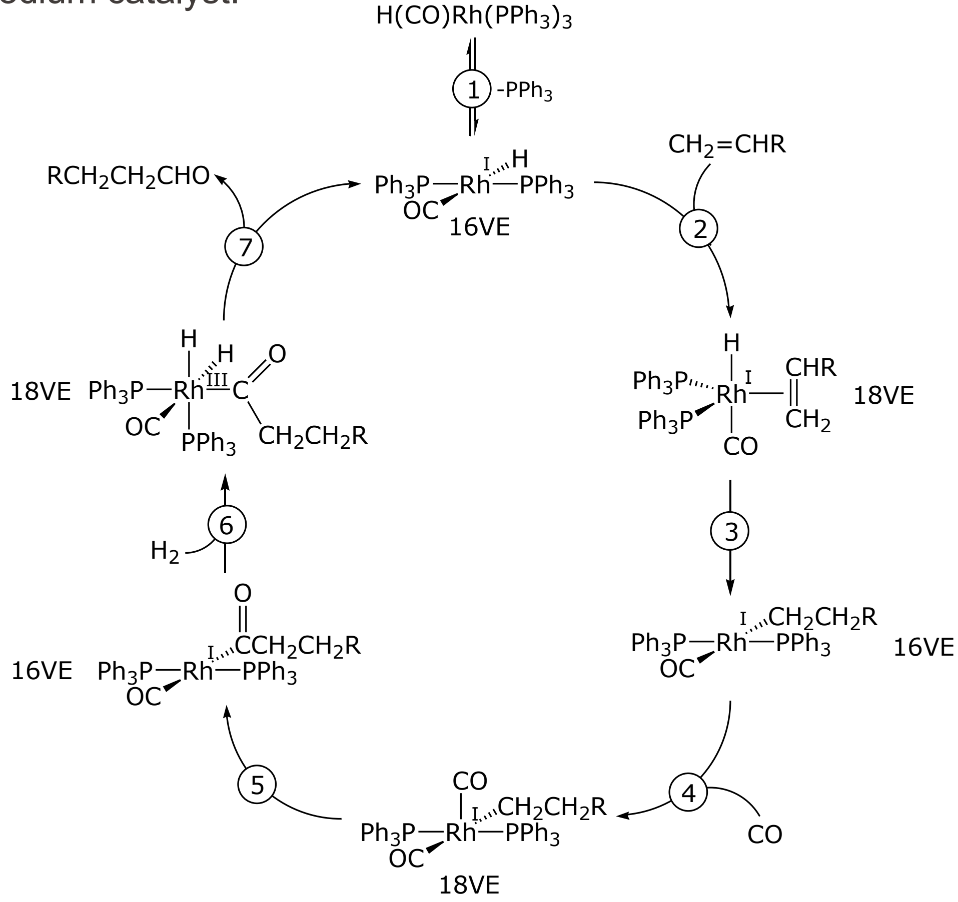


produces
highly syndiotactic
polypropylene

Hydroformylation:

Overall reaction formally entails the addition of H and HCO across a C=C double bond.
i.e. $RCH{=}CH_2 + H_2 + CO \rightarrow RCH_2\text{-}CH_2CHO$

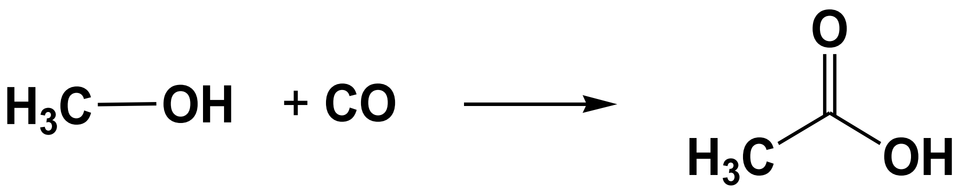
Union Carbide process using a rhodium catalyst:



The key steps are:

