Reagents in Organic Synthesis
Professor Subhash Ch. Pan
Department of Chemistry
Indian Institute of Technology Guwahati
Lecture No. 09
Reduction
Meerwein-Ponndorf-Verley (MPV) reduction

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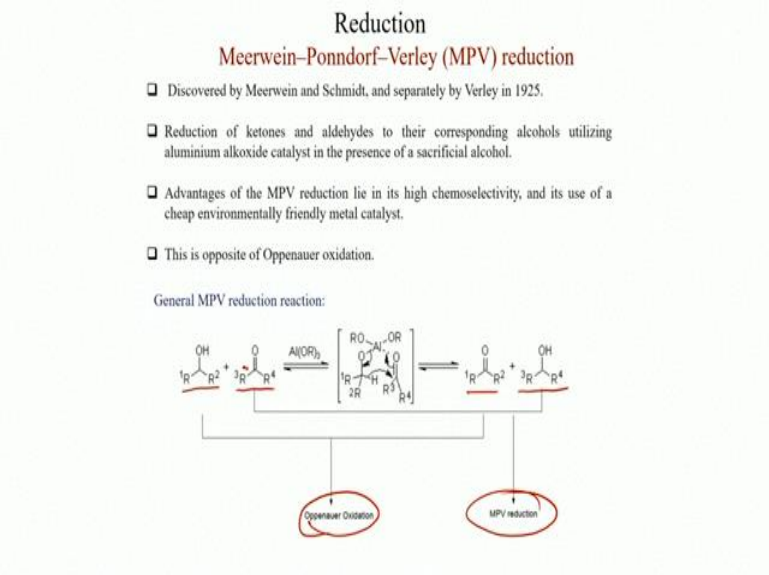

Welcome again, so today will discuss first MPV reduction and then metal catalysed hydrogenation. So first, we will discuss MPV reduction, which is called Meerwein-Ponndorf-Verley reduction discovered by Meerwein and Schmidt, and separately by Verley in 1925. Reduction of ketones and aldehydes to their corresponding alcohols utilising aluminium alkoxide catalyst in the presence of a sacrificial alcohol.

The advantage of the MTV reduction lies in its high chemoselectivity, and its use of a cheap environmentally friendly metal catalyst. This is opposite of Oppenauer oxidation, which we have already discussed. General MPV reduction is this that an alcohol which is the hydride source and this is the ketone which will be reduced. So this is R3 and now this aluminium alkoxide catalyst will see that the carbonyl compound is binding to the aluminium and this alcohol also binding to the aluminium because you want OR is replaced by this alcohol.

And now this hydride delivery will take place. So that R3, these R4 that ketone is going to alcohol and there are alcohol is going to ketones. So this process this ketone to alcohol. This process is called the MPV reduction. On the other hand, the alcohol is going to ketones. This R1, R2, the alcohol is going to ketones. So this is called Oppenauer Oxidation. So this

alcohol is going to ketone which is oppenauer oxidation and ketone going to alcohol. This is MPV reduction.

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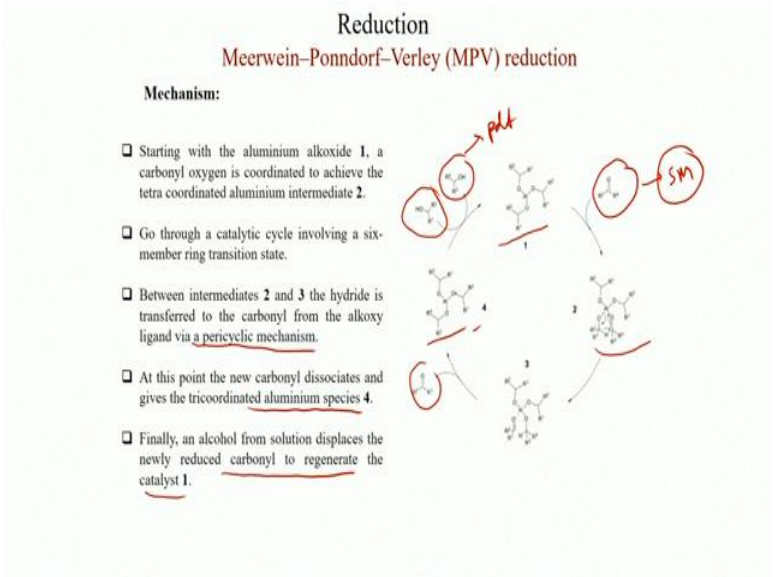

So the mechanism is similar like oppenauer oxidation, here this aluminium tri-alkoxide species is formed and here, this is the. Actually this starts from this one, and now the ketone is binding to the aluminium and this species is forming. So starting from the aluminium alkoxide, the carbonyl oxygen is coordinated to achieve the tetra coordinated aluminium intermediate 2. And after that, if this goes to a six membered cyclic transition state like oppenauer oxidation is hybrid delivery takes place and this ketone going to alcohol.

And better in it intermediate 2 and 3, the hybrid is transferred to the carbonyl from the alkoxy legend via a pericyclic mechanism. At this point the new carbonyl dissociates and get the try coordinated aluminium species 4. So this ketone is eliminated and now this alkoxide is forming and this is usually as the solvents. So this is in more quantity, this will displace, alkoxide displaces the newly reduced carbonyl to regenerate catalyst 1.

So this is the product, so this is product and this was the starting material. So the starting material ketone is going to the alcohol. So alcohol is liberating at the last step. Because this is the product alcohol and because this is the alcohol which is hydride source, so this is a generally as a solvent. This is large quantity, so this displace this alkoxide reagent to get this one.

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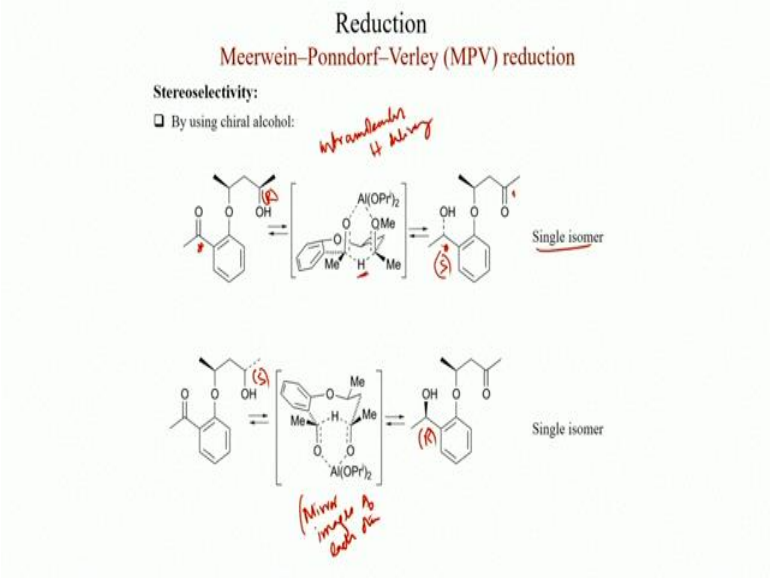

Stereoselectivity by using chiral alcohol, we can get stereoselectivity reduction. Because in the ketone reduction you generate a chiral centre, suppose this chiral centre is generating, when you reduce this carbonyl compound. Now you see this alcohol as a chiral centre. This is R centre. There is another extra chiral centre also is there. Now when this hydride delivery. This is intramolecular hybrid delivery and here you see this is actually an eight-member ring is forming. But this hydrogen this is the, this actually, this hydrogen. So this is the alcohol here, this is binding with aluminium isopropoxide here.

And now this, you can see this is the six membered transition state. This is the hydride which is delivered to the carbonyl compound and this takes this position. And now this alcohol becoming ketone and this chiral centre, newly regenerated each from the top face. So you get the S alcohol. This is the single isomeric form.

On the other hand if you consider this alcohol, where the stereochemistry just opposite. So either earlier case, it was R, now it is S. And now the hybrid delivery will take place from this way and now if you see this transition state and this transition state are mirror images. So mirror images of each other and now whatever earlier wise R. This oxygen, oxygen. Now they are down like this and now the hydride delivery takes place. So that you will get R alcohol and this is also selective, so highly selective. So with the chiral alcohol you can generate the chiral centre in a specific way.

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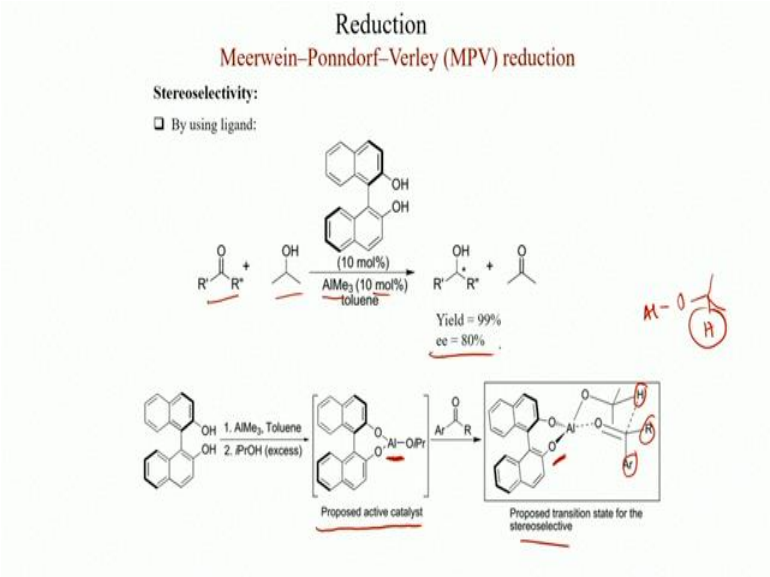

Also by legal it is possible like this ketone and this is the isopropyl alcohol and now with this binol catalyst and trimethylaluminium which is also catalyst in 10 mole percent, you will get this alcohol in 99 percent yield and ee is 80 percent. So what is the mechanism of this reaction? So binol first reacts with trimethylaluminium to generate the OAl methyl may be, and then isopropanol comes, isopropanol generate this isopropoxide catalyst. So this is the active catalyst.

And now hydride delivery will take place. So where from the hydride delivery take place. Now if you see the isopropoxide, this is the hydride and this is the hydride that will deliver to the carbonyl compound. Now it is binding, aluminium is binding to a chiral ligand. So everything is chiral. This transition state is chiral.

Now this ketone will take. The orient in a such fashion that this will be less sterically position. So that it will face the less spheric and that is why this Ar is in the axial and R is in equatorial. Now this is the hybrid from the isopropyl and this delivery will take place such in a way that you get a moderately in a selective way up to 80 percent the alcohol.

