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1. Learning Outcomes

After studying this module, you shall be able to

- Know what is meant by hydrogenation
- Learn about the types of hydrogenations and hydrogenation catalysts
- Identify the conditions used for hydrogenation, mechanism and stereochemical aspects
- Evaluate the type of catalysts to be used for a selective hydrogenation
- Be familiar about asymmetric hydrogenations
- Analyze the hydrogenation conditions for alkenes, alkynes and aromatic rings

2. Introduction

As is evident from the term “Hydrogenation”, i.e., addition of hydrogen, it involves the treatment of a chemical compound with hydrogen whereby the hydrogen molecule adds to the substrate. It is the most commonly reaction used for the reduction of unsaturated compounds such as alkynes and alkenes to form saturated compound i.e., alkanes. In addition, aromatic rings and carbon-heteroatom multiple bonds (imines, nitriles, carbonyls etc.) are also reduced by hydrogenation.

In order to carry out a hydrogenation reaction, gaseous hydrogen (H_2) is used in the presence of a catalyst. Without a catalyst, hydrogenation requires very high temperatures since the energy barrier to the reaction is huge as the H—H bond is very strong (bond enthalpy of 436 kJ mol^{-1}). The catalyst decreases the energy of activation by breaking the H—H bond. Hence, **catalytic hydrogenation** is an important method to reduce organic compounds via hydrogenation.

Usually, transition metals such as Platinum or Palladium are used in a finely divided state adsorbed on charcoal (Pt/C or Pd/C) and hydrogenation is done simply by stirring or shaking the substrate with the catalyst in a suitable solvent, in an atmosphere of hydrogen gas. For example, 2-butene gets reduced to butane by reaction with hydrogen in the presence of Platinum-charcoal. Hydrogenation is done in an apparatus which is arranged so that the uptake of H_2 can be measured.(FIG-1)

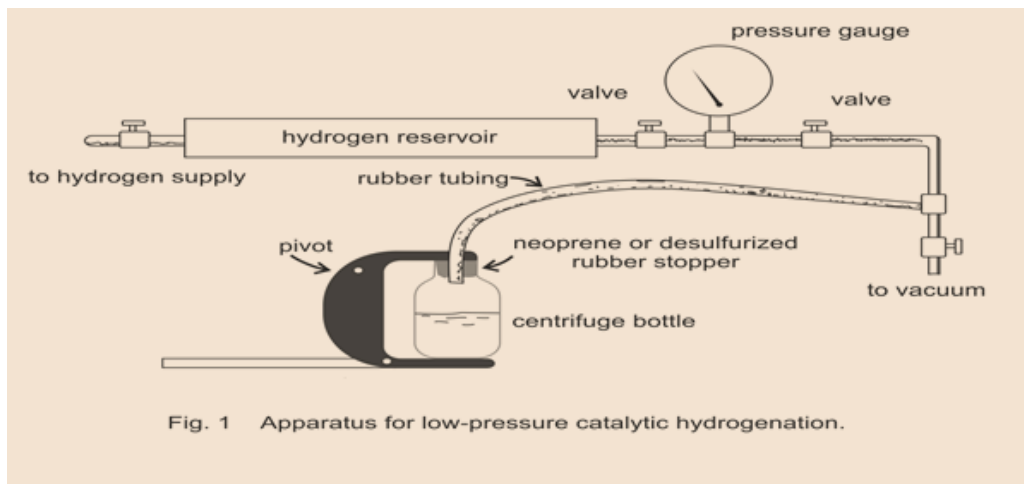


Fig. 1 Apparatus for low-pressure catalytic hydrogenation.

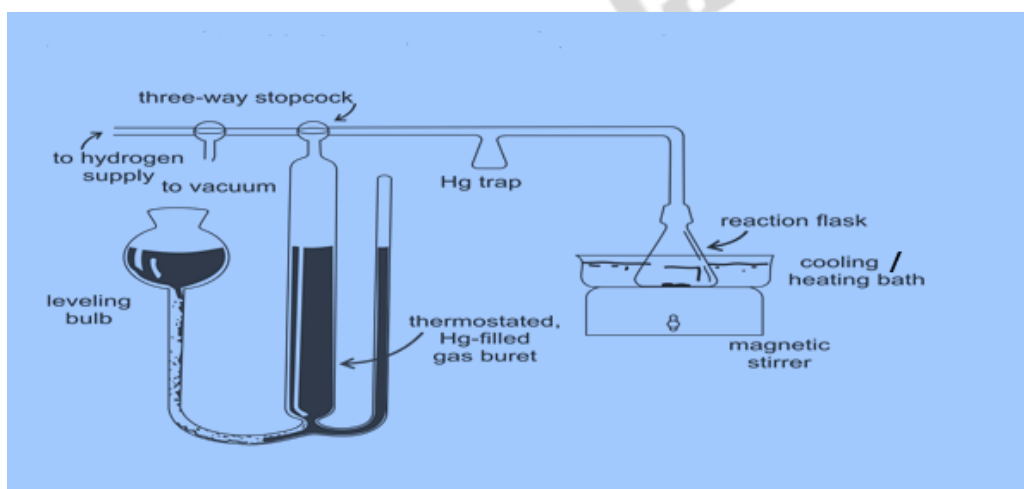
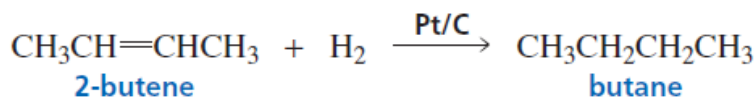


Fig. 2 Alternative set up for catalytic hydrogenation and dehydrogenation



The method is spoken as **heterogeneous hydrogenation**. (There are three phases namely a gas (H_2), a solid (insoluble catalyst) and a solution (substrate in a solvent)). Filtration is done to remove a heterogeneous catalyst. It can also be recycled, which is important from an economic and greener perspective.

