HOMOGENEOUS CATALYSIS

GENERAL INFO

Examination: Wednesday 13.12. 2023

Homework:

Write a short summary based on 2 publications.

Dead-line Monday 4. 12.

- Min. length 1 page max. length 2 pages.
- Introduction (why this reaction)
- Mechanism
- Conclusions (what was new)

HOMOGENEOUS CATALYSIS

Many species can act like catalysts (including e.g. H^+, OH^-, Al^{3+} and imidazole),

However, transition complexes metals are far and away the most selective of these.

Why this is so?

Variety of ligands can bind to transition metals

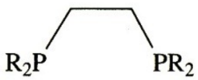
TM will bind virtually any other element in the Periodic Table and almost all organic molecules (L or X –type coordination).

Ligands can be directly (actor) or indirectly (spectator) involved in the catalysis by tuning steric and electronic properties of the complex.

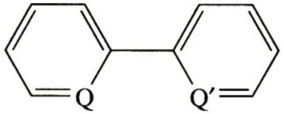
Spectator ligands are commonly polydentate with the donor atoms arranged in specific patterns.

ORGANOMETALLICS AS CATALYSTS

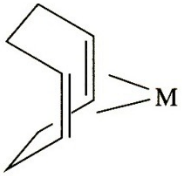
Bidentate, *cis*



dpe, R = Ph
dmpe, R = Me

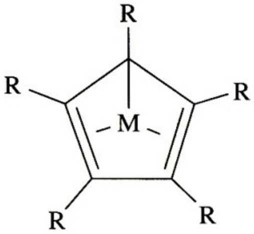


bipy, Q = Q′ = N
phpy, Q = C; Q′ = N
biph, Q = Q′ = C

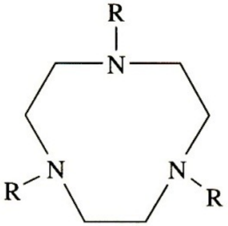


cod

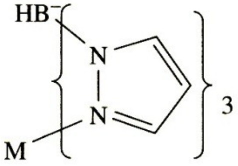
Tridentate, *fac*



Cp, R = H
Cp*, R = Me

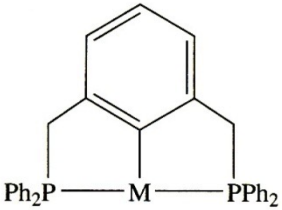


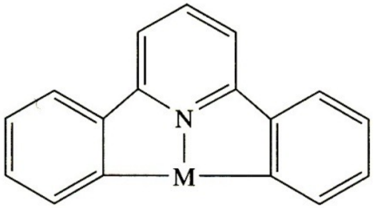
tacn, R = H
tacn*, R = Me



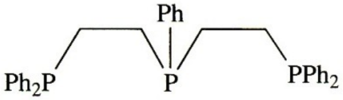
Tp

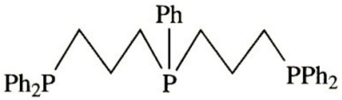
Tridentate, *mer*

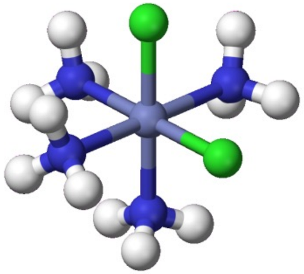




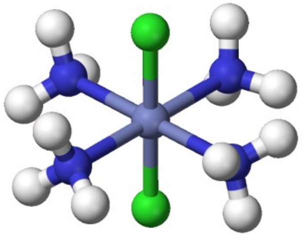
Tridentate, *fac* and *mer*



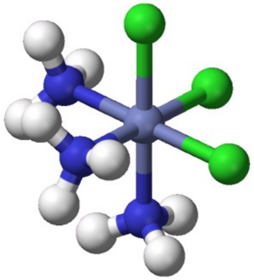




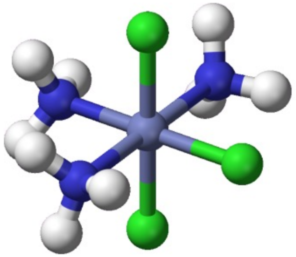
cis



trans



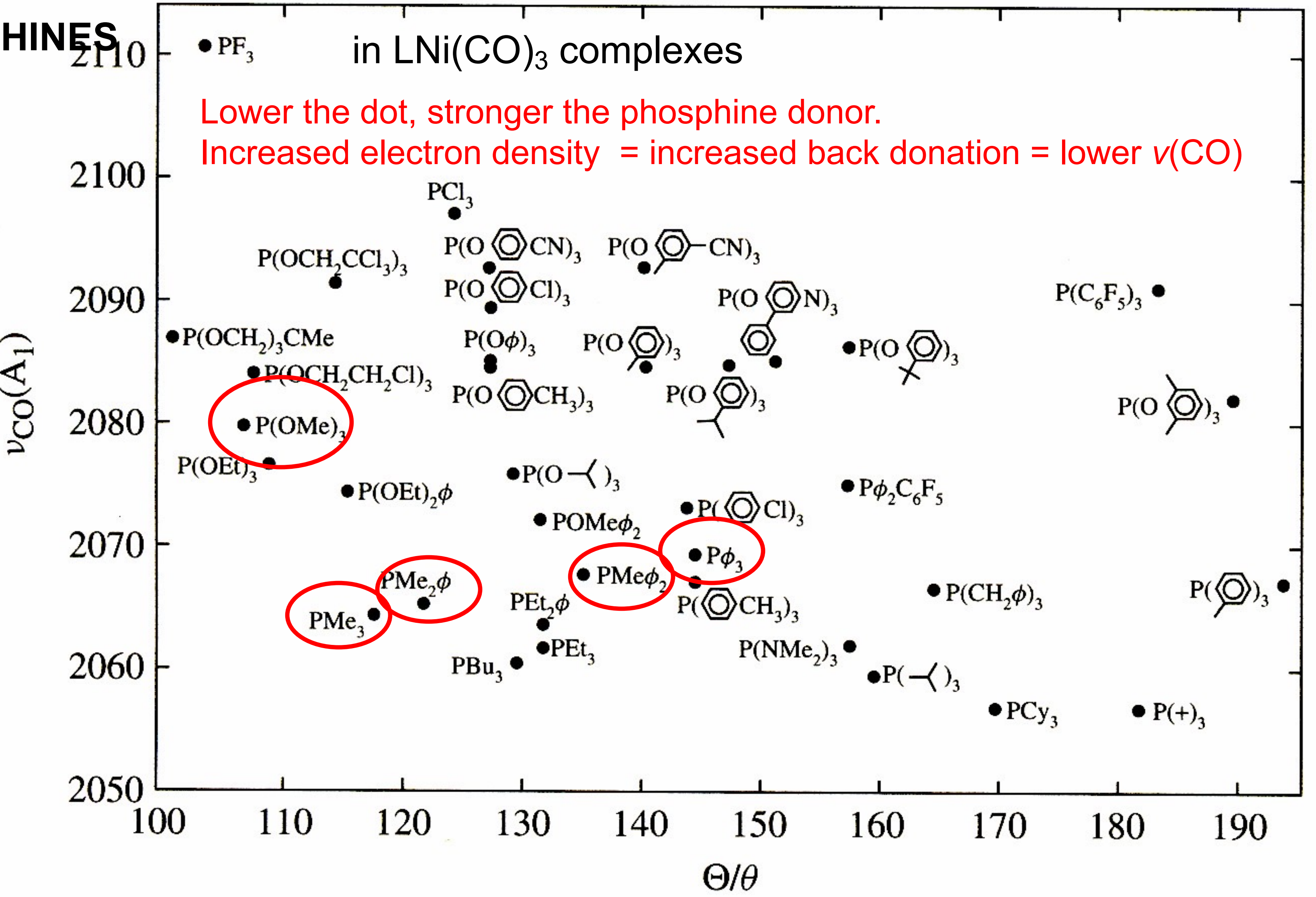
fac



mer

In a facial isomer (*fac*) the three identical ligands are mutually cis, and in a meridional isomer (*mer*) the three ligands are coplanar.

PHOSPHINES



in $LNi(CO)_3$ complexes

Lower the dot, stronger the phosphine donor.

Increased electron density = increased back donation = lower v(CO)

FIGURE 4.4 Electronic and steric effects of common P-donor ligands plotted on a m
according to Tolman (ν in cm^{-1}, θ in degrees). Reproduced from Ref. 26 with permissi
of the American Chemical Society.)

ORGANOMETALLICS AS CATALYSTS

Ligands can bind to transition metals in number of ways

The availability of d as well as s and p orbitals on the metal allows formation of σ and π bonds from metal to ligand. And a single ligand like alkene can bind in an η^1 or η^2 manner.

The hapticity can change change during a catalytic cycle.

The strenght of the metal-ligand bond is moderate (30-80 kcal/mole), bonds are formed and breaked relatively easily.

Variety of oxidation states is available

Ligands are added and removed from the metal by oxidative addition and reductive elimination. TMs have large number of different oxidation states available (compared to main group metals).

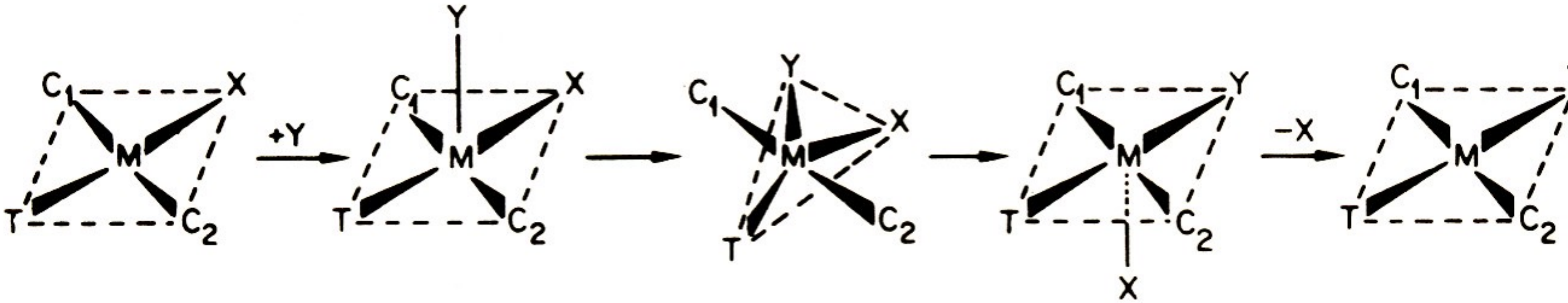
Group 8 to 10 have tendency for rapid, reversible two-electron change.

ORGANOMETALLICS AS CATALYSTS

TM complexes have several geometries

Linear, trigonal, square planar, tetrahedral, square pyramidal, trigonal bipyramidal, octahedral, and many more.

Remember, for reductive elimination and insertion actor ligands must be *cis*.



Correct stability of the complexes

By varying ligands and metals, TM complexes are available as intermediates that are not too reactive or unreactive.

In catalytic cycle each intermediate in the cycle must have enough reactivity to proceed
But not so much that decomposition becomes feasible.

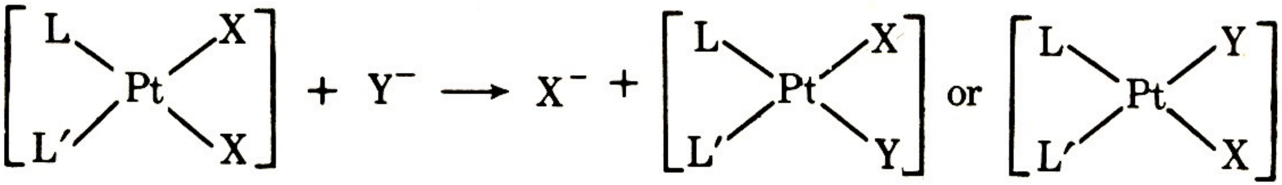
TM complexes are versatile

ORGANOMETALLICS AS CATALYSTS

Trans effect (of the spectator ligands)

Is important for ligand exchange reactions in square planar complexes.

Exchange reactions show distinct preferences for the site *trans* to one ligand rather than the other.



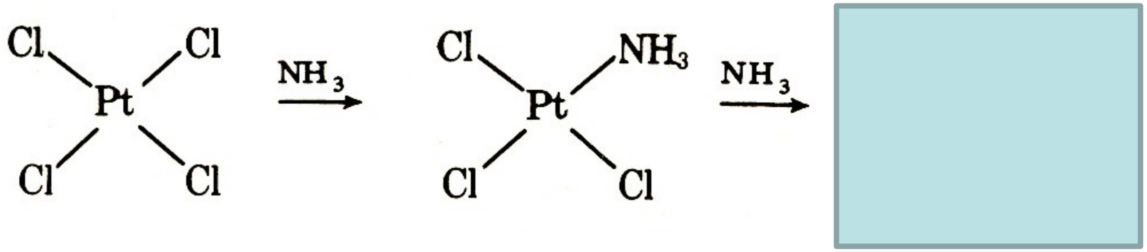
An extensive series of ligands has been arranged in the order of their tendency to facilitate the substitution in the position *trans* to themselves.

$$\mathrm{CO,\ CN^-,\ C_2H_4 > PR_3,\ H^- > CH_3^- > C_6H_5^-,\ NO_2^-,\ I^-,\ SCN^-}$$
$$\mathrm{> Br^-,\ Cl^- > py,\ NH_3,\ OH^-,\ H_2O}$$

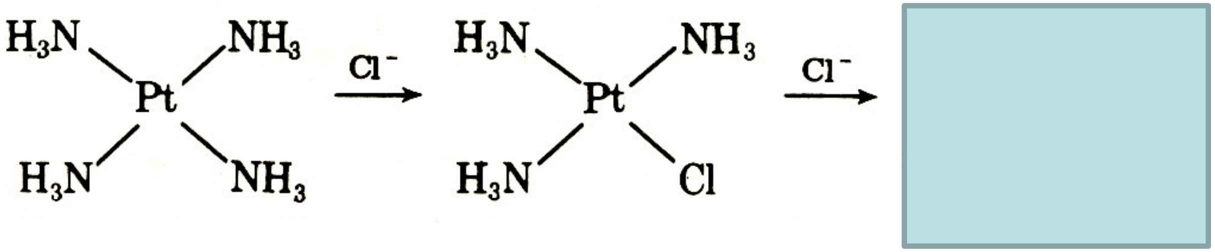
This order spans a factor of 10^6 in rate and holds for all square planar Pt complexes.

ORGANOMETALLICS AS CATALYSTS

Trans effect series is useful in rationalizing known synthesis procedures and in devising new ones.



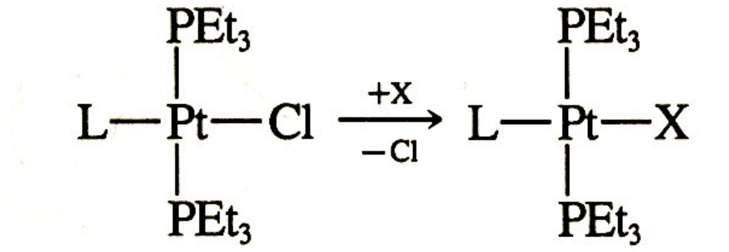
$$CO,\ CN^-,\ C_2H_4 > PR_3,\ H^- > CH_3^- > C_6H_5^-,\ NO_2^-,\ I^-,\ SCN^-$$
$$> Br^-,\ Cl^- > py,\ NH_3,\ OH^-,\ H_2O$$



ORGANOMETALLICS AS CATALYSTS

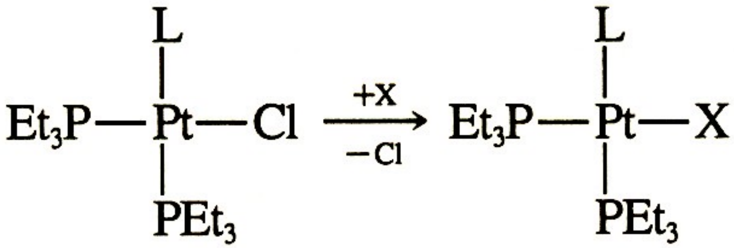
Cis effect

Is important for square planar complexes. Cis ligands have very little effect electronically on the reaction rates (max. factor of 3) but can be important sterically (because to the proximity of the site of replacement).



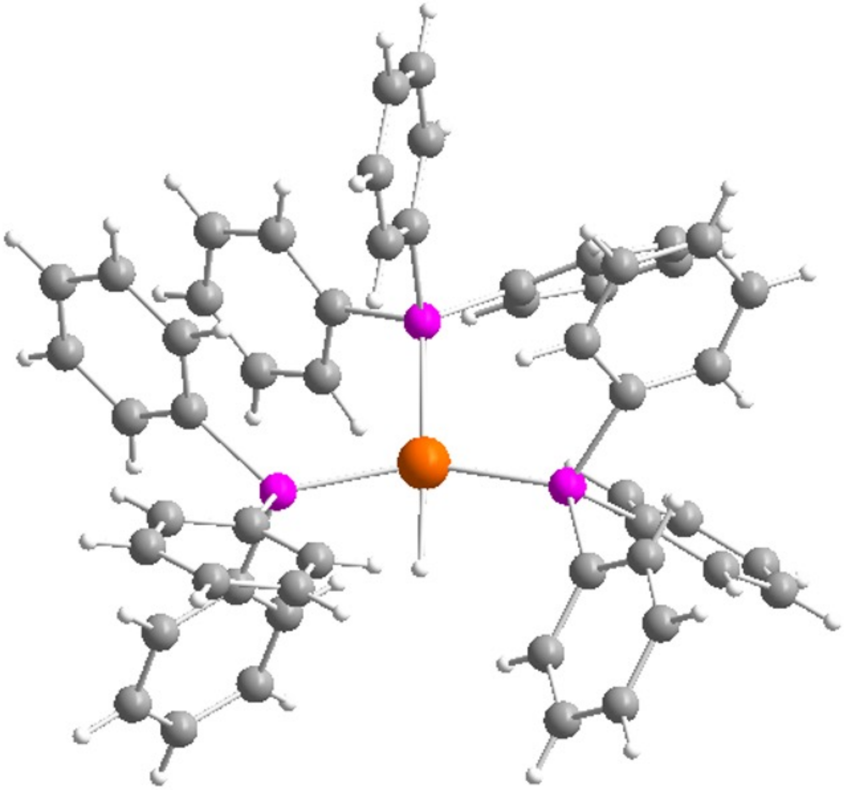
$$L-\overset{\overset{PEt_3}{|}}{\underset{\underset{PEt_3}{|}}{Pt}}-Cl \xrightarrow[-Cl]{+X} L-\overset{\overset{PEt_3}{|}}{\underset{\underset{PEt_3}{|}}{Pt}}-X$$

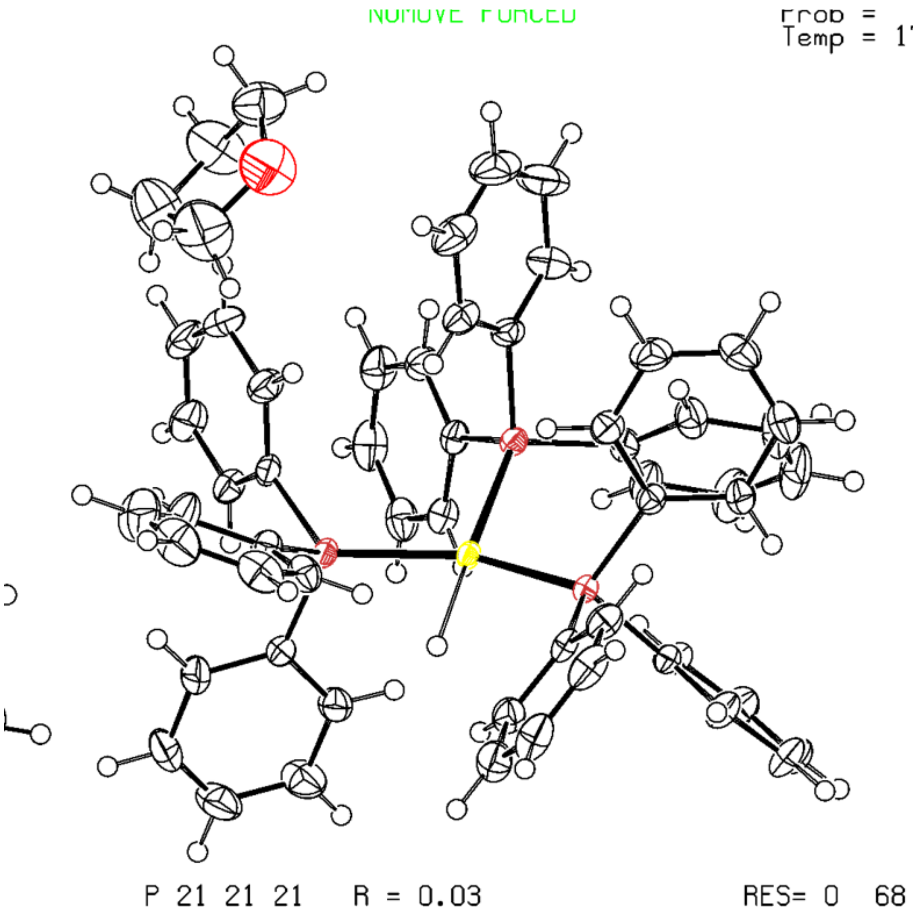
Changing L from phenyl to mesityl rate lowers 30 fold.



$$Et_3P-\overset{\overset{L}{|}}{\underset{\underset{PEt_3}{|}}{Pt}}-Cl \xrightarrow[-Cl]{+X} Et_3P-\overset{\overset{L}{|}}{\underset{\underset{PEt_3}{|}}{Pt}}-X$$

Changing L from phenyl to mesityl rate slows nearly10^5 fold.




