Advanced Transition Metal Organometallic Chemistry
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Module - 12
Lecture - 58
Organometallic Catalysis Reactions: Asymmetric Hydrogenation of Alkenes

Welcome to this course on Advanced Transition Metal Organometallic Chemistry. As a part of our discussion on organometallic catalysis reaction, we have been discussing an important reaction which is asymmetric hydrogenation reaction. And in this context, we have discussed about the Noyori catalyst in the previous class.

And in that discussion, what we had observed that Noyori catalyst is very much similar to that of the Schrock-Osborn catalyst which is nothing but L 2 rhodium bis solvated cationic complex which, in which L is a chiral phosphene based chiral ligand. Rhodium and solvent is the solvent coordinated to the metal centre. And in that sense, Noyori's catalyst is also of the similar type L 2 means L being a chiral ligand chelating phosphene ligand, rhodium bound to 2 carboxylate moieties.

Now, what we had seen that in a Noyori catalyst is extremely good for enantioselective hydrogenation. And this chiral PPh 2 phosphorus bound PPh 2 moieties exert van der Waals interaction on the rhodium centre which in turns transmit the chirality onto the substrates which are bound to rhodium after displacing the carboxylate. And we had seen how a heteroatom assisted carbonyl compounds can be selectively hydrogenated to alcohol in a enantioselective fashion using this Noyori catalyst.

So, this was a wonderful demonstration of applications of Noyori catalyst. And what we had seen that, the chelation of the heteroatom, the distant chelation of the heteroatom along with the carbonyl moiety was very much important in being enantioselectively obtaining the hydrogenation product. Continuing our discussion further on the Noyori catalyst we are going to look of some more examples which sort of highlights why this Noyori catalyst is have been so much appreciated in the domain of asymmetric hydrogenation catalysis.

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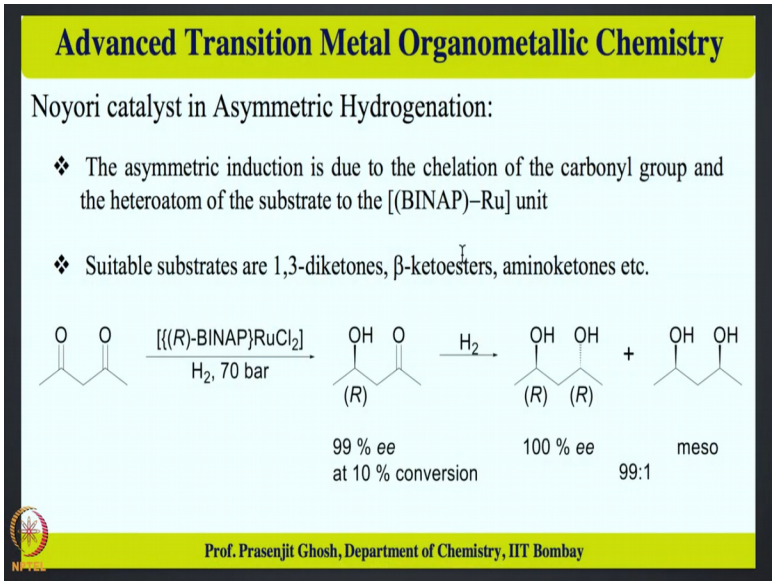

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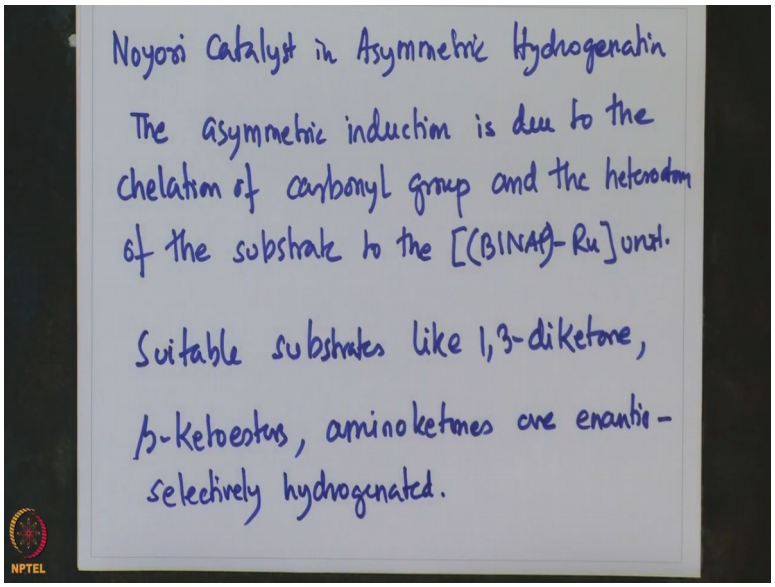

