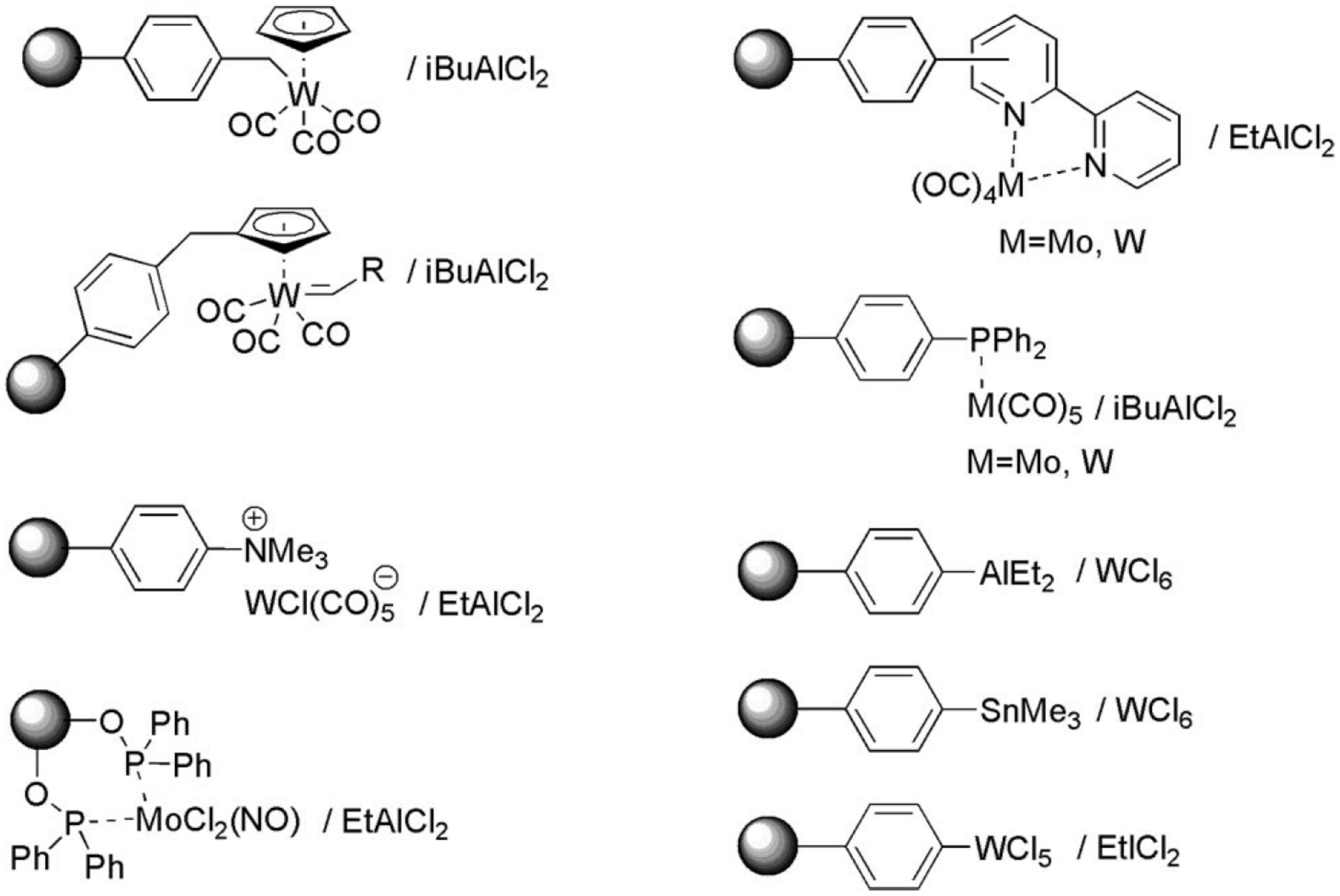
Organometallic Catalysis

- The catalysts we look at are soluble complexes, or ***homogeneous catalysts***, as opposed to catalysts such as *palladium on carbon*, or ***heterogeneous catalysts***.
- These terms are used because the catalyst and substrates for the reaction are in the same phase in the homogeneous, but not in the heterogeneous, type, where catalysis takes place at the surface of a solid catalyst.

Catalytic mechanisms are considerably easier to study in homogeneous systems, where such powerful methods as NMR can be used to both assign structures and follow reaction kinetics.

- Homogeneous catalysts have the disadvantage that they can be difficult to separate from the product.
- Homogeneous catalysts can also be chemically grafted on to solid supports for greater ease of separation of the catalyst from the reaction products.
- Although the catalyst is now technically heterogeneous, it often retains the characteristic reactivity pattern that it showed as a homogeneous catalyst, and its properties are usually distinct from those of any of the classical heterogeneous catalysts—these are sometimes called "heterogenized" homogeneous catalysts.



Representative selection of polymer-bound binary metathesis catalysts.

- The mechanistic ideas developed in ***homogeneous catalysis are also becoming more influential*** in the field of classical heterogeneous catalysis by suggesting structures for intermediates and mechanisms for reaction steps.
- By bringing about a reaction at ***lower temperature***, a catalyst can ***save energy*** in commercial applications. It often gives ***higher selectivity*** for the desired product, minimizing product separation problems and ***avoiding the need to discard the undesired product as waste***.
- Environmental concerns have promoted the idea of ***atom economy***, which values a process most highly when all the atoms in the reagents are used to form the product, minimizing waste.
- The selectivity can be changed by altering the ligands, allowing synthesis of products not formed in the un-catalyzed process.
- With growing regulatory pressure to synthesize drugs in enantiopure form, asymmetric catalysis has come to the fore, along with enzyme catalysis, as the only practical way to make such products on a large scale.

CATALYSIS IS GREEN CHEMISTRY !!!

- A catalyst may be defined by its ***Turnover Number*** **(TN)**. Each time the complete catalyst cycle occurs, we consider one catalytic turnover to have been completed (one mole of product formed per mole of catalyst).