Hydrogenation is an important reaction industrially and the most suitable example of its large scale industrial use is the manufacture of solid/semi-solid hydrogenated fat (margarine) from the vegetable oils (Figure 3).

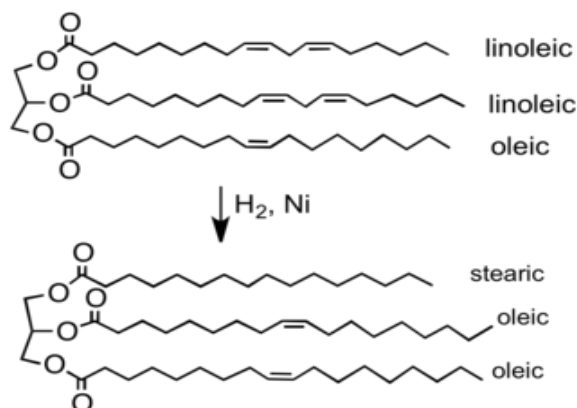
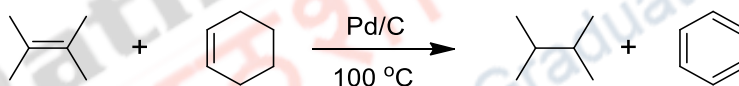
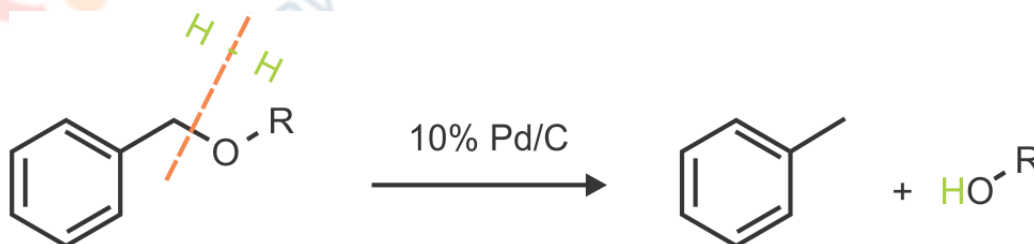


Fig. 3: Partial hydrogenation of typical plant oil to a typical component of margarine. Most of the C=C double bonds are converted to single bonds and increases product melting point.

In most of the cases hydrogen gas is used for hydrogenations, but sometimes other sources of hydrogen can also be used; these are termed **transfer hydrogenations**. For example, cyclohexene in the presence of Pd/C provides hydrogen to the substrate for its reduction and itself gets converted to benzene via cyclohex-1,3-diene as shown below.



Hydrogenolysis involves “lysis” of carbon–carbon or carbon–heteroatom single bond i.e. bond gets cleaved by hydrogen. Hydrogenolysis is most commonly used in protection/de-protection strategies in organic syntheses such as for de-benzylation. Also, hydrogenolysis can be a major side-reaction in multi-functional compounds.



3. Catalytic Hydrogenation

3.1 Catalysts for Hydrogenation

Catalytic hydrogenation can be done by number of catalyst. They lie under the two broad families of catalysts- **heterogeneous catalysts** and **homogeneous catalysts**. Heterogeneous catalysts remain suspended in the reaction mixture (or used in reactions where the substrate is gaseous). On the other hand, homogeneous catalysts become soluble in the solvent of the

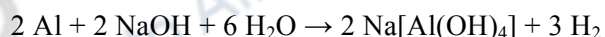
unsaturated substrate. The homogeneous catalyst is used for binding of unsaturated substrate and hydrogen. The catalysts development has not only enabled the implementation of hydrogenations at lower temperatures and pressure conditions. This has resulted in not only the reduced costs, but the advent of asymmetric hydrogenations has opened newer possibilities for the drug industry.

3.1.1 Heterogeneous Catalysts

Heterogeneous catalysts are mainly finely divided metals or their oxides or sulfides. Noble metal catalysts (platinum and/or palladium and rhodium, ruthenium and nickel) are commonly used. These catalysts are not specific and may be used for a variety of reductions.

The most extensively used are *palladium and platinum catalysts* either in the finely divided form or, more commonly, supported on a suitable support such as activated carbon, alumina or barium sulfate. In general, supported metal catalysts are active and unsupported metal are less active due to their larger surface area. However, their activity is influenced strongly by the support and by the method of preparation, which provides a means of preparing catalysts of varying activity. Platinum, which is pyrophoric and difficult to handle and optimize for a reaction, is not employed itself as a catalyst, but is often used in the form of its oxide PtO_2 (*Adams' catalyst*), which is reduced to metallic platinum by hydrogen. Palladium is used as a 5-10% w/w loading on activated charcoal and its hydroxide supported on activated carbon can also be used.

Nickel-based metal catalysts (such as *Raney nickel and Urushibara nickel*) can be an alternative but they are slow enough that they require higher temperatures and/or pressures conditions. Raney nickel is a porous, fine-grained solid obtained by treating a powdered nickel-aluminium alloy with sodium hydroxide and contains 25–100 mL adsorbed H_2 per g of nickel, when freshly prepared.



Raney nickel is alkaline and may be used only for hydrogenations that are not adversely affected by basic conditions. Due to its alkaline nature, Raney nickel gets deactivated by acids. However, it is highly active and can reduce any unsaturated substrate by optimal changes in temperature and pressure, and is usually used when all other methods have failed.