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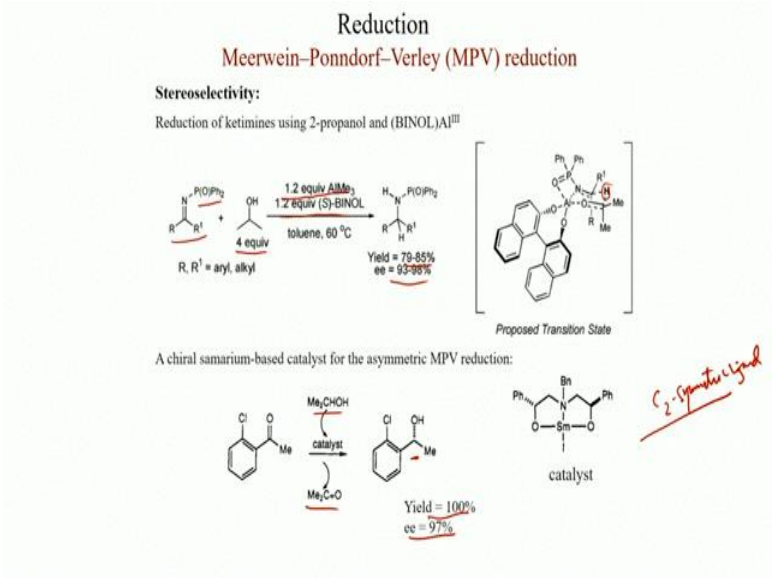

Also in this way ketimines can also be reduce like this. This is the phosphine oxide protecting group n. Phosphoryl oxygen is there and now 4 equivalent of isopropanol, it is not catalytic 1.2 equivalent time aluminium and 1.2 equivalent S binol, you get this amine product with 79 to 85 percent yield and 93 to 98 percent ee. And R, R1 can be arrive alkyl.

And this is the transition state, here also, you can see this imine nitrogen is coordinating the aluminium and this isopropanol oxygen also coordinating aluminium and this is the isopropanol hydrogen, which is delivered to the amine and now this transition state. It is chiral because of this ligand is chiral and the hydride delivery takes place in such a way that you get high enantioselectivity for this product.

Also chiral samarium catalyst for the asymmetric MPV reduction can be used. So this is isopropanol with catalyst and this reaction this is going to be this alcohol. And acetone you are getting a product, by-product of this reaction. And now with this samarium catalyst, you get 100 percent yield and 97 percent ee. So here you can see this is a chiral C2 symmetric ligand, C2 symmetric ligand is binary samarium and you get high enantioselectivity 97 percent yield you get for this product.

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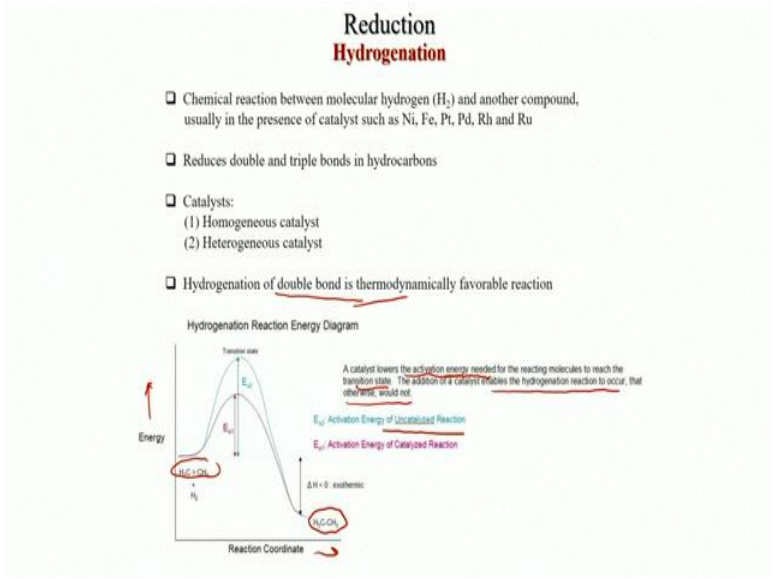

Now we will discuss hydrogenation. Chemical reaction between molecular hydrogen and another compound, usually in the presence of catalyst such as Nickel, Iron, Platinum, Palladium, Rhodium, Ruthenium, different metals can be used. Reduces double and triple bonds in hydrocarbons. Mainly catalyst, homogeneous catalysts, heterogeneous catalyst. Hydrogenation of double bond is thermodynamically favourable reaction. So this is the double bond reduction generally will perform with hydrogen and if you see this diagram energy and reaction coordinate and this green color is the uncatalyzed reaction and pink is the catalyzed reaction.

So what you see with catalyst reaction that transition state energy gets lower. So you need lesser activation energy needed for the reactive molecules to reach to the transition state. The addition of a catalyst enables the hydrogenation reaction to occur, otherwise it is not possible. Because the transition state so high, without catalyst it is not possible. Though the reaction is exothermic as you can see, alkane is here and alkene is high. So this reaction is exothermic. However, to get the transition state, it is not possible in uncatalyzed version.

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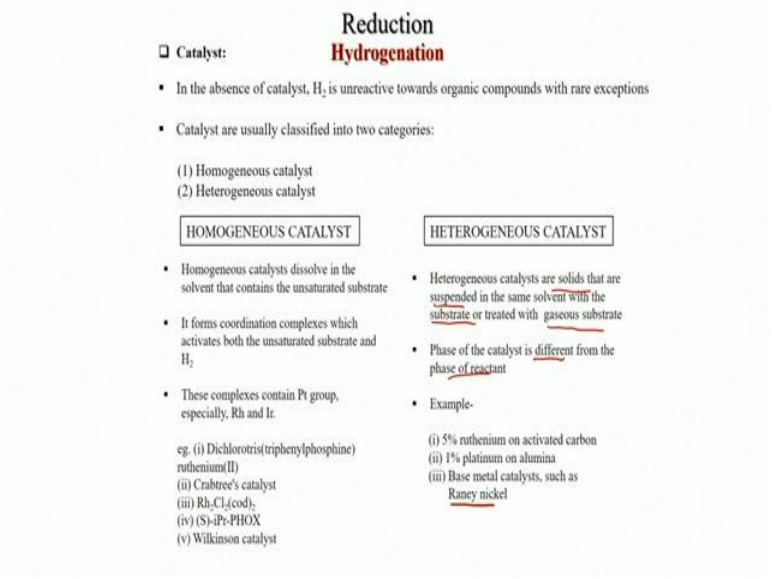

Catalyst hydrogen is unreactive towards organic compounds with rare exceptions. Catalysts are usually classified into two categories, homogeneous and heterogeneous catalyst. So in a homogeneous catalyst the catalyst dissolved in the solvent that contains the unsaturated substrate. It forms coordination complexes which activates both the unsaturated substrate and hydrogen. So this is very important. These complexes contain platinum group specially rhodium and iridium, as for example dichlorotrist triphenylphosphine, ruthenium, crabtrees catalyst, Rh2-Cl2 cod2, S-isopropyl-PHOX with rhodium may be and Wilkinson catalyst.

Heterogeneous catalyst are solids that are suspended in the same solvent with the substrate or treated with gaseous substrate. So these are solid heterogeneous catalyst they are really suspended, not in solution. Phase of the catalyst is different from the phase of reactant, example 5 percent ruthenium on activated carbon, 1 percent Platinum on alumina. Base metal catalyst such as Raney nickel. Lindlar catalyst that will discuss also.

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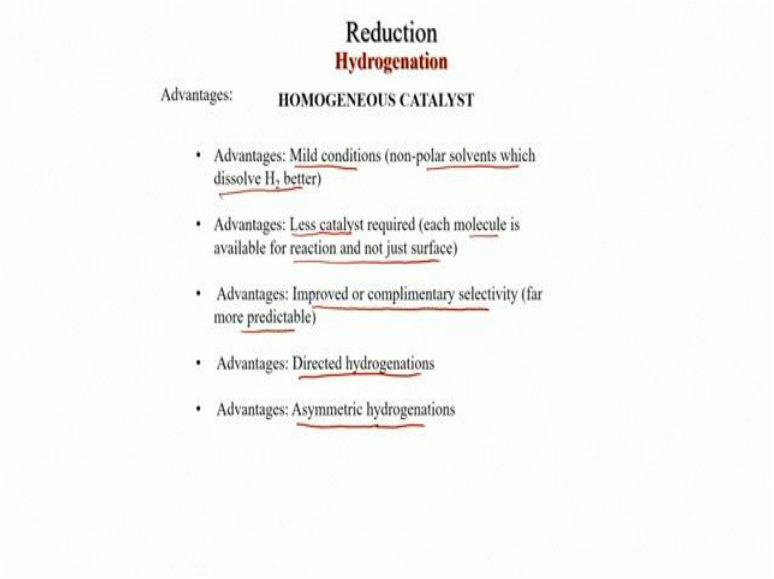

So there are several advantages of homogeneous catalyst. First advantages it is mild condition, non-polar solvents which dissolve hydrogen better and also less catalyst is required. These molecules is available for reaction and not just surface. So you do not need a whole surface like heterogeneous, where you need a molecule, particular amount of molecules. Advantage improved or complementary selectivity far more predictable. Advantage directed hydrogenations is also possible and asymmetric hydrogenations are also possible and mechanism can will understood for homogeneous catalysts.

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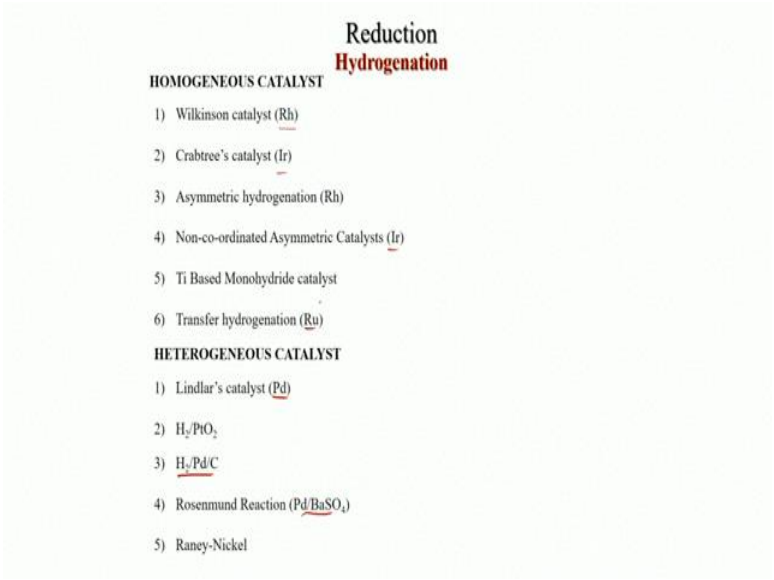

So this is the homogeneous catalysts. Wilkinson catalysts. Crabtrees catalyst, Wilkinson, rhodium and this is iridium base. Asymmetric hydrogenation, rhodium that will discuss. Non-

co-coordinated asymmetric catalyst iridium base. Titanium based monohydrate catalyst, will discuss this points. Transfer hydrogenation with ruthenium.

And heterogeneous catalyst will discuss Lindlars catalyst which is Palladium. Then H2/PtO2, H2, Palladium charcoal. Rosenmund reaction will discuss Palladium BaSO4 with hydrogen and Raney nickel.

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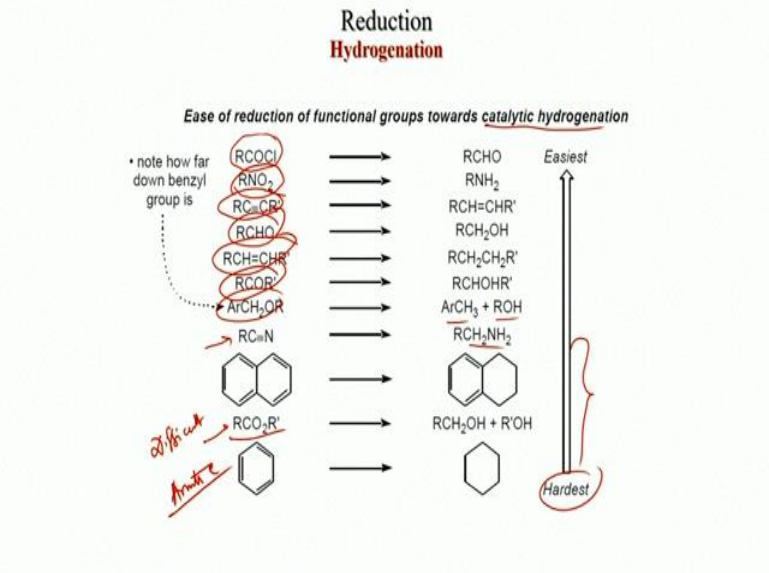

And these are the functional groups that can be reduced with the catalytic hydrogenation and these if you go from the top to the down the, this become hardest. So benzene is the hardest to reduce because of course it is aromatic. So also esters are difficult to reduce with because with LA you can easily reduce a stars are difficult, naphthalene derivative also difficult, nitrile also difficult.