NOMOVE FORCED
Prob =
Temp = 1'
P 21 21 21
R = 0.03
RES= 0 68

HYDROGENATION CATALYSTS

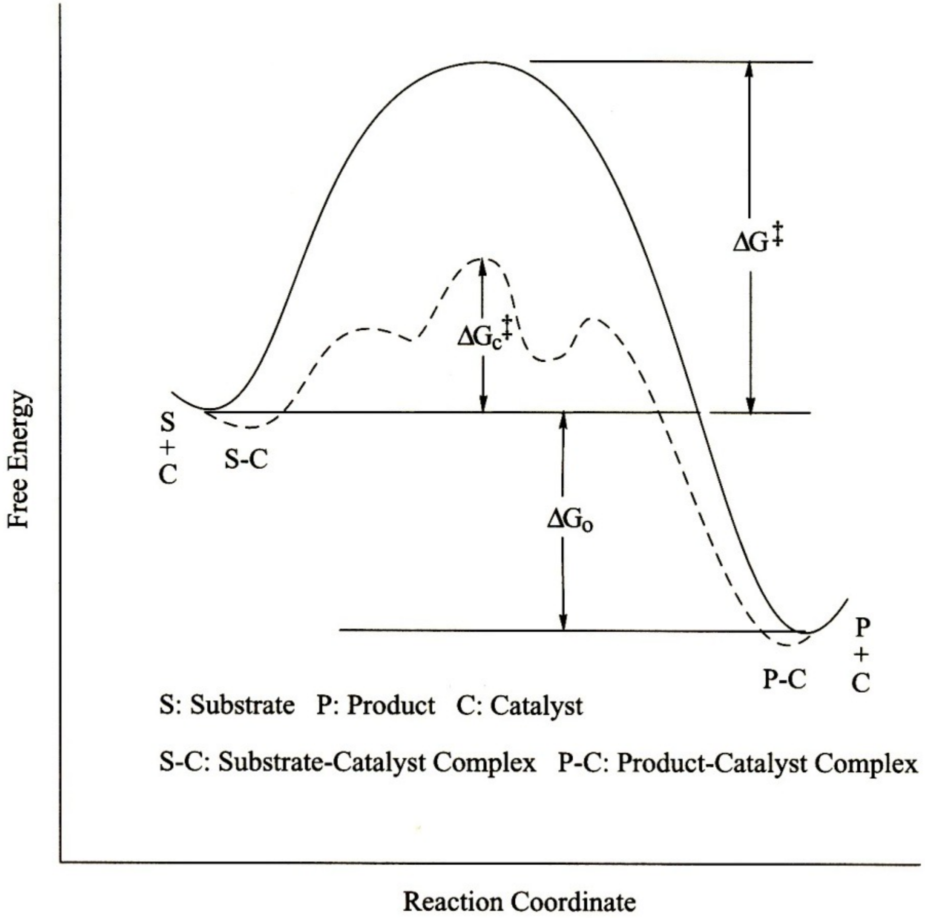
Homogeneously catalyzed hydrogenation of organic substrates is an important chemical transformations.

Olefins are the most studied substrates but there are many others
-acetylenes
-aldehydes
-ketones
-imines
-nitro compounds
-arenes

Beside molecular hydrogen also other sources of hydrogen can be used: hydyrogen transfer catalysts form the requisite metal hydrides from alcohols, $NaBH_4$, formic acid, or from hydrolysis of coordinated CO.

It is worth of notice that hydrosilylations and hydrocyanations are conceptually similar to hydrogenation.

ORGANOMETALLICS AS CATALYSTS



HYDROGENATION CATALYSTS

A large number of soluble transition-metal complexes can catalyse hydrogenation.

Precatalyst or catalyst precursor: compound that is added to a reaction

Catalyst: actual species that is doing the catalytic transformation.

For example, one of the ligands may dissosiate before the oxidative addition of hydrogen.

Majority of the homogeneous hydrogenation catalysts are coordinatively unsaturated. The vacant coordination site is needed for e.g. olefin coordination (or hydrogen activation).

Because of being coordinatively unsaturated, the catalysts are sensitive for impurities (traces of oxygen) and tend to associate.
The latter can be prevented by using bulky ligands like Cy_3P
or non-bridging labile ligands like MeOH.

HYDROGENATION CATALYSTS

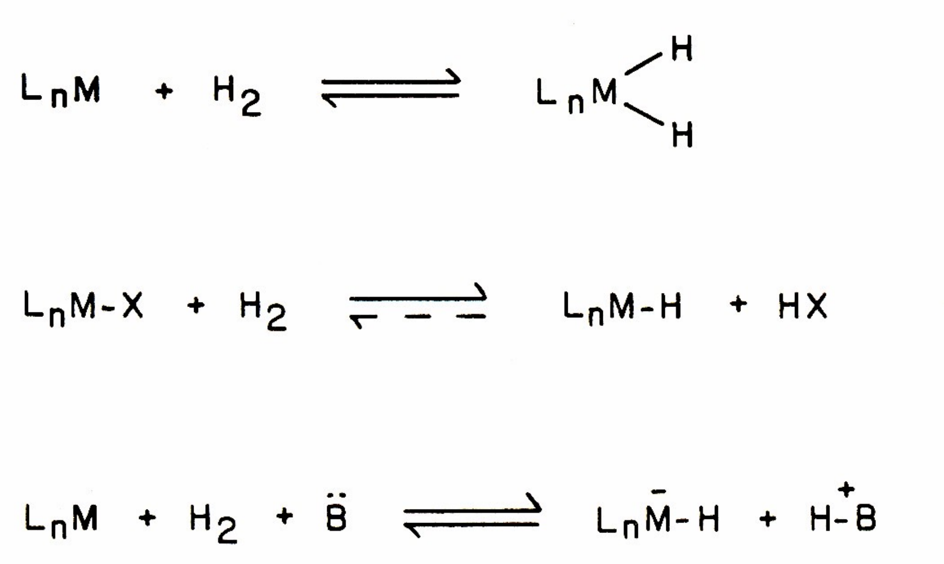
There are many several strategies to produce vacant coordination sites:

weakly coordinating ligands: $(Co(CO)_3(CH_3CN)_3$ and $[Rh(PR_3)_2(MeOH)_2]^+$

photolabile ligands: $Co(CO)_6$ and $Fe(CO)_5$

ligands destroyed by hydrogenation: olefins and allyls

Three different activation mecanisms are known:



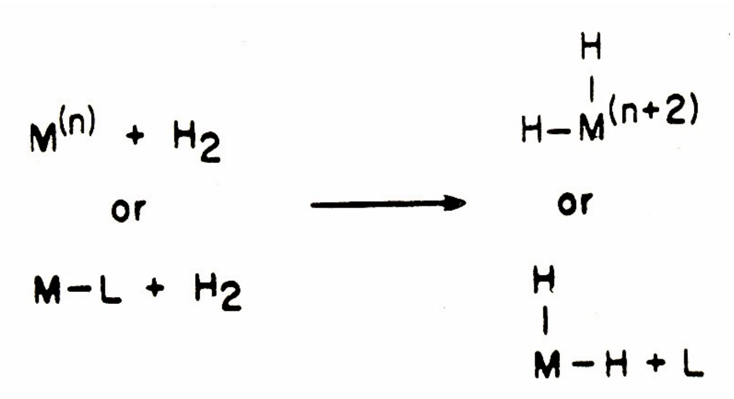
oxidative addition

hydrogenolysis

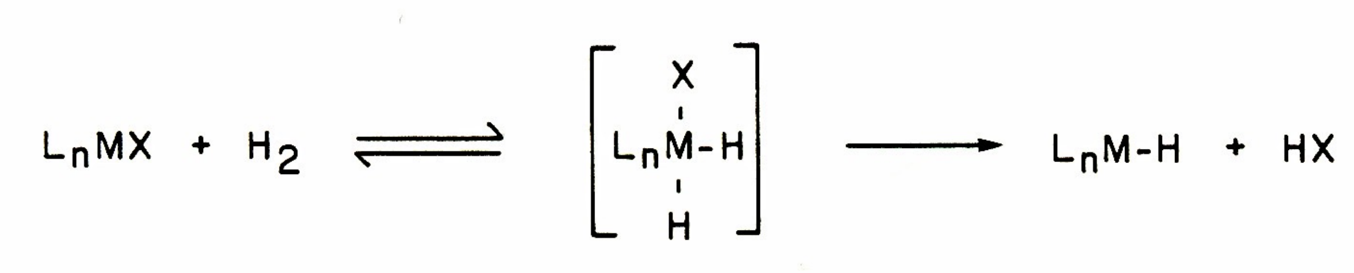
heterolytic hydrogen cleavage

HYDROGENATION CATALYSTS

oxidative addition



hydrogenolysis

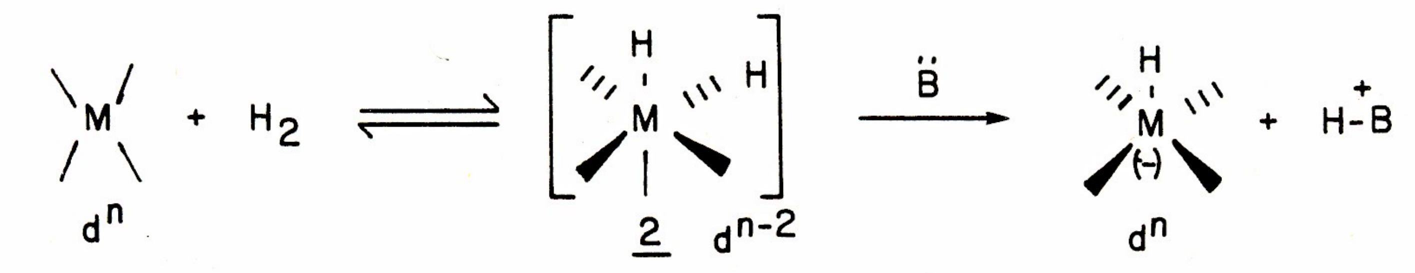


heterolytic hydrogen cleavage

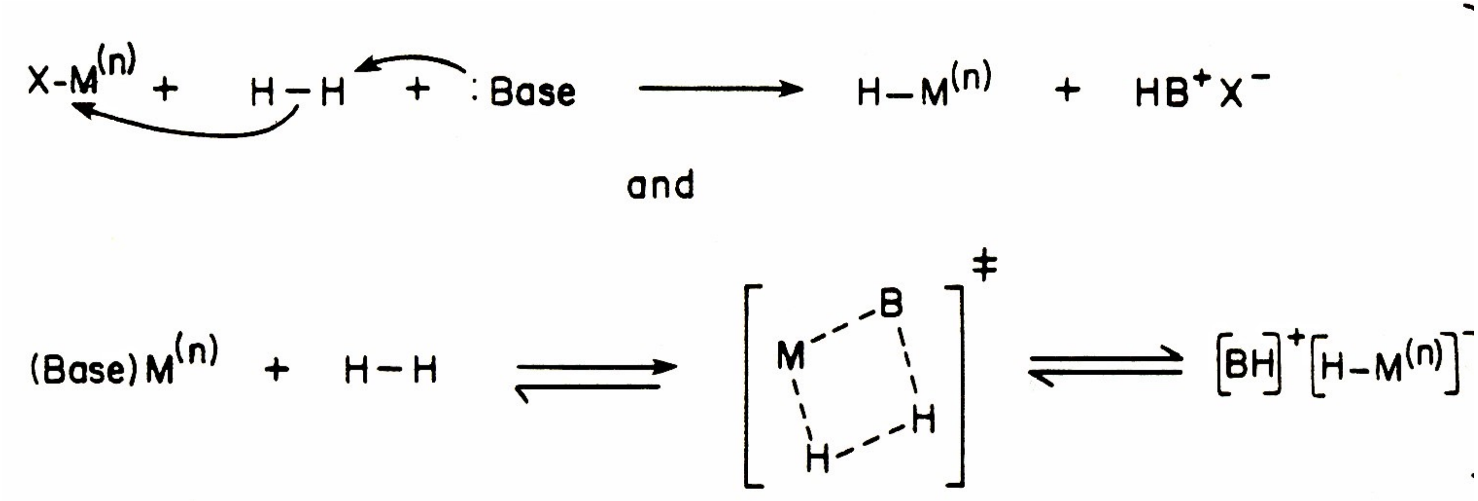
HYDROGENATION CATALYSTS

heterolytic hydrogen cleavage

After oxidative addition



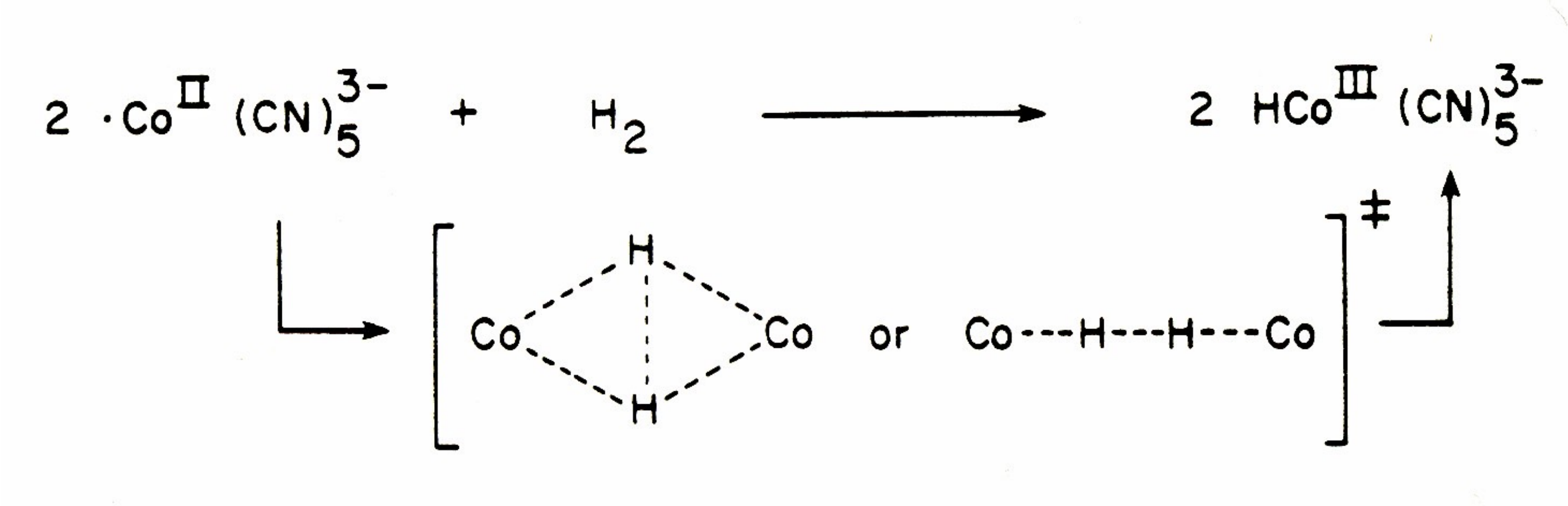
concerted



HYDROGENATION CATALYSTS

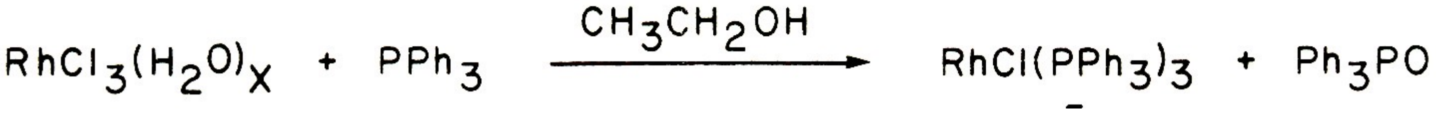
heterolytic hydrogen cleavage

concerted bimetallic



WILKINSONS'S CATALYST

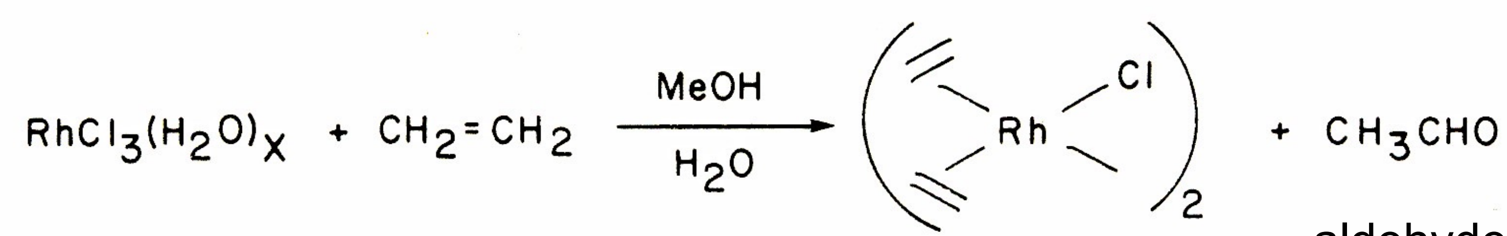
Two methods are routinely used to prepare Wilkinson's catalyst.



$$RhCl_3(H_2O)_x + PPh_3 \xrightarrow{CH_3CH_2OH} RhCl(PPh_3)_3 + Ph_3PO$$

phosphine oxide

This method is limited to PPh_3 or other triarylphosphines



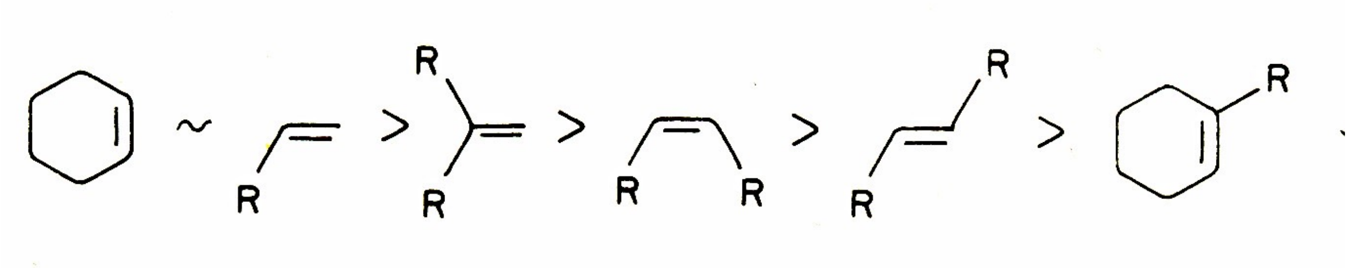
aldehyde

This method is more versatile, as olefins can be replaced by any tertiary phosphines.

WILKINSON'S CATALYST

Wilkinson and Coffey, 1964, discovered homogeneous hydrogenation catalyst for olefins. $RhCl(PPh_3)_3$ is commonly called as Wilkinson catalyst.

This catalyst is selective and efficient exhibiting high rates and turn over numbers.



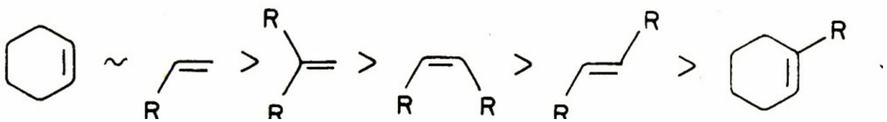
This order spans fifty fold

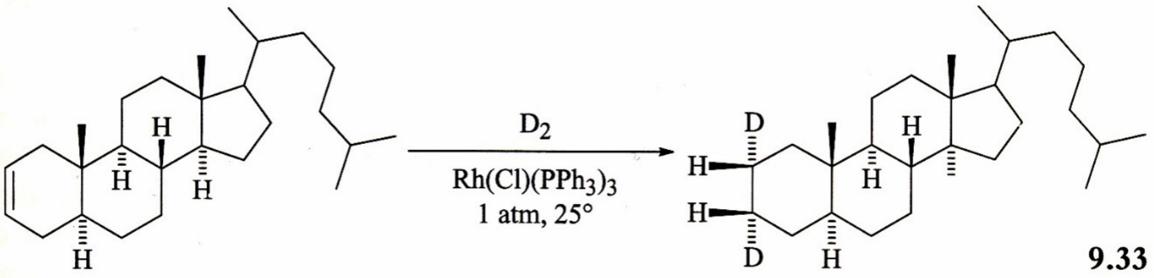
The reaction proceeds in the ambient hydrogen pressure and temperature in benzene with a polar cosolvent such as ethanol. Polar solvents seem to facilitate micratory insertion (see below).

No isotope scrambling between H_2 and D_2 and between protons in the solvent or on the olefin substrate. Clean *cis*-addition of hydrogen.

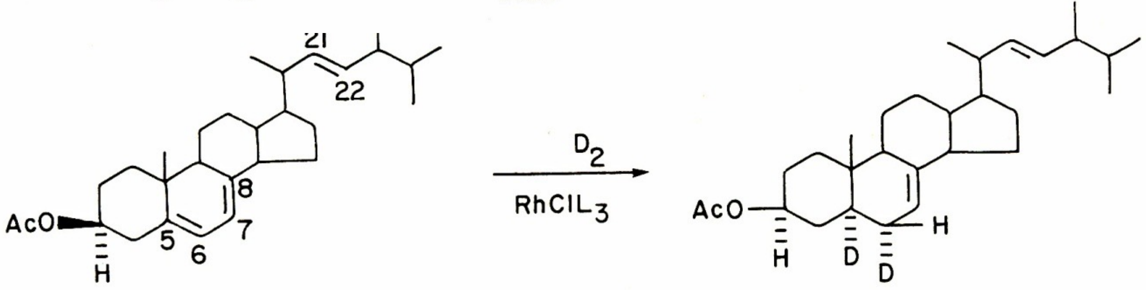
WILKINSON’S CATALYST

This catalyst is selective and efficient exhibiting high rates and turn over numbers.