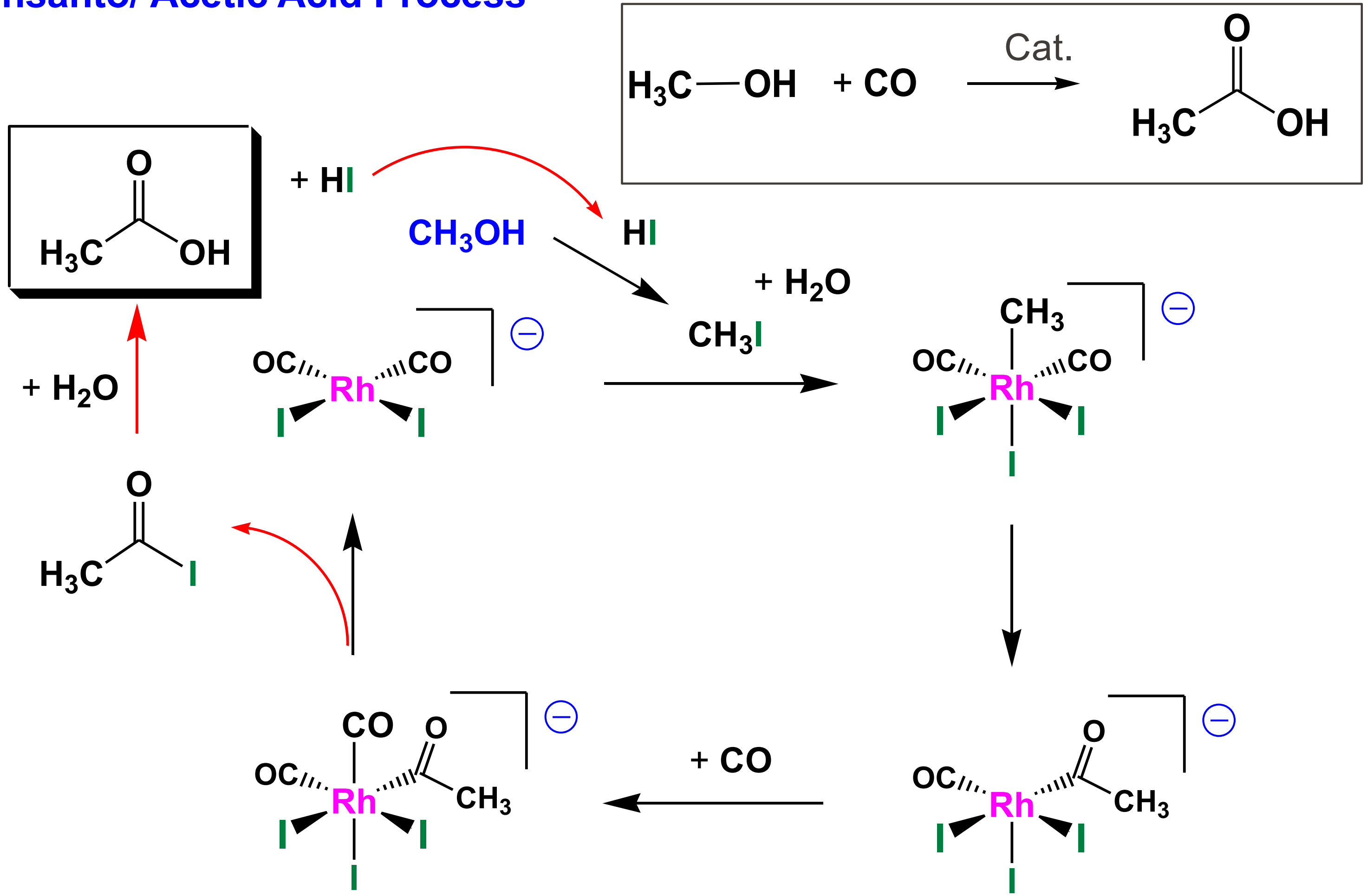
1) Ligand dissociation.
2) Coordination of alkene.
3) 1,2-Migratory insertion of the alkene.
4) Coordination of CO.
5) 1,1-Migratory insertion of CO.
6) Oxidative addition of $H_{2.}$
7) Reductive elimination of aldehyde.

Monsanto/BP/Celanese Acetic Acid Process



	Cobalt	**Rhodium**
Concentration	~ 10^{-1} M	~ 10^{-3} M
Temperature	~ 230°C	~180°C
Pressure	500-700 atm	30-40 atm
Selectivity	90%	> 99%
H_2 effect	CH_4, CH_3CHO, EtOH byproducts	no adverse effect

Monsanto/ Acetic Acid Process

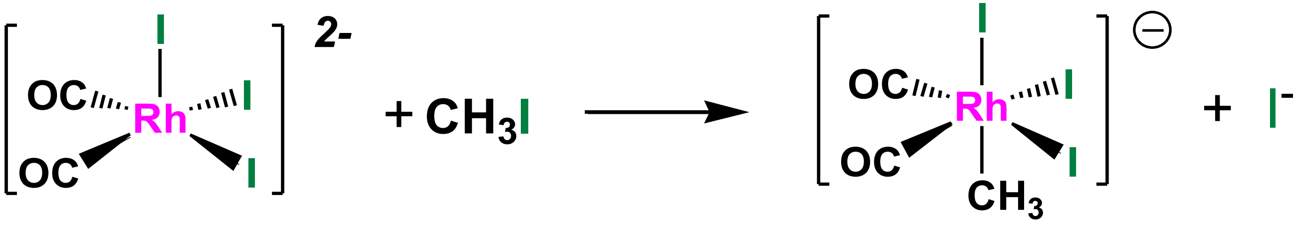


- The reaction is independent of CO pressure
- First order in both rhodium and MeI.
- Rate determining step is the oxidative addition of MeI to the $[Rh(CO)_2I_2]^-$ catalyst.

In the late 70's Celanese developed a major improvement on the Monsanto technology not covered by their narrow patent that involved the simple addition of LiI (and other proprietary modifiers) to reduce the amount of H_2O (and HI) used in the catalysis. Added LiI increased the catalyst stability by minimizing the side reactions that produced inactive Rh(III) species.

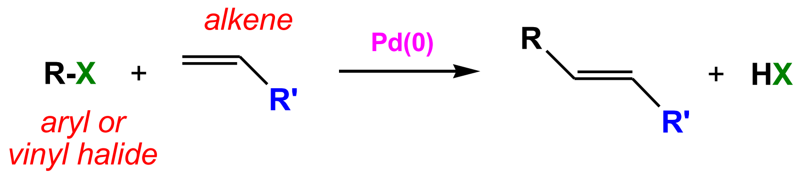
It also increased the amount of the more reactive dianionic $[RhI_3(CO)_2]^{2-}$ catalyst species. This considerably increased the catalyst activity, throughput, and efficiency.

Problem: Increasing the iodide concentration increases the amount of the following 18e- complex. Why is this more reactive and why doesn't this saturated 18e- complex slow down the subsequent oxidative addition reaction with MeI?