So what is easy? Acid chloride is easy, RNO2, you can reduce, alkyne reduce, aldehyde, alkyne, ketone you can reduce, also displacement reaction that benzyl group is liberated here, ArCH3 and ROH. So, following derivative is liberated and alcohol is generated. Also RCN can be reduced. So these are the difficult, but these can be also done that we will see. So acid chloride is the easiest reduction possible with the catalytic hydrogenation.

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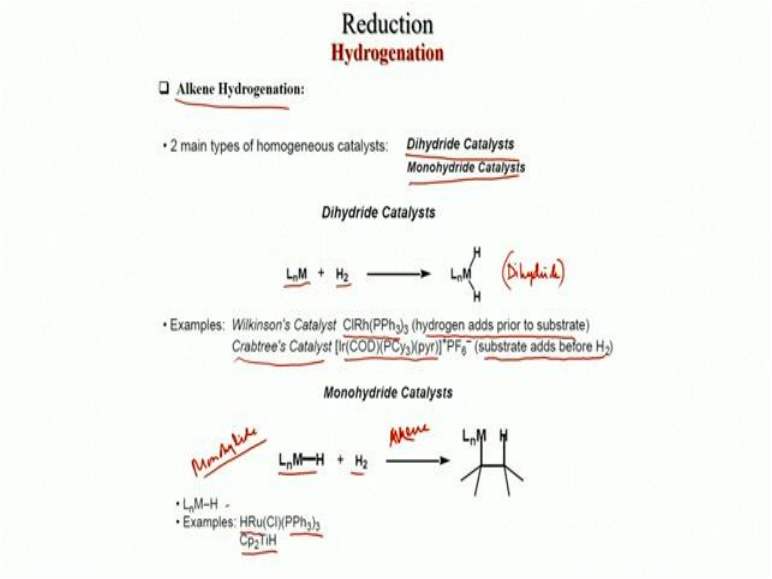

So first, will discuss Alkene hydrogenation, for alkane hydrogenation there are two main types of homogeneous catalysts, one is dihydride catalyst and another is monohydride catalyst. So in dihydride catalyst, this is the metallicant complex, this reacts with hydrogen and this is the dihydrides species will form. So in dihydride catalyst, this dihydride species will be formed an example is Wilkinsons catalyst this is chloro rhodium, 3 phosphine are there. So here also hydrogen adds prior to substrate. So hydrogen adds to this dihydride species prior to the substrate.

And in Crabtrees catalyst, this is the Crabtrees catalyst iridium COD PCy3 pyridine and hexachlorophosphate is there. Here substrate adds before hydrogen that will see details later and in monohydride catalyst, this is the monohydride species and monohydride plus hydrogen plus alkene will give this kind of inserted intermediate. An example is LnM hydrides. So hydrides species who is like this. H ruthenium chloro 2 phosphine and Cp2 cyclopentadienyl titanium hydride, this species can attract monohydride catalyst.

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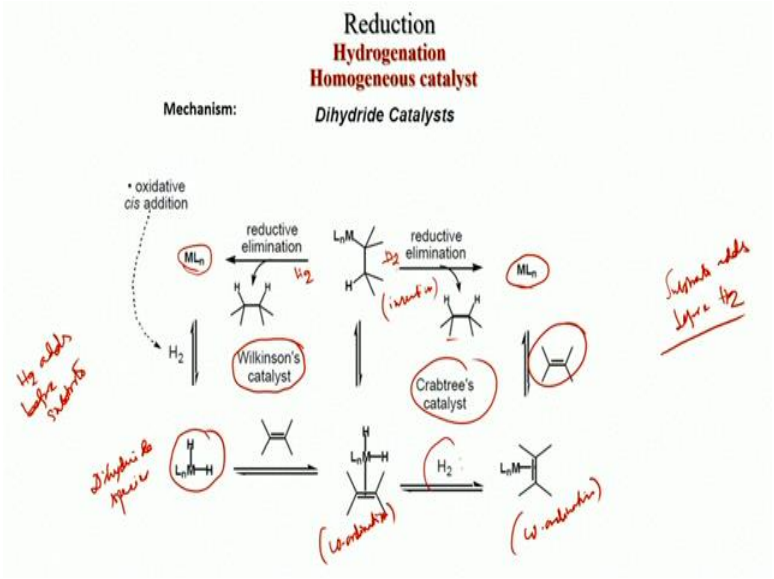

So First what is the mechanism of dihydride catalyst? So as we have seen that MLn this metallicant complex reacts with hydrogen to generate the dihydride species. So this is the active catalysts actually. So dihydride species is formed and oxidative addition is happening here, metal gets plus 2 more oxidation state. Now when it reacts with alkene. So first the coordination will happen, coordination with the metal and the pi bond of the olefin.

And then the insertion happen to get this intermediate and this one, if you put hydrogen more. Because the hydrogen will attract to this and then of course the reductive elimination will happen, and then you get your alkane and you are the metal ligand complex back. And these procedure followed in case of Wilkinsons catalyst. In Wilkinson catalyst the hydrogen adds before substrate, hydrogen adds before substrate.

Now in the case of Crabtree kind of things. So here MLn metal ligand complex is binding with olefin first. So here this coordination is happening, and now hydrogen comes to generate this coordination again. Because hydrogen their oxidation of metal is happening here by hydrogen and this is followed in crabtrees catalyst and then insertion will happen and after that the hydrogen will come, of course here. Hydrogen and then the reductive elimination you get the alkane and metal ligand complex is formed. So what is the name difference? Here substrate adds before hydrogen. So this is important, substrate is adding before hydrogen, hydrogen is adding later.

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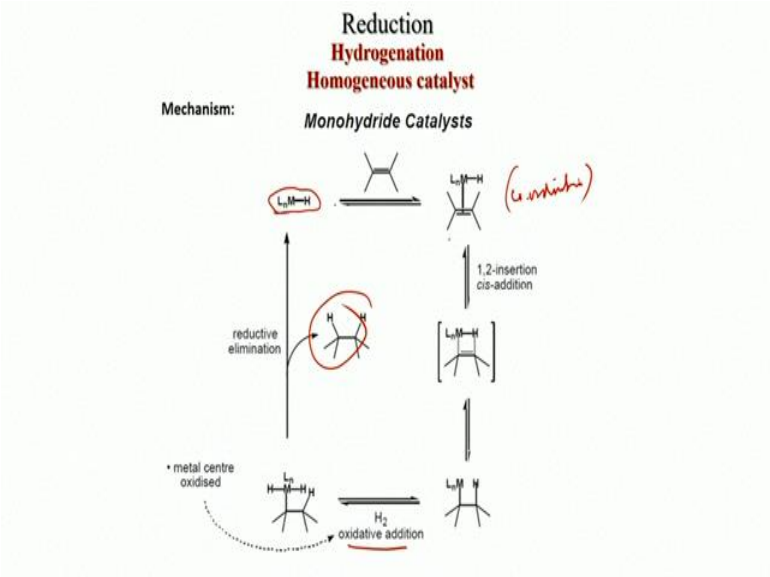

And in monohydride catalyst this is the co-ordination is happening with a metal hydride and alkene and now 1, 2 insertion will happen like this and you get this species. And now hydrogen will add this intermediate we have seen already in dihydride. So only difference is start with a ligand metal hydride complex and now oxidative addition is happening, metal centre is oxidised here and reductive elimination will generate the product alkene and you get your metal ligand hydride complex back.

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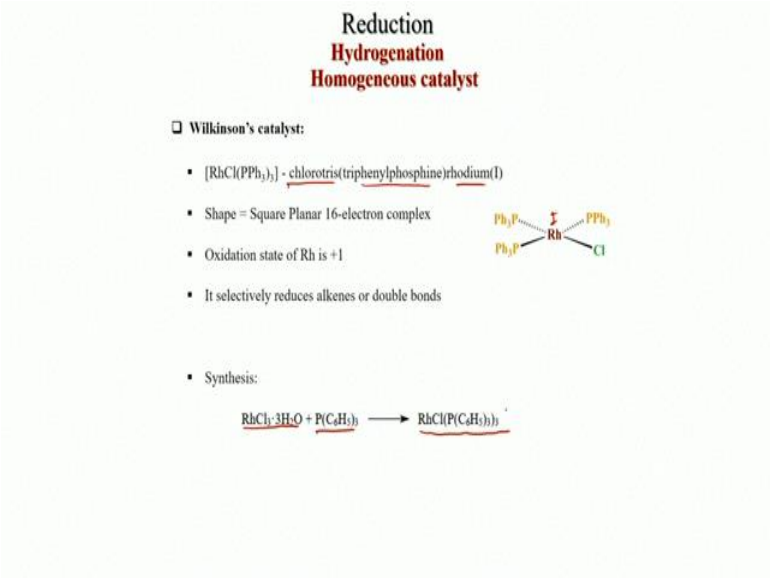

Wilkinsons catalyst first will discuss, this is the rhodium chlorotris triphenylphosphine rhodium 1. The charges coming because of chlorine and shape is square planar 16-electron complex. Oxidation state of rhodium is plus 1. It selectively reduces alkenes or double bonds

that it is main application. And what is the synthesis in a rhodium chloride 3H2O Triphenylphosphine you can get this Wilkinson catalyst which is chlorotris triphenylphosphine rhodium.

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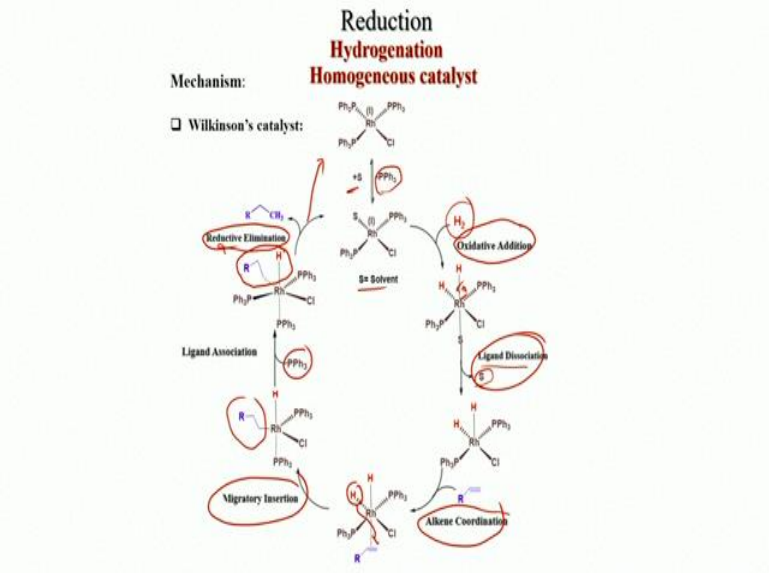

What is the mechanism of this reaction with Wilkinson catalyst? So this is the Wilkinson catalyst and this is solvent may come first one. PPh3 may liberated and this intermediate is forming. Now the hydrogen comes. So we have seen in Wilkinson catalyst hydrogen adds before substrate. So that is why this happening and oxidative addition is happening, so rhodium becoming (III).