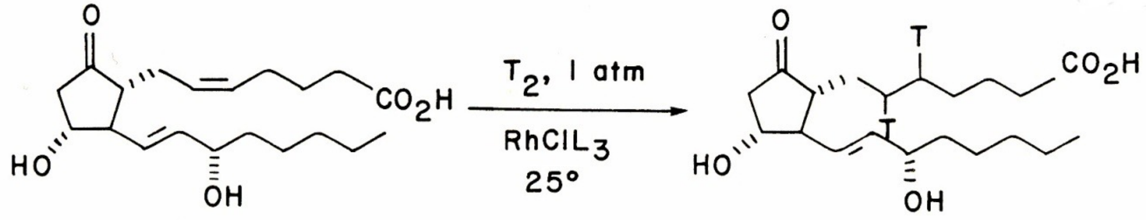




9.33



Ergosterol acetate

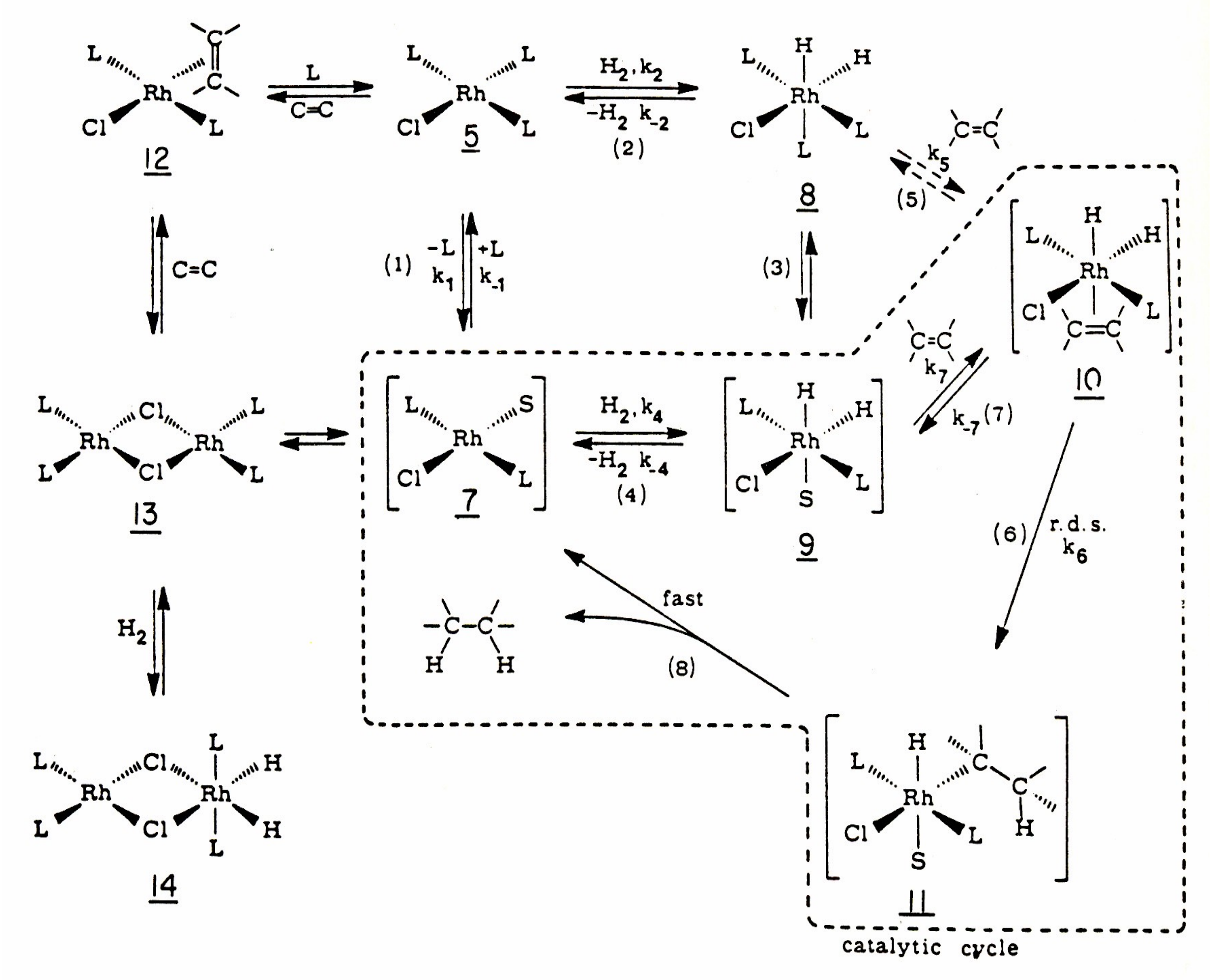


prostaglandine

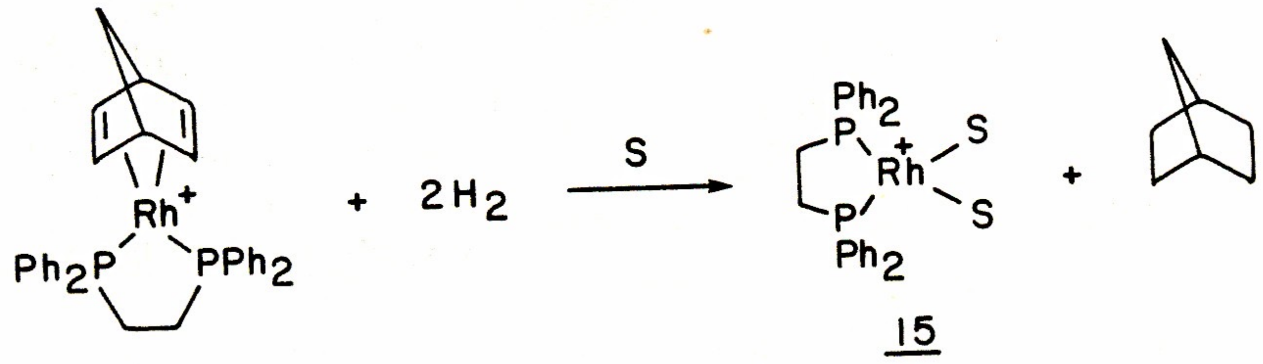
No isotope scrambling between H_2 and D_2 and between protons in the solvent or on the olefin substrate.

WILKINSON'S CATALYST

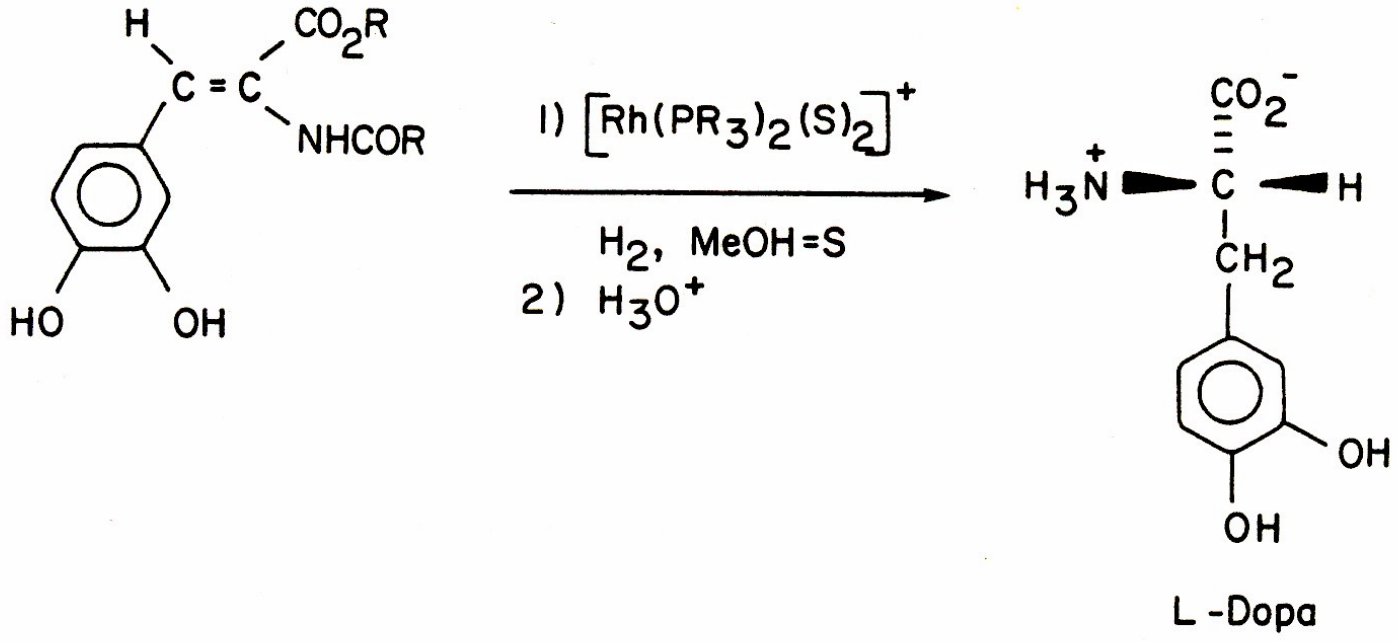
Halpern's stepwise analysis



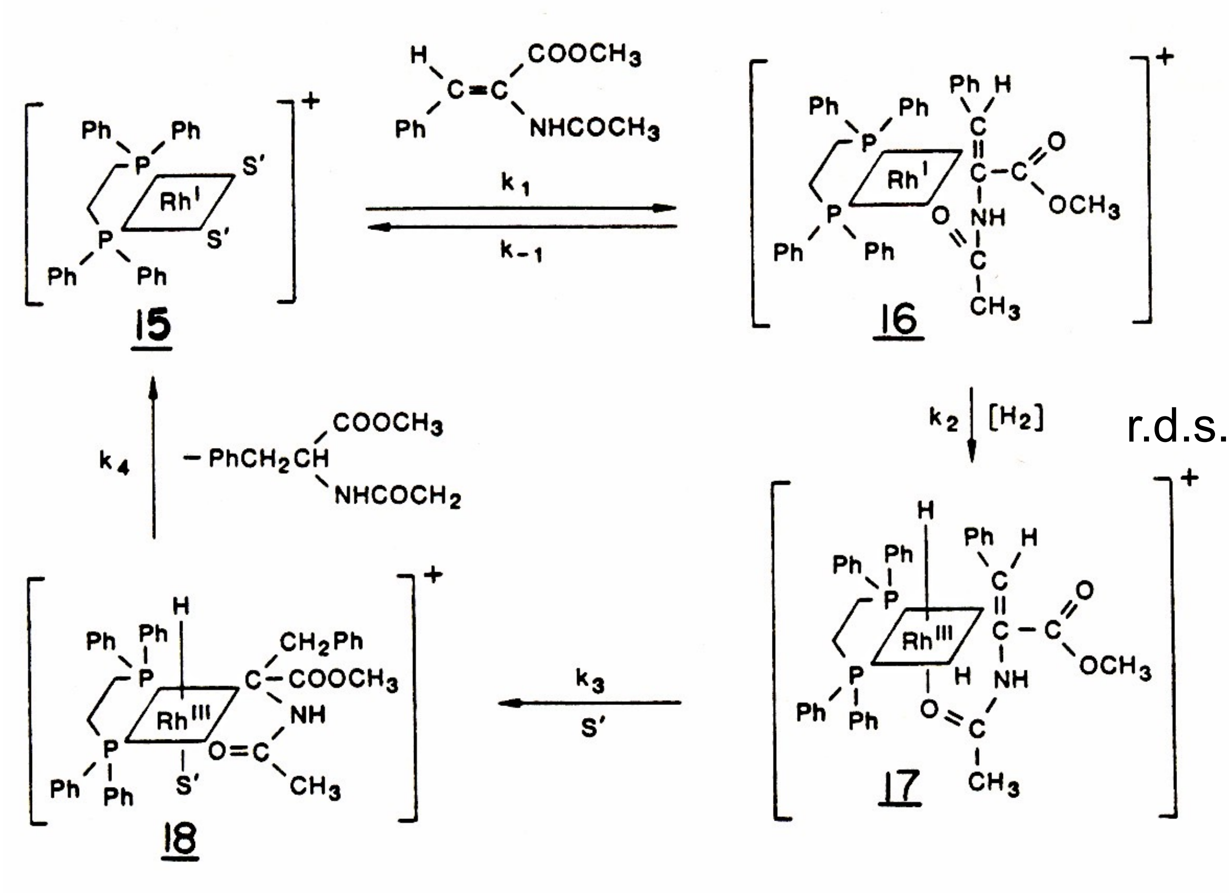
WILKINSON’S CATALYST



Monsanto process was developed for synthesis of L-Dopa, a drug for Parkinson- desease starting from aminocinnamic acids



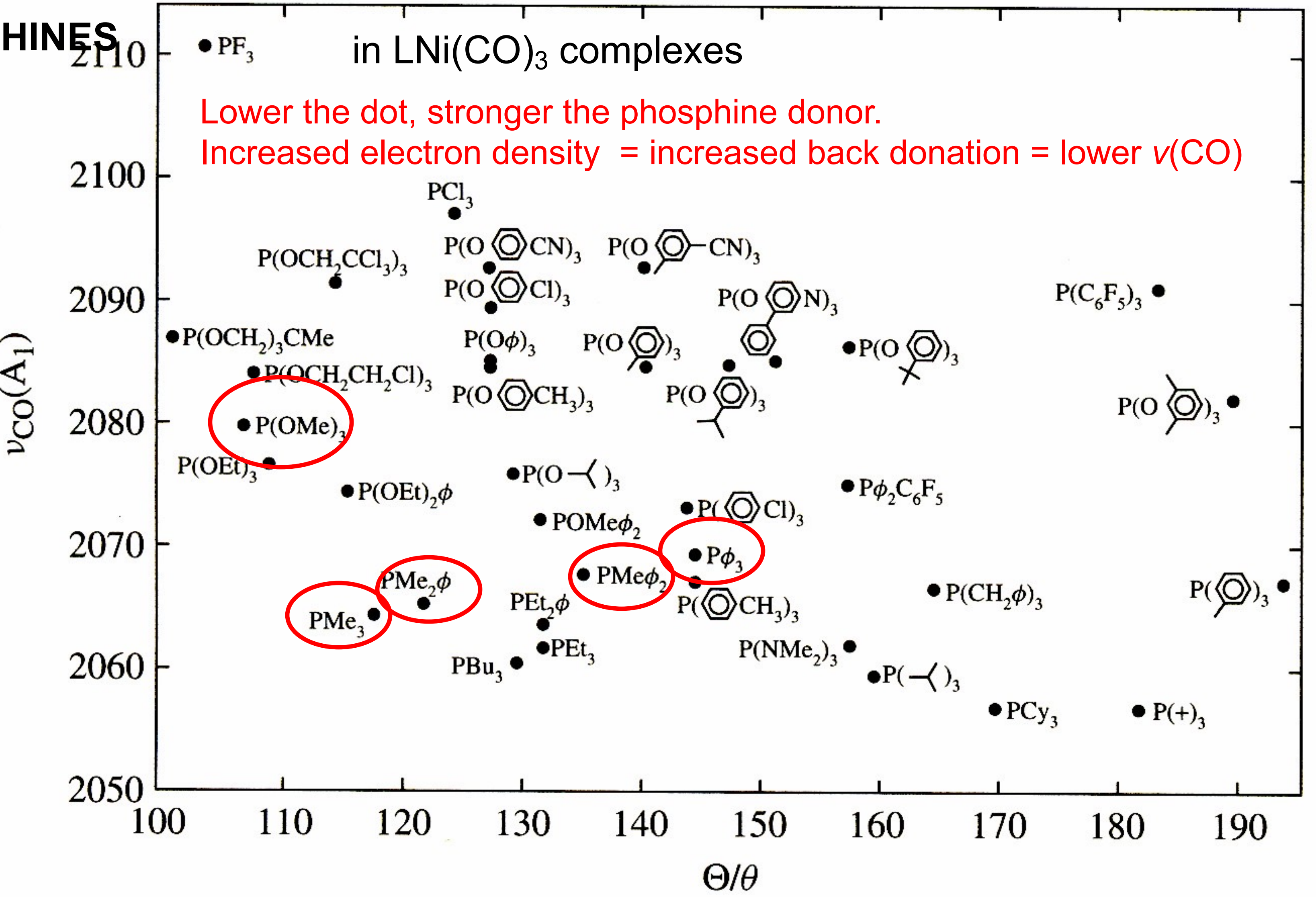
WILKINSON’S CATALYST



r.d.s.

The catalyst with chiral ligands like CHIRAPHOS and DIPAMP is highly selective and optical yields approach 100 % enantiomeric excess (ee) ([R]-[S]) / ([R] + [S])] x 100.

PHOSPHINES



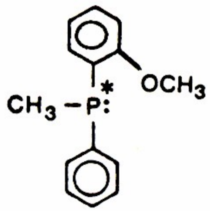
in $LNi(CO)_3$ complexes

Lower the dot, stronger the phosphine donor.

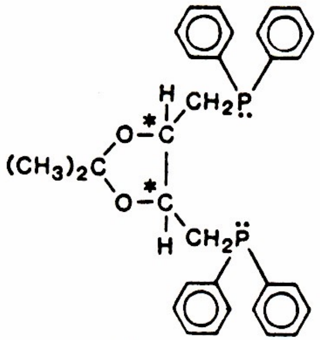
Increased electron density = increased back donation = lower v(CO)

FIGURE 4.4 Electronic and steric effects of common P-donor ligands plotted on a m according to Tolman (ν in cm^{-1}, θ in degrees). Reproduced from Ref. 26 with permissi of the American Chemical Society.)

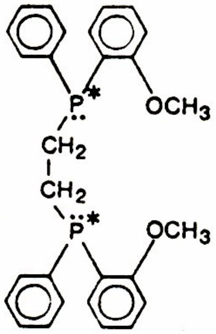
WILKINSON'S CATALYST



(PAMP)

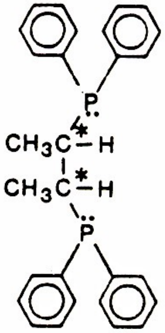


(DIOP)



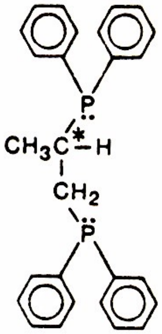
(DIPAMP)

21

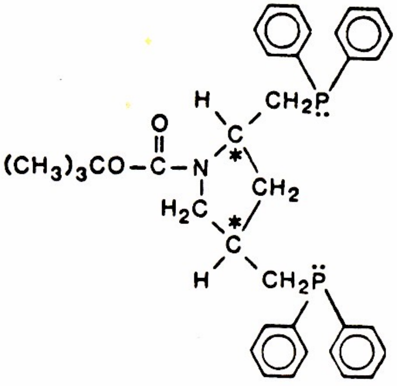


(CHIRAPHOS)

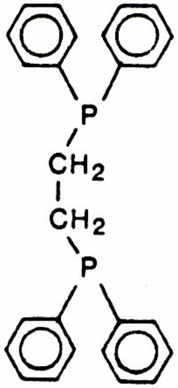
22



(PROPHOS)



(BPPM)

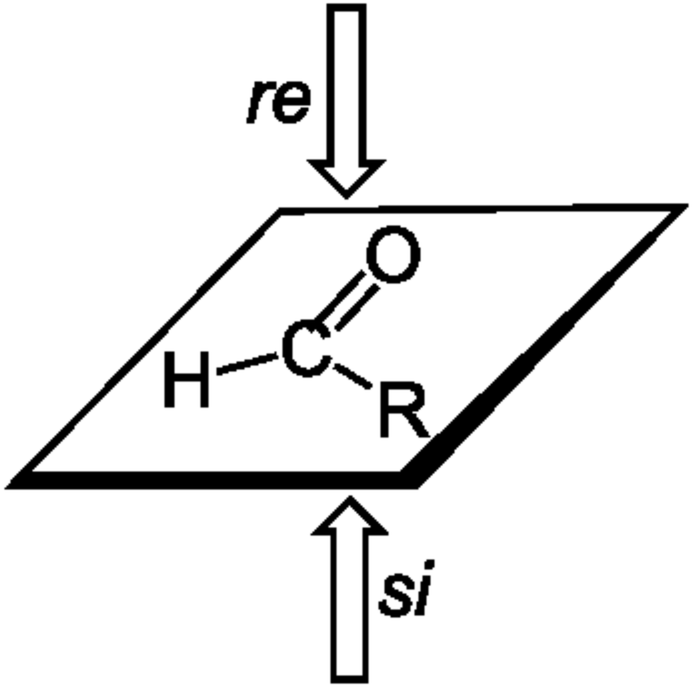


(DIPHOS)

Prochirality

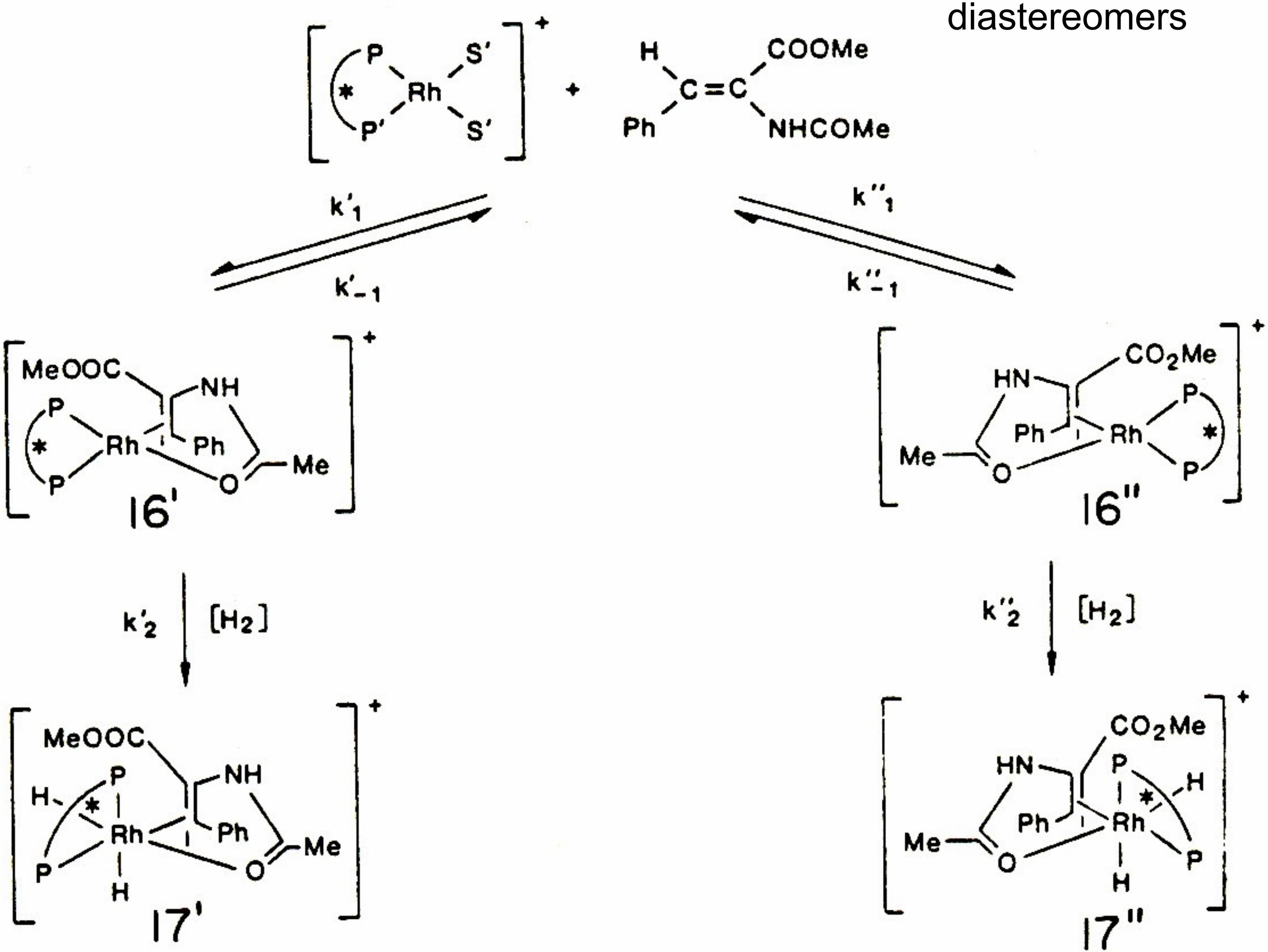
In stereochemistry, prochiral molecules are those that can be converted from achiral to chiral in a single step.[1] [2]

A trigonal planar sp^2-hybridized atom can be converted to a chiral center when a substituent is added to the *re* or *si* face of the molecule. These faces are labelled *re* if the substituents at the trigonal atom are disposed in decreasing Cahn-Ingold-Prelog priority order in a clockwise order, and *si* if the priorities decrease in counter-clockwise order; but the designation of the resulting chiral centre as R or S depends on the priority of the incoming group.