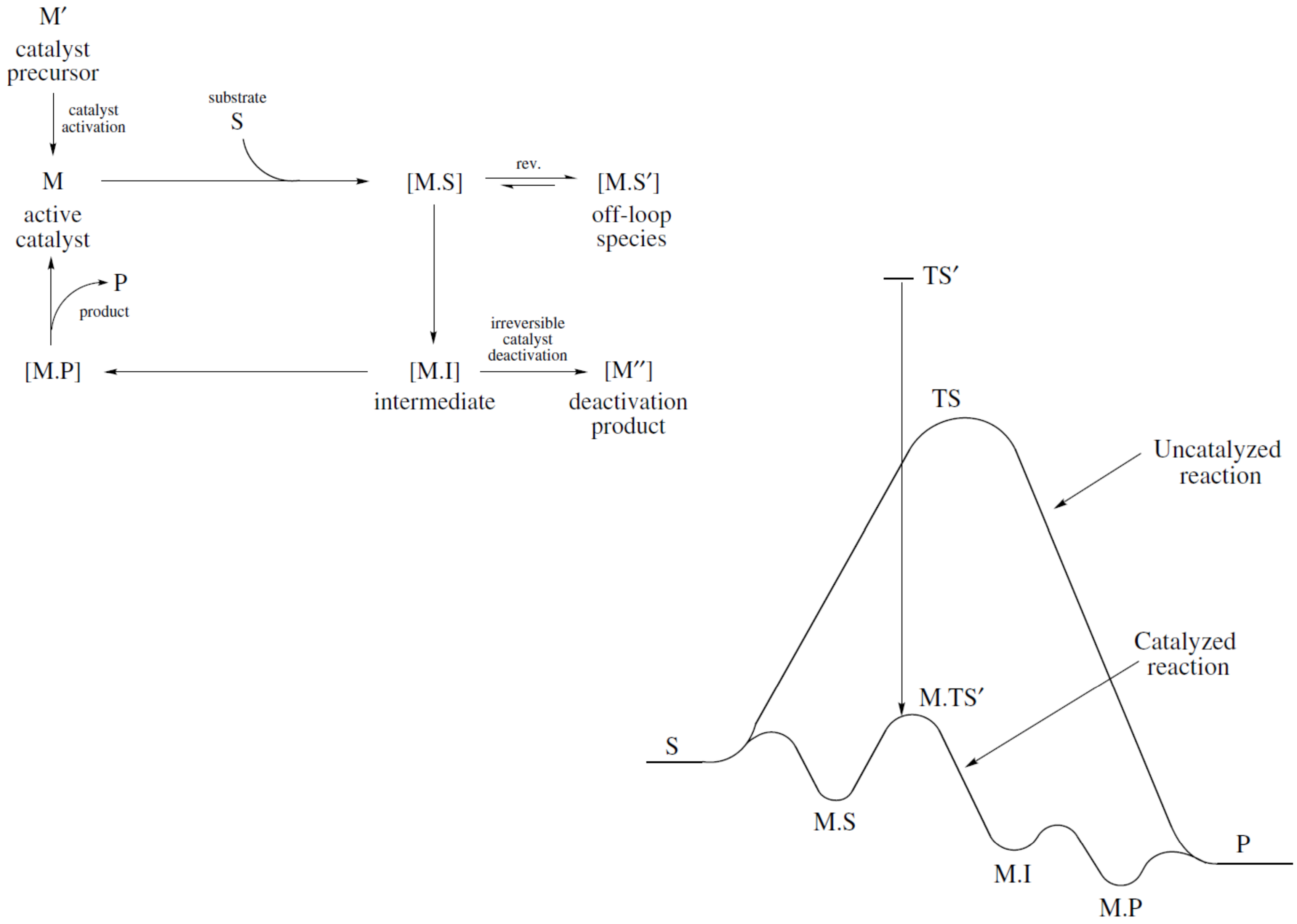
- The catalytic rate can be conveniently given in terms of the **Turnover Frequency (TOF)** measured in turnovers per unit time (often per hour).

- The ***lifetime of the catalyst*** before deactivation is measured in terms of total turnovers.

- For most transition metal catalysts, the catalyzed pathway is completely changed from the pathway of the uncatalyzed reaction. Instead of passing by way of the high-energy uncatalyzed transition state TS, the catalyzed reaction normally goes by a multistep mechanism in which the metal stabilizes intermediates that are stable only when bound to the metal.

- Normally, the catalyst only increases the rate of a process but ***does not alter its position of equilibrium***, which is decided by the relative thermodynamic stabilities of substrate and products.

- For example, if the substrate S is slightly less stable than the product P, so the reaction will eventually reach an equilibrium favoring P.


M′
catalyst precursor
catalyst activation
substrate
S
M
active catalyst
[M.S]
rev.
[M.S′]
off-loop species
P
product
[M.P]
[M.I]
intermediate
irreversible catalyst deactivation
[M″]
deactivation product
TS′
TS
Uncatalyzed reaction
Catalyzed reaction
M.TS′
S
M.S
M.I
M.P
P

- The TS structure in the absence of the metal would be extremely unstable, but the energy of binding is so high that M.TS is now much more favorable than TS and the reaction all passes through the catalyzed route.

- Different metal species may be able to stabilize other transition states TS—which may lead to entirely different products—hence different catalysts can give different products from the same starting materials.

- The slow step in a catalytic process is called the ***turnover limiting step***. ***Any change that lowers*** **the barrier for this step will increase the turnover frequency (TOF)**.

- Changes in other barriers will not affect the TOF. For a high TOF, we require that none of the intermediates be bound too strongly (otherwise they may be too stable and not react further) and that none of the transition states be prohibitively high in energy.

- Indeed, the whole reaction profile must not stray from a rather narrow range of free energies, accessible at the reaction temperature. Even if all this is arranged, a catalyst may undergo a catalytic cycle only a few times and then "die."

- This happens if undesired deactivation reactions are faster than the productive reactions of the catalytic cycle itself.

Alkene Isomerization

- Many transition metal complexes are capable of catalyzing the 1,3-migration of hydrogen substituents in alkenes, a reaction that has the net effect of moving the C=C group along the chain of the molecule.

- This is often a side reaction in other types of catalytic alkene reactions, desired or not according to circumstances.

- Two mechanisms are most commonly found:

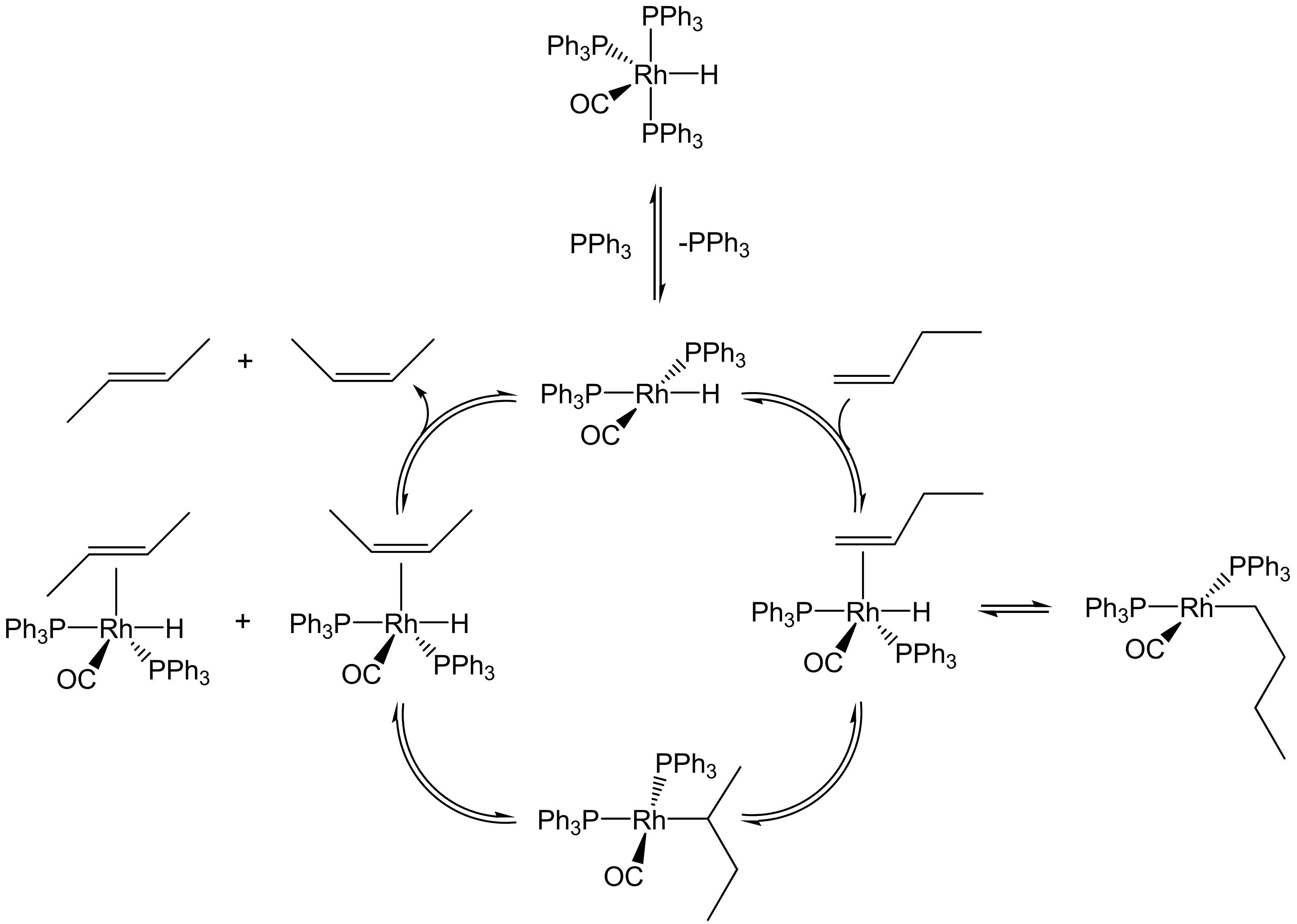
  1. via alkyl intermediates.

  2. via η^3-allyl intermediates.

- Note that in each cycle, all the steps are reversible, so that the substrates and products are in equilibrium, and therefore although a non-thermodynamic ratio of alkenes can be formed at early reaction times, the thermodynamic ratio is eventually formed if the catalyst remains active long enough.

Alkyl mechanism

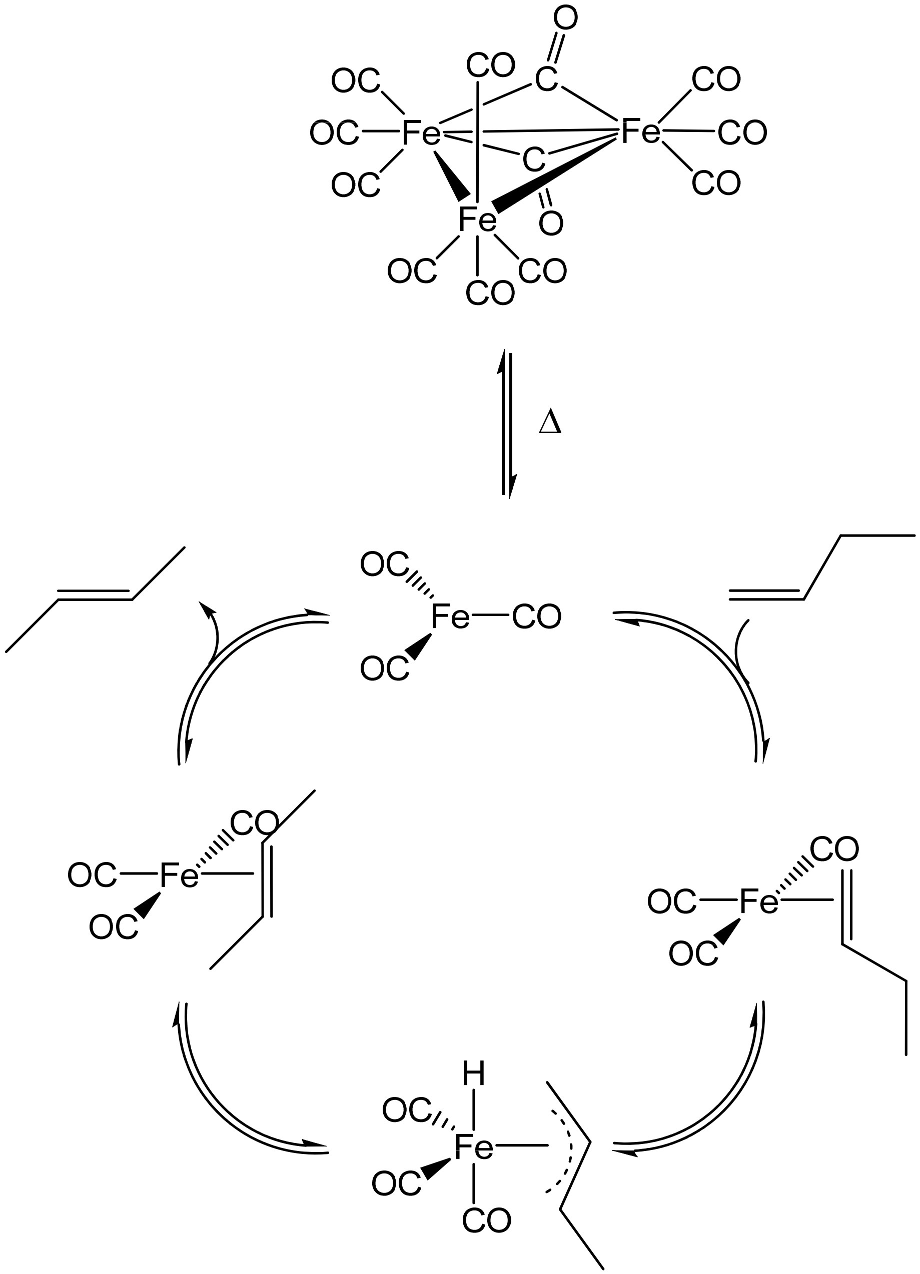
- The alkyl route ***requires an M–H bond and a vacant site***.
- The alkene binds and undergoes 1,2-insertion to give the alkyl.
- For 1-butene, the alkyl might be the 1° or the 2° one, according to the regiochemistry of the insertion.
- If the 1° alkyl is formed, β *elimination* can give back only 1-butene, but β *elimination* in the 2° alkyl, often faster, can give both 1- and *cis*- and *trans*-2-butene.
- Since insertion to give the 1° alkyl is favored for many catalysts, nonproductive cycling of the 1-butene back to 1-butene is common, and productive isomerization may be slower.
- The initial *cis*/*trans* ratio in the 2-butenes formed depends on the catalyst; the *cis* isomer is often favored.
- The final ratio depends only on the thermodynamics, and ***the trans isomer is preferred***.
- A typical isomerization catalyst is $RhH(CO)(PPh_3)_3$.
- As this is a coordinatively saturated 18e species it must lose a ligand,PPh_3 in this case, to form a coordinatively unsaturated intermediate (16e), able to bind the alkene.