And now the ligand dissociation will give you painter coordinated species and now alkane will coordinate. So in the painter coordinated species after began dissociation or solvent whatever, you get the alkene coordination like this. So get us six coordinated rhodium and now migratory insertion will happen one hydride will go to the alkene and you get a painter coordinated species and now ligand dissociation will happen to get this hexacoordinated species.

So PPh3 will add, and now from this hexacoordinated the reductive elimination will happen. So these two groups eliminate and now you get your, actually you get here, this one and get here again by solvent this will form. So this is the overall mechanism, the oxidative addition of hydrogen ligand dissociation and alkene coordination, migratory insertion is happening, this is the fast one hydride is coming to the double bond to get to get a alkene species here. Now, after a ligand association it becomes six coordinated and form their reductive

elimination is possible. So six becomes four here, four coordinated and you get your alkane product.

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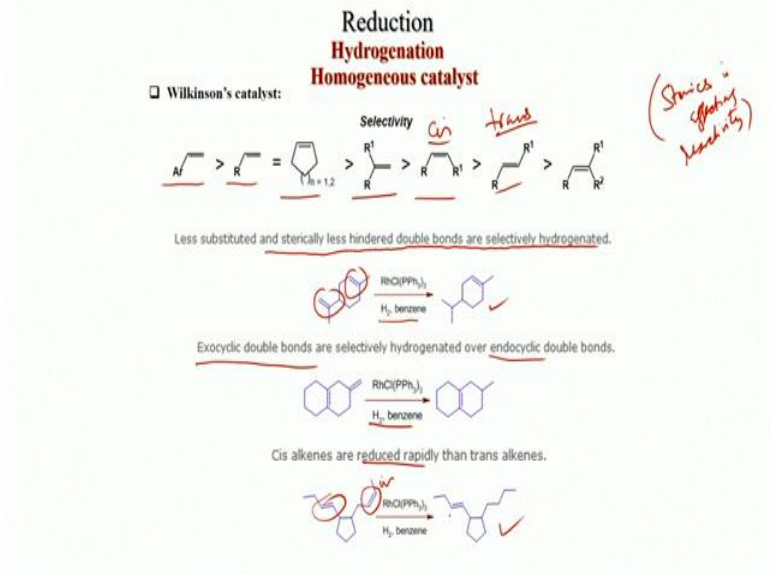

This is the reactivity for the alkene. So here you can see styrene derivatives are more reactive. Than mono substituted olefin, then cyclic olefin, then 1, 1 disubstituted olefins, then 1 to 2 disubstituted olefins. This is cis and this is trans. So this will see the cis olefins are reactive than trans and then trisubstituted. So what you see the sterics is affecting the activity. So if you are allowing is highly substituted or in the spherical in that position than Wilkinson catalyst cannot come. Because the coordination will not be possible in that case.

Less substituted and sterically less hindered double bonds are selectively hydrogenated. This is an example you can see there are two double bonds are present, this and this and this one is in the endocyclic, this is outside and with this catalyst, Wilkinson catalyst hydrogen benzene will get only this product. So only this double bond is reduced.

Also exocyclic double bonds are selectively hydrogenated over endocyclic bonds, like this is endocyclic, this is exocyclic and exocyclic are more hydrogenated, selectively hydrogenated over endocyclic, here also hydrogen benzene is used. And cis alkenes are reduced rapidly than trans alkenes. So we already discuss, so this is the example, here can say this is the cis, this is cis olefin, this is trans olefin and selectively you get reduction of the cis double bond and trans double bond is untouched in this condition.

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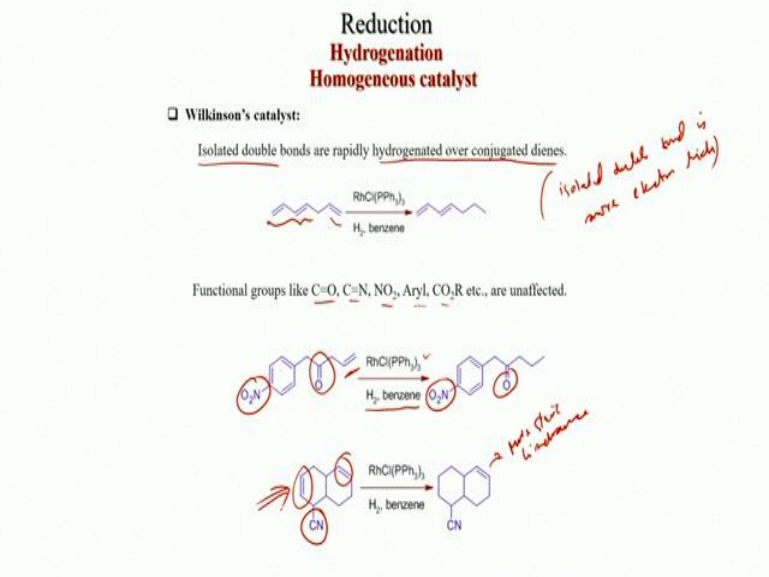

Also isolated double bonds are rapidly hydrogenated over conjugated dienes. Like this is conjugation and this is isolated and the isolated double bond is reactive. So that means isolated double bond is more electron rich. So electron rich double bond is reacting here. And functional groups like carbonyl, amine, NO2, Aryl, CO2R etc are unaffected and this is the example here NO2 group is there, carbonyl is there and double bond is there.

Selectively Wilkinson catalyst in hydrogen benzene reduce the double bond and these two functional groups are untouched in this condition. Also here you can see a CN group present and two double bonds are there. However, these double bond is close to a tertiary carbon centre. So this is more steric, more steric hindrance. That is why Wilkinson catalyst selectively only this double bond.

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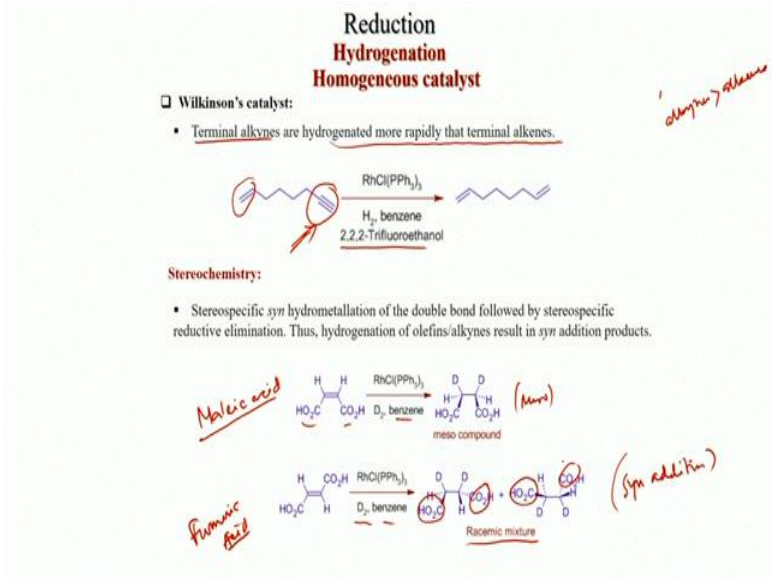

Terminal alkynes are hydrogenated more rapidly than terminal alkenes. So alkynes are more reactive than alkenes and here terminal, both are terminal. However, only the alkyne is getting hydrogenated, where 2,2,2 trifluoroethanol is used also as a proton source. Stereospecific syn hydrometallation of the double bond, followed by stereospecific reductive elimination. Thus hydrogenation of olefins alkynes result in syn addition product. So this is maleic acid. Maleic acid two carboxyl groups are syn to each other.

Now it would do Wilkinson catalyst D2 and benzene. Then two deuterium, adding as the syn fashion. So this is a meso compound. Because in, here is the syn is there, that means the orientation of the groups will not change, here they are syn, here also syn. If this is a fumaric acid and here they are terms to each other and now it is Wilkinson catalyst D2 benzene you get racemic mixture. So the racemic mixture is forming because syn addition is happening. Because here they are trans to each other and here also, they are trans and two trans products are possible. So you get racemic mixture.

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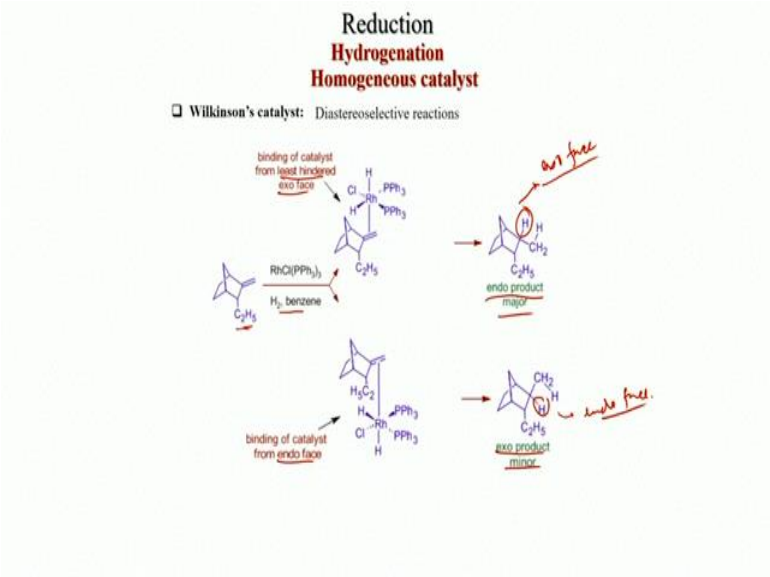

Now we will see diastereoselective reaction. this is a norborane system, here an exocyclic olefin is there and C2H5 is there in the endo position. Now, which rhodium chloride triphenylphosphine that is Wilkinson catalyst hydrogen benzene. The binding happens from the least hindered exo face. So selectively the binding happens exo face. So that means steric effect is very important in Wilkinson catalyst reduction and that is why hydride delivery takes place from exo face and you get endo product major.

Hydride these coming from the exo face. So top face. So because exo face is less hindered. And binding of catalyst from endo face. Now this is steric group is there, already ethyl group, and that is why exo product will be minor. Here hydride from the endo face. So this product will be minor.

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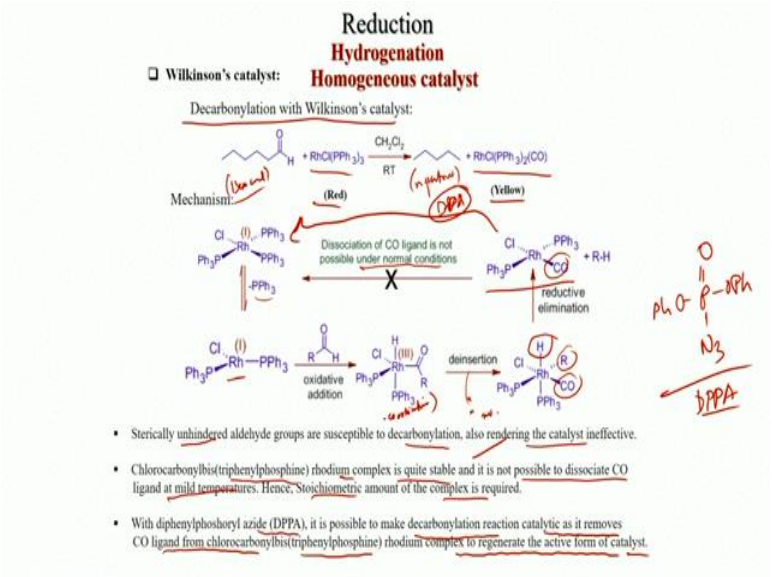

Decarbonylation with Wilkinsons catalyst is also possible, like this in a long chain aldehyde. So this is hexanal, hexanal on reduction with Wilkinson catalyst in dichloromethane at room temperature, you get n Petane. So one carbonyl less, that carbonyl is going here. This is stoichiometry of the reaction, here you can get a carbonyl with displacement of a phosphine. And this is also red and this is yellow. So this decarbonylation is happening that you can understand by a color also.