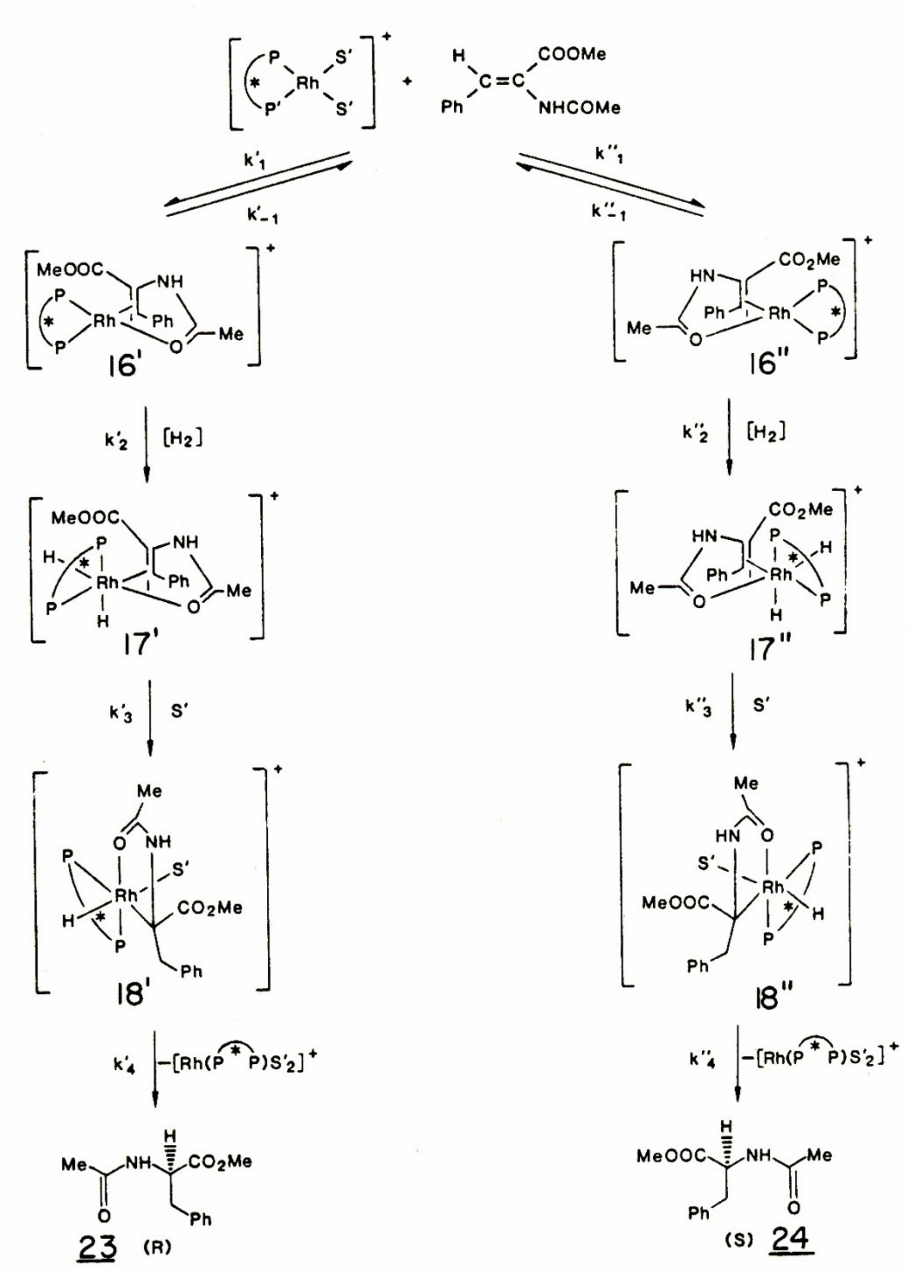


WILKINSON’S CATALYST

With a chiral ligand two diastereomers

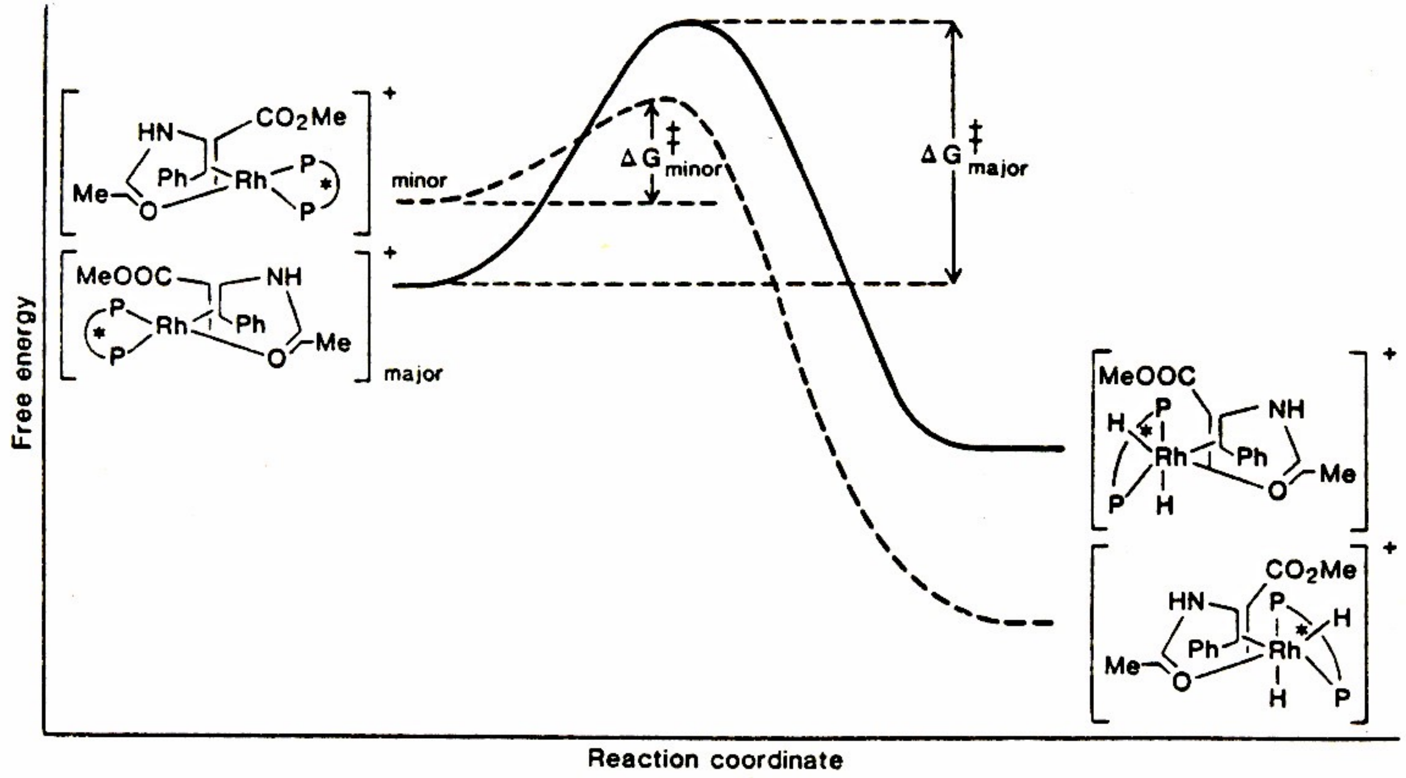


WILKINSON'S CATALYST



WILKINSON'S CATALYST

Fischer's *lock and key* assumption is not valid here



Principles of Organometallic Chemistry

Definition:

Organometallic compound (complex) contains at least on metal-carbond bond.

Also inorganic complexes with alike properties are counted (at least when M-C bond is generated *in situ*).

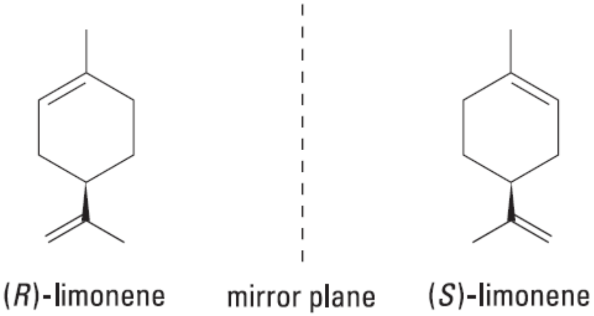
Importance:

Organometallic complexes are in the center of many industrial, catalytic processes and in the major chemical transformations (oxidation, reduction, C-C coupling and C-H activations).

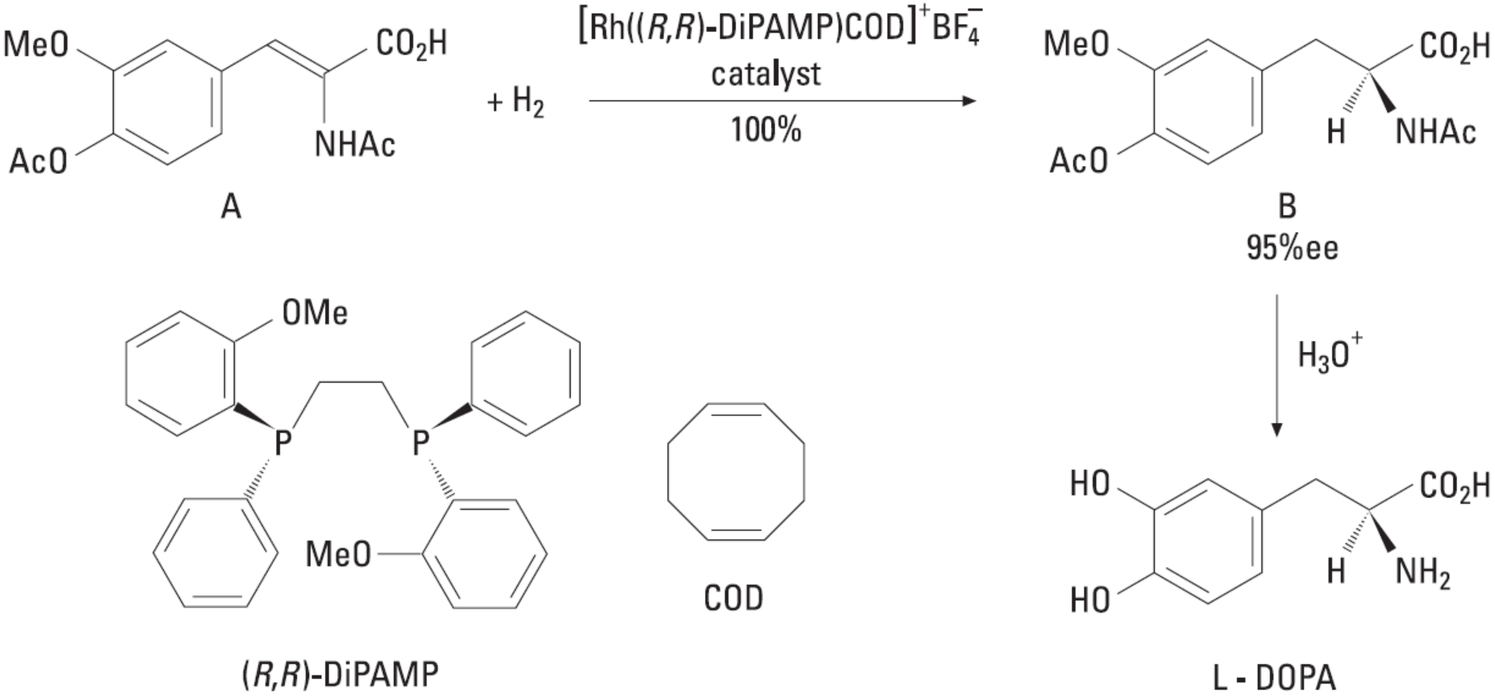
Nobel Prize in Chemistry for 2001 for the development of catalytic asymmetric synthesis William S. Knowles, Ryoji Noyori and Barry Sharpless.

http://nobelprize.org

Principles of Organometallic Chemistry



(*R*)-Limonene smells of oranges and (*S*)-limonene smells of lemons.



The Monsanto synthesis of L-DOPA using catalytic asymmetrichydrogenation.

HYDROGENATION CATALYSTS
industrial applications

Monsanto amino acid process was the first homogeneous transition-metal catalyzed hydrogenetion on industrial scale.

In this enantioselective process 200 tons of L-dopa is produced. Wilkinson type Rh catalyst with DIPAMP ligand gives 94% ee.

HYDROGENATION CATALYSTS
industrial applications

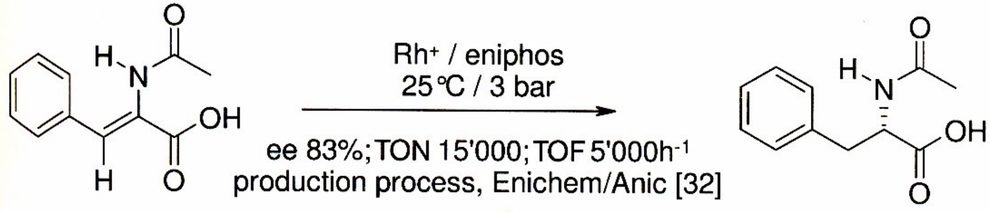
Monsanto amino acid process was the first homogeneous transition-metal catalyzed hydrogenetion on industrial scale.

In this enantioselective process 200 tons of L-dopa is produced. Wilkinson type Rh catalyst with DIPAMP ligand gives 94% ee.

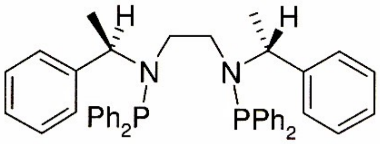
Nowadays for preparation of pharmaceuticals, ees below 99% are not aceptable!

$$ee = \frac{(R-S)}{(R+S)} \times 100$$

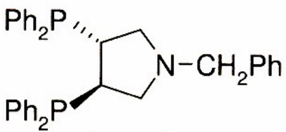
Another homogeneous enantioselective hydrogenetion is Epichem process for hydrogenation of a dehydroamino acid for synthesis of (S)-phenylalanine, needed for the sweeterner aspartame. Production:35,000 metric tons a year.



After crystallization ee 99%

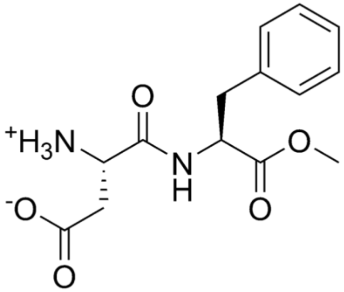


eniphos



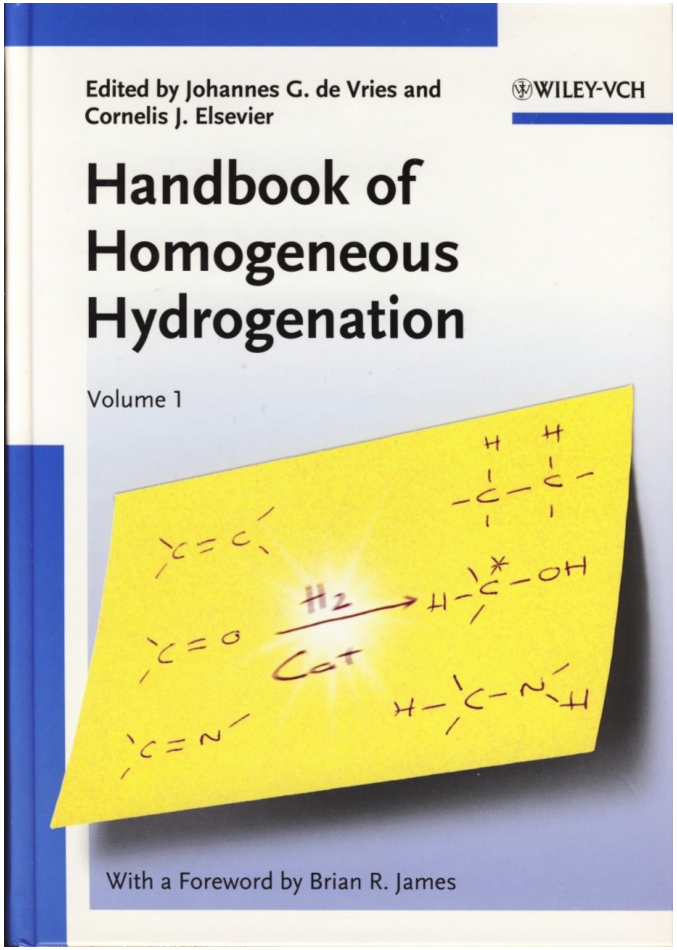
deguphos

TON 10 000, TOF 3000 h^{-1}



aspartame

HYDROGENATION CATALYSTS



Edited by Johannes G. de Vries and
Cornelis J. Elsevier

WILEY-VCH

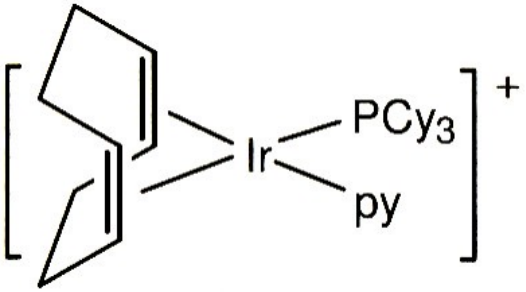
Handbook of
Homogeneous
Hydrogenation

Volume 1

With a Foreword by Brian R. James

HYDROGENATION CATALYSTS

Crabtree's iridium catalyst



Coordinatively highly unsaturated catalysts,
Which catalyzes reduction of hindered olefins
At high rates.

It is rather inert for other functional groups.

Alcohols and polar solvents deactivate the catalyst.

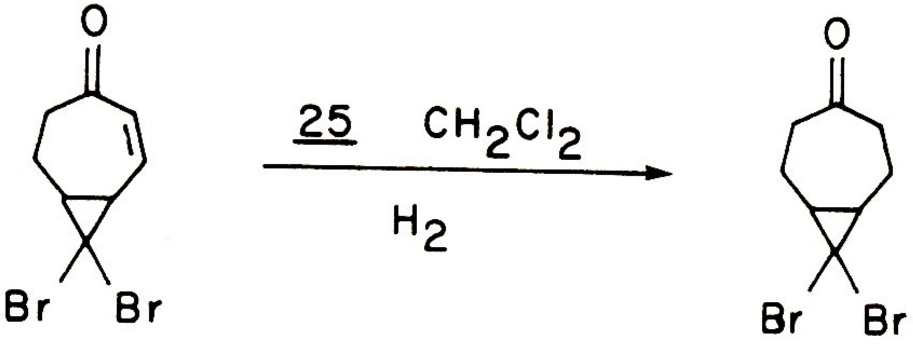
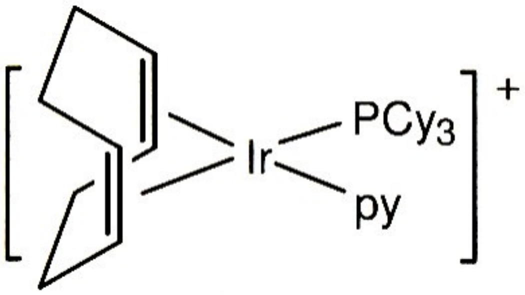


Table 10.1. Turnover Frequencies for Homogeneous Olefin Hydrogenation Catalysts.

Catalyst precursor	Temp.(°C)	Solvent	Turnover Frequency(Hr.$^{-1}$)		
			1-hexene	cyclohexene	tetramethyl-ethylene
$[Ir(cod)(PCy_3)(Py)]^+$	0°	CH_2Cl_2	6,400	4,500	4,000
$[Ir(cod)(PMePh_2)_2]^+$	0°	CH_2Cl_2	5,100	3,800	50
$[Ir(cod)(PMePh_2)_2]^+$	0°	CH_3COCH_3	10	0	0
$[Rh(cod)(PPh_3)_2]^+$	25°	CH_2Cl_2	4,000	10	0
$[Ru(H)Cl(PPh_3)_3]$	25°	C_6H_6	9,000	7	0
$[RhCl(PPh_3)_3]$	25°	C_6H_6/EtOH	650	700	0
$[RhCl(PPh_3)_3]$	0°	C_6H_6/EtOH	60	70	0

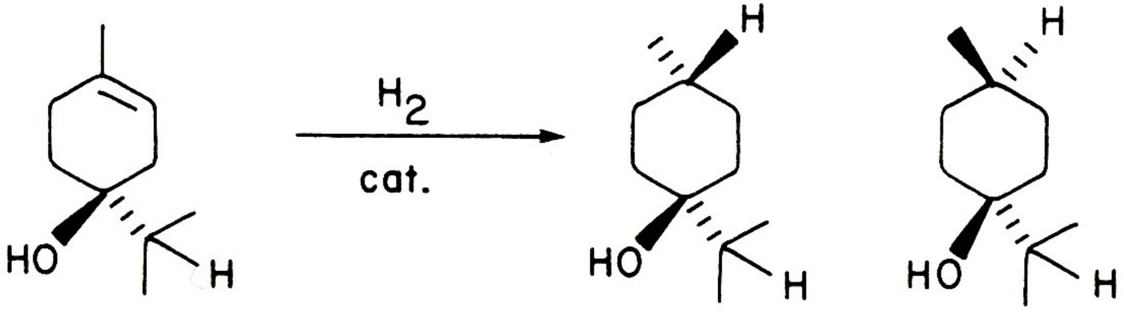
HYDROGENATION CATALYSTS

Crabtree's iridium catalyst



As shown below, enols are easily hydrogenated, but the rate is reduced (about 30 h^{-1}).

Because the catalyst have high affinity to for polar ligands, hydrogen come from the same face of a molecule which bears an alcohol group.



Notice the contrast to palladium on charcoal

cat. = Pd/C	20	30
cat. = [Ir(COD)PCy_3py]	99.9	< 0.1

HYDROGENATION CATALYSTS

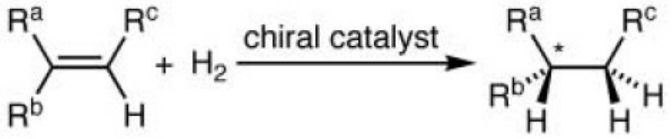
Asymmetric hydrogenation of olefins is one of the most useful reactions for the synthesis of optically active compounds, especially in industry.

However, the application range of the catalysts developed was for a long time limited to alkenes with a coordinating functional group or an aryl substituent next to the double bond.