I must note that Noyori has been conferred the Nobel Prize for his work on this asymmetric hydrogenation catalysis. And that is why his catalyst are so famous and have been recognised duly by the scientific community. The asymmetric hydrogenation as observed in our previous discussion was due to this chelation of the distant heteroatom. And one can sort of extend the concept from a carbonyl with distant heteroatom to the substrates like diketones.

And there, one can see that the stereo induction arises due to chelation of the carbonyl groups. So, the main principle or the main success of the Noyori catalyst in asymmetric induction is due to the chelation of carbonyl group and the heteroatom of the substrate to the BINAP ruthenium unit. And substrates like 1 3 diketone, beta ketoesters or amino ketones are also enantioselectively hydrogenated.

Suitable substrates like 1 3 diketone, beta ketoesters, amino ketones are enantioselectively hydrogenated. So, this is beautifully illustrated by this equation given over here.

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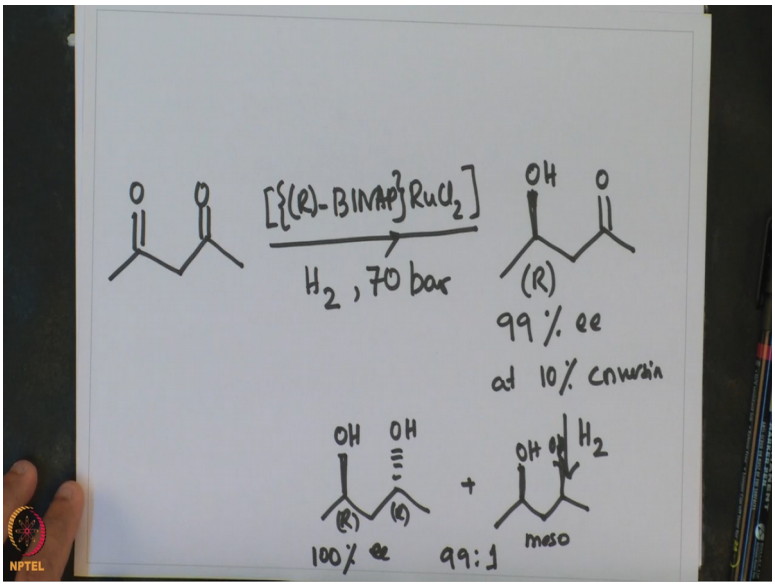

1 3 diketone reacting with R BINAP Ru Cl 2 in presence of hydrogen 70 bar gives alcohol R 99% ee at 10% conversion. And which, if allowed to react more with hydrogen then; so, the first obviously is the reduction of the diketone to alcohol and a ketone. So, one of the group that reduce the other chelates, but if one continues with the hydrogenation, then both the carbonyl compounds are reduced to alcohol.

And the stereo chemistry of the alcohol is R R 100% ee. And little bit of the meso product like OH, OH. And the ratio of this R R 2 meso is 99:1. So, one can really appreciate, or the power of this Noyori catalyst in terms of achieving this enantioselectivity. So, you know the, using this concept of chelation of carbonyl, the group getting reduced with one of a distant heteroatom can be successfully used for the diketones the diketoester substrates, where the first one of the carbonyl compound is reduced in high selectivity, about 99% ee.

And then, subsequent treatment with hydrogen reduces both the carbonyl giving the RR product in 100% ee. And about 99 to 1 selective product selectivity towards the RR compound as opposed to the meso compound. So, one can sort of appreciate the power of these the diketone Noyori catalyst on diketone substrates. So, Noyori catalyst can also be used on used to produce beta hydorxo carboxylic ester.