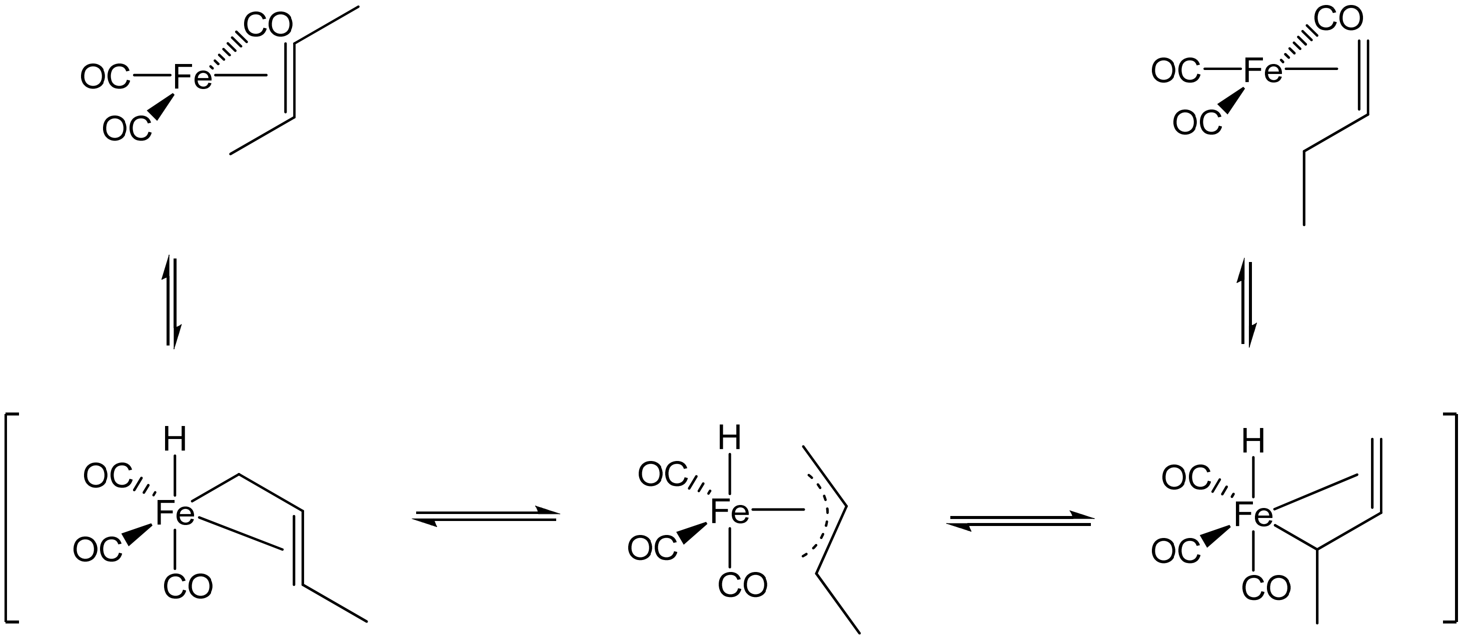
PPh$_3$
Ph$_3$P
Rh
H
OC
PPh$_3$
PPh$_3$
-PPh$_3$
+
+

Allyl mechanism

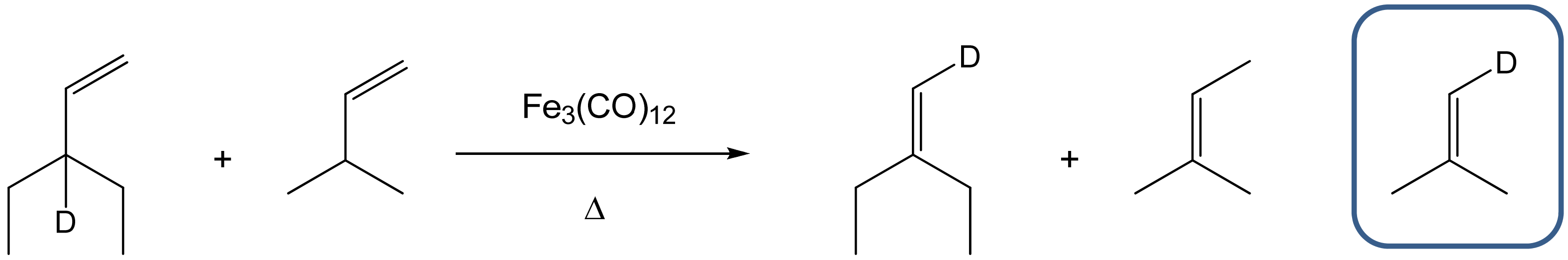
- The second common mechanism involves allyl intermediates and is adopted by catalysts having ***two 2e vacant sites but no hydrides***.
- It has been established for the case of $Fe_3(CO)_{12}$ as catalyst, a system in which "$Fe(CO)_3$," formed by fragmentation of the cluster on heating, is believed to be the active species.
- Thus the cluster itself is an example of a catalyst precursor.
- As a 14e species, $Fe(CO)_3$ may not have an independent existence in solution, but may always be tied up with substrate or product (***or even solvent***).
- In this mechanism the C−H bond at the activated allylic position of the alkene undergoes an ***oxidative addition*** to the metal.
- The product is an **η^3-allyl hydride**. Now, we only need a reductive elimination to give back the alkene.
- Again, we can have nonproductive cycling if the H returns to the same site it left, rather than to the opposite end of the allyl group.