What is the mechanism of this reaction? So four coordinated, one ligand dissociation happens then this tri coordinated species is formed. Now aldehyde can add oxidative addition. So earlier rhodium was 1 now it is 3 and this is penta coordination, penta coordination is there. Now deinsertion will happen and deinsertion what happens? The oxidation number increases. So oxidation number increases, here what happens? Here, this COR becomes RCO, you can see here.

And now reductive elimination is possible here. So reductive elimination, this hydrogen and R. They liberates and this carbonyl states here, so you get this carbonyl species. And dissociation of carbonyl ligand is not possible under normal condition. That is why this catalyst is regenerated, not regenerated. Sterically unhindered aldehyde groups are susceptible to decarbonylation, also rendering the catalyst ineffective.

Chlorocarbonylbis triphenylphosphine rhodium complex, which is this byproduct here, this one. It is quite stable and it is not possible to dissociate CO ligand and mild temperatures. Hence, stoichiometric amount of the complex is required. However, with diphenylphosphoryl

azide. So this is diphenylphosphoryl azide. This is the DPPA. So with DPPA it is possible to make decarbonylation reaction catalytic as it removes CO ligand from chlorocarbonylbis triphenylphosphine rhodium complex to regenerate the active form of catalyst. So these on DPPA you can get this one. So simply it is not possible, but if you add DPPA in the reaction medium, then you can use this as a catalytic amount.

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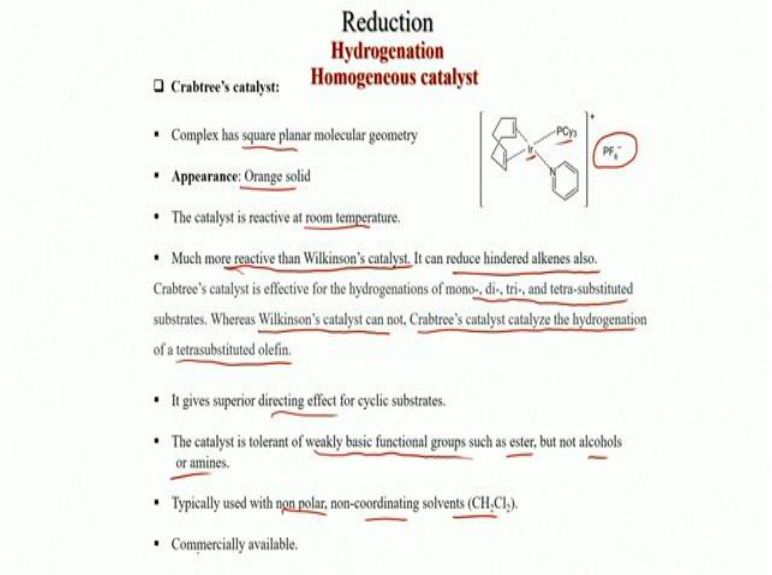

This is Crabtrees catalyst as you can see this complex is iridium complex is there, cyclooctyne is there, pyridene is there and PCy3 is there and hexachlorophosphate is the counter ion. Complex has square planner molecular geometry, this is orange solid. The catalyst is reactive at room temperature, it is much more reactive than Wilkinsons catalyst. It can reduce hindered alkanes also. So this is very important for Crabtrees catalyst.

Crabtrees catalyst is effective for the hydrogenations of mono-, di-, tri-and tetra-substituted substrates. Whereas Wilkinsons catalyst can not, Crabtree catalyst catalyze the hydrogenation of a tetrasubstituted olefin also. It gives superior directing effects for cyclic substrates and the catalyst is tolerant of weakly basic functional groups such as ester, but not alcohols or amines. Typically used with non-polar, non-coordinating solvents like dichloromethane and this is commercially available.

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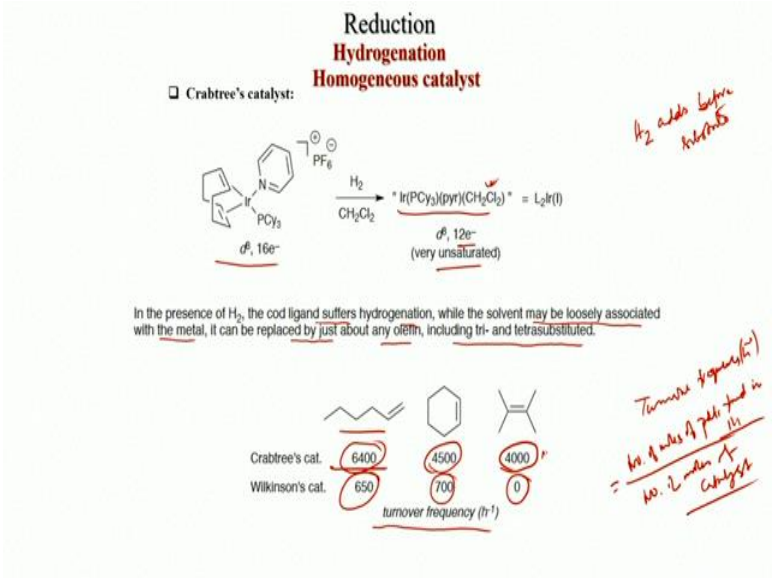

And in Crabtrees catalyst this is the thing hydrogen adds, H2 adds before substrate and after H2 addition. This is the Crabtree catalyst, this is d8, 16 electron system. So COD group is getting reduced and that is liberated and then solvent is coming. And here d6 system and 12 electron. In the presence of hydrogen, the cod ligand suffers hydrogenation, while the solvent may be loosely associated with the metal, it can be replaced by just about any olefin, including tri- and tetrasubstituted. So now here the olefin association will happen.

And this is the turnover frequency. So turnover frequency in hour means a number of molecules or number of moles of product formed in 1 hour divided by number of moles of catalyst. So you can see in Crabtree catalyst, simple this one, this is 1 hexene. This Crabtree catalyst is the turnover frequency is 6400 and here one 10^{th} Wilkinson catalyst, also cyclohexane receipts 4500, this is 700 almost one 8^{th} and tetrasubstituted olefin Crabtree catalyst 4000 and Wilkinson catalyst 0. So Wilkinson catalyst does not react with tetrasubstituted olefin, but there is high reactivity with tetrasubstituted olefin with Crabtree catalyst.

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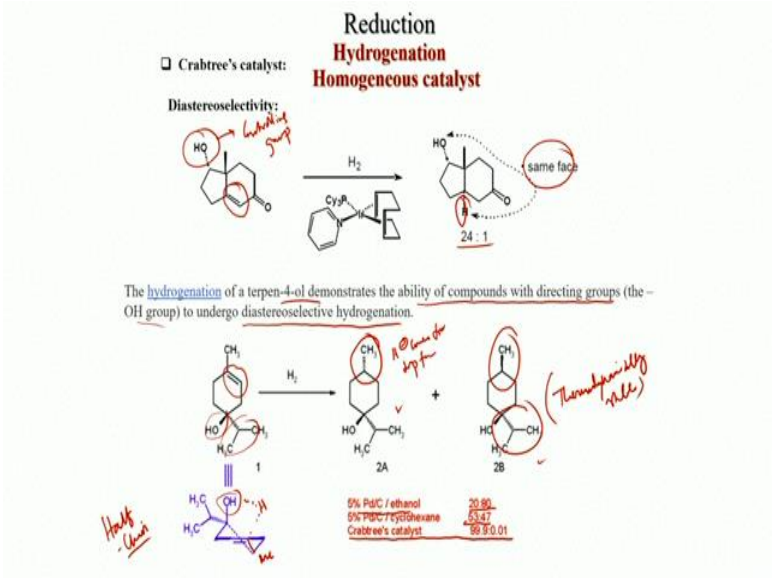

This possible also diastereoselective reduction and here the hydroxyl group is important for Crabtree catalyst. This is the bicyclic compounds and here enone is there and this hydrogen adds to this double bond and the facial selectivity is controlled by the hydroxyl groups. So this is the control, controlling group. And you get 24 :1 diastereo selective product. So this hydride is coming from the same face, same phase here down hydroxide and here also down.

The hydrogenation of a terpen-4-ol demonstrates the ability of compounds with directing groups, likewise OH group to undergo diastereoselective hydrogenation. This is the terpen-4-ol system, you can see there is the hydroxyl group and there is an isopropyl group, this is down this is up and this is the double bond that will be reduced.

Now this is the half chair, half chair and there will be a methyl group actually here, methyl group will be there with the double bond and hydroxyl is up and this isopropyl is down. So hydride delivery will take place from the up. So it will reduced and the methyl will be down. And this is the methyl is down and this methyl is up. So with 5 percent palladium circle ethanol you get 20 :80. So this product we measure.

So this product might be thermodynamically stable, thermodynamically stable because these two groups are trans to each other and with 5 percent palladium charcoal in cyclohexane you get almost 1 raise to 1 mixture. However, Crabtree catalyst is gave 99.9 of this product and 0.1 of this product. So that means a Crabtree catalyst is the hydroxide group is the controlling group. Hydroxide detect hydrogenation, hydroxyl is up. That is why hydride comes, hydride comes from top face and you get this product.

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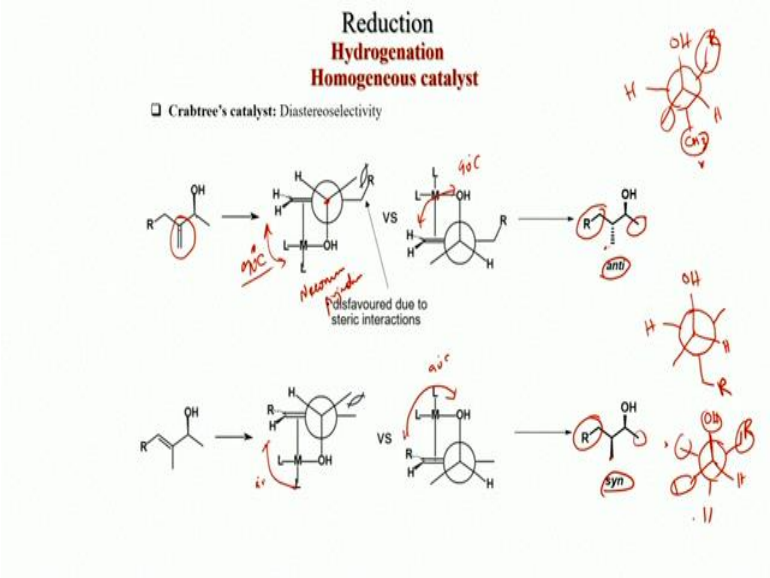

This is a Crabtree catalyst, also the diastereoselectivity hydrogenation here, here a alcohol is chiral here and here is a exocyclic double bond is present. And now if you draw Newman projection, so this Newman projection and if you look this carbon and this carbon, so this carbon is at top, this is, the hydroxide is there, hydrogen methyl. If you draw like this way and this double bond if you draw a 90 degree angle with the hydroxy. This double bond is there, this is the CH2R group and this double bond is getting reduced and here it is also coordinate with the metal and hydroxyl group. So their perpendicular 90 degree angle.