Pd-Catalyzed C-C Coupling Reactions

Heck reaction:



Stille coupling:

organotin

$$R\text{-}X + R'\text{-}SnR_3 \xrightarrow{Pd(0)} R\text{-}R' + XSnR_3$$

aryl or
vinyl halide

Negishi coupling:

organozinc

$$R\text{-}X + R'\text{-}ZnR \xrightarrow{Pd(0)} R\text{-}R' + XZnR$$

aryl or
vinyl halide

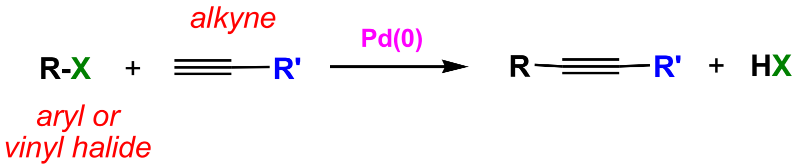
Suzuki coupling:

organoboron

$$R\text{-}X + R'\text{-}B(OH)_2 \xrightarrow{Pd(0)} R\text{-}R' + XB(OH)_2$$

aryl or
vinyl halide

Sonogashira coupling:

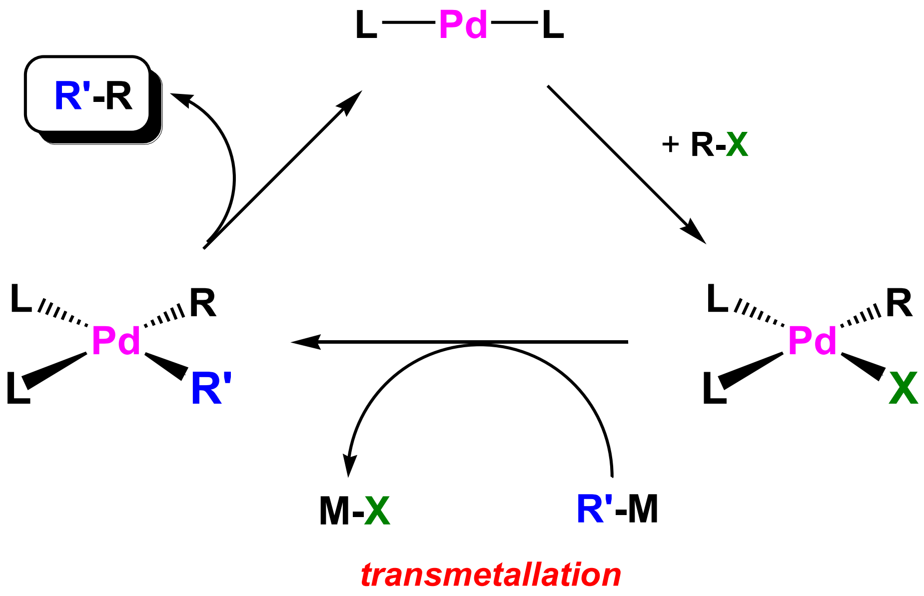


Cross-Coupling of Organometallics and Halides

$$R\text{-}X \quad + \quad R'\text{-}M \xrightarrow{Pd(0)} R\text{-}R' \quad + \quad MX$$

M = MgX, $ZrCp_2Cl$, ZnX, SnR_3, $B(OR)_2$, $AlMe_2$, SiR_3, Cu,…

The mechanism involves oxidative addition of the halide or triflate to the initial Pd(0) phosphine complex to form a Pd(II) species. The key slow step is a **transmetallation**, so called because the nucleophile (**R'**) is transferred from the metal in the organometallic reagent to the palladium and the counterion (**X** = halide or triflate) moves in the opposite direction. The new Pd(II) complex with two organic ligands undergoes reductive elimination to give the coupled product and the Pd(0) catalyst ready for another cycle.