OC
OC
OC
CO
O
C
CO
CO
CO
Fe
Fe
C
O
Fe
OC
CO
CO
Δ
OC
Fe
CO
OC
CO
OC
Fe
OC
CO
OC
Fe
OC
H
OC
Fe
OC
CO


CO
OC
Fe
OC
CO
OC
Fe
OC
H
OC
Fe
OC
CO
H
OC
Fe
OC
CO
H
OC
Fe
OC
CO

- An experimental distinction can be made between both the alkyl and allyl routes by means of a crossover experiment using the mixture of C_5 and C_7 alkenes.
- For the allyl mechanism, we expect the D to end up only in the corresponding product having undergone an intramolecular 1,3 shift.
- **For** the hydride mechanism, the D will be transferred to the catalyst that can in turn transfer it by crossover to the C_5 product.



not observed

Alkene Hydrogenation

- Hydrogenation catalysts add molecular hydrogen to the C=C group of an alkene to give an alkane.
- Three general types have been distinguished, according to the way each type activates H2.

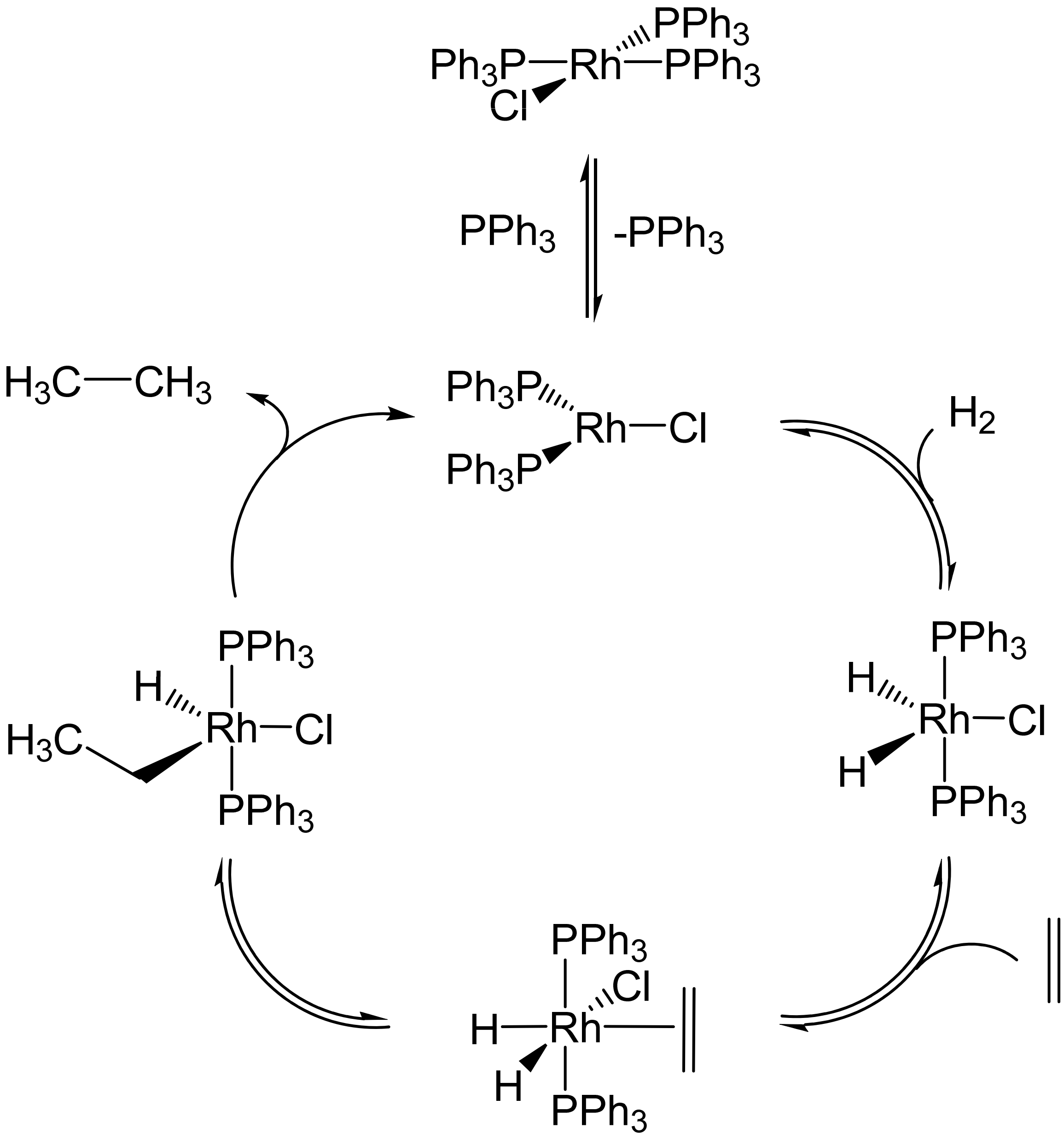
1. ***oxidative addition***

2. ***heterolytic activation***

3. ***homolytic activation***

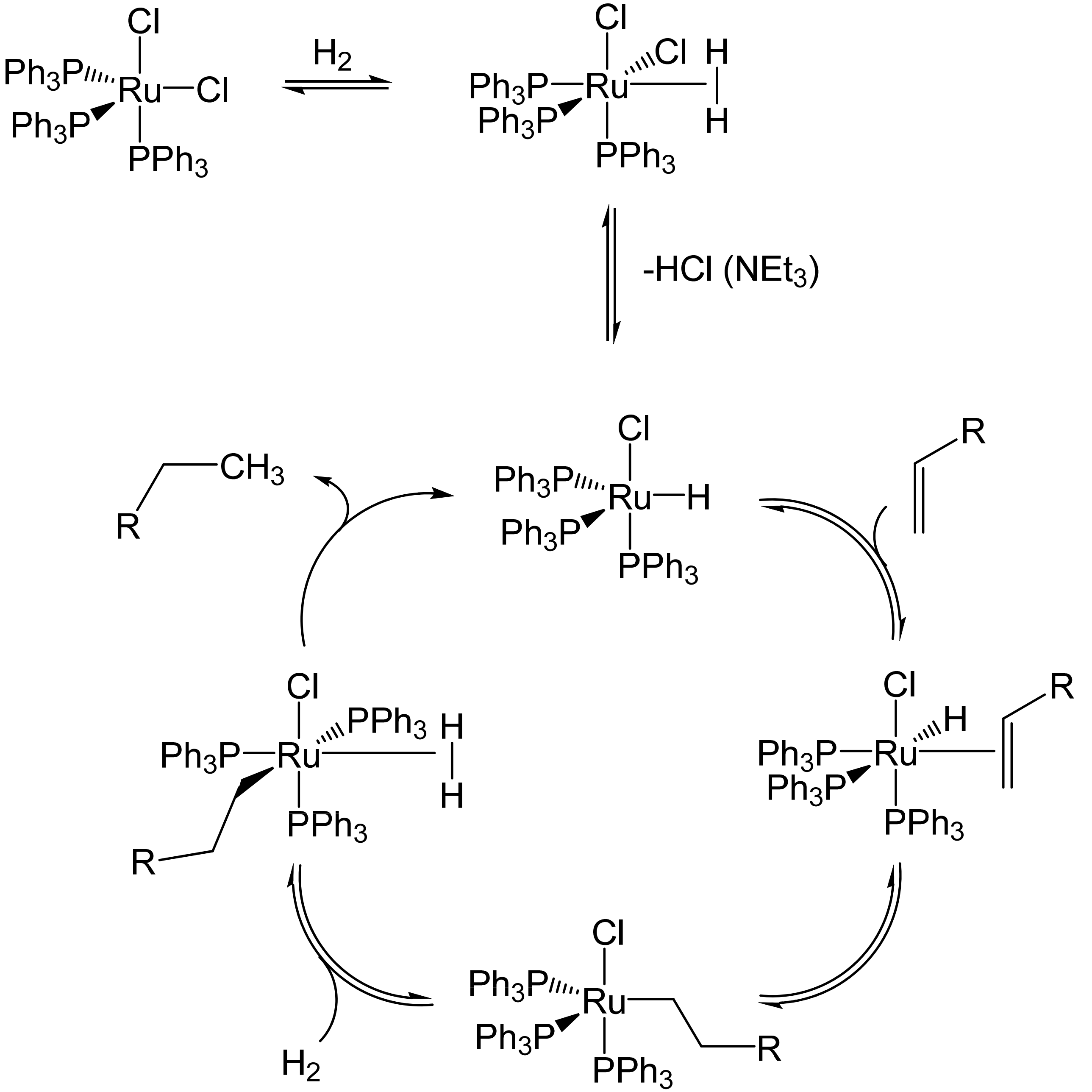
Alkene Hydrogenation via oxidative addition