However this way the steric repulsion is happening between these and this group. Alternatively, here also 90 degree angle is possible and now metal is coordinative with the double bond and this way you get the anti-alcohol. So what happens? This hydrogen. Now, after hydrogenation this is becoming, this you can draw CH2R, this is the methyl group that is the generated and this is the hydrogen.

Hydrogen is coming from this way, this said and if you see this one in this zigzag, this CH2 group and this group are trans. So here CH2 R and this are trans. And now this OH and methyl are also trans. So this is anti -OH and methyl, so this methyl, this methyl is this methyl, this with is here. So they are anti-to each other.

On the other hand, so this is due to steric interaction. On the other hand if there is a internal double model like this alkaline alcohol and now you can draw same way, this is the 90 degree angle, this is the OH hydrogen methyl and now this is R group, there is the extra methyl

group is here and due to this methyl there is a steric interaction. Now you can draw this way, here also 90 degree angle, 90 degree angle and this way, this way there is no steric repulsion.

Because this methyl is now with hydrogen. So no steric interaction and this should be with syn. So this also you can draw OH hydrogen and after reduction this groups comes here, this here and this, this is the hydrogen and this is the CH2 R, and now we have seen that this and this CH2 R and this a groups are trans to, and zigzag they are trans to each other. So you have to move it and if you move it, then with the OH hydrogen and these the methyl group.

Now if you draw CH2R here, then methyl here, hydrogen here and now you see these two are trans to each other and OH and methyl, this methyl is this methyl they are cis to each other, so they are syn.

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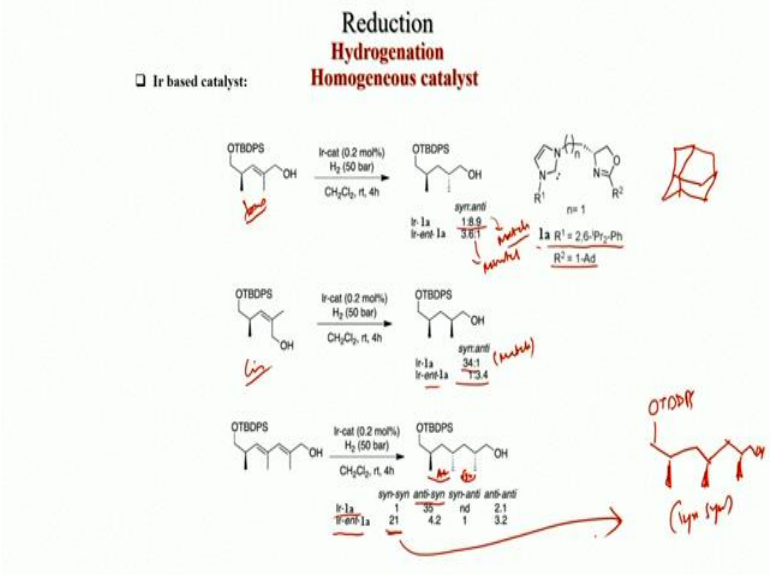

Iridium-based catalyst has also been used for hydrogenation, in fact, this asymmetric hydrogenation here, this carbene complex is there, oxazoline motif, iridium, then iridium cod used with hydrogen 50 bar in dichloromethane room temperature, this allylic alcohol it gets reduced with IR 1a, so iridium 1a, R1 is equal to 2, 6 diisopropylphenyl group, then R1 is there and R2 1 is adamantane group is there, this is the adamantane group, then you get 8.9 raise to 1. So anti is more, this is the match case and this is the mismatch case.

Also this kind of alcohol when it is cis, so this is the trans actually, trans alcohol this is cis allylic alcohol and in this case same condition, you get here syn is 34. So this is match case and anti-with ent 1a, you get one raise to 3.4, this is the mismatch case. Now if you are dying

this is also trans, here it has been found that iridium 1a, it gave anti-syn products. So this is anti, this is syn. So this product is measure with iridium 1a and ent 1a, you get syn-syn. So this means syn-syn. So that means OTDDPS, this is syn and this also syn, so this is syn-syn. That is from with this 21 ratio. So ent 1a, you get that product as major.

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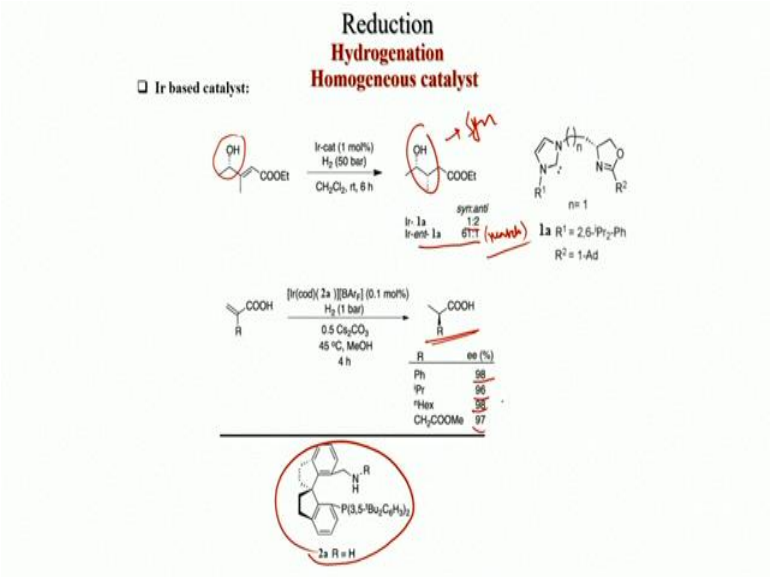

Also here a chiral alcohol is there and this same catalyst can be used for diastereoselectivity hydrogenation of this alpha beta unsaturated) ester, here also you can see 1a , they are good, it is not good. But ent 1a is the enantiomer of this, you get this is match case actually. The syn product is measure, this is syn, 6 to 1 raise to 1 ratio and this is the hydrogenation of alpha, beta unsaturated carboxylic acid with iridium cod and 2a this is the ligand, the ammonium.

There is a nitrogen as well as phosphine is there which hydrogen 1 bar cesium carbonate 45°C methanol, you get good enantioselectivity for this alpha substituted carboxylic acid and the phenyl acid 98 percent, isopropyl 96 percent, n hexane 98 percent, this group 97 percent, ees you can get.

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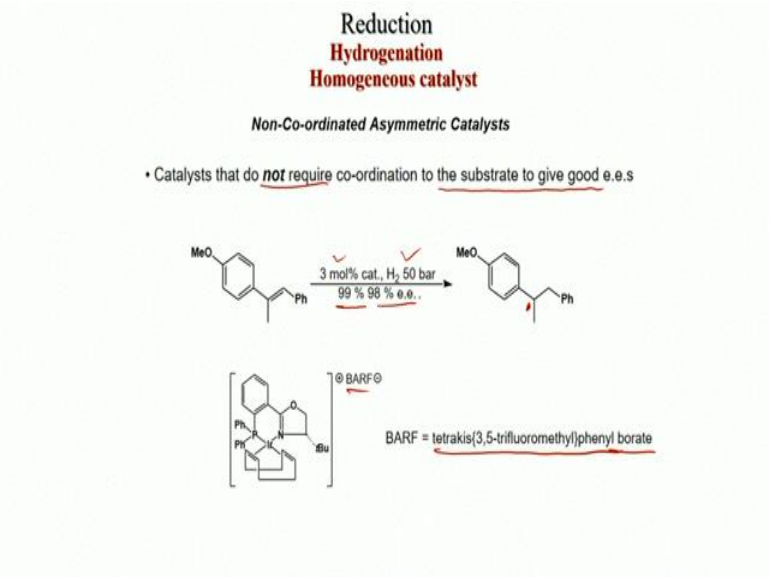

Non-coordinated asymmetric catalysts also is possible, catalyst that do not require coordination of the substrate to give good ees, like this catalyst. The iridium based catalyst with BARF tetrakis 3,5 trifluoromethyl phenyl borate. And if this catalyst does not bind exactly with the olefin but you get high enantioselectivity there is a chiral centre here, with only 3 mole percent catalyst, 50 bar hydrogen you get 99 percent yield and 98 percent enantioselectivity for this product.

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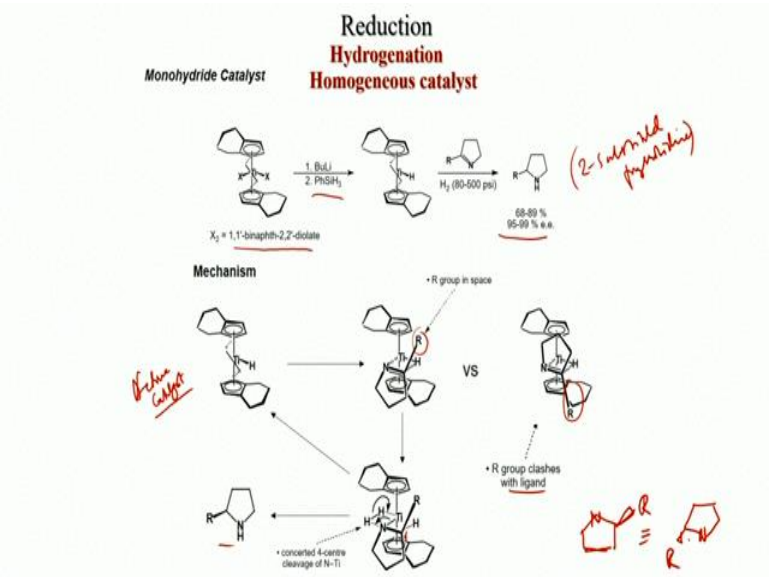

And this is an example of monohydrate catalyst, X2 is 1,1 binaphthyl 2,2-diolates. So this is binaphthyl ligand is there, with butyllithium and silane, you get this is the active one. And now this is the two substituted Pyrrolidine. This is an imine and now two substituted

pyrrolidine is forming in good yield as well as good enantioselectivity. So what is the mechanism of this reaction? So this is the active catalyst after this phenylsilane and butyllithium.

And now this substrate is binding to this, here you can see 4 member ring is forming and this is more stable because R is outside and in this case R is down, where the, it is finding a steric repulsion with the ligand and this is the stable. Then the hydride confirmed the down face and you get the chiral centre here. Now again another 4 member ring is forming here which cleaved under this condition. This N titanium bond is cleaved and you get this product. So actually from this you get. This is the product and this is same like this. So two substituted pyrethrin is forming.