3.1.2 Homogeneous Catalysts

Homogeneous catalysts provide better results as compared to heterogeneous catalysts in the form of improved, more predictable selectivity, milder conditions and lower catalyst loadings. Further, the stereochemistry of reduction becomes easier to predict, since it depends not on chemisorption but on reactions between molecules. These soluble catalysts, which allow hydrogenation in homogeneous solution, are thus, increasingly used for asymmetric hydrogenations as their spatial configurations can direct the addition of hydrogen molecule to one or more favored 3-dimensional arrangements.

There are a large number of homogeneous catalysts. The most common are based on rhodium and ruthenium complexes. For example, $[(\text{Ph}_3\text{P})_3\text{RhCl}]$ (tris(triphenylphosphine)chloro rhodium, **Wilkinson's catalyst**) and $[(\text{Ph}_3\text{P})_3\text{RuClH}]$. Another example of homogeneous catalyst is a complex of Iridium with 1,5-cyclooctadiene, tris-cyclohexylphosphine, and pyridine, developed by Robert H. Crabtree (**Crabtree's catalyst**). (Figure 4)

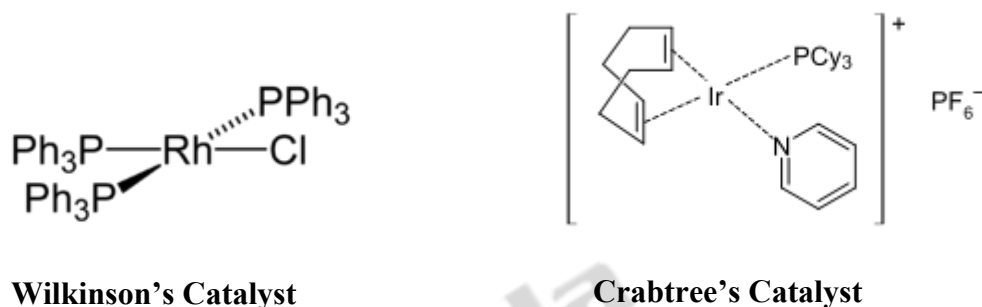


Fig. 4: Structures of Wilkinson and Crabtree's catalyst

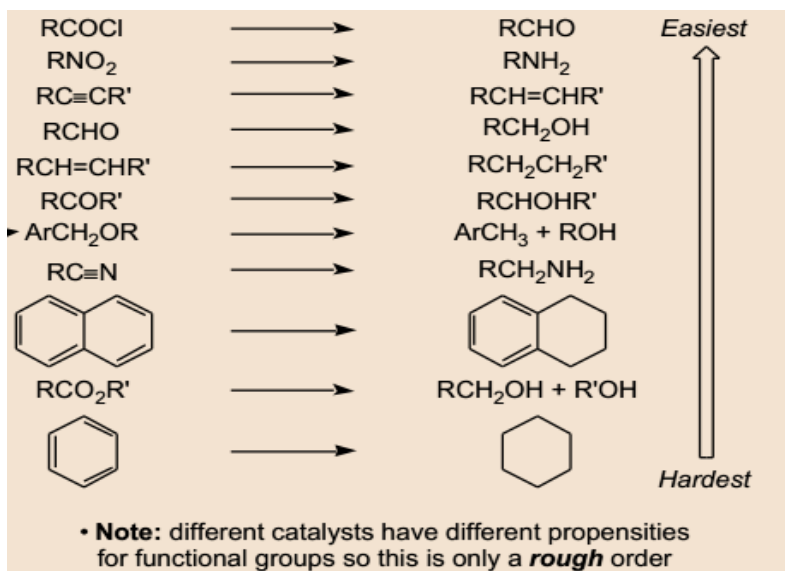
3.2 Selectivity of Hydrogenation

The selectivity of a hydrogenation catalyst becomes important in the light of the numerous hydrogenation catalysts available with a chemist. A question arises that what type of catalyst must be used for a particular type of hydrogenation reaction? The answer is not simple and for heterogeneous catalysts, highly empirical observations and modifications form the basis of their selectivity for hydrogenation. In general, one must remember the governing principle ***that more active the catalyst, the less discriminating it is in its action.*** Other parameters to be kept in mind are:

- The rate of a given hydrogenation reaction may be increased by raising the temperature, by increasing the pressure or by increasing the amount of catalyst used.
- For greatest selectivity, reactions should be run with the least active catalyst and under the mildest possible conditions consistent with a reasonable rate of reaction.
- Sometimes, the *role of solvent* is important and can decide the course of hydrogenation.
- It is important to select an *appropriate catalyst* and reaction conditions for selective hydrogenation. Sometimes the catalyst itself may be more active towards certain classes of compound than others. For example, Pt, Rh, and Ru will selectively hydrogenate aromatic rings in the presence of benzylic C–O bonds, while with Pd catalysts the benzylic C–O bonds are hydrogenolysed faster.
- The *functional groups* present on the substrate are also important. Not all functional groups are reduced with equal ease. In general, the reactivity of functional groups towards catalytic hydrogenation decrease in the order as listed in Table 1. In general, groups at the top of the list can be reduced selectively in the presence of those at the bottom. For example, reduction of an unsaturated ketone to a saturated ketone can be accomplished readily by hydrogenation over palladium, but the hydrogenation of unsaturated ketone to unsaturated alcohol is not possible. Similarly, benzonitrile can be

converted into benzylamine, but selective reduction to cyclohexanecarbonitrile is not possible.