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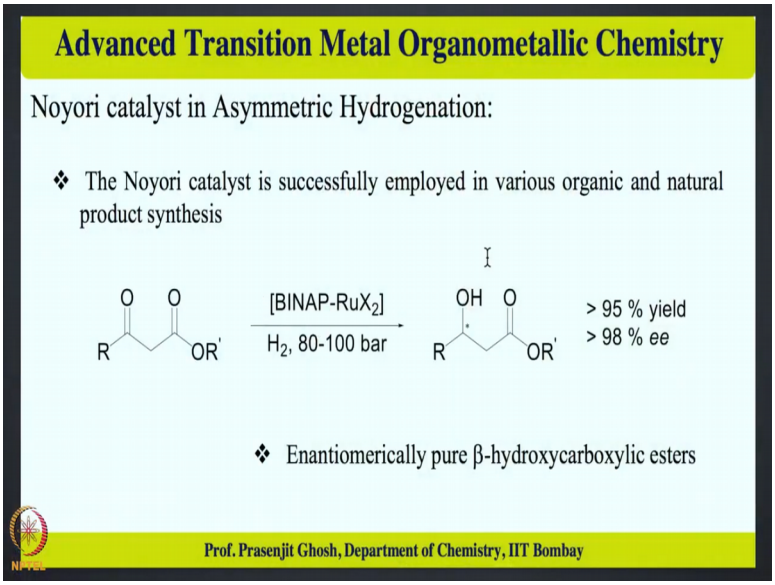

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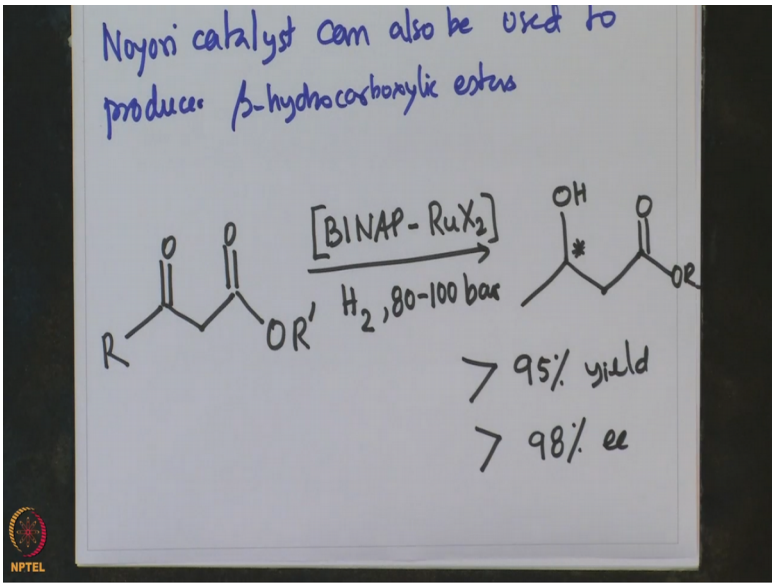

So, Noyori catalyst can also be used to produce beta hydroxo carboxylic esters which are important as intermediates towards very organic and natural products. And this is beautifully illustrated by this beta ketoester substrates which is OR dashed and R, BINAP, Ru X 2, H 2, 80 to 100 bar giving O, R, OH, star. And the yield is over 95% and selectivity over 98%.

So, one can see this chelation concept of a heteroatom chelation bound in distant to the carbonyl being so effective in using Noyori catalyst for producing alpha hydroxo carboxylic esters of which are important components of many natural products. Now, this chelation can also be used to do an enantioselective catalysis with halides.