Asymmetric Hydrogenation of Unfunctionalized, Purely Alkyl-Substituted Olefins

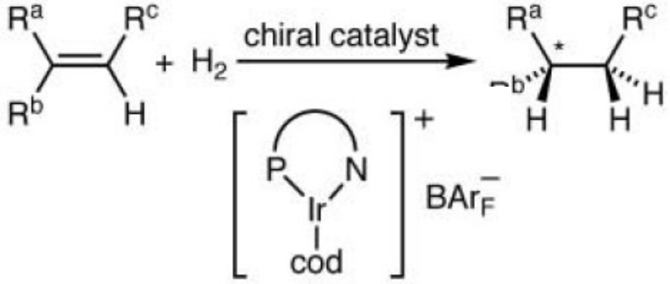
Sharon Bell,[1*] Bettina Wüstenberg,[1*] Stefan Kaiser,[1] Frederik Menges,[1] Thomas Netscher,[2] Andreas Pfaltz[1]†

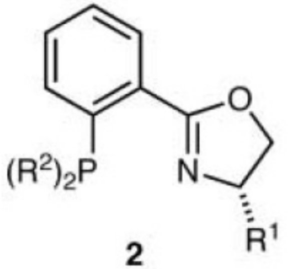
SCIENCE 2006,311, 642



HYDROGENATION CATALYSTS

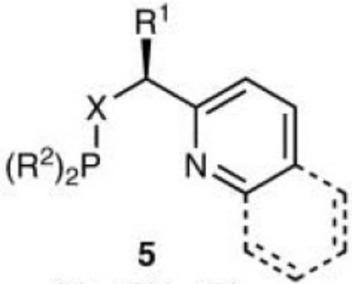
Asymmetric Hydrogenation of Unfunctionalized, Purely Alkyl-Substituted Olefins



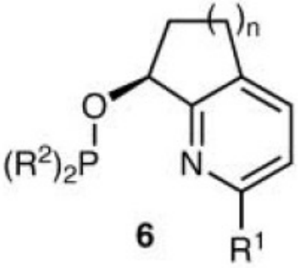


2

Oxazoline based P,N ligands

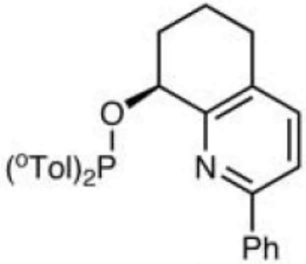


5
(X = CH_2, O)

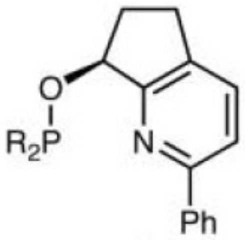


6

Pyridine based P,N ligands



11

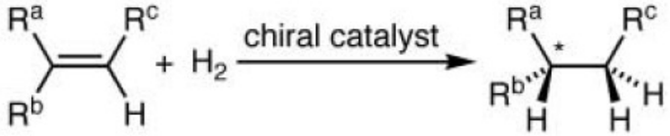


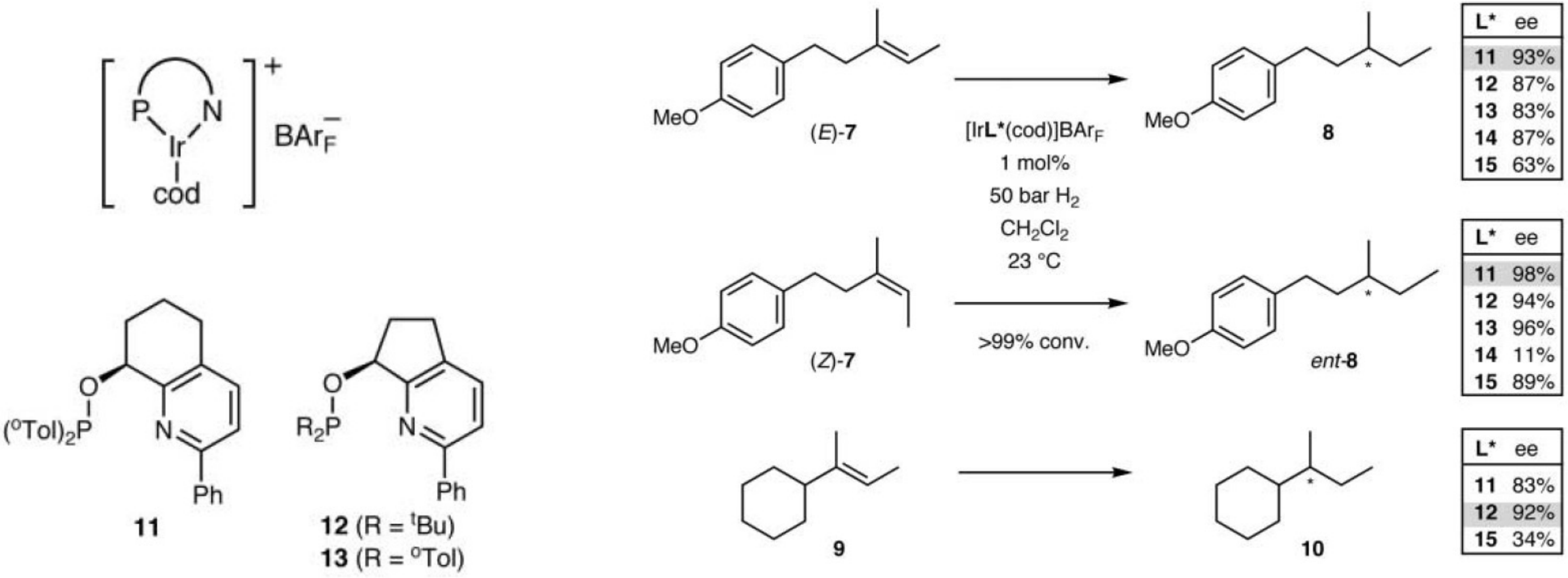
12 (R = ᵗBu)
13 (R = °Tol)

SCIENCE 2006,311, 642

HYDROGENATION CATALYSTS

Asymmetric Hydrogenation of Unfunctionalized, Purely Alkyl-Substituted Olefins





L*	ee
11	93%
12	87%
13	83%
14	87%
15	63%

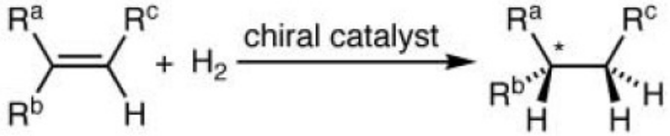
L*	ee
11	98%
12	94%
13	96%
14	11%
15	89%

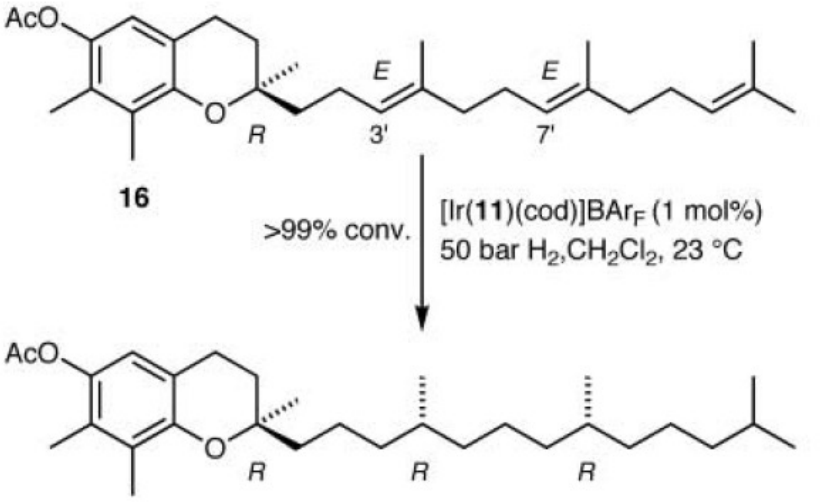
L*	ee
11	83%
12	92%
15	34%

SCIENCE 2006,311, 642

HYDROGENATION CATALYSTS

Asymmetric Hydrogenation of Unfunctionalized, Purely Alkyl-Substituted Olefins





16

17 >98% *RRR* (<0.5% *RRS*; <0.5% *RSR*; <0.5% *RSS*)

Tocopherols are the principal components of vitamin E.

Hydrogenation of γ-tocotrienyl acetate **16** (AcO = acetate)

SCIENCE 2006,311, 642

HYDROGENATION CATALYSTS

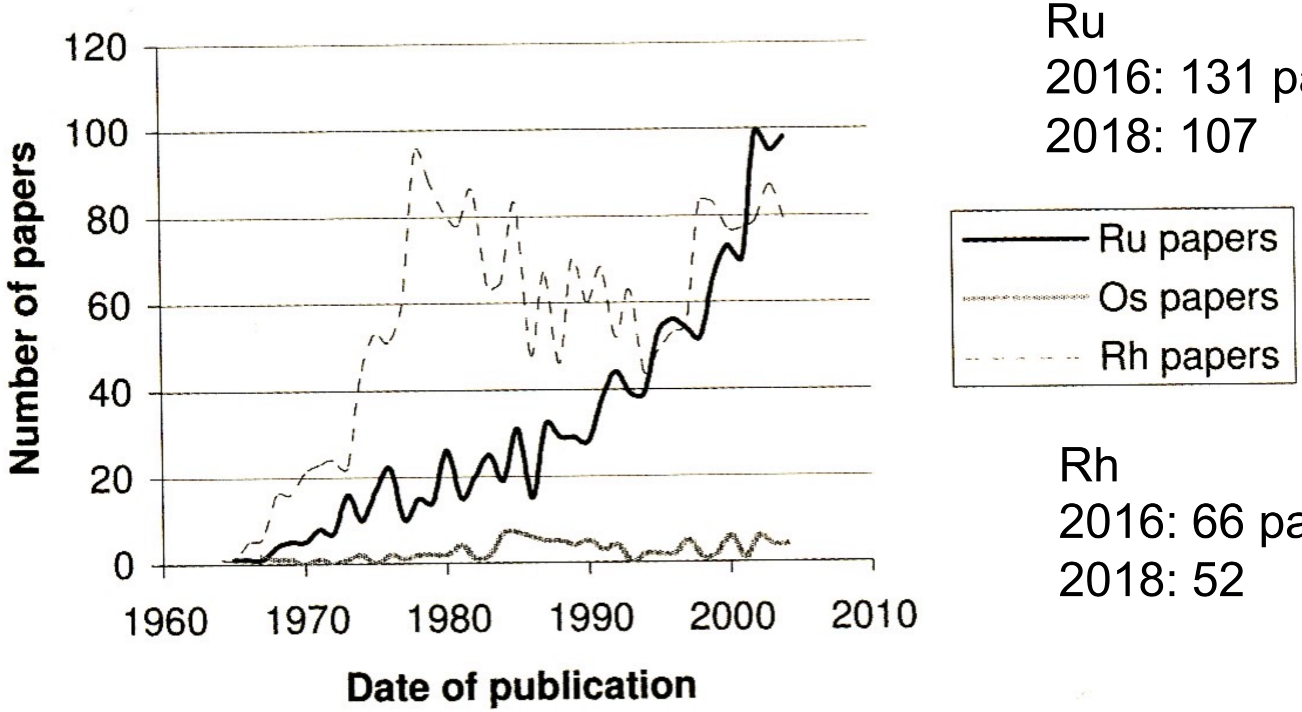


Fig. 3.1 Graphical illustration of numbers of reports per year versus date of publication. Data were obtained by searching the Chemical Abstracts Database using the term "hydrogenation catalyzed by ruthenium complexes" or osmium complexes or rhodium complexes. These are not comprehensive searches but are still representative of the activity in the field.

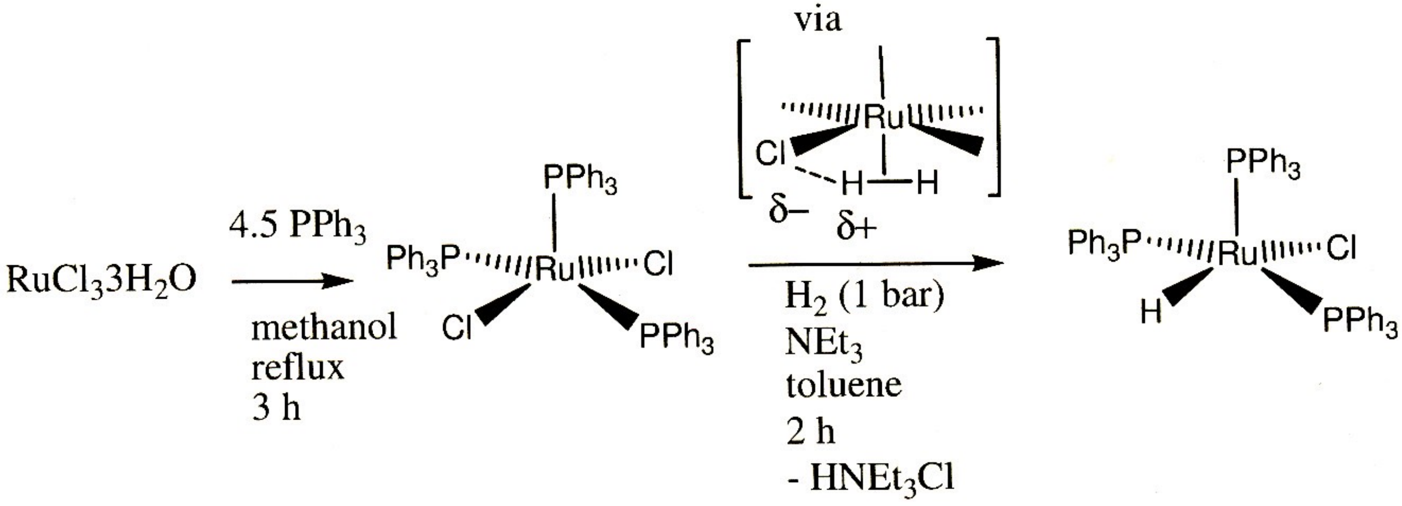
Ru
2016: 131 papers
2018: 107

Rh
2016: 66 papers
2018: 52

Os
2016: 5 papers
2018: 3

HYDROGENATION CATALYSTS

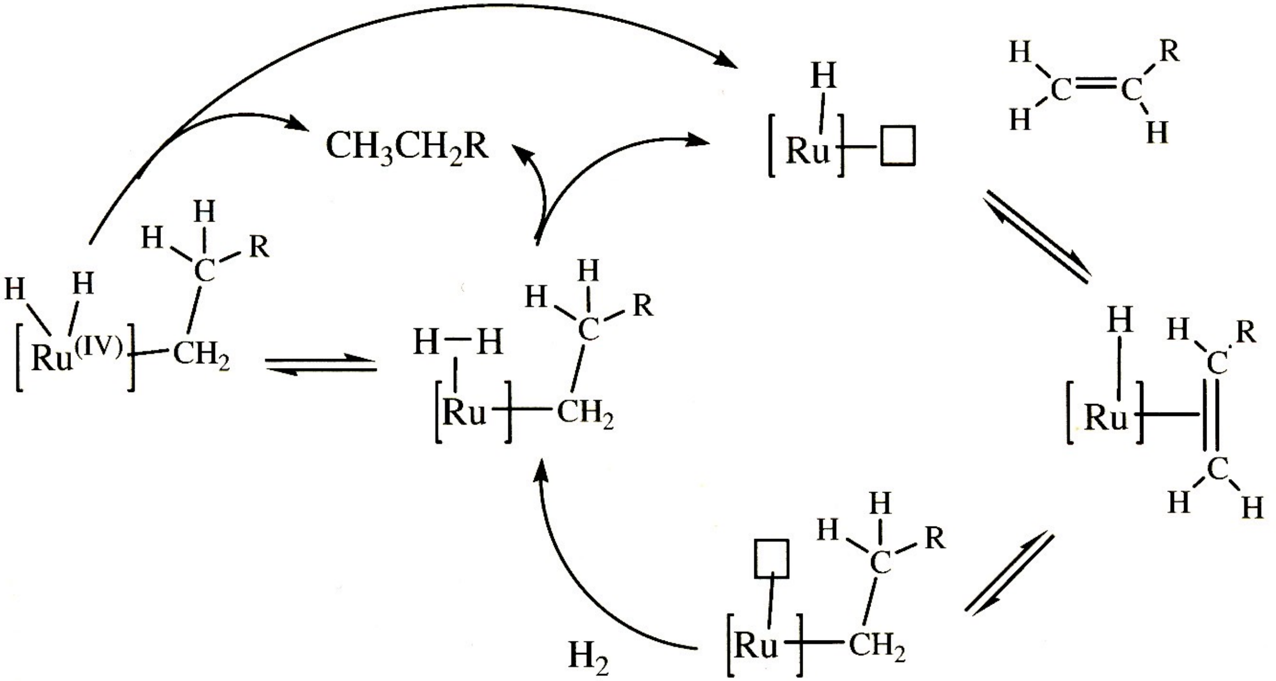
Ruthenium complexes as hydrogenation catalysts.



Scheme 3.2 Preparation of the alkene hydrogen catalyst $RuHCl(PPh_3)_3$.

Beside of being hihgly active in hydrogenation of olefins, ruthenium complexes are highly useful for hydrogenation of aldehydes, ketones and imines.

HYDROGENATION CATALYSTS



Scheme 3.3 Mechanism for the hydrogenation of 1-alkenes catalyzed by $RuHCl(PPh_3)_3$. [Ru] represents the $RuCl(PPh_3)_n$ fragment. The box represents an empty coordination site on ruthenium(II).

Principles of Organometallic Chemistry

Definition:

Organometallic compound (complex) contains at least on metal-carbond bond.

Also inorganic complexes with alike properties are counted (at least when M-C bond is generated *in situ*).

Importance:

Organometallic complexes are in the center of many industrial, catalytic processes and in the major chemical transformations (oxidation, reduction, C-C coupling and C-H activations).

Nobel Prize in Chemistry for 2001 for the development of catalytic asymmetric synthesis William S. Knowles, Ryoji Noyori and Barry Sharpless.

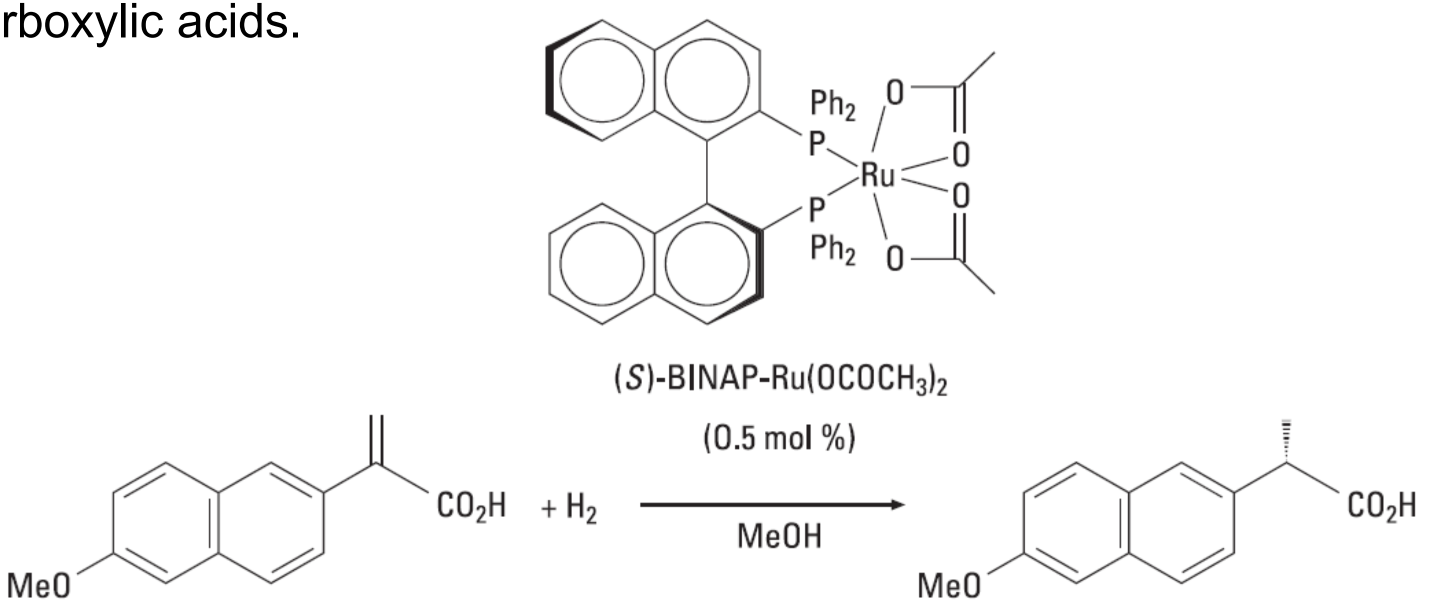
http://nobelprize.org

HYDROGENATION CATALYSTS

Noyori’s general hydrogenation catalysts

Noyori’s discovery of the BINAP-Ru(II) complex catalysts was a major advance in stereoselective organic synthesis. The scope of the application of these catalysts is far reaching.

These chiral Ru complexes serve as catalyst precursors for the highly enantioselective hydrogenation of a range of α,β- and β,γ-unsaturated carboxylic acids.

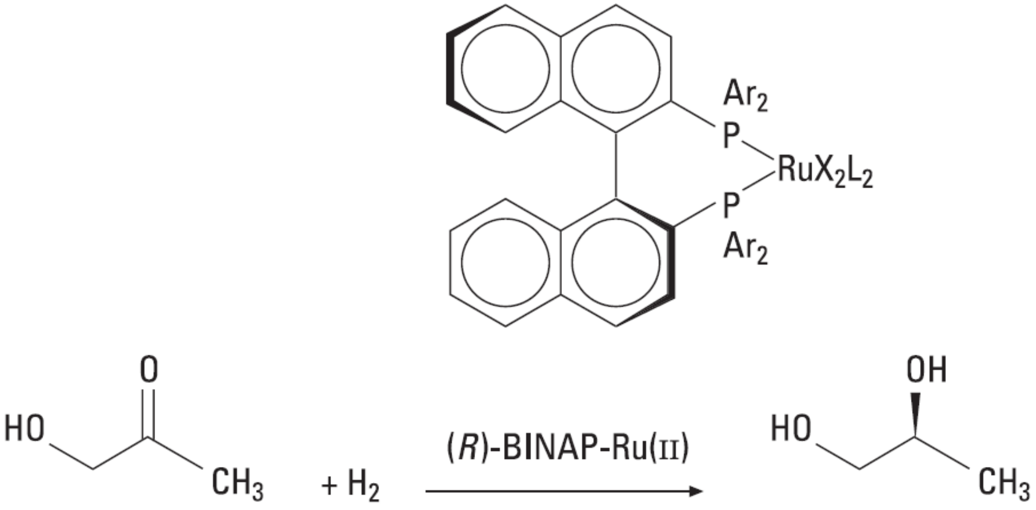


(S)-naproxen
an anti-inflammatory agent
92% yield, 97%ee

HYDROGENATION CATALYSTS

This reaction, unlike Rh(I)-catalyzed olefin hydrogenation, proceeds via a metal monohydride mechanism.The enantioselectivity is much higher than when utilizing the Rh catalyst and the sense of asymmetric induction is the opposite.

Various functionalities can act as directing groups.

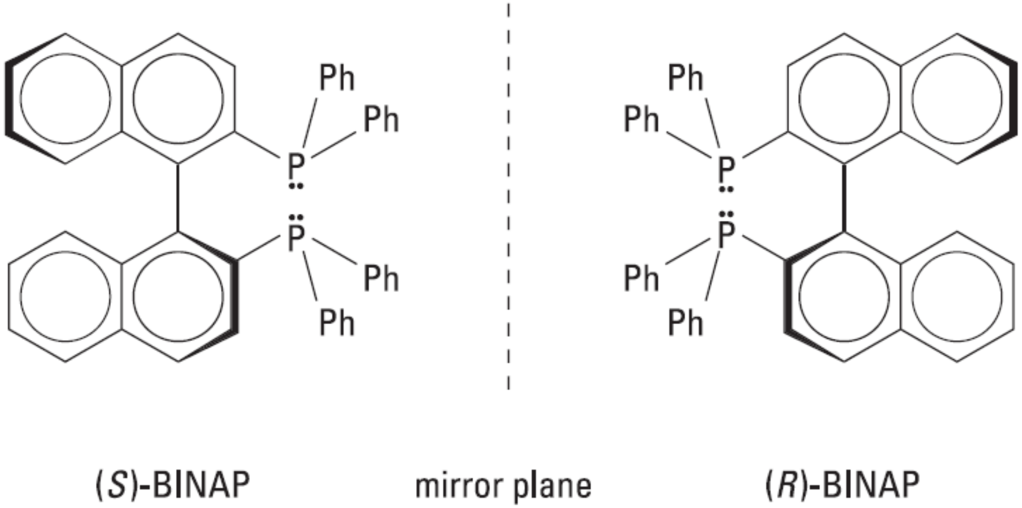


Ar = aryl; L = ligand; X = Cl, Br or I

The (*R)-BINAP-Ru-(II)-catalyzed hydrogenation of acetol to (R)-1,2-*propanediol is currently used for the industrial synthesis of antibacterial levofloxacin.