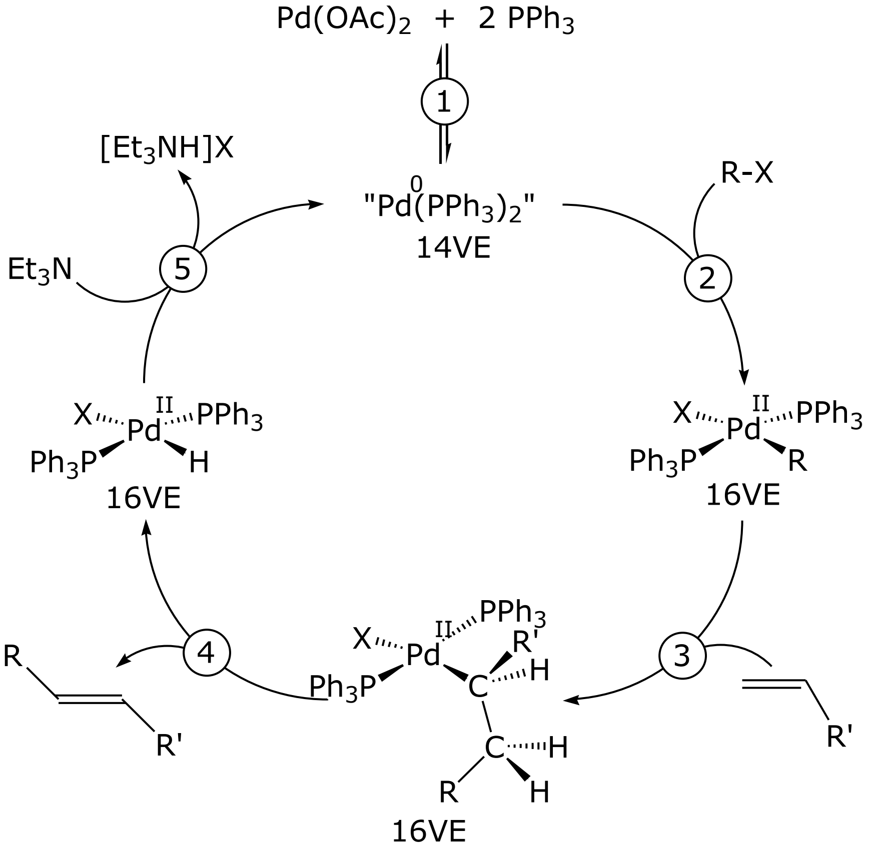


The halide partner (**R**–**X**) must be chosen with care, as β-hydride elimination would decompose the first intermediate during the slow transmetallation step. The choice for **R** is restricted to substituents without β-hydrogen atoms: vinyl, allyl, benzyl, and polyfluoroalkyl halides, triflates, and phosphates have all been coupled successfully.

The Heck Reaction:

The key steps are:

1) In situ reduction of Pd(II) → Pd(0).
2) Oxidative addition of R-X.
3) Coordination of alkene and 1,2-migratory insertion (this requires dissociation of one L).
4) β-hydride elimination of alkene.
5) Reductive elimination of HX.



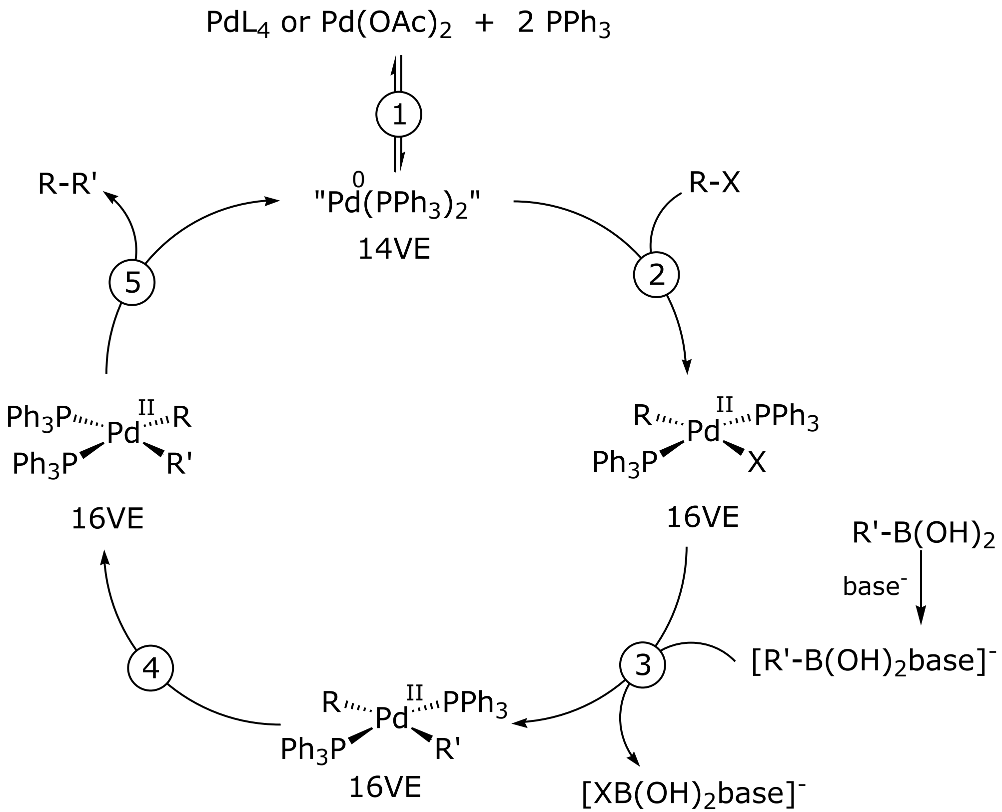
Note, this reaction requires a stoichiometric quantity of Et$_3$N for step 5.

This reaction works best for X = Br or I. X = Cl is an outstanding challenge.

In order to prevent rapid decomposition of the intermediate after step 2 by β-elimination, R can only be aryl, benzyl, or vinyl in nature.

The Suzuki Reaction:

The key steps are:



1) In situ reduction of Pd(II) → Pd(0).
2) Oxidative addition.
3) X/R’ exchange.
4) *Trans* → *cis* isomerisation.
5) Reductive elimination.

R’ = alkyl, alkenyl, or aryl.