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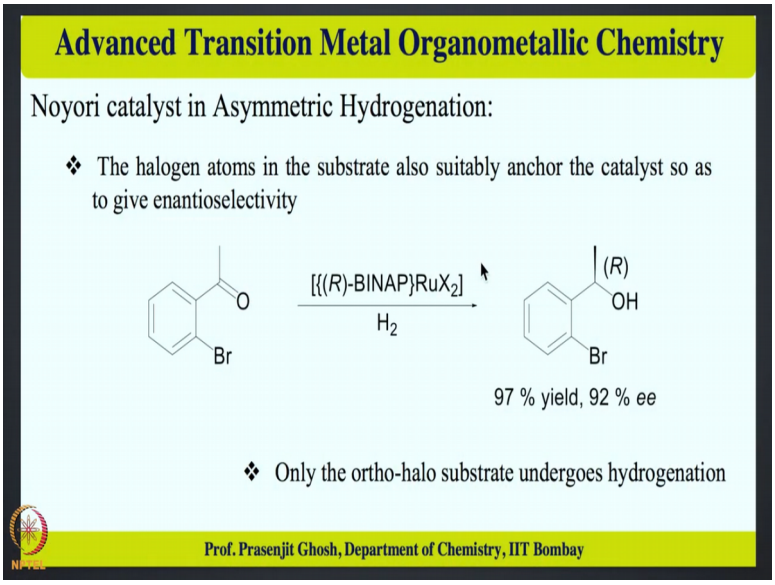

So, halogen atoms in substrate can also suitably anchor the catalyst through chelation to give high enantioselectivity.

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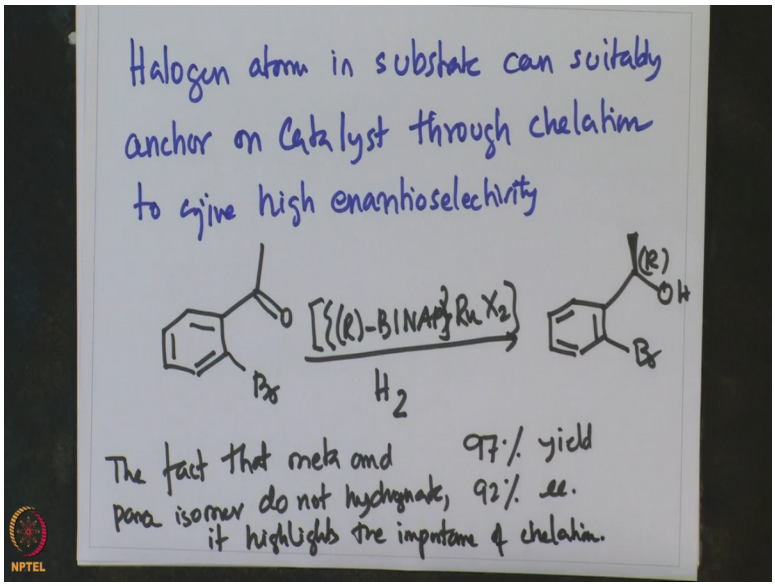

In substrate, can suitably anchor on catalyst through chelation to give high enantioselectivity. And this is beautifully illustrated by the example, bromo, R BINAP ruthenium X 2 + hydrogen, bromide, OH, R. So, 97% yield and 92% ee. Now, the fact that only ortho-halo substrate undergoes hydrogenation and the para and the meta does not give hydrogenation; that sort of underscores that the importance of chelation in being able to hydrogenate.

The fact that meta and para isomers do not hydrogenate; it highlights the importance of chelation. So, this is a important point in explaining the high enantioselectivity observed in case of Noyori catalyst that this hetero, there is, there has to be a heteroatom bound chelation

distant to the carbonyl moiety which results in higher chirality transfer leading to higher enantioselectivity.

So, in substrates where such chelation is not possible; for example, the ortho and the meta and the para substrates. Such kind of hydrogenation does not proceed at all, which further highlights the importance of chelation in hydrogenation reaction. Now, asymmetric hydrogenation with other catalyst has also been used for synthesis of many natural product. For example, have been successfully used in the synthesis of anti-inflammatory S naproxen.

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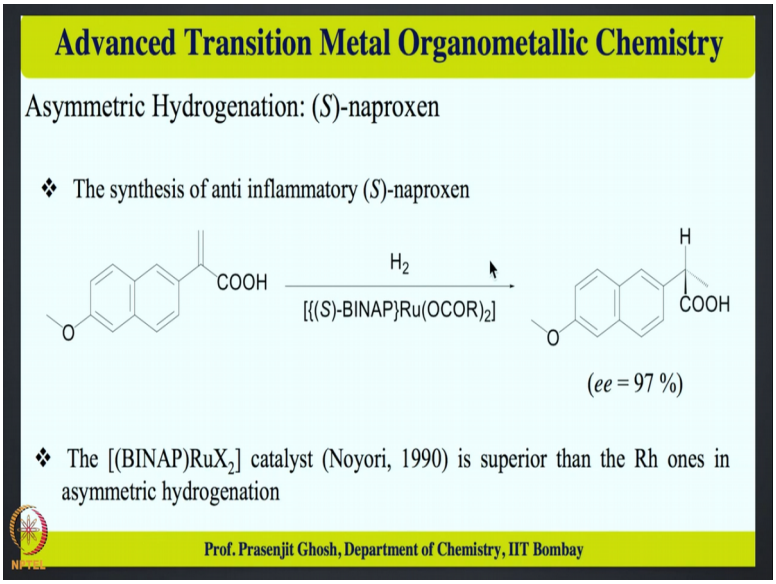