HYDROGENATION CATALYSTS

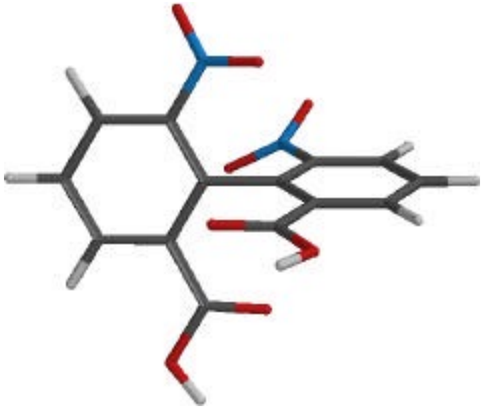
In 1980, Noyori, together with Takaya, discovered an **atropisomeric chiral** diphosphine, BINAP. Rh(I) complexes of the enantiomers of BINAP are remarkably effective in various kinds of asymmetric catalysis.

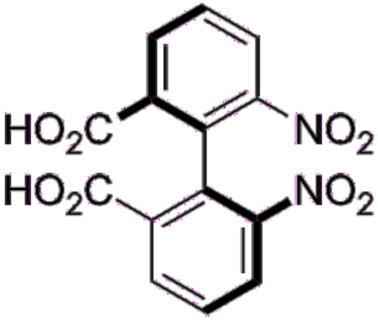


The two enantiomers of the versatile diphosphine ligand BINAP is shown.

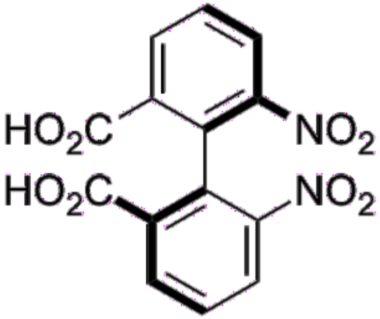
Atropisomers

are stereoisomers resulting from hindered rotation about single bonds where the steric strain barrier to rotation is high enough to allow for the isolation of the conformers. The word atropisomer is derived from the Greek a, meaning not, and tropos, meaning turn. The name was coined by Kuhn in 1933, and atropisomerism was first detected in 6,6’-dinitro-2,2’-diphenic acid by Cristie in 1922.





S_a

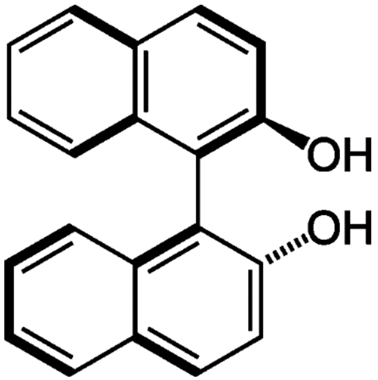


R_a

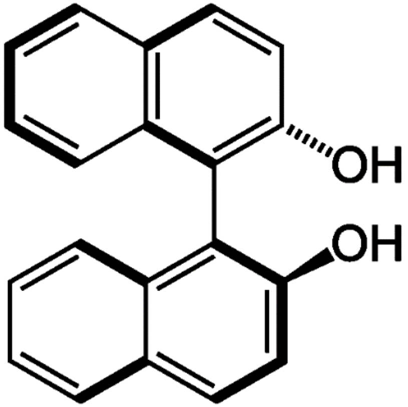
Axial chirality is a special case of chirality in which a molecule does not possess a stereogenic center (the most common form of chirality in organic compounds) but an axis of chirality – an axis about which a set of substituents is held in a spatial arrangement that is not superposable on its mirror image.

Axial chirality is most commonly observed in atropisomeric biaryl compounds wherein the rotation about the aryl-aryl bond is restricted, for example, biphenyl, binaphthyls, e.g., 1,1'-bi-2-naphthol, and certain dihydroanthracenone compounds [1] . Certain allene compounds also display axial chirality. The enantiomers of axially chiral compounds are usually given the stereochemical labels Ra and Sa, although the plus (P) or minus (M) notation (or alternatively Δ / Λ) is occasionally employed.[2] P/M or Δ/Λ is used particularly for molecules that resemble a helix, such as hexahelicene, in which case a right-handed helix is denoted P or Δ and a left-handed helix is denoted M or Λ.

This can also be called helicity, which is the chirality of a helical, propeller or screw-shape molecular entity. P (plus) or Δ is a right-handed helix, where M (minus) or Λ is a left-handed helix

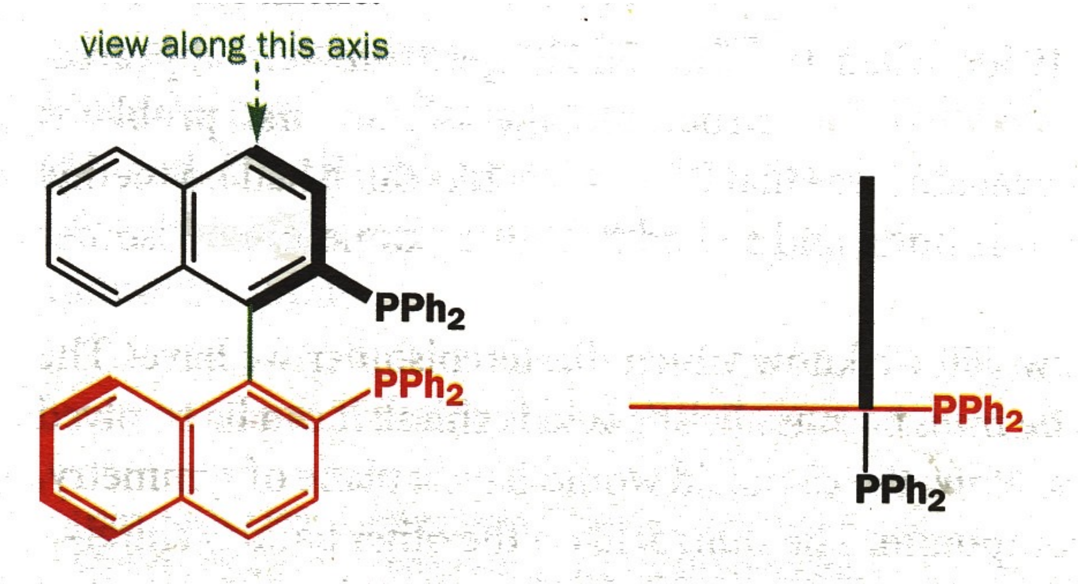


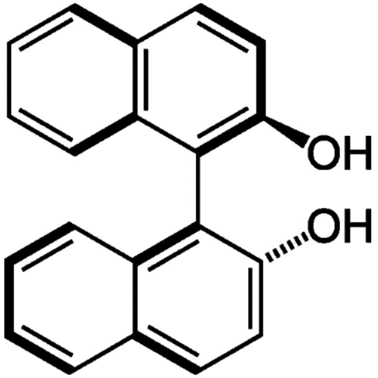
R-binol



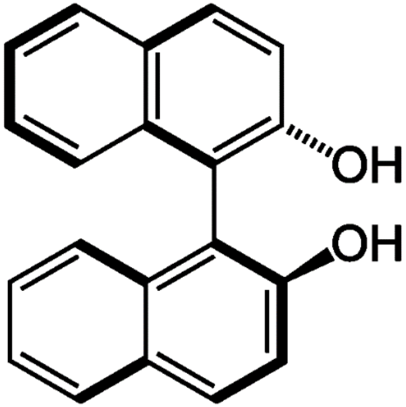
S-binol

a rotational half-life of over 5 million years.



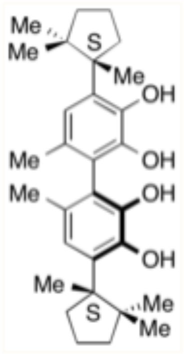


R-binol

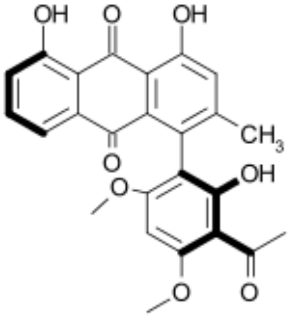


S-binol

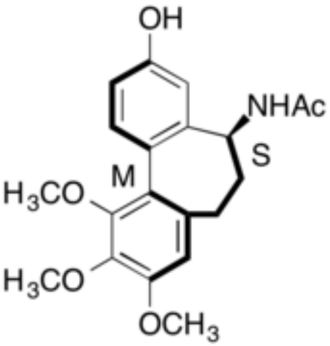
Atropisomeric Natural Products



Mastigophorene A



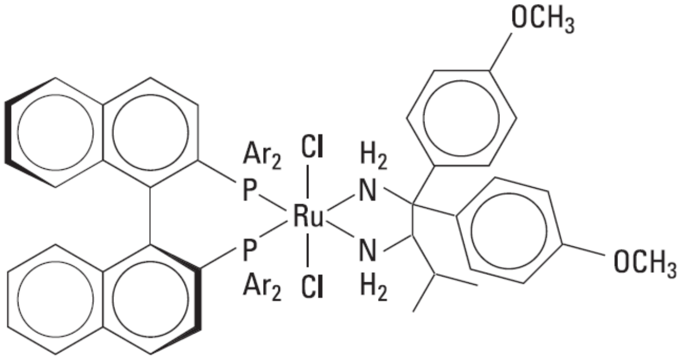
Knipholone



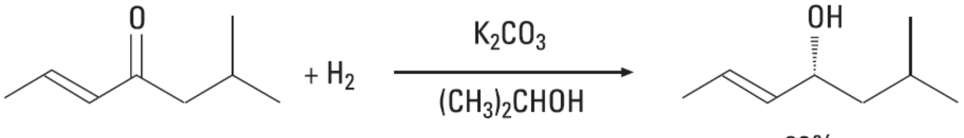
(–)-*N*-Acetylallocolchinol

HYDROGENATION CATALYSTS

Noyori recently reported a remarkable enhancement in the reactivity of the Ru(II) catalyst by the addition of ethylene diamine and KOH in 2-propanol.



Ar = 3,5-$(CH_3)_2C_6H_4$



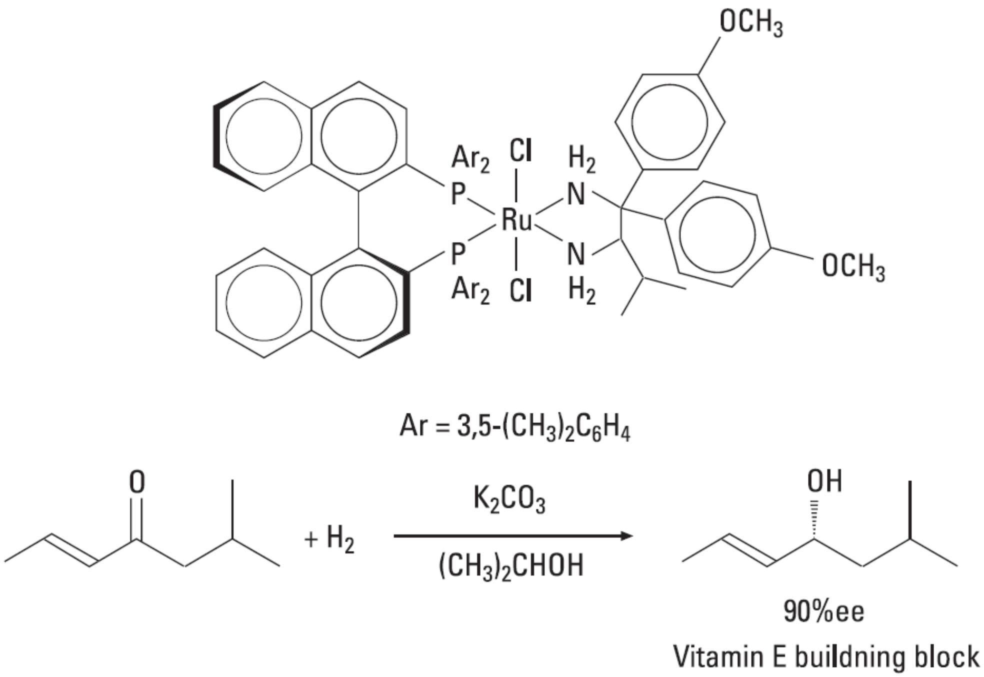
90%ee

Vitamin E buildning block

$RuCl_2$(xylylbinap)(diamine) and the weak base K_2CO_3 transforms a simple enone by enantioselective hydrogenation into a chiral allylic alcohol. The substrate/catalyst ratio approaches 100 000. This chemoselectivity is remarkable in view of the large catalytic activity of diamine-free BINAP-Ru complexes for hydrogenation of CC double bonds in allylic alcohols.

HYDROGENATION CATALYSTS

Noyori recently reported a remarkable enhancement in the reactivity of the Ru(II) catalyst by the addition of ethylene diamine and KOH in 2-propanol.



Ar = $3,5\text{-}(CH_3)_2C_6H_4$

90%ee

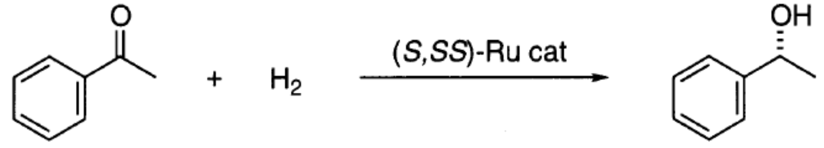
Vitamin E buildning block

The Ru hydride species generated in this asymmetric hydrogenation saturates a C=O linkage selectively, leaving C=C bonds intact, because of the operation of a metal-ligand bifunctional mechanism.

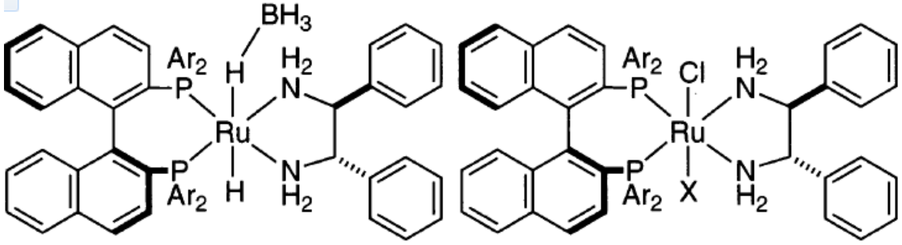
HYDROGENATION CATALYSTS

enantioselectivity is unaffected by hydrogen pressure, the nature of the solvent (protic or aprotic,bulkiness and chirality of alcohols), substrate concentration, the extent of conversion, the presence or absence of base, base concentration, or the nature of the base or coexisting metallic and organic cations.

This feature indicates that the stereodetermining step involves a common Ru hydride.



1 (*R*)-**2**



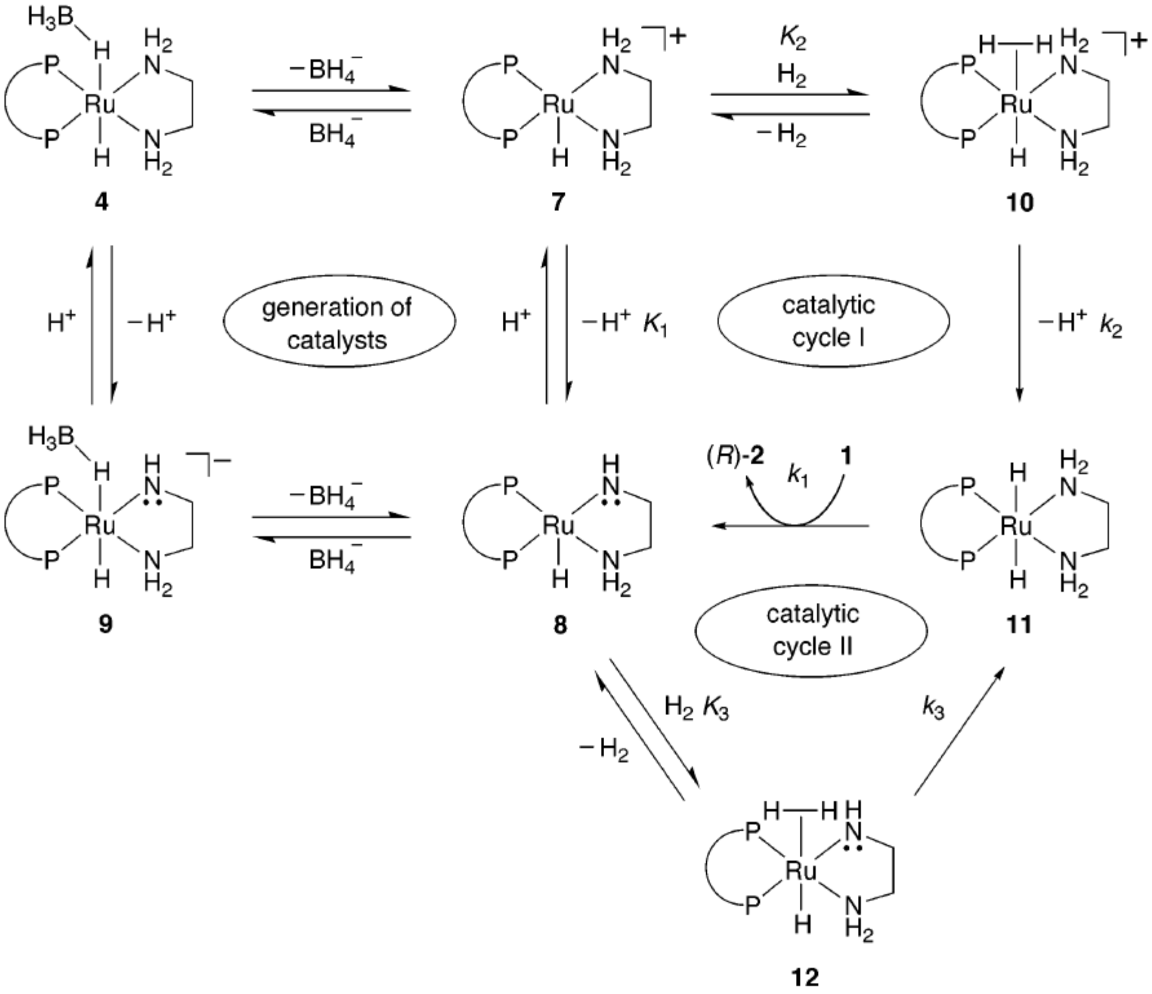
(*S*,*SS*)-**3**: Ar = 3,5-$(CH_3)_2C_6H_3$
(*S*,*SS*)-**4**: Ar = 4-$CH_3C_6H_4$

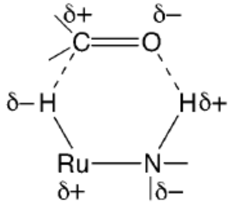
(*S*,*SS*)-**5**: Ar = 4-$CH_3C_6H_4$; X = Cl
(*S*,*SS*)-**6**: Ar = 4-$CH_3C_6H_4$; X = H

Acetophenone (**1**) (102 g) is hydrogenated to (R)-1-phenylethanol [(R)-**2**] in 99% ee and 100% yield in 2-propanol (106 mL) containing trans-RuH(è1-BH4)[(S)-xylbinap][(S,S)-dpen] [(S,SS)-3] (9.0 mg). The reaction with a substrate/catalyst molar ratio (S/C) of 100 000 takes place smoothly at 8 atm of H_2 and 45 °C and is completed within 7 h.

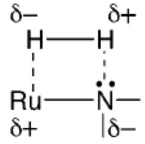
JACS, 2003, 13499.

HYDROGENATION CATALYSTS

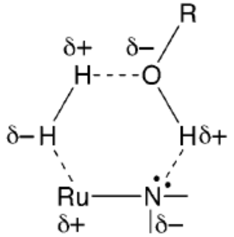




13 (TS)



14 (TS)

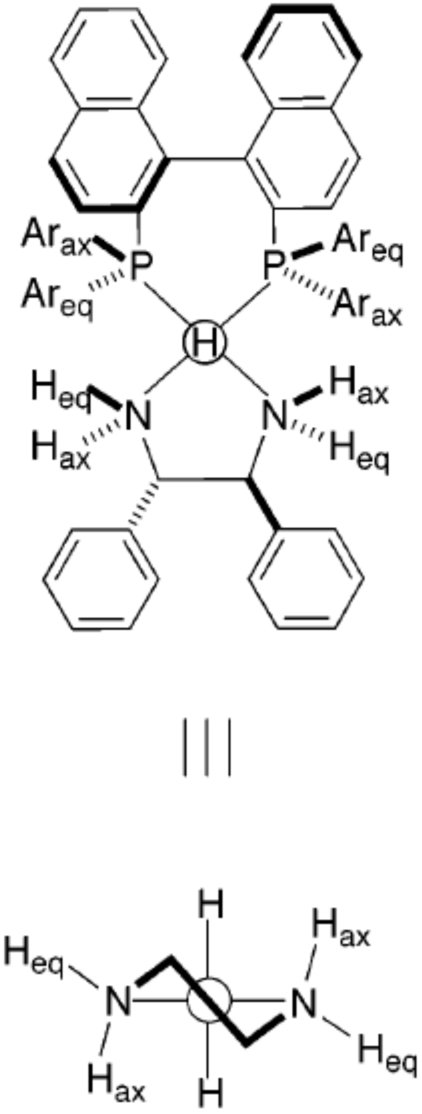


15 (TS)

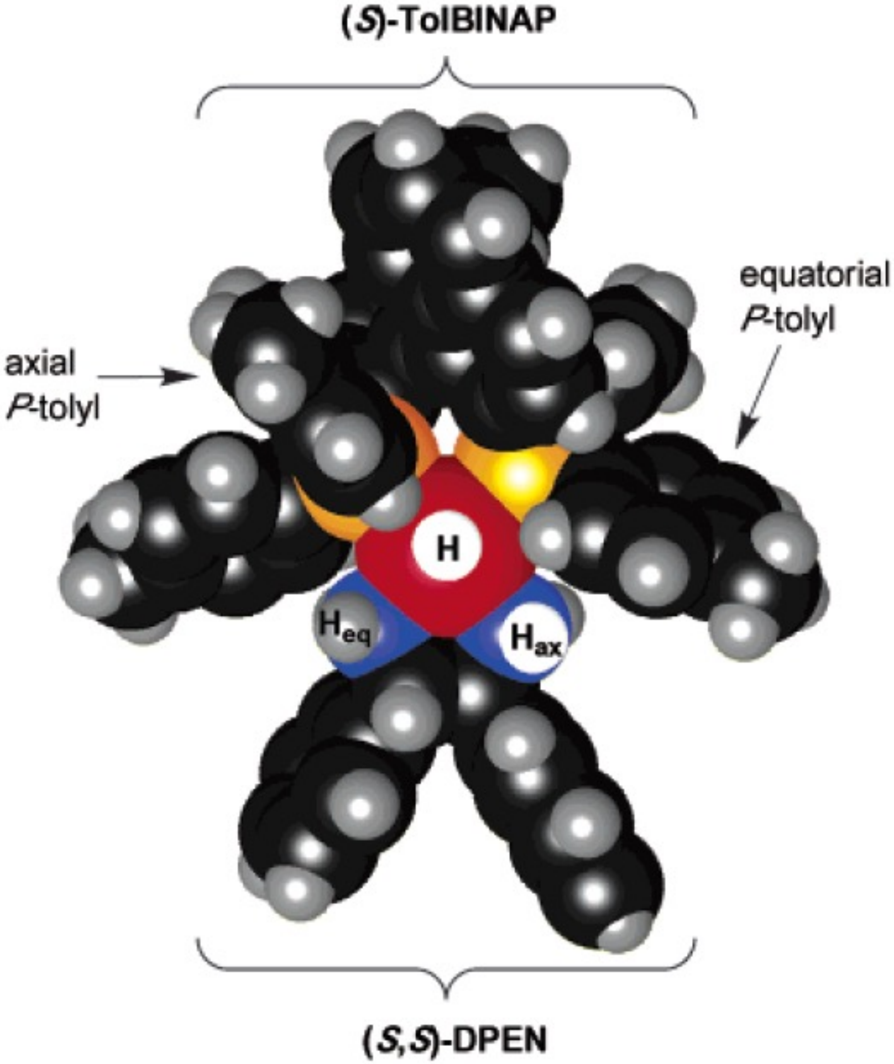
In **13** the Ru center delivers a hydride to the electrophilic C=O carbon, while the nitrogen supplies a proton to the oxygen atom simultaneously.