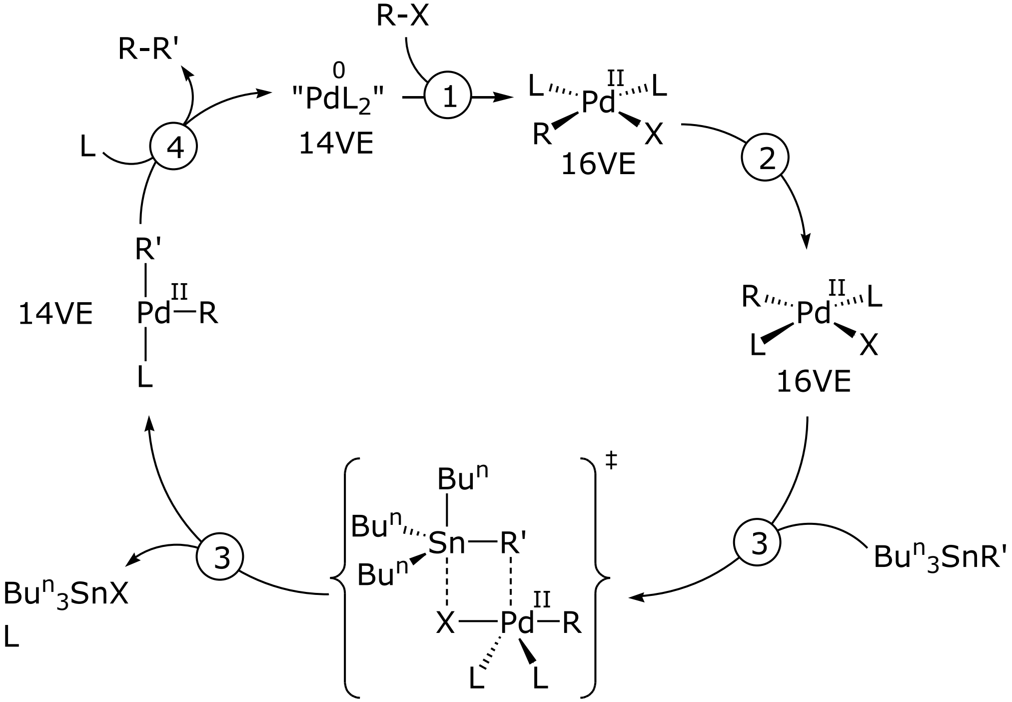
Base = NaOH, NaOEt, Na_2CO_3, etc.

In addition to the air- and water-stable nature of boronic acids, this reaction is tolerant of OH, NH, C=O, NO_2, and CN groups and is therefore the method of choice for C–C coupling.

The Stille Reaction:

The key steps are:

1) Oxidative addition.
2) Cis → trans isomerisation.
3) Transmetallation of R’ from Sn → Pd with displacement of L in a concerted step.
4) Reductive elimination.



Step 3 is slow, but step 4 is faster than typical β-hydride eliminations so the absence of β-hydrogens is only required for R and not R’.

A wide range of functional groups are tolerated.

If the reactions are conducted under CO, ketones are generated (migratory insertion of CO before step 4).

Reactivity at tin: alkyl < acetonyl < benzyl ≈ allyl < aryl < alkenyl < alkynyl.

X = Br or I is best, but the use of sterically demanding phosphines such as Bu^t_3P allows coupling reactions with aryl chlorides to proceed.

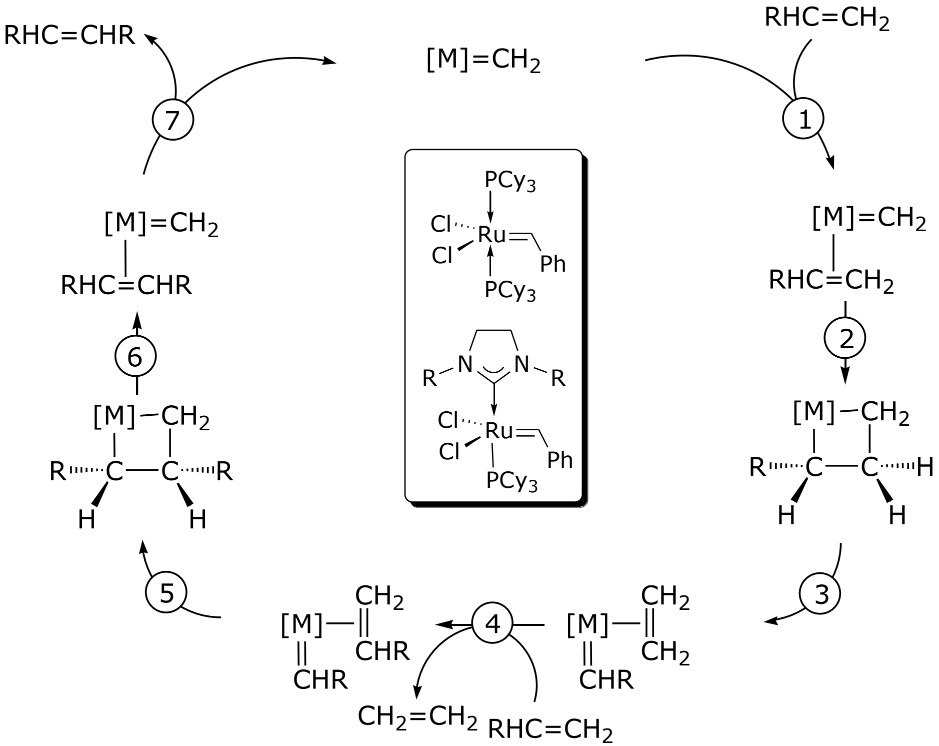
Alkene Metathesis:

This Nobel Prize 2005 in chemistry winning reaction is an incredibly important and versatile method for breaking and forming C=C double bonds. It has extensive applications in organic and polymer synthesis.

Yves Chauvin
Robert H. Grubbs
Richard R. Schrock

The key steps are:

1) Alkene coordination.
2) [2 + 2] Cycloaddition.
3) Retro-cycloaddition.
4) Alkene coordination/ displacement.
5) [2 + 2] Cycloaddition.
6) Retro-cycloaddition.
7) Alkene loss.