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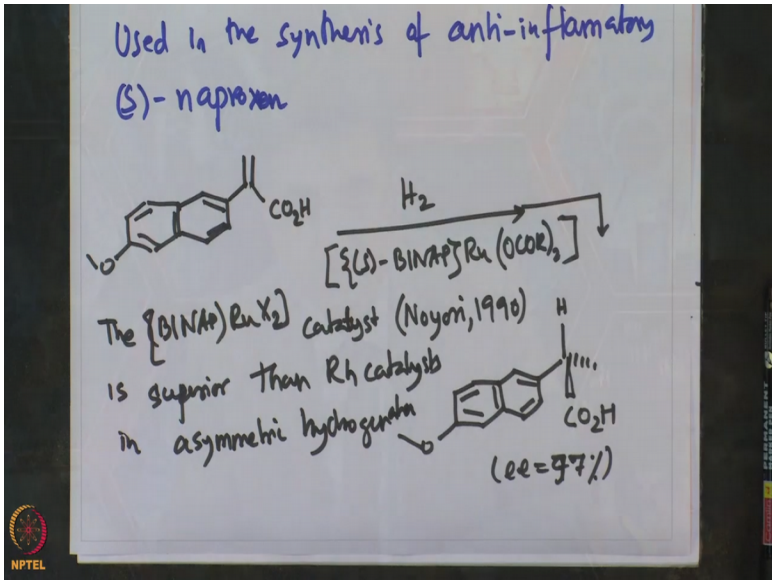

And this is given as CO 2 H, H 2, S BINAP ruthenium R 2 giving O methyl CH 3, CO 2 H; ee is extremely high, 97%. And 1 interesting thing about Noyori catalyst is that Noyori

catalyst is even superior to rhodium catalyst in hydrogenation, asymmetric hydrogenation reaction. So, this is an important aspect of Noyori catalyst. The BINAP ruthenium X 2 catalyst Noyori 1990 is superior than rhodium catalyst in asymmetric hydrogenation.

So, this is a important information, as here we have a catalyst which is based on ruthenium. And usually the rhodium is more catalytic active as it is called a magic metal. But here, we have a ruthenium catalyst in form of Noyori catalyst performing better. Then this rhodium based asymmetric hydrogenation reaction. So, another interesting way is the enantioselectivity through carbonyl coordination. And we are going to take a look at this example individually.

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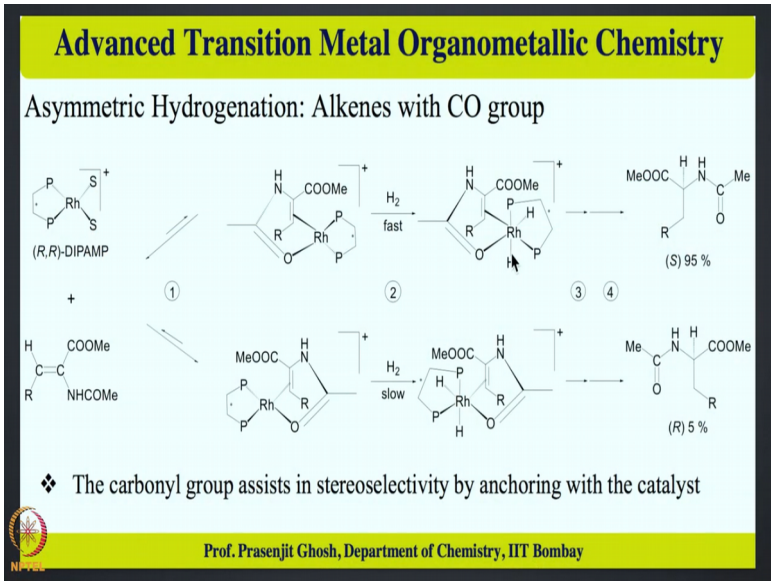