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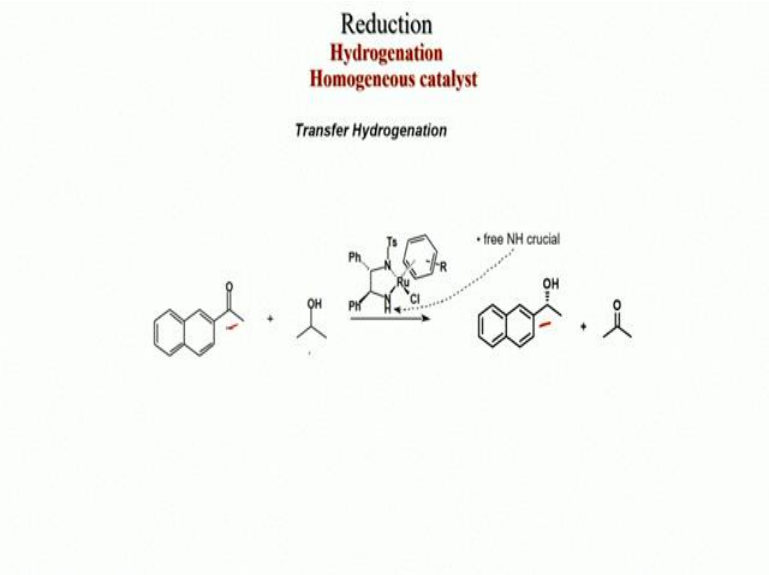

Transfer hydrogenation like MPV reduction is possible like this one, want to diphenidine diamine with ruthenium catalyst and you get this ketone, naphthyl containing ketone to get this chiral alcohol and isopropanol becomes acetone.

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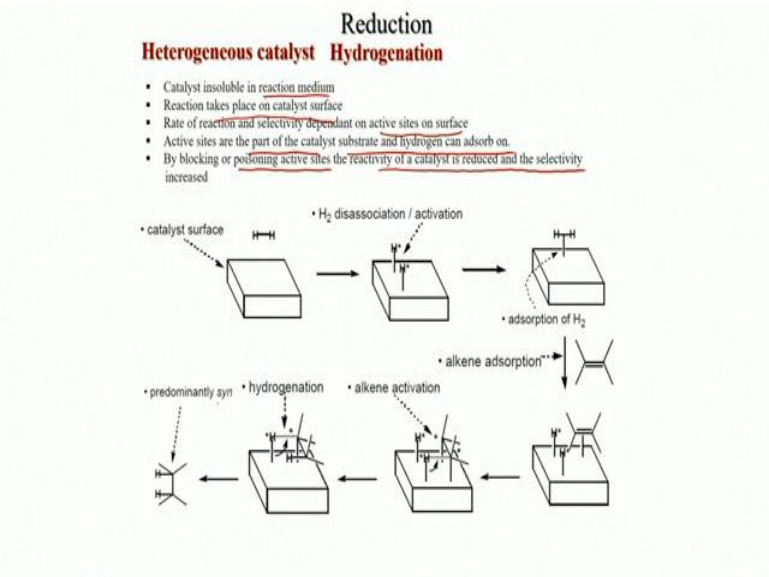

Now will discuss heterogeneous catalyst. In heterogeneous catalyst, catalyst is insoluble in reaction medium and a reaction takes place on catalyst surface. Rate of reaction and selectivity dependant on active sites on surface. Active sites are the part of the catalyst substrate and hydrogen can absorb on. By blocking or poisoning active sites the reactivity of the catalyst is reduced and the selectivity is increased.

This is the catalyst surface. Then hydrogen adds, hydrogen dissociation activation is happening here and now absorption of hydrogen, alkene absorption, then alkene activation is forming and then hydrogenation is giving the predominantly syn product.

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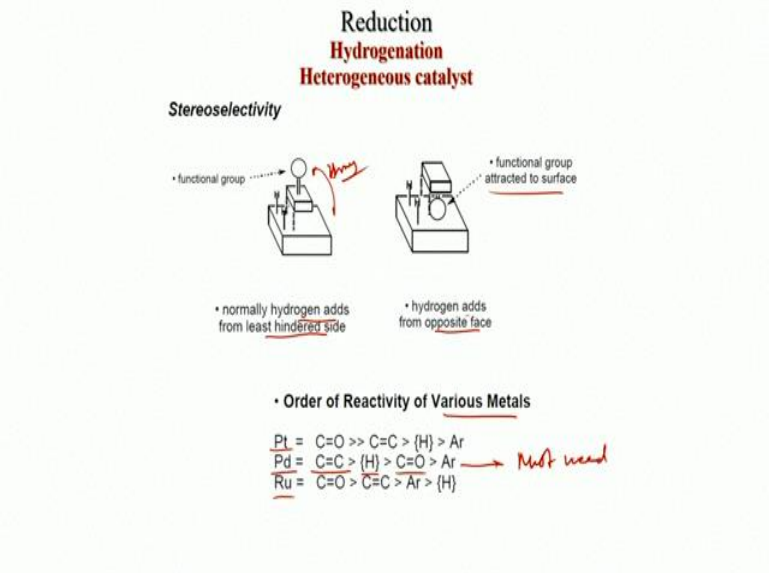

Stereoselectivity also possible if you have a functional group. Then, in case normally hydrogen adds from the least hindered side, and functional group away from the surface here and here functional group attracted to surface and in this case, hydrogen adds to from the opposite side. And this is the order of reactivity of various metals, platinum, palladium, ruthenium. Palladium, C=C, then alkene then carbonyl. So this is the most used.

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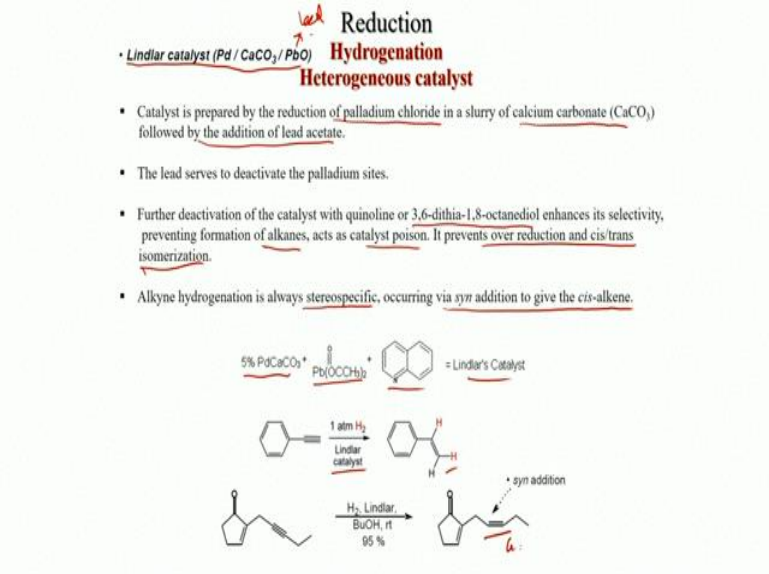

First will discuss lindlar catalyst, which palladium, calcium carbonate and lead. So this is lead oxide lead acetate is use, by reduction palladium chloride in a slurry of calcium carbonate followed by addition of lead acetate. The lead serves to deactivate the palladium sites. Further deactivation of the catalyst with quinoline or 3,6 dithia 1, 8 octanediol enhances its selectivity, preventing formation of alkanes, acts as catalyst poison. It prevents over reduction and cis/trans isomerization.

Alkyne hydrogenation is always stereospecific, occurring via syn addition to give the cis-alkene. This is the Lindlar catalyst 5 percent palladium, calcium carbonate lead acetate quinoline, this is the lindlar catalyst and this is very effective for syn addition, like here the alkyne phenyl acetylene goes to styrene to hydrogen come from the same side and here a triple bond is getting reduced with this condition raise to lindlars catalyst butanol, you get the cis olefin and this moiety is untouched.

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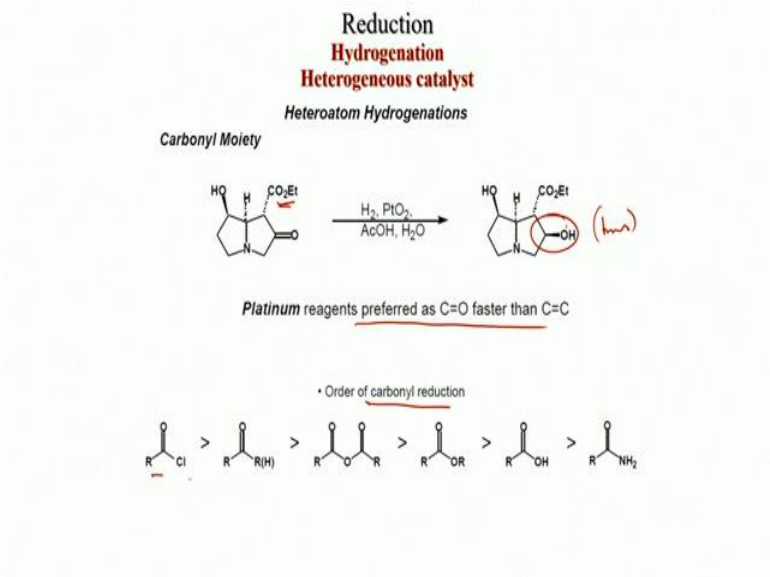

Carbonyl moiety can be also be reduced like these a hydroxy group is present and this is ester group and carbonyl groups reduce alcohol this is the trans with H2 palladium oxide acetic acid water, here platinum refers CO reduction faster than C=C and this is the carbonyl reduction , acid chloride ketone, anhydride ester, carboxylic acid amide.

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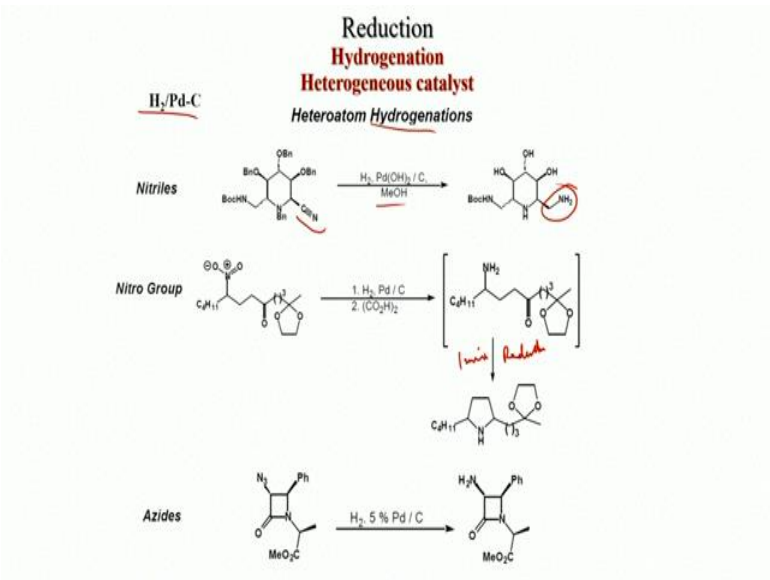

And H2 PDC also can do the hydrogenation, heteroatom hydrogenation, a nitriles getting reduced to amine with H2 palladium hydroxide charcoal, in methanol solvent. And then nitro group is getting reduced to the amine with this condition and which is cyclizing to get the imine and then reduce. So reduction is happening here, amine followed by reduction. Azides can also be reduced to amine.