Alkene metatheses are essentially thermoneutral equilibria. A shift in the desired direction is achieved by removal of a volatile component (e.g. ethylene).

https://www.youtube.com/watch?v=uYzv9D0Lf0s

Amino-alkene Hydroamination/Cyclisation:

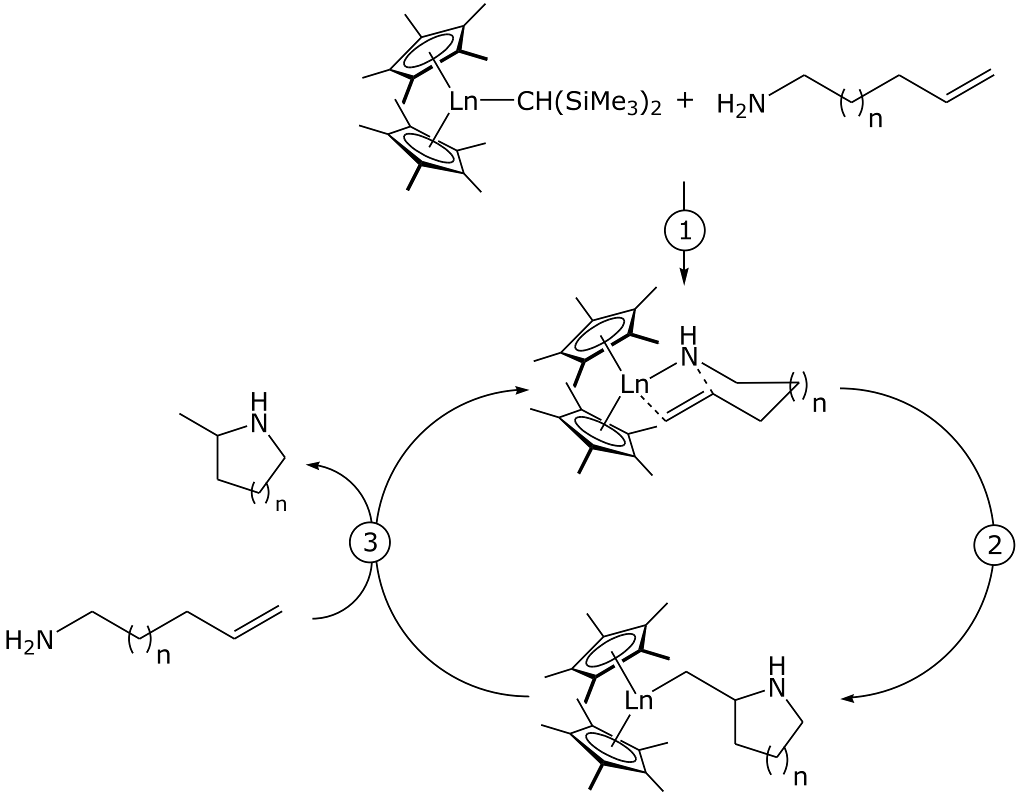
This is an elegant method for constructing N-heterocycles, and overall is the formal addition of H and NHR across a C=C double bond.

The key steps are:

1) Protonolysis.
2) σ-bond metathesis.
3) Protonolysis.

This chemistry also works very well for amino-alkynes, hydrophosphination, and hydrosilylation.

Note, the Cp* ring maintains a spectator/ancillary role.



Course Checklist

These are the most important concepts and facts you should know and be able to explain :

- Assign formal oxidation states.
- Assign a formal d^n count to a metal.
- Count the valence electrons for a metal (18/16-electron rule).
- Recognise where the 18-electron rule is inappropriate (e.g. coordination complexes).
- Draw a complex from a formula.
- Understand the impact of thermodynamic and kinetic factors on stability.
- Identify principal reaction types and when they are appropriate to use.
- Appreciate how to synthesise organometallic complexes.
- Describe synergic bonding (Dewar-Chatt-Duncanson model of synergic bonding).
- Describe the bonding in metal-carbon single, double, and triple bonds.
- Describe the bonding in complexes with π-bonding.
- Appreciate dynamic processes which may occur with bound π groups.
- Annotate catalytic cycles.

Summary Of Key Knowledge To Be Acquired

d^n Electron Count in Transition Metal Compounds:

d^n gives you the number of electrons formally associated with metal-centred (i.e. d) orbitals in a transition metal compound:

d^n = metal group number – O.S.