- Perhaps the most important group employs oxidative addition, of which $RhCl(PPh_3)_3$ ***(Wilkinson's catalyst)*** is the best known.
- Hydrogen addition to give a dihydride leads to labilization of one of the PPh_3 ligands (high trans effect of H) to give a site at which the alkene binds.
- The alkene inserts, as in isomerization, but the intermediate alkyl is irreversibly trapped by reductive elimination with the second hydride to give an alkane.
- This is an idealized mechanism. In fact, $RhCl(PPh_3)_3$ can also lose PPh_3 to give $RhCl(PPh_3)_2$, and dimerize via halide bridges and each of these species have their own separate catalytic cycles that can be important under different conditions.
- Indeed, $RhCl(PPh_3)_2$ reacts so much faster with H_2 than does $RhCl(PPh_3)_3$ that the vast majority of the catalytic reaction goes through $RhCl(PPh_3)_2$ under most conditions.
- By reversibility arguments, the more rapid oxidative addition of H_2 to the 3-coordinate d^8 $RhCl(PPh_3)_2$ to give 5-coordinate d^6 $RhH_2Cl(PPh_3)_2$ relative to the corresponding 4-coordinate→6-coordinate conversion is consistent with the tendency for faster reductive elimination from 5-coordinate d^6 species discussed in previous lectures
(TBP Y-type intermediate).
- The following mechanism in illustrates a case where H_2 adds before the olefin. Sometimes the olefin adds first (the olefin mechanism) as is found for $[Rh(dpe)(MeOH)_2]BF_4$.


PPh3
Ph3P—Rh—PPh3
Cl
PPh3
-PPh3
H3C—CH3
Ph3P
Rh—Cl
Ph3P
H2
PPh3
H
Rh—Cl
H
PPh3
PPh3
H
Rh—Cl
H3C
PPh3
PPh3
Cl
H—Rh
H
PPh3

Heterolytic alkene hydrogenation (H2 activation)

- We now look at the second mechanistic class of hydrogenation catalyst.
- $RuCl_2(PPh_3)_3$ is believed to activate H_2 ***heterolytically***, a reaction accelerated by bases, such as NEt_3.
- The base abstracts a proton from H_2, leaving an H−bound to the metal ultimately giving $RuHL_4$, the true catalyst.


H_2
-HCl (NEt_3)
Cl
Ph_3P
Ru
PPh_3
H
R
CH_3
H_2

- It is likely that the intermediate in the heterolytic activation of H_2 is a dihydrogen complex.

- The protons of a dihydrogen ligand are known to be more acidic than those of free H_2, and many H_2 complexes can be deprotonated by NEt_3.

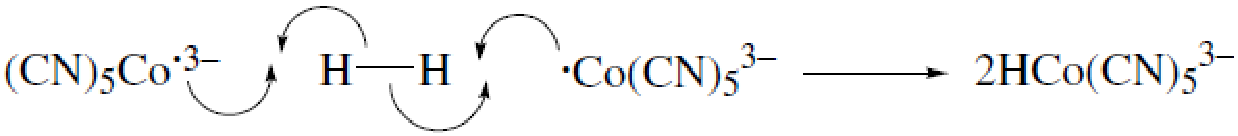
- In this way the metal gives the same products that would have been obtained by an oxidative addition–reductive elimination pathway, but by avoiding the oxidative addition, the metal avoids becoming Ru(IV), not a very stable state for Ru.

- Other than in their method of activating H_2, these catalysts act very similarly to the oxidative addition group.

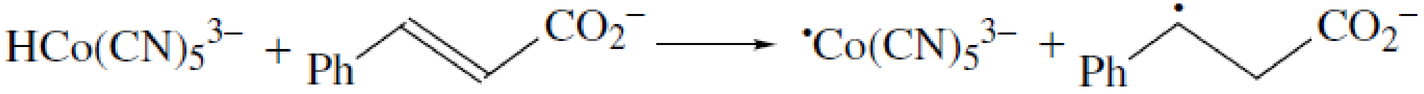
- As a 16e hydride complex, $RuCl_2(PPh3)_3$ can coordinate the alkene, undergo insertion to give the alkyl, then liberate the alkyl by a heterolytic activation of H_2, in which the alkyl group takes the proton and the H^- goes to the metal to regenerate the catalyst.

Homolytic H_2 activation

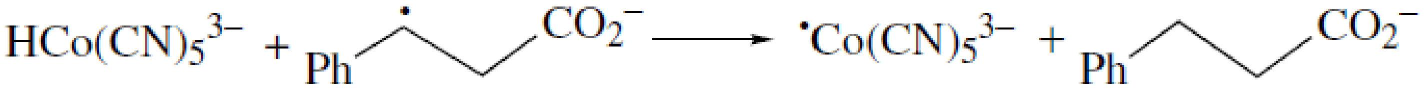
- Iguchi's paramagnetic d^7 $Co(CN)_5^{3-}$ system was a very early (1942) example of a homogeneous hydrogenation catalyst.
- It is an example of the third and rarest group of catalysts, which activate hydrogen homolytically.
- Another way of looking at this is to say the cobalt system activates H_2 by a binuclear oxidative addition.
- This is not unreasonable for this Co(II) complex ion, a metal-centered radical that has a very stable oxidation state, Co(III), one unit more positive.
- Once $CoH(CN)_5^{3-}$ has been formed, a $H^\bullet$ atom is transferred to the substrate in the second step, a reaction that does not require a vacant site at the metal, but does require the resulting organic radical to be moderately stable—hence the fact that the Iguchi catalyst will reduce only activated alkenes, such as cinnamate ion, in which the radical is benzylic and therefore stabilized by resonance.
- Finally, the organic radical abstracts $H^\bullet$ from a second molecule of the cobalt hydride to give the final product.