Table 1: Order of reactivity of various functional groups towards catalytic hydrogenations

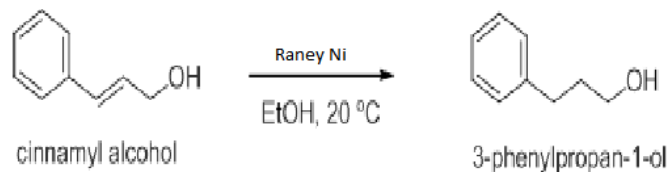


In heterogeneous hydrogenation catalysts, the **active sites** (the metal surface on the support which is exposed for the reaction) are important and selectivity (or reducing the activity of the catalyst) can also be achieved by blocking some of these by means of “**poisons**” which can include halides, metal cations, amines, sulfides and phosphines. Effect of poisoning agents is not the same for every catalyst and their use is based solely on observation. For example partial hydrogenation of alkynes give high yield alkenes with a palladium–calcium carbonate catalyst that has been partially deactivated by lead acetate or quinolone (**Lindlar’s catalyst**). Sometimes, the substrate itself can have a functional group which may act as catalyst poison and can lead to selectivity or may even make the substrate less active to catalytic hydrogenation.

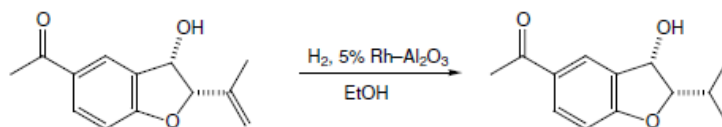
4. Hydrogenation of Alkenes

4.1 Aspects of Carbon-Carbon double bond Hydrogenations

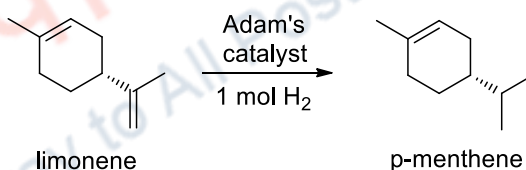
Hydrogenation of alkenes takes place easily and in most cases can be effected under mild conditions. However, as hydrogenation is sensitive to steric hindrance, highly hindered alkenes are resistant to hydrogenation, but even these can generally be hydrogenated under more vigorous conditions. Pd and Pt are the most frequently used catalysts. Both are very active and their use depends upon the type of substrate and degree of selectivity required. In general, Pt is more active than Pd-catalysts.



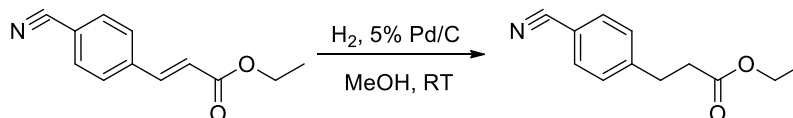
Other catalysts that can be used are Raney-Nickel (only in some cases as it is highly reactive) and Rhodium and Ruthenium catalysts. Rh and Ru catalysts sometimes show useful selectivity. For example, in the reaction shown below, rhodium allows hydrogenation of alkenes without affecting the hydrogenolysis of the ether (an oxygen functional group).



The degree of substitution of the double bond decreases the ease of reduction of an alkene, and this sometimes selectively reduce one double bond over other in a molecule with more than one double bond. *Out of the exocyclic and endocyclic double bonds, exocyclic double bonds are easier to be reduced.* For example, limonene can be converted into p-menthene by hydrogenation over Adam's catalyst if the reaction is stopped after absorption of one molar equivalent of hydrogen.



The reactivity order of various functional groups towards hydrogenation reflects that alkenes can be selectively hydrolyze in many cases excluding when aromatic nitro, alkynes or acyl halides are present in the same molecule with Pd being the catalyst of choice. For example, in the following reaction, C=C is reduced selectively without affecting the nitrile.



For different hydrogenation metal catalysts, an empirical generality has been observed in their selective hydrogenations of a functional group in preference to another which is depicted in figure 3. Similarly, when the substrate is alkene, more is the steric hindrance; less is the reactivity (Figure 4).

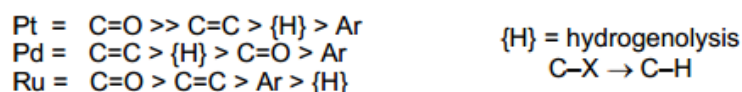


Fig. 3: Order of reactivity of functional groups for different metals as catalysts

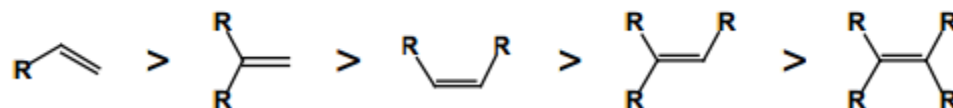
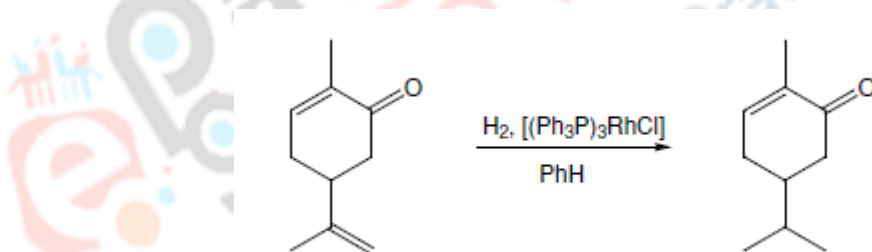
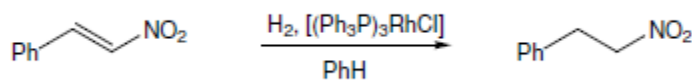