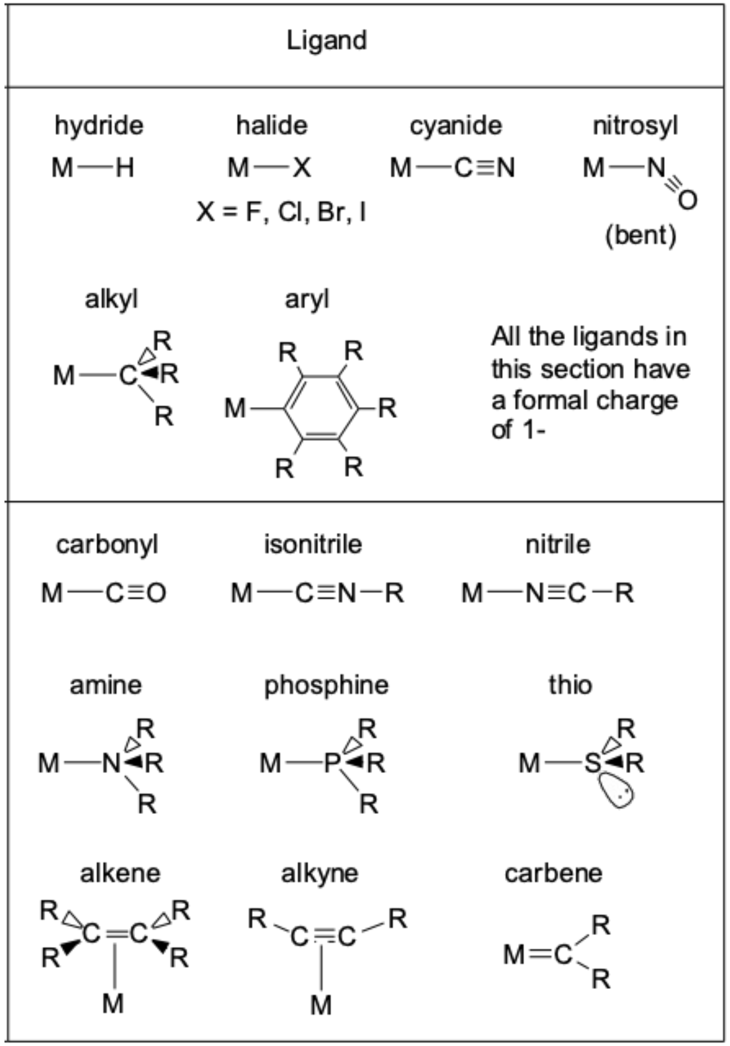
Do not confuse ion configurations in *complexes* with *atomic* configurations.

d^3 d^{10}

21 Sc $3d^14s^2$	22 Ti $3d^24s^2$	23 V $3d^34s^2$	24 Cr $3d^54s^1$	25 Mn $3d^54s^2$	26 Fe $3d^64s^2$	27 Co $3d^74s^2$	28 Ni $3d^84s^2$	29 Cu $3d^{10}4s^1$	30 Zn $3d^{10}4s^2$
39 Y $4d^15s^2$	40 Zr $4d^25s^2$	41 Nb $4d^35s^2$	42 Mo $4d^55s^1$	43 Tc $4d^55s^2$	44 Ru $4d^75s^1$	45 Rh $4d^85s^1$	46 Pd $4d^{10}5s^0$	47 Ag $4d^{10}5s^1$	48 Cd $4d^{10}5s^2$
57 La $5d^16s^2$	72 Hf $5d^26s^2$	73 Ta $5d^36s^2$	74 W $5d^46s^2$	75 Re $5d^56s^2$	76 Os $5d^66s^2$	77 Ir $5d^76s^2$	78 Pt $5d^96s^1$	79 Au $5d^{10}6s^1$	80 Hg $5d^{10}6s^2$
89 Ac $6d^17s^2$	104 Rf $6d^27s^2$	105 Db $6d^37s^2$	106 Sg $6d^47s^2$	107 Bh $6d^57s^2$	108 Hs $6d^67s^2$	109 Mt $6d^77s^2$	110 Ds $6d^97s^1$	111 Rg $6d^{10}7s^1$	112 Cn $6d^{10}7s^2$

Common Ligands (to know by Heart)

Ligands with Charge 0



Ligand

hydride: M—H

halide: M—X, X = F, Cl, Br, I

cyanide: M—C≡N

nitrosyl: M—N=O (bent)