JACS, 2003, 13499.

HYDROGENATION CATALYSTS

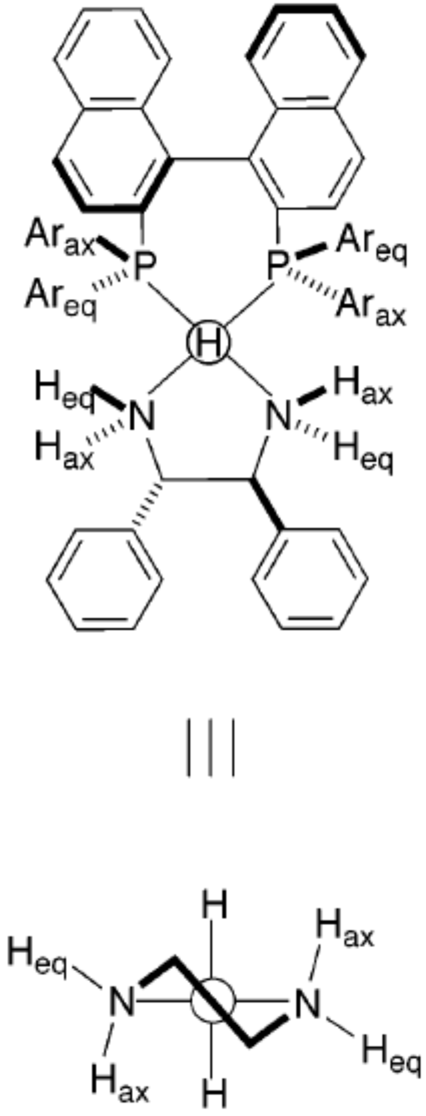


(*S*,*SS*)-**11**

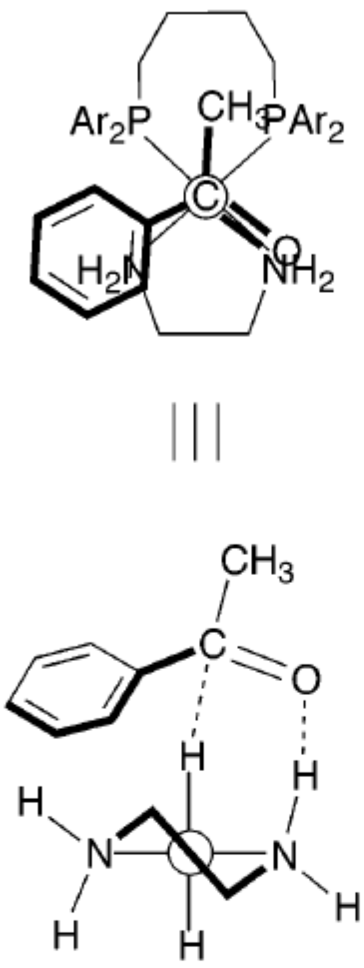


JACS, 2003, 13499.

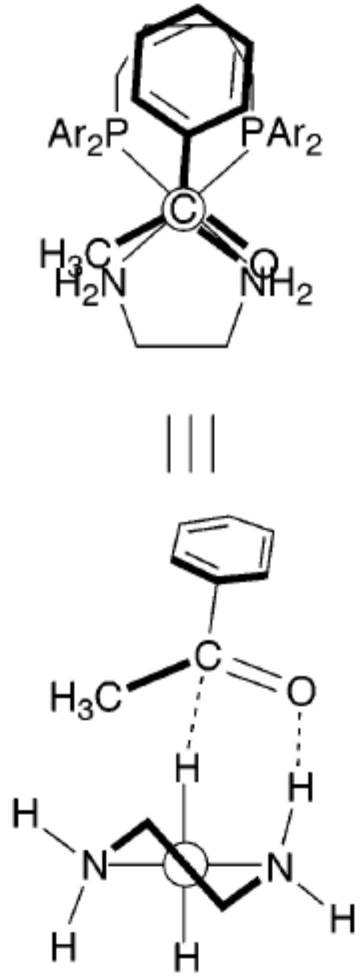
HYDROGENATION CATALYSTS



(*S*,*SS*)-**11**



17$_{Si}$ (favored)

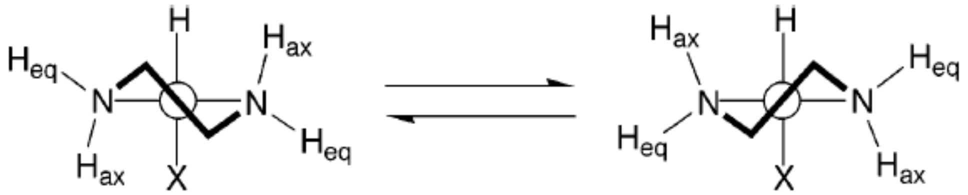


17$_{Re}$ (unfavored)

axially oriented hydrogens, H_{ax}, are more reactive

JACS, 2003, 13499.

HYDROGENATION CATALYSTS



δ,δ-**18**$_{\mathbf{H}}$: X = H
δ,δ-**18**$_{\mathbf{OR}}$: X = OR

δ,λ-**18**$_{\mathbf{H}}$: X = H
δ,λ-**18**$_{\mathbf{OR}}$: X = OR

Figure 11. Conformationally flexible diastereomeric reducing species formed from *trans*-RuH(η^1-BH$_4$)[(*S*)-tolbinap]($H_2NCH_2CH_2NH_2$). Ar = 4-$CH_3C_6H_4$.

The reaction in 2-propanol under the standard conditions (S/C) 2000, [ketone]) 0.83 M, [catalyst]) 0.41 mM, [KO-t-C_4H_9]) 18 mM, P_{H2}) 4 atm, T) 30 °C) gave (R)-1-(4-bromophenyl)ethanol in 53% ee (cf. R enantiomer in 83% ee with (S,SS)-**4**).

The observed moderate enantioselection is largely due to the conformational flexibility of the simple, unsubstituted ethylenediamine ligand. Thus two diastereomeric species δ,δ-18H and δ,λ18H are possible for the RuH_2 complex

JACS, 2003, 13499.

HYDROGENATION CATALYSTS

Most existing homogeneous and heterogeneous catalyses using molecular hydrogen saturate carbon-carbon multiple bonds preferentially over a carbonyl moiety. Thus $RuCl_2[P(C_6H_5)_3]_3$ normally shows feeble catalytic activity in the hydrogenation of simple ketones such as acetophenone.

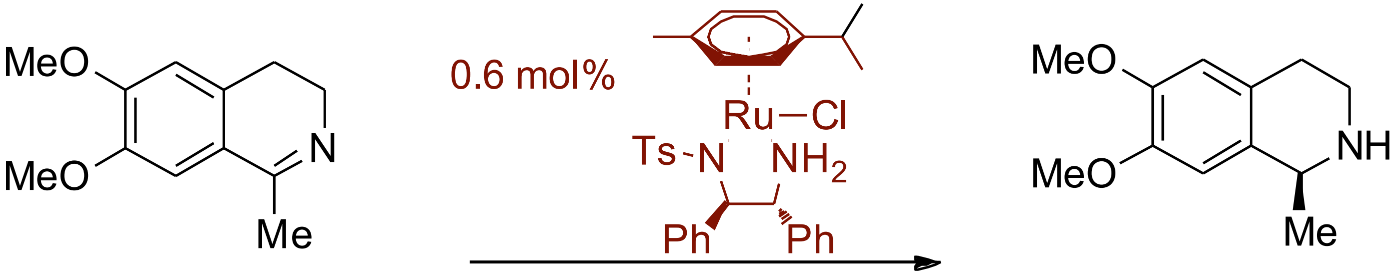
A simple enone is transformed by enantioselective hydrogenation into a chiral allylic alcohol using a novel Noyori catalyst.

Apart from asymmetric catalysis, this carbonyl-selective hydrogenation provides a real advance in organic synthesis. A wide range of ketones and aldehydes possessing carboncarbon multiple bonds are hydrogenated preferentially at the carbonyl group, leading to unsaturated alcohols. Both conjugated and unconjugated enones and enals may be used.

This transition metal catalysis is clean, simple and economical to operate and hence is capable of conducting a reaction on any scale from<100 mg to>100 kg with a very high (up to 50%) substrate concentration in organic solvents. In addition to industrial production of compounds such as *(R)-1,2-*
propanediol (10 tons/year) and a chiral azetidinone for carbapenem synthesis (120 tons/year), this hydrogenation method is utilized in academic and industrial research laboratories to develop pharmaceuticals, agrochemicals, flavours and fragrances.

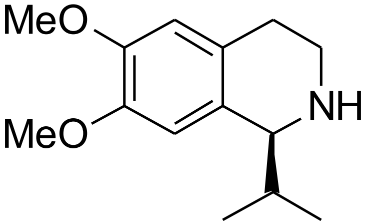
HYDROGENATION CATALYSTS

The Noyori catalyst

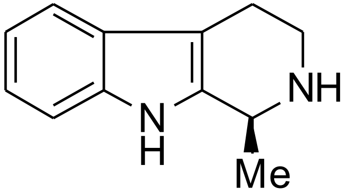


HCOONa, cetyltrimethylammonium bromide (CTAB),
H_2O
rt or 40 °C

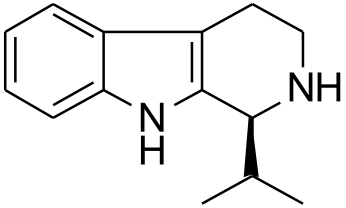
90%, 99% ee



87%, >99% ee (40 °C)



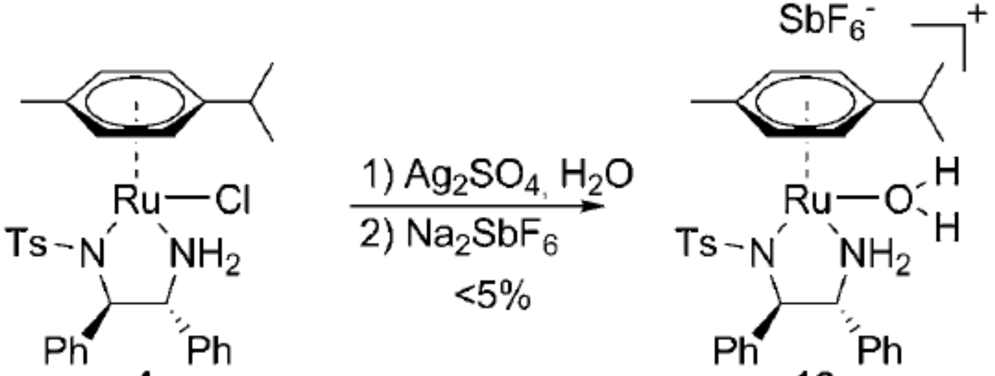
90%, >99% ee (rt)



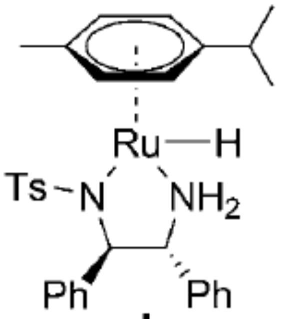
92%, >99% ee (40 °C)

Evanno, L.; Ormala, J.; Pihko, P. M. *Chem. Eur. J.* **2009**, *15,* 12963.

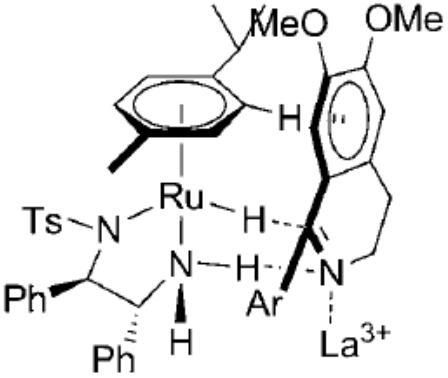
HYDROGENATION CATALYSTS



4 **16**



I
active catalytic species

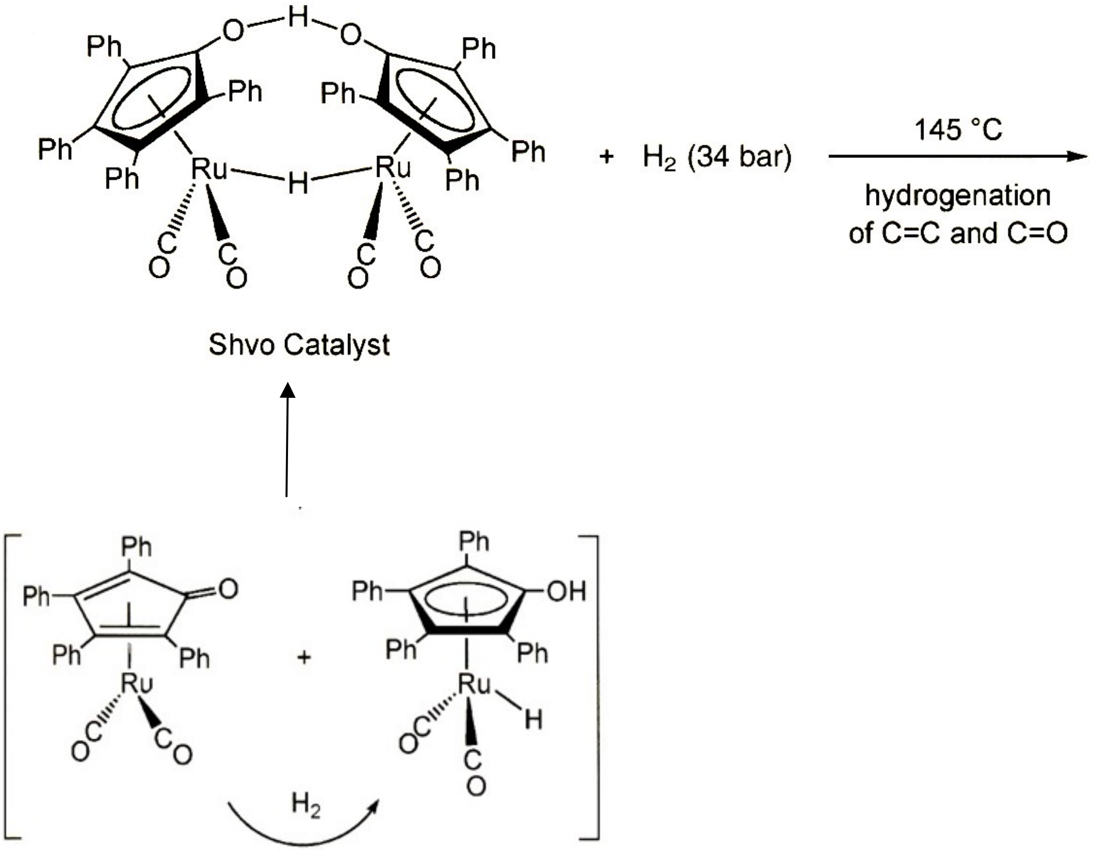


II

Evanno, L.; Ormala, J.; Pihko, P. M. *Chem. Eur. J.* **2009***, 15,* 12963.