Fig 4: Order of reactivity of different alkenes

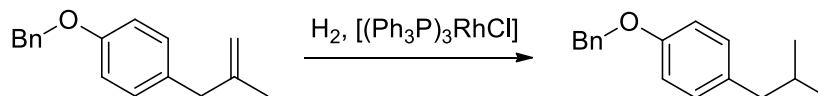
For homogeneous hydrogenation of non-conjugated alkenes, Wilkinson's catalyst is an extremely efficient catalyst (and also for alkynes) at ordinary temperature and pressures. Functional groups such as $-\text{C}=\text{O}$, $-\text{CN}$, $-\text{NO}_2$ and $-\text{Cl}$ are not reduced under these conditions. Tri- or tetra-substituted double bonds are reduced much more sluggishly than mono- and di-substituted ones, permitting the selective hydrogenation of compounds containing different kinds of double bonds. For example, in the reduction of carvone, the hydrogenation occurred at the non-conjugated double bond.



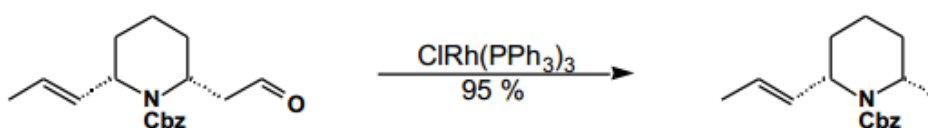
Another example is the selective reduction of β -nitrostyrene to 2-phenyl-nitroethane by reduction of double bond without affecting the nitro group.



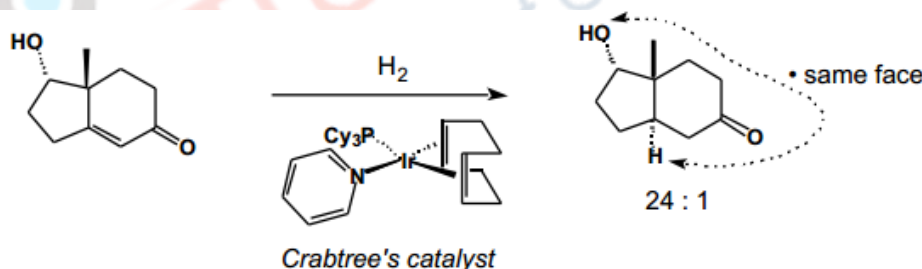
Another synthetically useful feature of the Wilkinson's catalyst is that it does not lead to hydrogenolysis of the susceptible functionalities in the molecule and hence can be employed in multi-step synthetic strategies for selective double bond hydrogenation without hydrogenolysis of protecting groups. Another important aspect is that on reaction with deuterium, only two deuterium atoms are added, at the site of the original double bond and no allylic scrambling is observed as with heterogeneous catalyst.



However, one disadvantage associated with the Wilkinson's catalyst is that substrates containing aldehyde group undergo de-carbonylation due to strong affinity of this catalyst towards carbon-monoxide



The Ir-based Crabtree's catalyst is even more reactive than Wilkinson's catalyst and is good for hydrogenating hindered alkenes. Also, this catalyst gives superior directing effect for cyclic substrates as high degree of stereo-control can be achieved in the hydrogenation of cyclic allylic and homoallylic alcohols. This directing effect is due to a bonding interaction of the hydroxyl group with the iridium center.

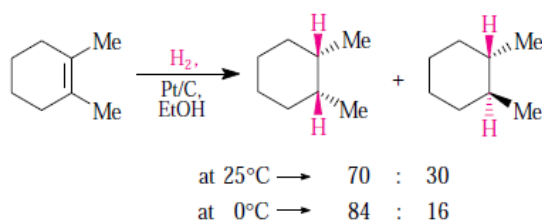


4.2 Mechanism of Hydrogenation and Stereochemical aspects

4.2.1 Mechanism of Heterogeneous catalytic hydrogenation

In the mechanism of catalytic hydrogenation, the surface of metal catalyst absorbs hydrogen. The alkene complexes with the metal by reversible π -complex formation with vacant metal orbitals. After this hydrogen from the catalyst is transferred to the side of the molecule that is adsorbed on it. The adsorption onto the catalyst is largely controlled by steric factors, and it is found in general that hydrogenation takes place by *cis* addition of hydrogen atoms to the less-hindered side of the unsaturated center and thus *cis*-hydrogenated product is usually obtained. However, *trans* product may form occasionally. The most plausible mechanism which can explain these outcomes is in

which transfer of hydrogen atoms from the catalyst to the adsorbed substrate takes place in number of steps as shown in the figure5.



The process involves equilibria between π -bonded forms 1 and 2 and a half hydrogenated form 3, which can either take up another atom of hydrogen (to give the reduced product 4) or revert to starting material or to an isomeric alkene 5. Subsequently, the new iso-alkene is hydrogenated. In principle it may add hydrogen from either of its diastereotopic faces and would eventually lead to trans-hydrogenated product. Similarly, the formation of allylic deuteration products may be explained when an alkene is reacted with D_2 in presence of Pd catalysts.