$(CN)_5Co^{\bullet 3-}$
H—H
$^{\bullet}Co(CN)_5^{3-}$
$2HCo(CN)_5^{3-}$

(9.13)


$HCo(CN)_5^{3-}$
+
Ph
CO_2^-
$^{\bullet}Co(CN)_5^{3-}$
+
Ph
CO_2^-

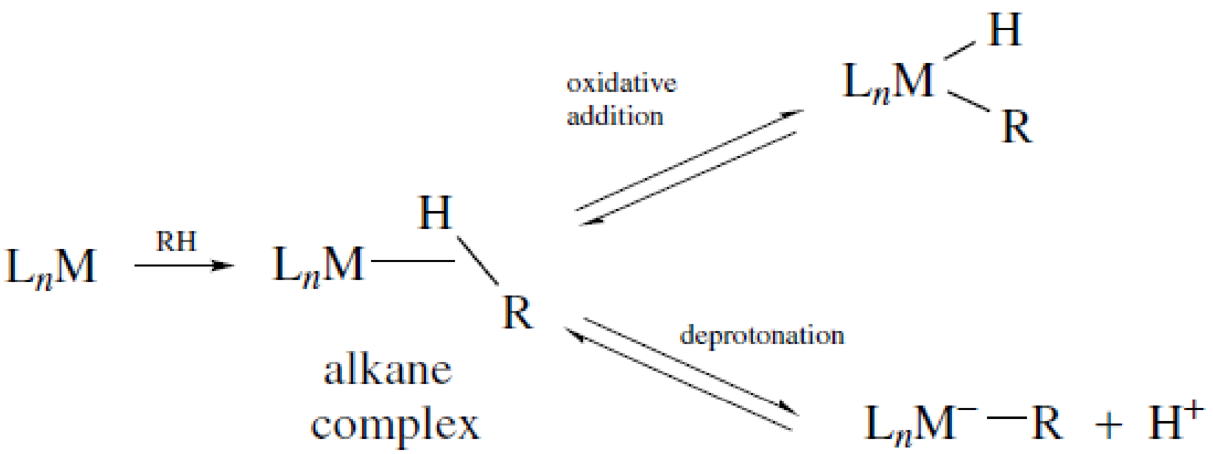
(9.14)


$HCo(CN)_5^{3-}$
+
Ph
CO_2^-
$^{\bullet}Co(CN)_5^{3-}$
+
Ph
CO_2^-

(9.15)

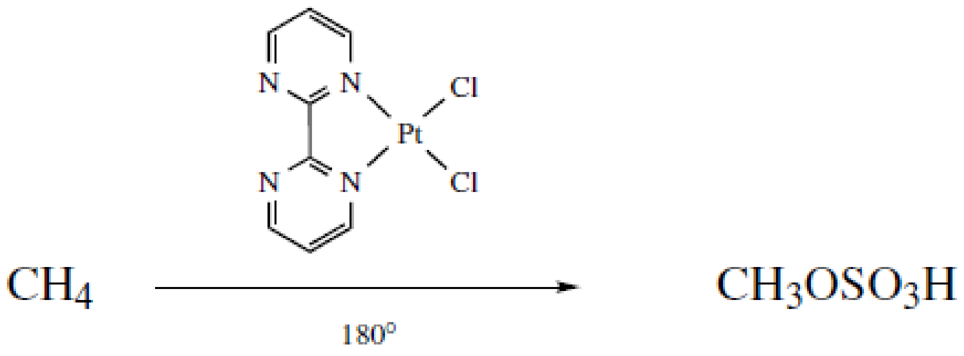
C-H activation

- The goal is ***the conversion of an alkane RH into the more valuable species RX***, where X is any of a variety of useful groups.
- Classical organic procedures tend to give branched products, such as *i*-PrX from propane, but linear products are very desirable, hence the potential of transition metal complexes, where formation of *n*-PrX is favored.
- For the moment <u>no system has proved economically viable, but steady progress is being made</u>.
- The term CH activation emphasizes the selectivity difference between low-valent metal complexes and classical organic reagents. In a classical electrophilic or radical route, radicals such as $OH^{\bullet}$ abstract an $H^{\bullet}$ atom from alkanes, PrH, but always to give the branched radical *i*-$Pr^{\bullet}$.
- Superacids, abstract H^{-} ion from PrH, but always to give the branched ion *i*-Pr^{+}.
- By such classical routes, the ultimate functionalization product, *i*-PrX, is branched.
- An alkane CH bond can oxidatively add to a variety of low-valent transition metals preferentially to give the linear product, *n*-Pr-M-H, however, and in any subsequent functionalization, the linear product, *n*-PrX, is often obtained.
- In addition, ***methane activation holds promise as methane seems likely to become a more important feedstock for the chemical industry***.