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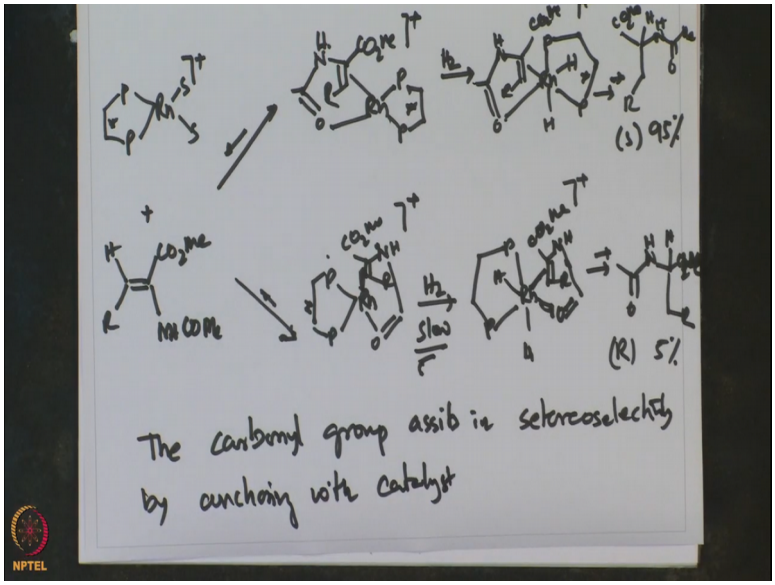

So, through steps. So, we have a chiral ancillary rhodium, the chiral catalyst + the substrate hydrogen R, NH CO Me, you know. That can react in 2 pathways. So, in which this substrate binds in 1 particular way which is N H, R, CO 2 Me, rhodium, P, P, star + H 2. So, now the hydrogen comes and gives the same N, H, R, CO, rhodium, hydride, hydride, phosphorus, prosperous and then CO 2 Me, overall +.

So, that in many steps gives CO 2 Me, hydrogen, R, NH, CO, Me. Now, the other pathway is shown over here in which the olefin binds in a the different way as is shown, rhodium, NH, R CO 2 Me bound to rhodium; overall it is a +. Adding hydrogen, but in a slow fashion for this particular enantiomer giving rhodium hydride, phosphene, hydrogen, O, NH, R, CO 2 Me and this rhodium is bound to that.

This is still monionic. And then, after several steps, one can see the formation of ketone NH H, CO 2 Me and R. So, what we see, the configuration over here is S 95%. The configuration over here R is 5%. And this hydrogen addition is slow. So, this is how the stereo differentiation occurs in this complex. The carbonyl group assist in stereo selectivity by anchoring with catalyst.

So, what we see that this Noyori catalyst is successful because of its ability to carry out face facial discrimination. And that is why it can carry out enantioselectively all this asymmetric catalysis reaction. So, here is another nice example on asymmetric catalysis reaction that we had be talking about;

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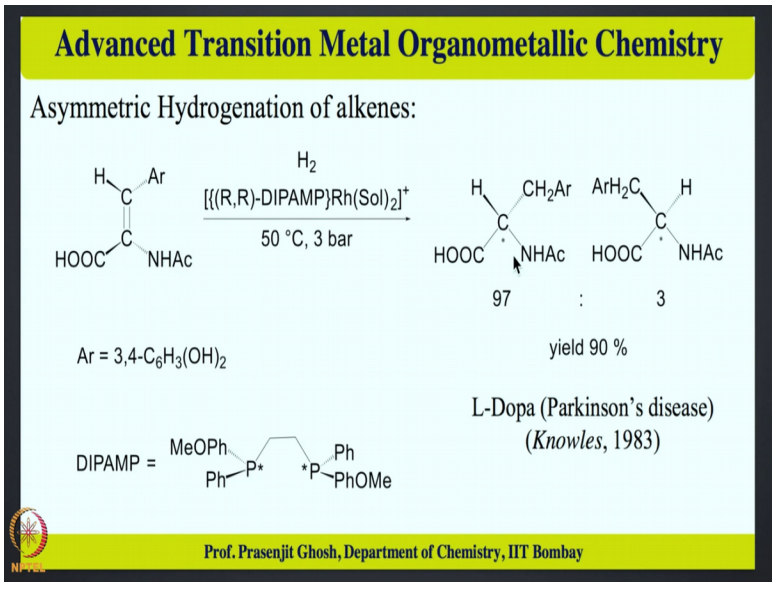