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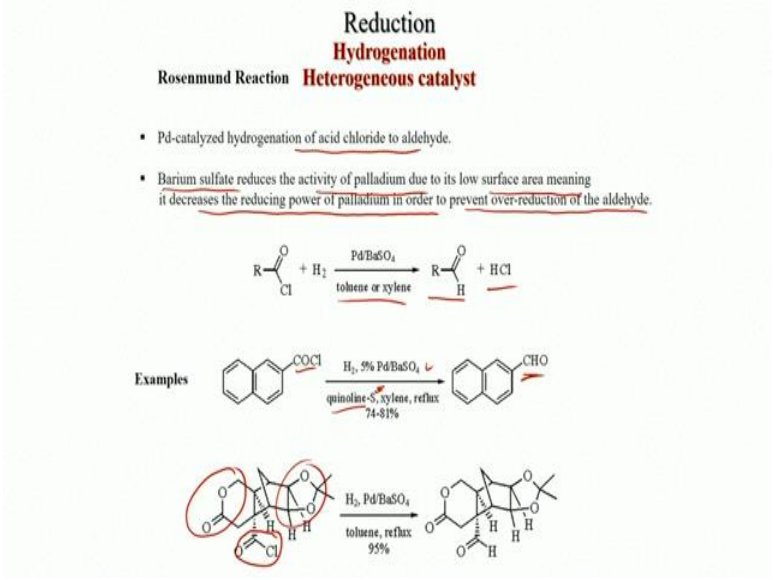

And then we discussed Rosenmund reaction. This is palladium catalyst hydrogenation of acid chloride to aldehyde. Barium sulphate reduces the activity of palladium due to its low service area meaning it decreases the reducing power of palladium in order to prevent over reduction of the aldehyde. R, Cl, hydrogen palladium BaSO4 toluene, xylene. It gives the aldehyde and HCl.

This is the example that a carbonyl provide is reducing to aldehyde with H2, 5 percent Palladium barium sulphate, quinoline-S that is the safety reason, xylene, reflux condition gives the aldehyde and here different groups are there, acid chloride, lactone and ketal is there, and with this condition selectively the acid chloride is reduced to the aldehyde.

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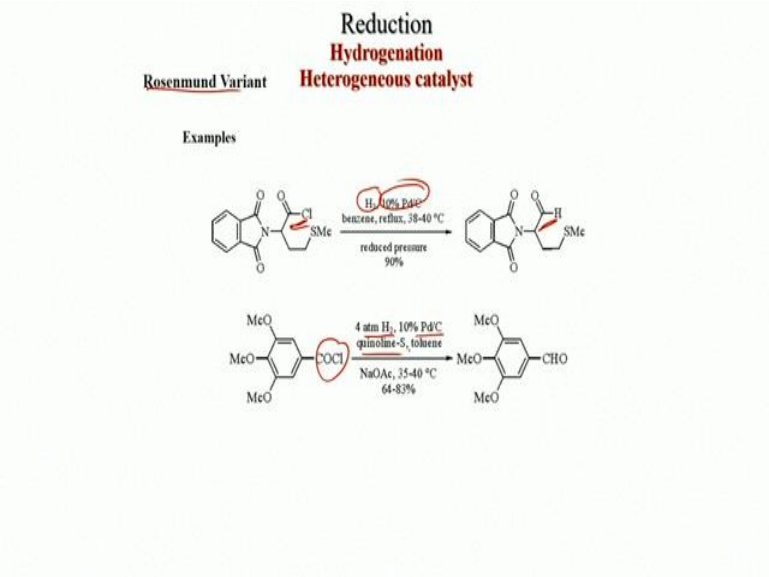

This are another examples of Rosenmund variant, here. Palladium charcoal is enough to do this reaction, with hydrogen you get the acid chloride to aldehyde. And here also acid chloride to hydride is possible. Hydrogen Palladium charcoal quinoline, toluene and sodium acetate.

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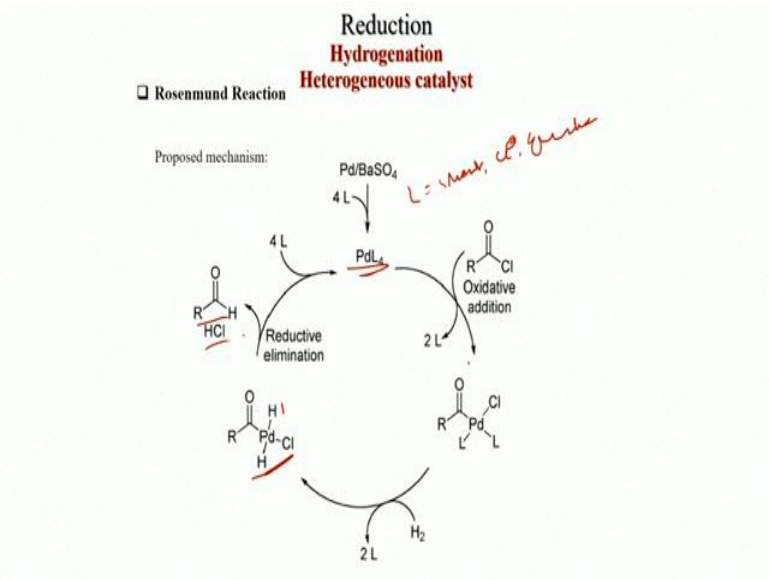

So what is a mechanism here? The ligand which is generally solvent, solvent or Cl minus quinoline. That is this species is generated than the oxidative addition is happening to generate this intermediate and now hydrogen adds to get this intermediate and after that reductive elimination is happening. So this two groups eliminate and you get aldehyde and HCl.

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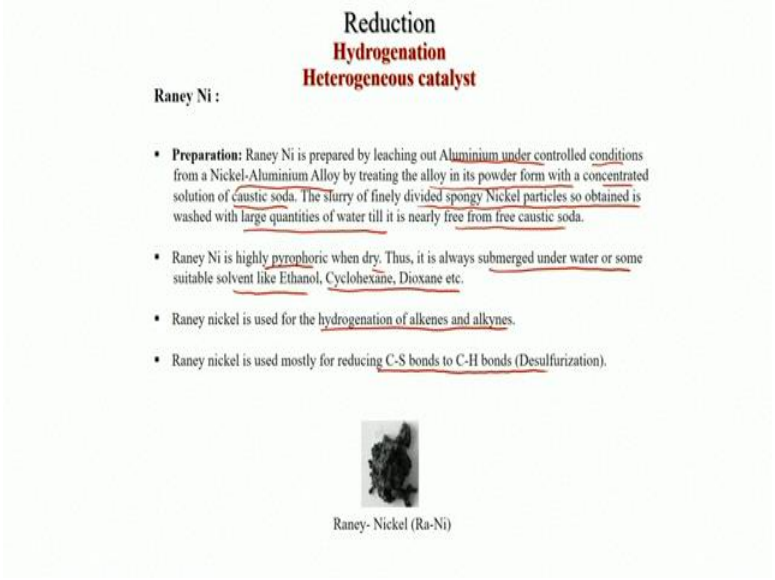

Raney nickel will discuss last. So Raney nickel is prepared by leaching out aluminium under controlled conditions from a nickel, aluminium alloy by treating the alloy in its powder with a concentrated solution of caustic soda. The slurry of finely divided spongy nickel particles, so obtained is washed with large quantities of water till it is nearly free from free caustic soda.

Raney nickel is highly pyrophoric when dry. Thus it is always submerged underwater or some solvent like Ethanol, Cyclohexane, Dioxane. Raney nickel is used for the hydrogenation of alkene and alkynes. Raney nickel is also used for reducing C-S bonds to C-H bonds, which is Desulfurization. This is the Raney nickel picture.

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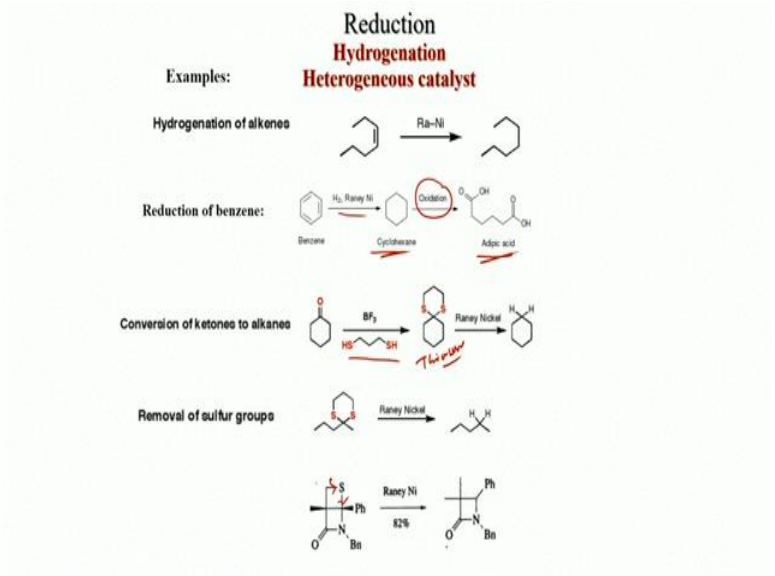

And examples here double bond is reduced, also benzene is reduced with hydrogenation Raney nickel cyclohexane, which an oxidation give the adipic acid. Conversion of ketones to alkenes is possible first that, keep thioketal formation is forming with thioketal with BF 3 and dithane. Then Raney nickel gives the cyclohexane here also Raney nickel removing this thioketal moiety and here these two bond, the sulfurization happening to get this lactam.

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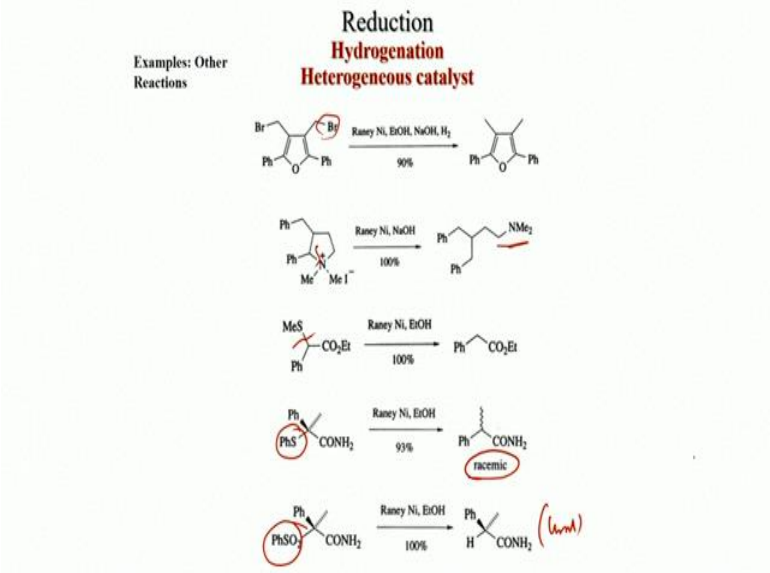

More examples, here the CH2 here is going to methyl group in Raney nickel, here, this bond is cleaved to get this amine. Here, this bond is cleaved with Raney nickel ethanol and interestingly here when it is liberated than it becomes racemic. However this sulphonate to SO2 Ph then you get a chiral. So this is chiral.

So today we have discussed first the MPV reduction and then hydrogenation with metal catalyst. We have seen homogeneous, heterogeneous catalysts and with homogeneous catalyst, there are certain advantage and we have seen first the Wilkinson reduction which a little bit less reactive. But different selective reduction can be done and also you have seen the steric enhance is very important for Wilkinson catalyst. So less sterically double bond is getting reduced.

And Crabtree catalyst, it is much more reactive than a. Here also tetrasubstituted olefins can be reduced and also the hydroxide deducted thus to selective reduction is possible. Then we have seen asymmetry hydrogenation, different ligand can be used, which is ligand catalyst based and diastereoselectivity and enantioselectivity reduction will be possible.

Then we have seen the lindlars catalyst, lindlars catalyst is very useful, here selective you can reduce the alkyne to cis olefin. Then we have seen the Rosenmund reaction, Rosenmund reaction is very good to reduce the carbonyl chloride to aldehyde group and lastly you have seen Raney nickel, Raney nickel is reduce mainly double bond also aromatic system like benzene and its main application in desulfurization reaction. Define tau thetas as well as disulfides moiety can be cleaved under this solution. Thank you.