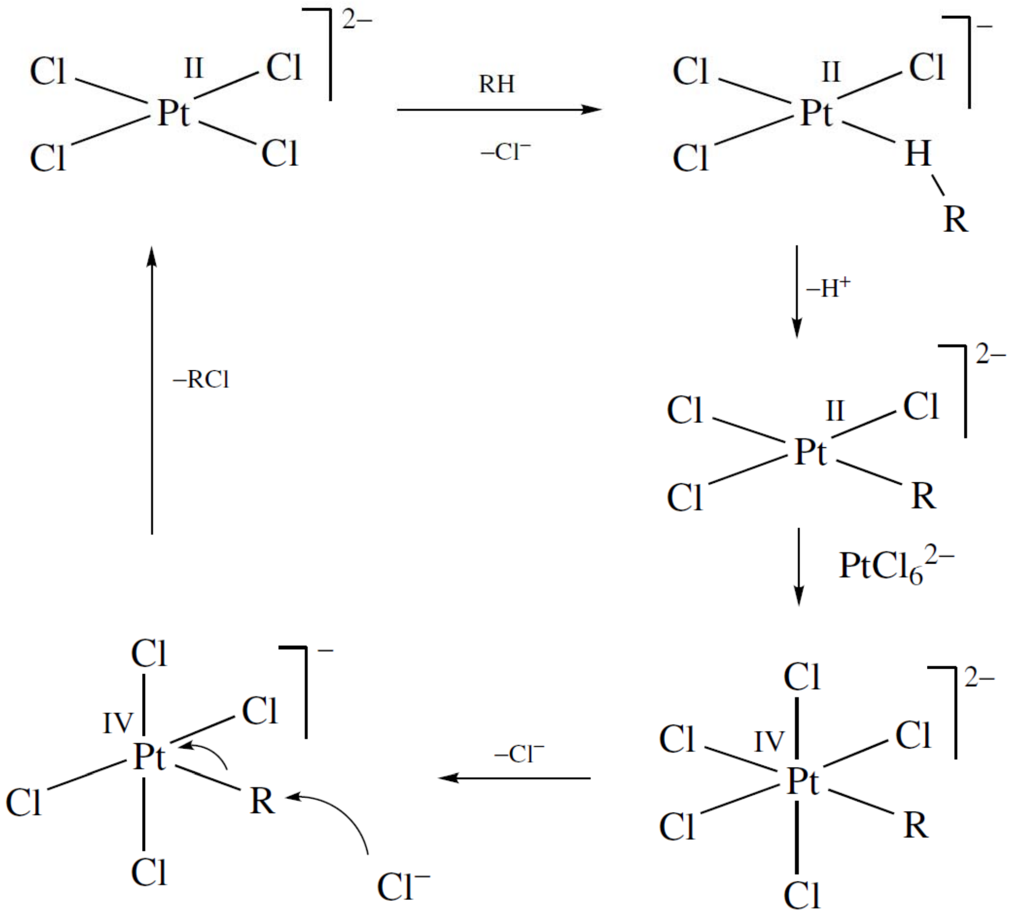
(12.29)

$$CH_4 \xrightarrow[180^\circ]{Hg(II),\ H_2SO_4} CH_3OSO_3H \qquad (12.30)$$

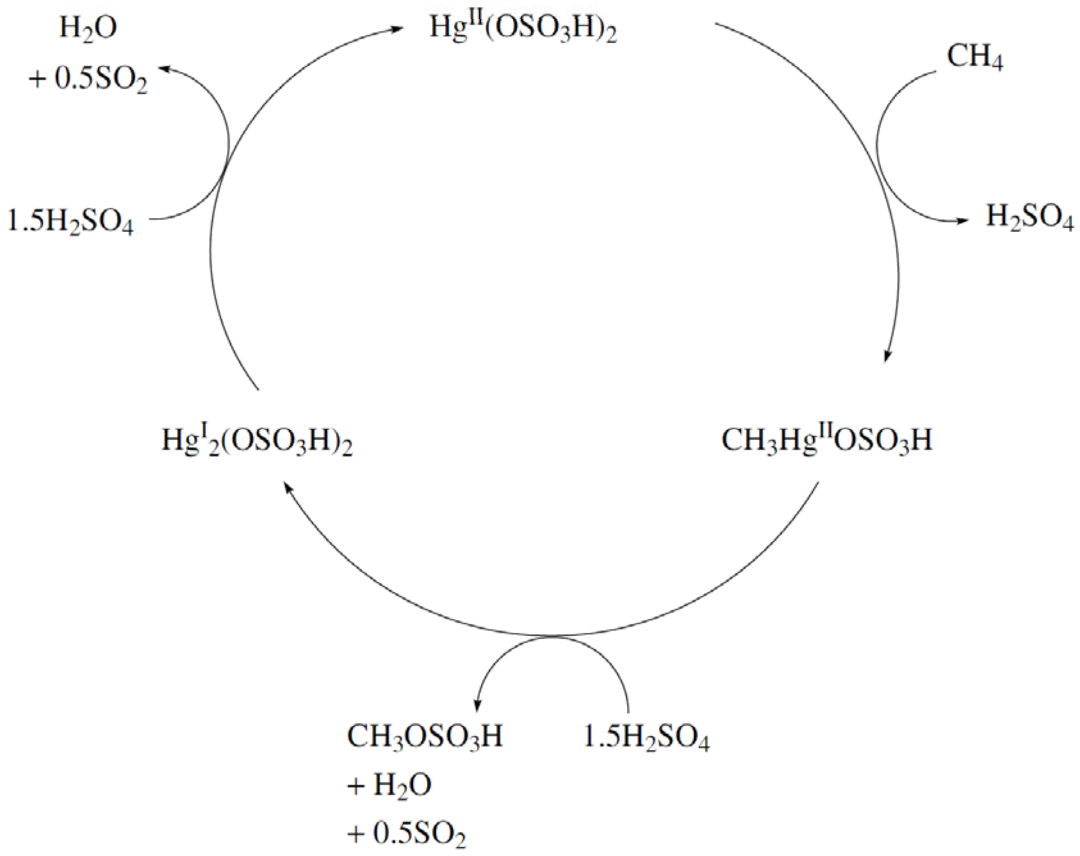


(12.31)

- During the 1970s, Shilov saw preferential activation of primary CH bonds in H/D exchange in alkanes catalyzed by Pt(II) in D_2O/DOAc.
- This was the first indication of the special reactivity pattern associated with oxidative addition.
- Moving to $[Pt(IV)Cl_6]^{2-}$ as oxidant, alkanes were oxidized to ROH and RCl with the same Pt(II) catalyst with linear product still preferred, so the Pt(IV) clearly intercepts the same intermediate alkyl that led to RD in the deuteriation experiments.
- With methane as substrate, a methylplatinum intermediate was seen.
- Labinger and Bercaw revisited the system in the 1990's using a series of mechanistic probes that confirmed Shilov's main points as well as extending the picture.


RH
−Cl⁻
−H⁺
PtCl6 2−
−Cl⁻
−RCl
Cl⁻
Pt
II
IV
Cl
H
R
2−
−

- With Hg(II) salts in H_2SO_4 at 180°, the acid is both solvent and mild reoxidant .
- Methane was converted to the methanol ester, methyl bisulfate, $MeOSO_3H$, in which the $-OSO_3H$ provides a powerful deactivating group to prevent overoxidation.
- At a methane conversion of 50%, 85% selectivity to methyl bisulfate (ca. 43% yield) was achieved with the major side product being CO_2.
- The expected intermediate $MeHg^+$ cation was seen by NMR spectroscopy, and a Shilov-like mechanism proposed.
- Since Hg(II) is not expected to give oxidative addition, Hg(IV) being unknown, the initial activation step must occur via deprotonation of a σ complex.
- Similar selectivity is seen as for Pt(II) and indeed deprotonation of a Pt(II) σ complex still cannot be excluded for this case.


$Hg^{II}(OSO_3H)_2$
CH_4
H_2SO_4
$CH_3Hg^{II}OSO_3H$
$1.5H_2SO_4$
CH_3OSO_3H
$+ H_2O$
$+ 0.5SO_2$
$Hg^{I}_2(OSO_3H)_2$
$1.5H_2SO_4$
H_2O
$+ 0.5SO_2$