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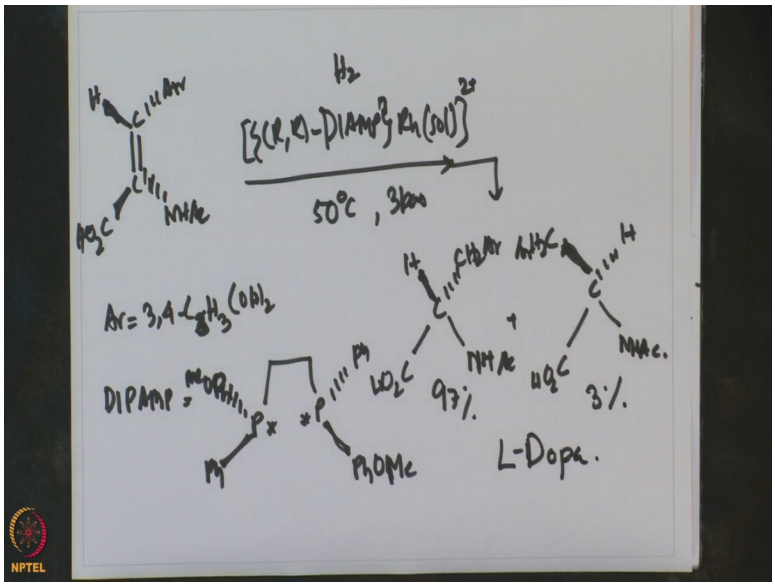

Is Ar, hydrogen, C, NH, AC, C, O 2 H. Ar = 3 4 C 3 C 6 H 3 OH whole 2. DIP AMP = O Ph O Me, phosphorous, Ph. This is a chiral entity. P, this phosphorus is also chiral; Ph, Ph O Me. So, this is the DIAMP ligand. And this is used for preparation of L-Dopa which is R R DIAMP rhodium Sol 2 + 50 degree centigrade 3 bar in presence of hydrogen, gives a highly 2 isomers in highly enantiopure form; CH 2 Ar, N H Ac, C O 2 H and H.

This is 97% and the other isomer thus is C, H, C H 2 Ar, C O 2 H, NHAC. And this is formed in 3% yield. And this is a useful method for preparations of L-Dopa. So, with this, I would like to conclude our discussion on asymmetric hydrogenation reaction. And what we have looked at is the reason behind the tremendous success of asymmetric hydrogenation reaction in regard to chirality transfer.

And what we had observed is that there is a chelation of a distant heteroatom bound to the hydrogenation moiety which can be a carbonyl, which allows for such enantioselective discremination towards 1 product over the other. Now, we had also looked at the substrates which will have such a ability to form such a type of chelation in terms of enantioselective discrimination.

And we found that substrates like diketones (()) (29:56) betaketoesters, all can be enantioselectively hydrogenated with Noyori's catalyst to give the corresponding hydrogenated product. We have also seen alpha bromo acetoxybenzene can also give such a hydrogenated product. Then, that primarily is because of the presence of the bromo moiety on

the benzene atom or bromine having lone pairs which can chelate to the metal complex or anchor to the metal complex and help in enantioselective reaction.

So, with this, I conclude today's discussion on asymmetric hydrogenation reaction. And we are going to take up another very interesting discovery in the next form, next lab which is this hydroformylation reaction. That also is a important reaction from industrial perspective. So, more on hydroformylation reaction when we make, meet next in the class.

I sincerely thank you for your time and attention that you have given to me for and for being with me in this class. And I look forward to take to being with you in the next class while we take up hydrogenation in lot more detail. So, till then, goodbye and thank you.