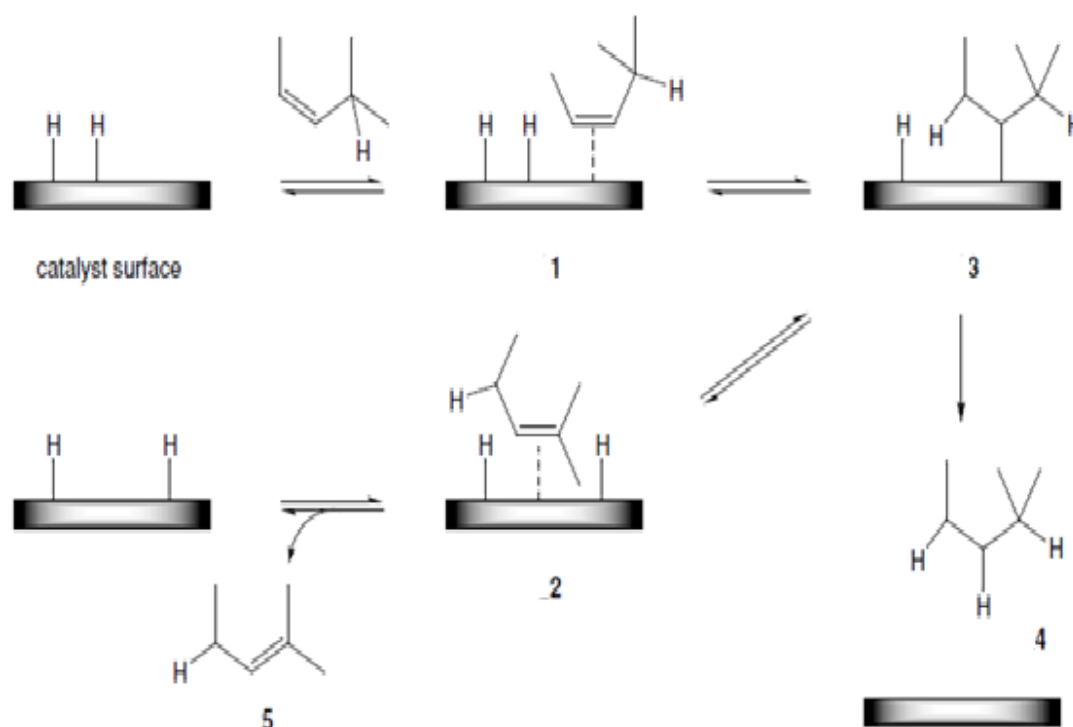


Fig.5: Mechanism of heterogeneous catalytic hydrogenation

4.2.2 Mechanism of Homogeneous Hydrogenation

Homogeneous hydrogenations with Wilkinson's catalyst $[(\text{Ph}_3\text{P})_3\text{RhCl}]$ also occur *cis* selectively *sans* the side reactions as observed with heterogeneous ones. In this mechanism initially the reaction involves dissociation of one or two triphenylphosphine ligands to give 14- or 12-electron complexes, respectively, then H_2 is added to the metal. Alkane product is rubbed out by Subsequent π -complexation of alkene, intramolecular hydride transfer (olefin insertion), and reductive elimination. Here we observe that PPh_3 is readily lost due to steric crowding and that the inner catalyst cycle with a weakly coordinated solvent molecule (resulting in a 16-electron complex) is about 1000 times faster than 3 PPh_3 ligands coordinated to the metal (Figure 6). The Crabtree's catalyst has a similar mechanism but the substrate adds before H_2 .

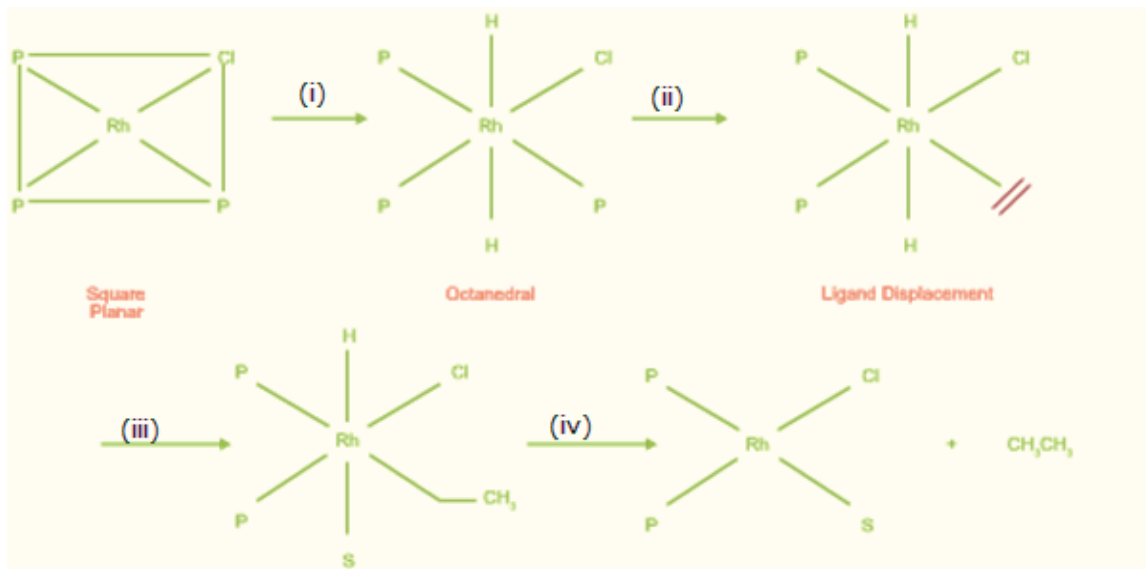


Fig. 6: Mechanism of hydrogenation by Wilkinson's catalyst; (i) H_2 addition, (ii) alkene addition, (iii) migratory insertion, (iv) reductive elimination of the alkane and regeneration of the catalyst

