Hydrogenation Catalysis

Hydrogenation is the addition of H₂ to a multiple bond (C=C, C≡C, C=O, C≡N, N=O, N=N, N≡N, etc) to reduce it to a lower bond order. The most common and simple type of hydrogenation is the reduction of a C=C double bond to a saturated alkane:

\[
\text{R} + \text{H}_2 \rightarrow \text{R}
\]

There are three different ways that transition metal catalysts can activate H₂ for performing hydrogenation catalysis:

\[
\text{L}_n\text{M} + \text{H}_2 \rightleftharpoons \text{L}_n\text{M} + \text{H} \quad \text{oxidative addition}
\]

\[
\text{L}_n\text{M-X} + \text{H}_2 \rightleftharpoons \text{L}_n\text{M-H} + \text{HX} \quad \text{hydrogenolysis}
\]

\[
\text{L}_n\text{M} + \text{H}_2 + \text{B} \rightleftharpoons [\text{L}_n\text{M-H}]^- + \text{H}^+:\text{B} \quad \text{heterolytic cleavage}
\]

**Oxidative addition**: the most common method of activating H₂ on a metal with d electrons (d² or higher). Metal center typically needs to have an empty coordination site in order to bind the H₂ first, prior to the oxidative addition.

**Hydrogenolysis**: the only way that early transition metals with d⁰ counts can activate H₂. Lanthanides and actinides also typically use hydrogenolysis. As with oxidative addition, the metal center needs to have an empty orbital to bind the H₂ and an anionic ligand (e.g., alkyl, halide) that can be protonated off. No change in oxidation state of the metal.

**Heterolytic cleavage**: in many ways quite similar to hydrogenolysis except that the proton produced does not directly react with an anionic ligand coordinated to the metal, but rather with an external base that typically has to transfer it back to the metal center to complete the catalytic cycle. Ru(+2) is the most common metal that uses heterolytic cleavage as a mechanism. No change in oxidation state of the metal.
**Wilkinson’s Catalyst:** RhCl(PPh₃)₃ was the first highly active homogeneous hydrogenation catalyst and was discovered by Geoffrey Wilkinson (Nobel prize winner for Ferrocene) in 1964. R. Coffey discovered it at about the same time while working for ICI (Imperial Chemical Industries). It was very simply prepared by reacting RhCl₃•3H₂O with excess PPh₃ in EtOH:

\[
\text{RhCl}_3 \cdot \text{H}_2\text{O} + \text{xs PPh}_3 \rightarrow \text{RhCl(PPh}_3\text{)}_3 + \text{Ph}_3\text{P}=\text{O} + \text{oxidized solvent}
\]

The proposed mechanism is as follows:

It has been clearly shown that PPh₃ is readily lost due to steric crowding and that the inner catalyst cycle with a weakly coordinated solvent molecule (not shown) is about 1000 times faster than the outer cycle that has 3 PPh₃ ligands coordinated to the metal.
This hydrogenation catalyst is compatible with a variety of functional groups (ketones, esters, carboxylic acids, nitriles, nitro groups, and ethers) and indicates that the metal hydride intermediate is primarily covalent in character.

Coordinatively unsaturated cationic catalysts that were considerably more active for hydrogenation were later discovered. The reason for this is that the cationic metal center is more electrophillic and this favors alkene coordination, which is often the rate determining reaction step.

The ability to coordinate to the catalyst directly influences the rate of hydrogenation. Thus, unsaturated substrates containing polar functionality which can assist in binding to the catalyst have faster hydrogenation rates. Terminal alkynes are hydrogenated as well and at a faster rate than terminal alkenes (better binding and insertion). The following is the general trend in hydrogenation rates:

\[
\begin{align*}
\text{CN} & > \text{OH} > \text{OH} > \text{OEt} > \equiv \equiv R > \equiv \equiv R > \equiv \equiv R > \equiv \equiv R > \equiv \equiv R > \equiv \equiv R \\
\end{align*}
\]
Selectivity:

Hydrogenation catalysts typically will selectively hydrogenate the most reactive multiple bonds first. Steric and electronic effects play an important role in this. Consider the following examples:

Typically NOT hydrogenated under mild conditions:

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

Crabtree has demonstrated some very interesting substrate directing effects in hydrogenation:

\[
\begin{align*}
\text{HO} & \quad \text{H}_2 \\
\text{i-Pr} & \quad \text{HO} \\
\text{HO} & \quad \text{i-Pr} \\
\text{HO} & \quad \text{i-Pr}
\end{align*}
\]

\[
\begin{align*}
Pd/C & \quad 20\% \\
\text{[Ir(cod)(PCy}_3\text{)(py)]}^+ & \quad 99.9\% \\
& \quad < 0.1\%
\end{align*}
\]

The weak ligand bonding of the OH group on the substrate directs one specific side of the alkene to coordinate to the metal center in order to form an alkene-OH chelate to the Ir.