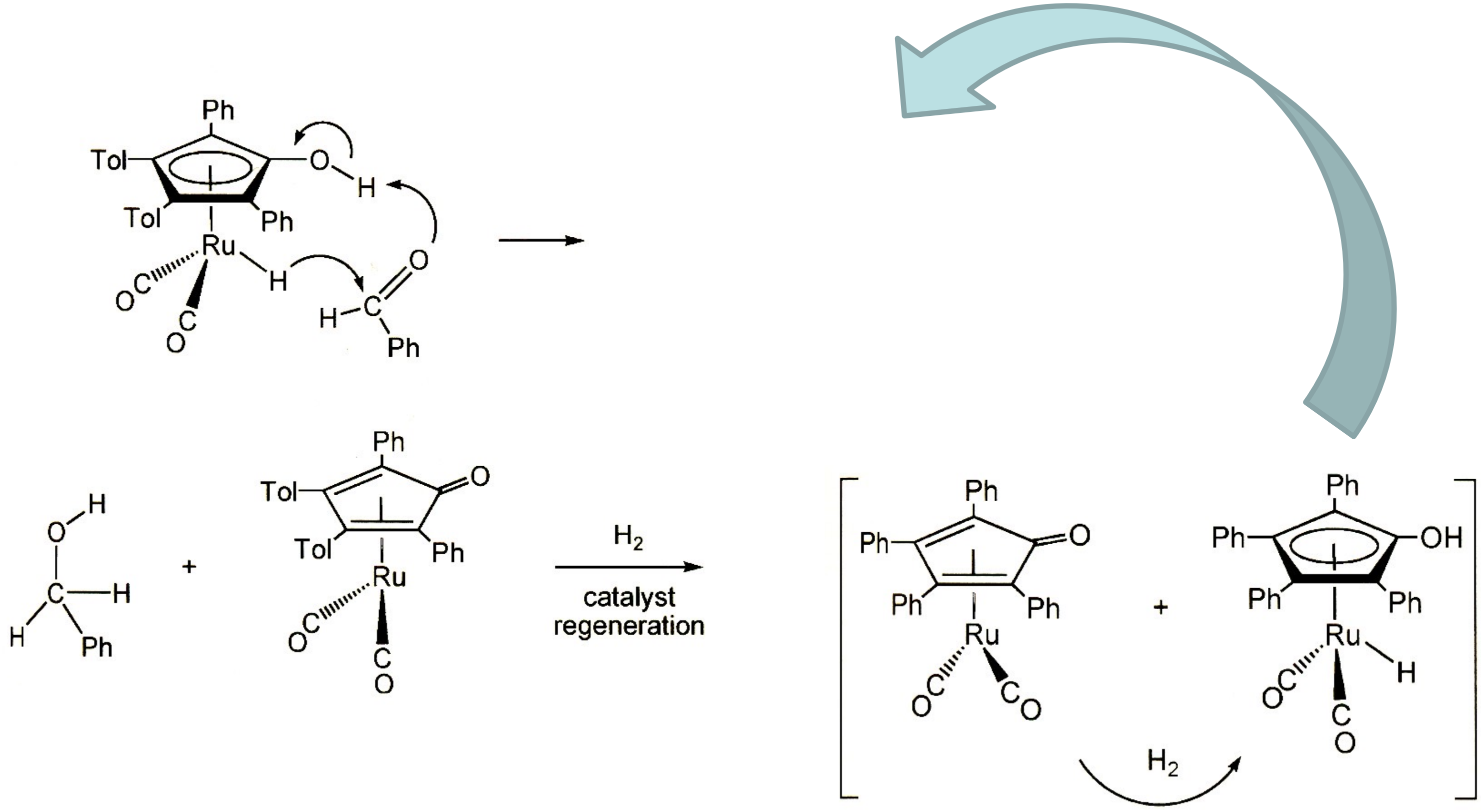
HYDROGENATION CATALYSTS

The Shvo catalyst

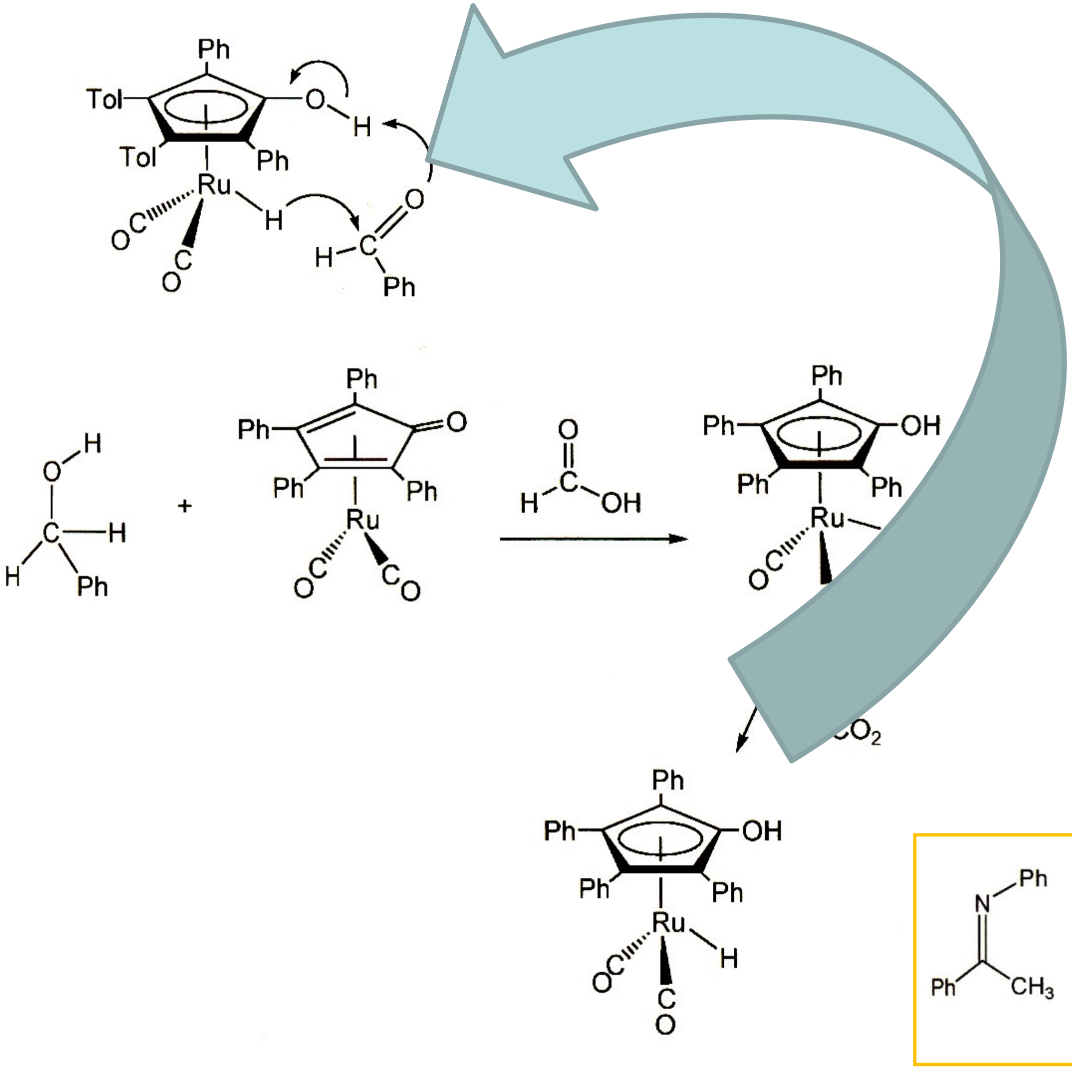


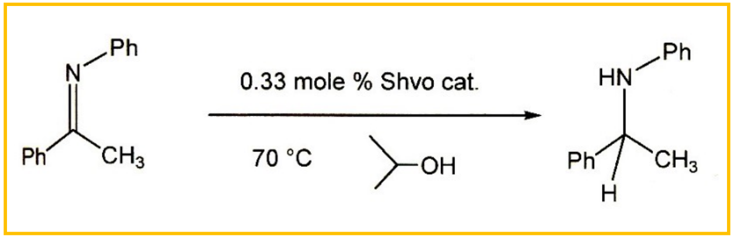
Shvo Catalyst

HYDROGENATION CATALYSTS

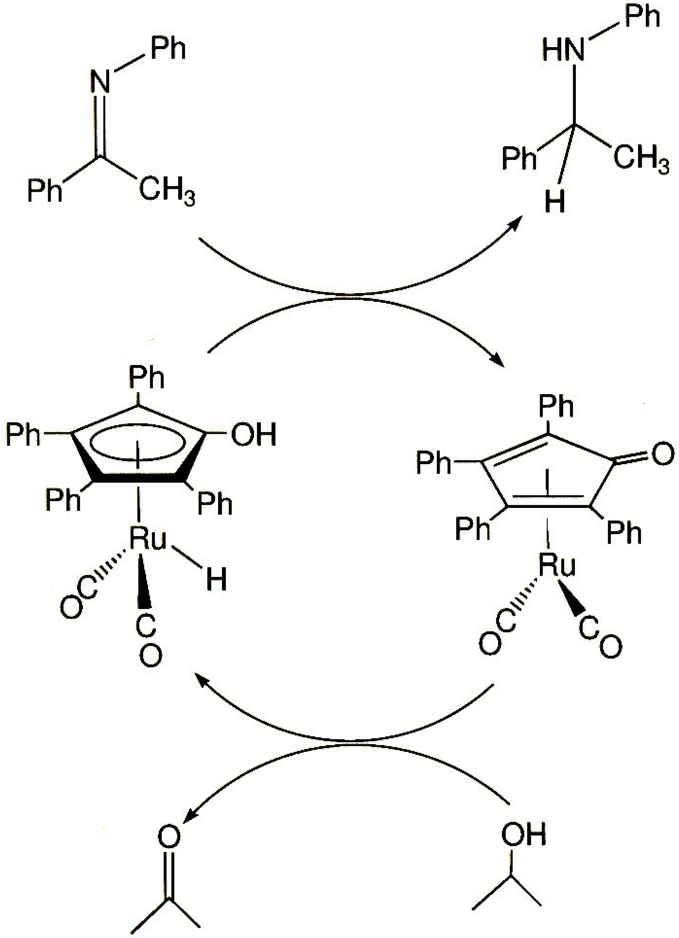


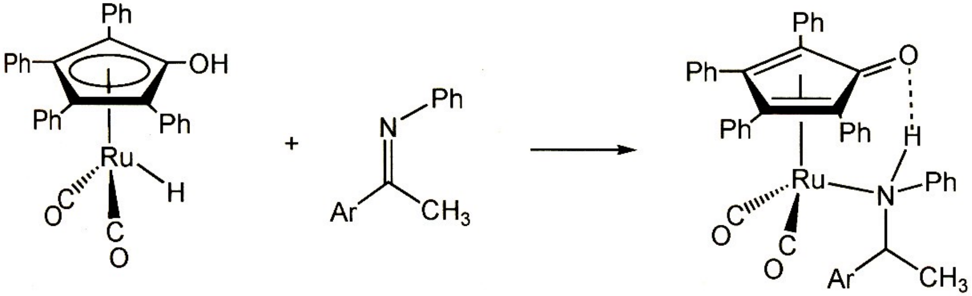
HYDROGENATION CATALYSTS





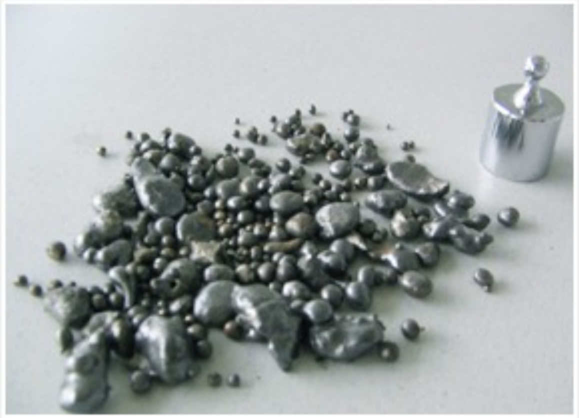
HYDROGENATION CATALYSTS

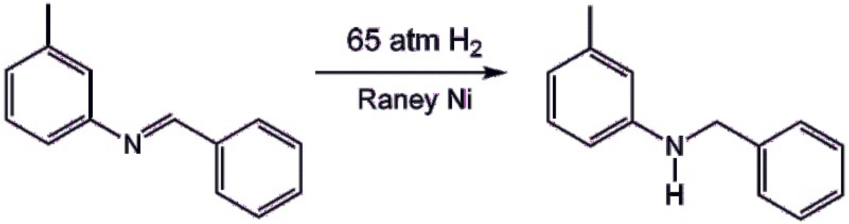




HYDROGENATION CATALYSTS
industrial applications

Raney nickel is a solid catalyst composed of fine grains of a nickel-aluminium alloy, used in many industrial processes. It was developed in 1926 by American engineer Murray Raney as an alternative catalyst for the hydrogenation of vegetable oils in industrial processes. More recently it is used as a heterogeneous catalyst in a variety of organic syntheses, most commonly for hydrogenation reactions.



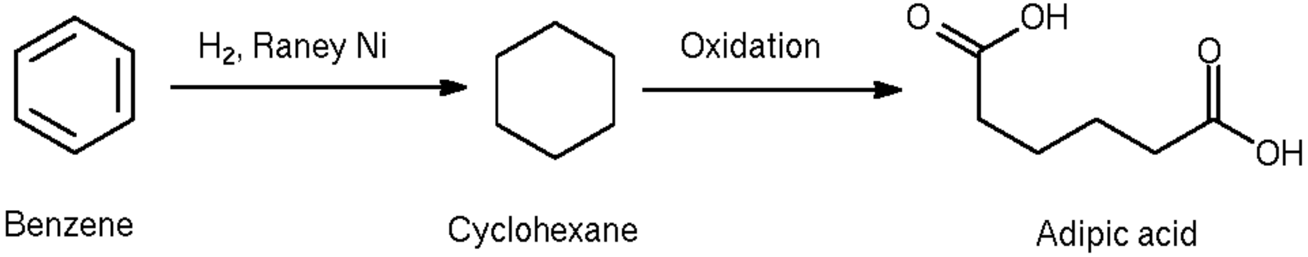


Alloys are prepared commercially by melting the active metal (nickel in this case, but iron and copper "Raney-type" catalysts can be prepared as well) and aluminium in a crucible and quenching the resultant melt, which is then crushed into a fine powder.

HYDROGENATION CATALYSTS
industrial applications

A practical example of the use of Raney nickel in industry is shown in the following reaction, where benzene is reduced to cyclohexane.

Other heterogeneous catalysts, such as those using platinum group elements, may be used instead to similar effect, but these tend to be more expensive to produce than Raney nickel. The cyclohexane thus produced may be used in the synthesis of adipic acid, a raw material used in the industrial production of polyamides such as nylon.



HYDROGENATION CATALYSTS
industrial applications

Millions of tons of benzene are hydrogenated to cyclohexane, which is further converted by oxidation to *adipic acid*, a major intermediate in production of nylon.

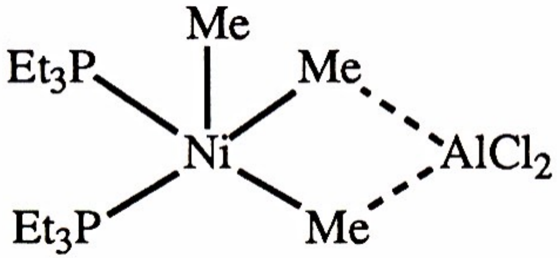
Previously heterogeneous Raney-nickel and palladium-on-carbon catalysts.

Homogeneous Ziegler-type catalysts are recently developed.

They are based on nickel and cobalt salts and trietylaluminum and hydrogenate benzene under relative mild conditions (155 ºC, 10 bar). (Compare to lab-scale Adam's catalyst PtO_2 x H_2O (25 ºC, 3 bar).

Mechanical and thermal advantage of the soluble catalysts outweight the problems in catalyst separation and recycling.

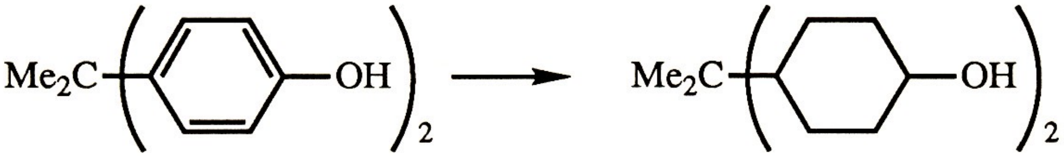
$(Et_3P)_2NiCl_2 + Al_2Me_3Cl_3$ =>



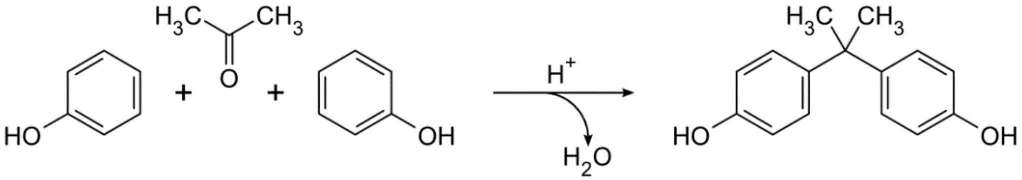
The nature of Ziegler catalyst is poorly defined!

HYDROGENATION CATALYSTS
industrial applications

The catalyst, although based on higly Lewis acidic Al-alkyls is tolerant against hydroxyl groups and can be applied also for reduction of bisphenol A.



Bisphenol A is applied as plasticiser in polymers.

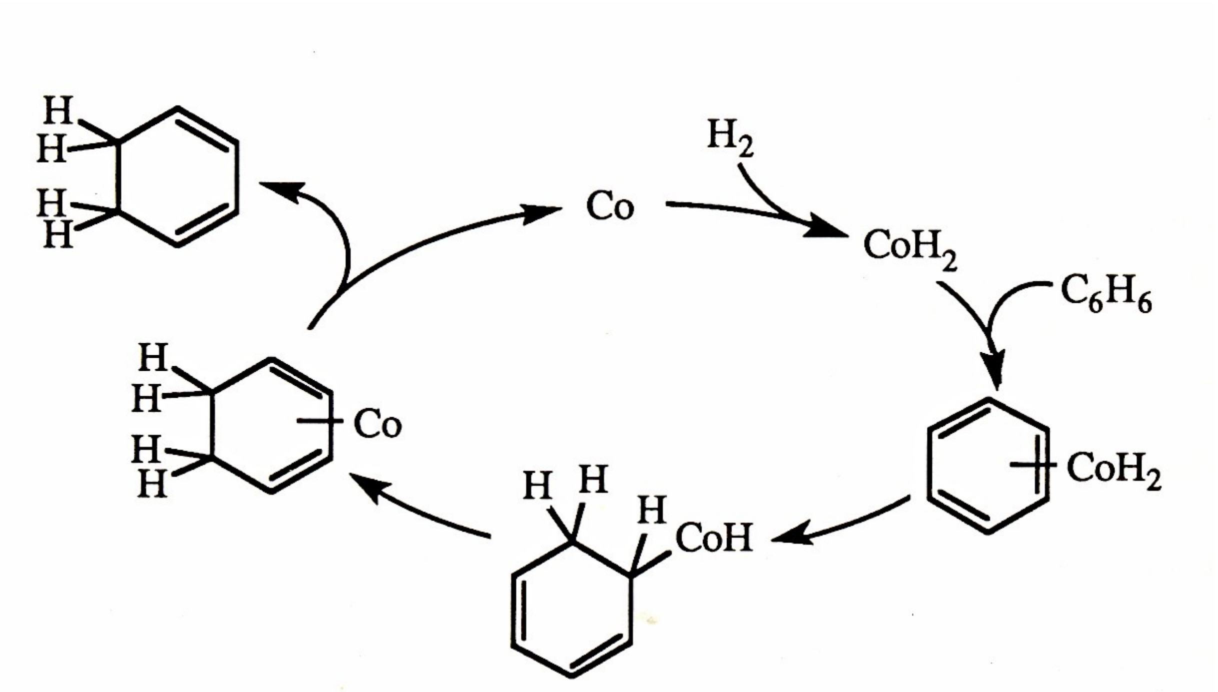


Catalysts based on Co(II) acetylacetonate in the presence of tributylphosphine are efficient for hydrogenation of olefins and arenes. Benzene is hydrogenated to cyclohexane at mild conditions (30 ºC, 1.5 bar).

Olefins are hydrogenated much faster than arenes. For example, styrene is selectively converted to ethylbenzene.

HYDROGENATION CATALYSTS
industrial applications

A proposed mechanism for hydrogenation of arenes. It includes oxidative addition of H_2 and coordination of arene followed by insertion of double bond to Co-H. Reductive elimination gives Co-species and partially hydrogenated arene.



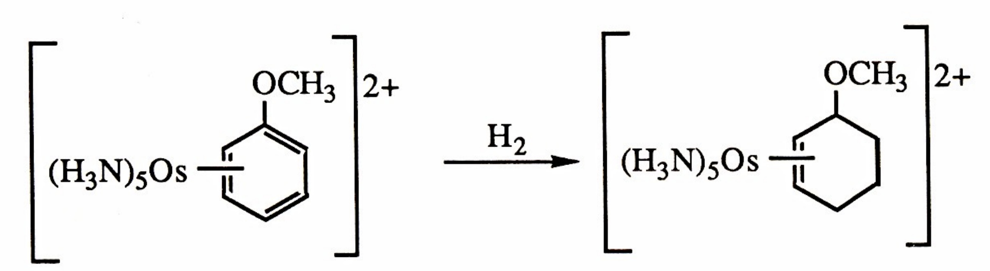
The substrate remains coordinated untill all double bonds are consumed. The overall mechanism is very similar as the one for Wilkinson’s catalyst.

HYDROGENATION CATALYSTS

industrial applications

Partial oxidation of benzene is higly valuable, as oxidation of cyclohexene to adipic acid is more clean process than oxidation of cyclohexane.

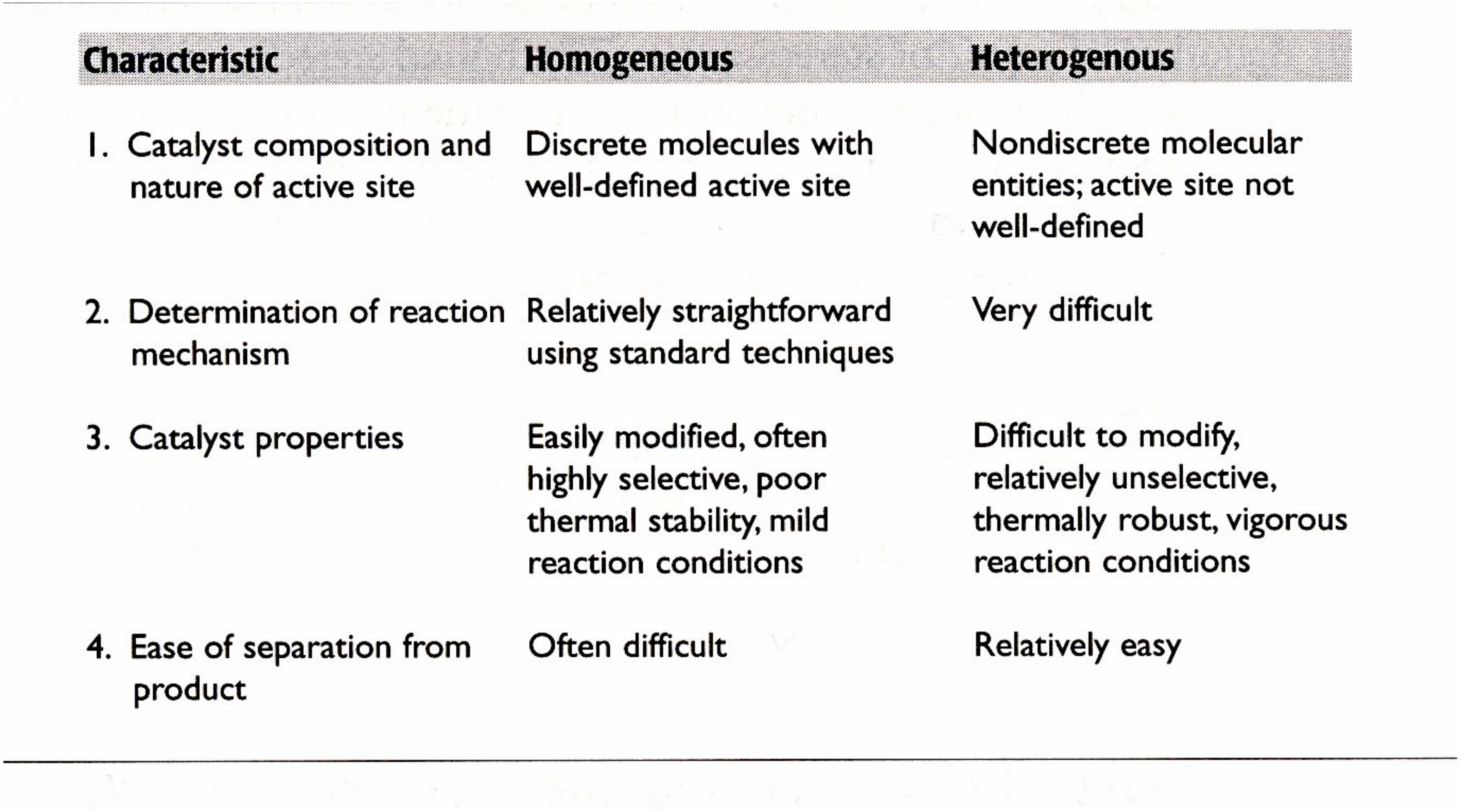
Most of the research is centered around heterogeneous Ru-catalysts, because with these catalysts tend to produce cyclohexene (50 %).



Homogeneous model with Os-bound arenes show, that the double bond coordinated with the Os is not reduced.

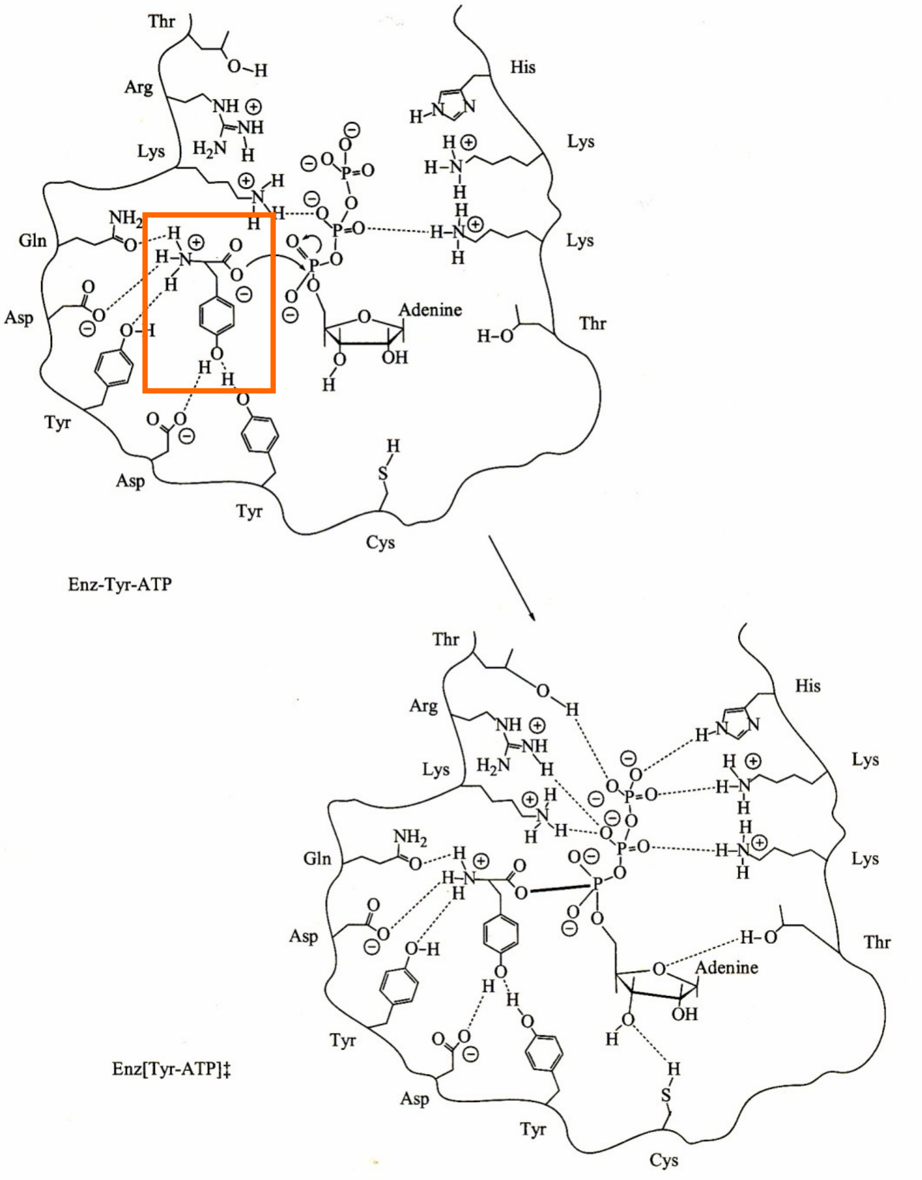
It has been though that benzene coordinates selectively to certain sites on Ru-surface and is protected. The uncoordinated double bonds are then reduced by other Ru-sites.

HOMOGENEOUS VS HETEROGENEOUS CATALYSTS



Characteristic	Homogeneous	Heterogenous
1. Catalyst composition and nature of active site	Discrete molecules with well-defined active site	Nondiscrete molecular entities; active site not well-defined
2. Determination of reaction mechanism	Relatively straightforward using standard techniques	Very difficult
3. Catalyst properties	Easily modified, often highly selective, poor thermal stability, mild reaction conditions	Difficult to modify, relatively unselective, thermally robust, vigorous reaction conditions
4. Ease of separation from product	Often difficult	Relatively easy

HOMOGENEOUS VS HETEROGENEOUS CATALYSTS


Enz-Tyr-ATP

Enz[Tyr-ATP]‡

HYDROSILYLATION