4.2.3 Asymmetric hydrogenation

Homogeneous hydrogenations are well-suited to asymmetric induction using chiral ligands on the rhodium or ruthenium metal centre. Chiral phosphines are most common and many have been studied. Recently monodentate phosphine ligands such as MonoPhos(1) have been shown to be very effective for enantioselectively reducing the N-acyl dehydro-amino acids or their corresponding esters, to amino-acid derivatives, for example giving N-acetyl phenylalanine in

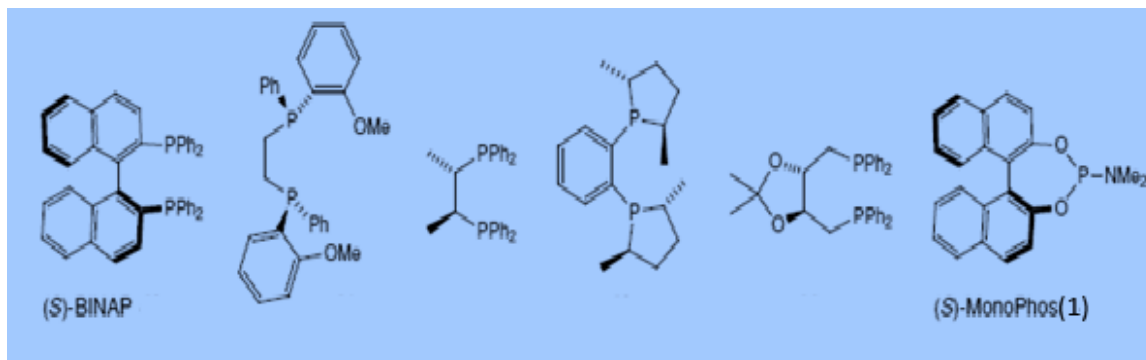
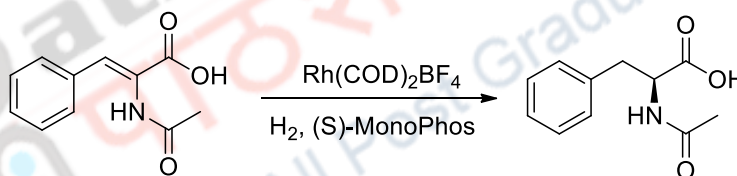


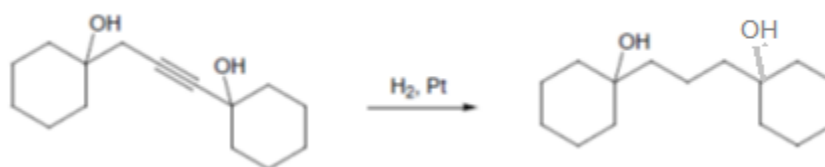
Fig. 5: Various chiral phosphine ligands used for asymmetric hydrogenations

quantitative yield and with 97% ee. The N-acyl dehydro-amino acid is thought to complex with the rhodium metal via its alkene and N-acyl carbonyl oxygen atom, leaving co-ordination sites for the ligand and hydrogen, which is then delivered asymmetrically to the alkene. Thus, asymmetric hydrogenation depends on the nature of substrate and a second functional group which can coordinate to the metal catalyst often aids to the asymmetric induction of hydrogen.



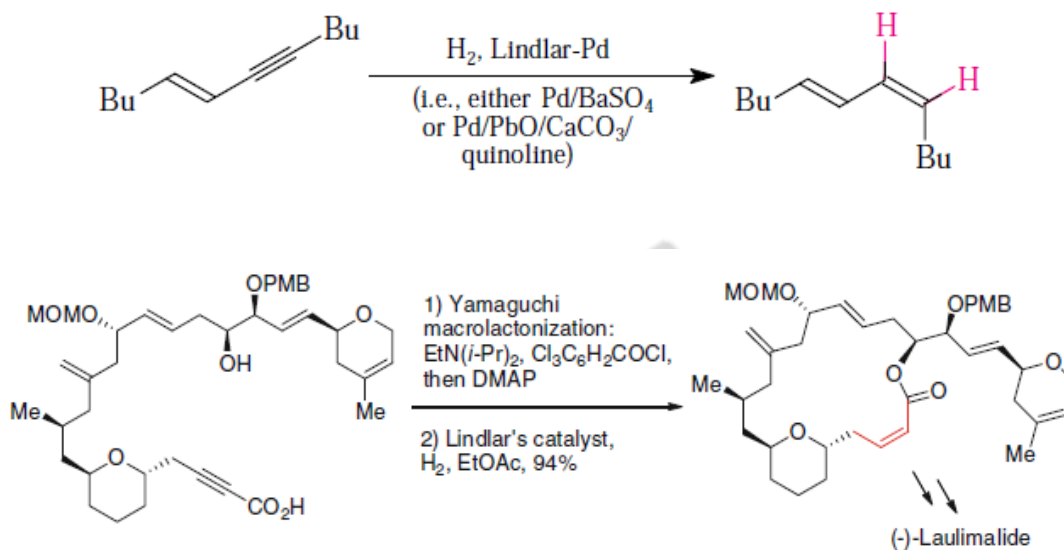
5. Hydrogenation of Alkynes

Alkynes are catalytically hydrogenated to alkene and further to alkane in a step-wise manner as discussed earlier. Both alkene and alkane may be isolated. For complete conversion of alkyne to alkane, Pt, Pd catalysts or Raney-Nickel are used. However, if a propargylic alcohol group is present, it may occasionally undergo hydrogenolysis, especially when Pt-catalysts are used.