Group binding affinities: amide > OH > OR > ester ~ ketone

Amine groups bind too strongly and inhibit catalysis. Rigid structures with stronger chelates, like the norbornene ligand shown to the right, are also poor substrates.

For a comprehensive review of cyclic and acyclic substrate-directed hydrogenations see: Hoveyda, Evans, and Fu, Chem. Rev. 1993, 93, 1307.
Asymmetric Hydrogenation

95% of all hydrogenations use heterogeneous catalysts like Pd on carbon (Pd/C) or Raney Nickel. One area where homogeneous catalysis rules is asymmetric hydrogenation. This involves the use of a chiral catalyst and an alkene substrate that generates a chiral carbon center on hydrogenation.

The first dramatic example of this was reported in 1968 by Bill Knowles and coworkers at Monsanto. Knowles found that a bidentate, C$_2$ symmetric version of the cationic Schrock-Osborn catalyst afforded extraordinarily high levels of enantioselectivity in the hydrogenation of $\alpha$-acetamidocinnamatic acid which is used to produce L-Dopa, an important pharmaceutical for the treatment of Parkinson’s disease (Knowles, *JACS* 1975, 97, 2567). Knowles went on to win the Nobel Prize in 2001, sharing it with B. Sharpless and R. Noyori, for this discovery.
As you can see, the mechanism of this hydrogenation differs from that observed with neutral catalyst ligated with monodentate ligands. That is, olefin complexation occurs prior to H₂ oxidative addition and this oxidative addition is the rate-limiting step. What is even more amazing is that the major olefin complex diastereomer, which was isolated and characterized by NMR and X-ray techniques, gives the WRONG product. In elegant mechanistic studies, Halpern showed that the minor diastereomer (olefin complex) REACTS 580x FASTER to give the final hydrogenated chiral product in a 60:1 ratio!

**Problem:** Draw a reaction coordinate diagram that clearly shows the difference in reactivity between the two diastereotopic olefin complexes.
Ru Heterolytic H₂ Activation

Ru has a strong tendency to perform a **heterolytic activation of H₂** instead of oxidative addition to make a metal dihydride. This can occur either via hydrogenolysis or heterolytic cleavage mechanisms. Complexation of the dihydrogen to the metal leads to a *decrease* in H-H σ-bond character. This decrease in bonding leaves it with a partial positive charge hence making it more *acidic*, or easier to deprotonate with a ‘base’ (either internal or external). Both hydrogenolysis (σ bond metathesis) and heterolytic cleavage mechanism give the same net result:

Shown below is a proposed catalytic cycle for Ru(+2) catalyzed hydrogenation:

Note that there is no change in oxidation state of the Ru(+2)!
Tobin Marks reported the extraordinary activity of \((\text{Cp}^*\text{LuH})_2\) 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\(_2\), 25°C!! This is one of the most active hydrogenation catalysts known.

The proposed mechanism is shown below:
Hydrogenation 10

Other H-X additions: Hydrosilylation and Hydrocyanation

Hydrosilylation (addition of H-SiR₃)

These H-X additions are very similar to hydrogenation (addition of H-X where X=H). Platinum and Palladium catalysts are most widely used for the hydrosilylation of alkenes.

\[
\text{R} + \text{H-SiR}_3 \xrightarrow{\text{Pd(PPh}_3)_4} \text{R}_3\text{SiH} + \text{R}
\]

Hydrosilylation of alkynes has been achieved with rhodium and ruthenium catalysts.

Parish JOMC 1978, 161, 91

\[
\text{H-SiEt}_3 + \text{R} \xrightarrow{0.001 \text{ mol} \% \text{ Rh Ph}_3\text{PPh}_3} \text{R}_3\text{SiEt}_3 + \text{SiEt}_3
\]

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 HSiR₃ to the isolated trans product leads to isomerization)
**Hydrocyanation (addition of H-CN)**

Hydrocyanation is used industrially to prepare adiponitrile from butadiene. Adiponitrile is the key intermediate in synthesizing Nylon-6,6.

\[
\text{Butadiene} + \text{HCN} \xrightarrow{\text{Ni}[P(\text{O-o-tol})_3]_3 \text{ cat.}} \text{Adiponitrile}
\]

\[
\text{Lewis Acid (e.g. AlCl}_3, \text{ ZnCl}_2\right) \Rightarrow \eta^3-\text{organo nickel intermediate identified by NMR}
\]

**Problem:** Draw a detailed reaction mechanism that shows the conversion of butadiene to adiponitrile.