alkyl

aryl

All the ligands in this section have a formal charge of 1-

carbonyl: M—C≡O

isonitrile: M—C≡N—R

nitrile: M—N≡C—R

amine

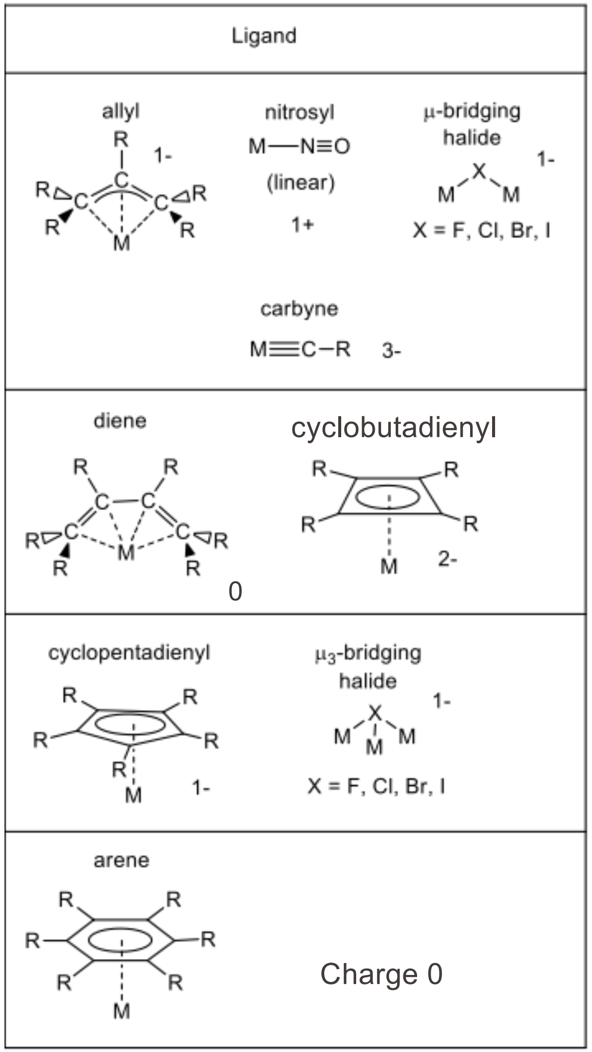
phosphine

thio

alkene

alkyne

carbene: M=C(R)R



Ligand

allyl, 1-

nitrosyl: M—N≡O (linear), 1+

μ-bridging halide, 1-, X = F, Cl, Br, I

carbyne: M≡C—R, 3-

diene, 0

cyclobutadienyl, 2-

cyclopentadienyl, 1-

μ_3-bridging halide, 1-, X = F, Cl, Br, I

arene

Charge 0

Ligand	Covalent (Neutral)	Ionic (Charged)	Charge (ionic model)
Alkyl, aryl, H, η^1-allyl, η^1-cyclopentadienyl (Cp), halide	1	2	−1
NO (bent)	1	2	−1
CO, N_2, PR_3, NR_3, OR_2, RNC, pyridine	2	2	0
CR_2 (Fischer carbene)	2	2	0
Alkene, alkyne[b]	2 or 4 (alkyne only)	2 or 4	0 (or −2)
CR_2 (Schrock carbene)	2	4	−2
η^3-allyl or η^3-Cp	3	4	−1
NO (linear)	3	2	+1
η^4-butadiene, η^4-C_6H_6, alkyne[b]	4	4	0
η^5-Cp,	5	6	−1
η^6-arene,	6	6	0
η^7-C_7H_7 (cycloheptatrienyl)	7	6 (as cation) 8 (as anion)	+1 (or −3)
η^8-C_8H_8 (cyclooctatetraenyl)	8	10	−2
Each metal–metal bond	1	1	0
OR (alk- or aryl-oxide)	1 or 3	2 or 4	−1
NR_2 (amide) PR_2	1 or 3	2 or 4	−1
O (oxo) or NR (imido) PR	2 or 4	4 or 6	−2

Principal Reaction Types: Identify , Predict , Mechanism

Salt Elimination

1) Protonolysis

2)Substitiution

3) Oxidative Addition

4) Reductive Elimination

5) Oxidative Coupling **X**

6) Reductive Cleavage **X**

7) Migratory Insertions

8) Elimination Reactions

9) σ-Bond Metathesis

There is a simple formal relationship between 4 and 5, 6 and 7, and 8 and 9 in that they are the *reverse* of each other, respectively.

Key types of ligand : Nature of Bonding , synthesis , reactivity

- σ-donor ligands:

(i) neutral: CO (carbonyl), PR_3 (phosphine), C(R)OR (Fischer carbene).

(ii) charged: CH_3^- (alkyl), H^- (hydride), Cl^- (halide), R_2C^{2-} (Alkylidene), RC^{3-} (Alkylidyne).

- π-donor ligands:

(i) alkene, alkyne, allyl, diene.

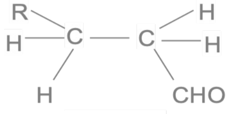
(ii)delocalised hydrocarbon rings:

cyclopentadienyl ($C_5H_5^-$), arene (C_6R_6),

Cycloheptatrienyl ($C_7H_7^+$ or $C_7H_7^{3-}$), cyclo-octatetraenyl ($C_8H_8^{2-}$).

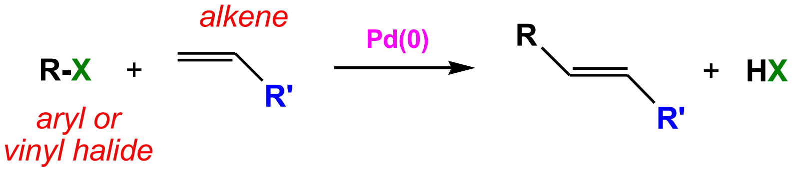
- Most ligands also act as π-acceptors -synergic bonding.

Homogeneous catalysis :General concepts and main catalytic cycles

Process	Catalyst	Substrates	Product
Hydrogenation	$RhCl(PPh_3)_3$ (Wilkinson)	alkene	alkane
Monsanto Acetic Acid	$[RhI_2(CO)_2]^-/HI$	MeOH/CO	MeCOOH (acetic acid)
Hydroformylation (Oxo process)	$HCo(CO)_4$ $HRh(CO)(PPh_3)_3$	$H_2C{=}CHR/$ CO/H_2	 aldehyde
Alkene metathesis	Ru(carbene) Grubbs catalyst	$R_2C{=}CH_2$ $R'_2C{=}CH_2$	$R_2C{=}CR'_2$ $H_2C{=}CH_2$
Alkene polymerisation	Ziegler Natta (Ti) or metallocene (Zr)	alkenes	Polyethylene Polypropylene

Pd-Catalyzed C-C Coupling Reactions

Heck reaction:



Stille coupling:

$$\underset{\text{aryl or vinyl halide}}{R\text{-}X} + \overset{\text{organotin}}{R'\text{-}SnR_3} \xrightarrow{Pd(0)} R\text{-}R' + XSnR_3$$

Negishi coupling:

$$\underset{\text{aryl or vinyl halide}}{R\text{-}X} + \overset{\text{organozinc}}{R'\text{-}ZnR} \xrightarrow{Pd(0)} R\text{-}R' + XZnR$$

Suzuki coupling:

$$\underset{\text{aryl or vinyl halide}}{R\text{-}X} + \overset{\text{organoboron}}{R'\text{-}B(OH)_2} \xrightarrow{Pd(0)} R\text{-}R' + XB(OH)_2$$

Sonogashira coupling:

$$\underset{\text{aryl or vinyl halide}}{R\text{-}X} + \overset{\text{alkyne}}{\equiv\!\!-R'} \xrightarrow{Pd(0)} R-\!\!\equiv\!\!-R' + HX$$