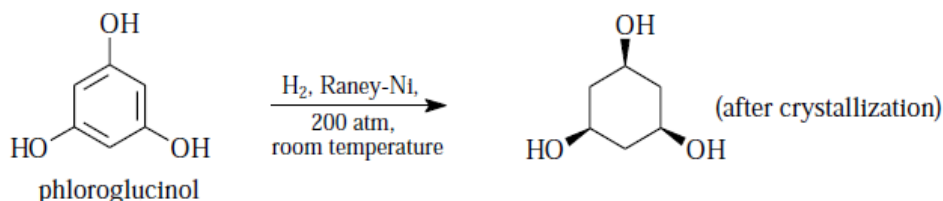
As mentioned earlier, it is possible to partially hydrogenate alkynes to alkenes by the use of catalyst poisons. The use of **Lindlar's catalyst** to get Z-alkenes is a most important example of such transformation. More electrophilic alkynes absorb more strongly on the electron-rich

catalyst surface than the corresponding alkenes, aids such partial hydrogenations. However, when using Lindlar's catalyst, it is important to prevent over-hydrogenation by carefully monitoring the reaction conditions and limiting the hydrogen consumption to around 1 mol. Such selective hydrogenation to Z-alkenes has found significant use in the synthesis of natural products and some pharmaceutically important intermediates.



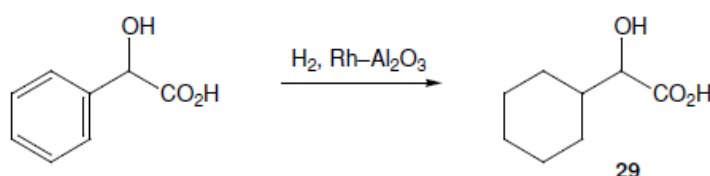
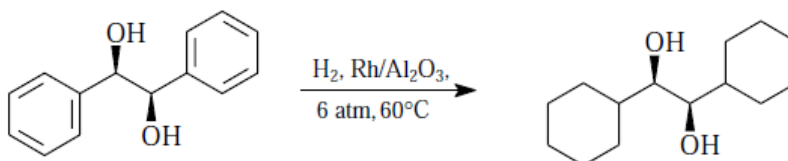
6. Hydrogenation of Aromatic rings

Aromatic rings are among the hardest to be hydrogenated and even with precious metal catalysts, require higher temperatures and pressures. But, once a benzene ring starts to hydrogenate, there is nothing like partial hydrogenation, and it hydrogenates to cyclohexane. This is because when benzene has been converted to cyclohexadiene (the first hydrogenation and the hardest, endothermic step), it is associated with the loss of resonance energy and the subsequent hydrogenations are exothermic and faster than the first one.

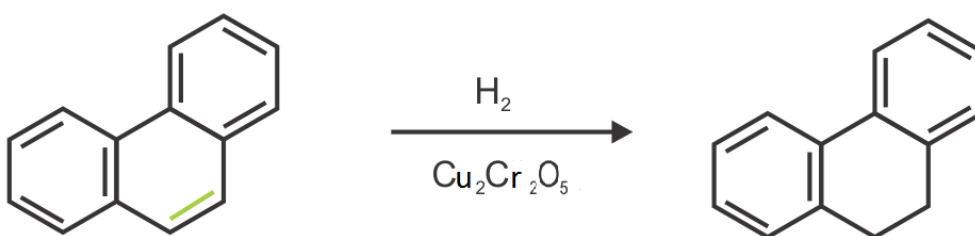


Pt and Rh catalysts are common and used at ordinary temperatures whereas Raney-Nickel or Ru-catalysts require higher temperatures and pressures and Raney-Nickel is used for large scale

hydrogenations involving heating at 150 °C at high pressures (100-200 atm). Rh over Alumina is another prominent catalyst used and requires milder conditions than others. Also, it does not cause hydrogenolysis of the sensitive C—O bonds present in the molecule.



Hydrogenation of polycyclic aromatic rings such as naphthalenes and phenanthrenes are also performed and by varying the reaction conditions, partially hydrogenated or fully hydrogenated products may be obtained. For example, Raney-Nickel may be used to obtain tetrahydro or decahydro-naphthalene by varying the reaction conditions. Similarly, 9,10-dihydro phenanthrenes or anthracenes can be obtained by reduction over copper-chromite and to fully reduce them, more active catalysts are required.



7. Summary

- Hydrogenation involves the treatment of a chemical compound with hydrogen and H_2 is added to a multiple bond.
- Hydrogenolysis (hemolytic fission of a bond by action of hydrogen) is an associated reaction and can be an unwanted side reaction in hydrogenation reactions.
- Hydrogenation requires use of a catalyst (homogeneous or heterogeneous) as the uncatalysed reaction requires very high temperatures and pressures.
- Different catalysts have different chemo-selectivities and their selection depends upon empirical observations and variations of reaction conditions.
- Catalyst poisons are added to decrease the activity of a catalyst and thereby bringing more selectivity, Lindlar catalyst to form alkene from alkynes being the most prominent example.
- The most plausible mechanism of heterogeneous hydrogenation is chemisorption of H_2 and unsaturated substrate over the catalyst surface and *cis*-addition of hydrogen atoms to the less-hindered side of the unsaturated centre a stepwise manner.
- Homogeneous hydrogenations involve a cycle of oxidative addition of H_2 to the metal, subsequent π -complexation of alkene, intramolecular hydride transfer (olefin insertion), and reductive elimination to give the product.
- Asymmetric hydrogenations are also possible in homogeneous hydrogenations by use of chiral ligands.
- Alkenes, alkynes and aromatic rings can be successfully hydrogenated by the variety of hydrogenation catalysts available to any feasible level of chemo-selectivity.