Advanced Transition Metal Chemistry
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Lecture - 44
Oxidative Addition and Reductive Elimination Reactions

Hello everyone. Once again welcome you all to MSB lecture series on transition metal chemistry. Now since couple of last lectures we have been discussing about the oxidative addition and reductive elimination reactions. Let me continue from where I had stopped in my previous lecture. So, I showed you how C-H bond can be activated and how C-C bond can be activated and what are the difficulties we come across.

Now let us look into another important method of addition of substance molecules that means here we are considering polar molecules. When we consider polar molecules having a electronegative atom, how it follows a pathway that is different from the neutral molecules we considered. So, neutral molecules, I showed you C-H, I showed you H_2 and even SiH bond addition and similarly one can also think of B-H bonds.

Now let us look into the second mechanism that is followed by polar molecules that is called nucleophilic oxidative addition. So, at the end of this one you will be knowing why we call this one as nucleophilic oxidative addition.

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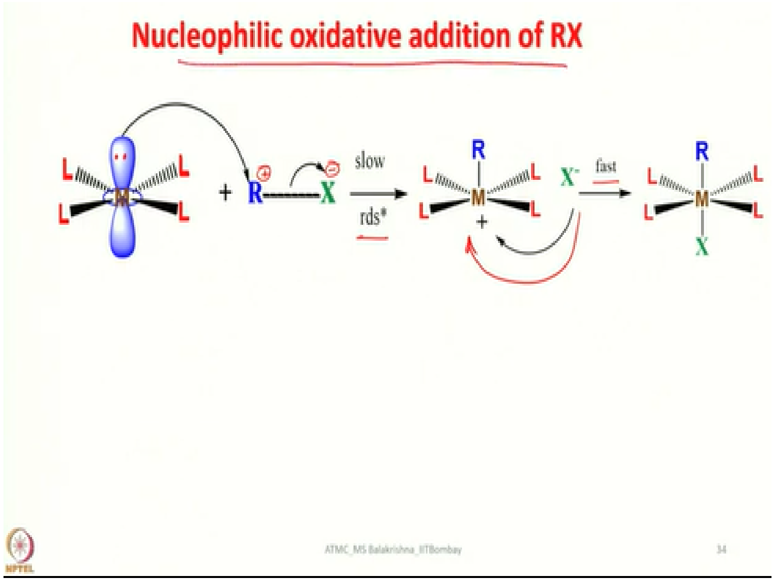
Nucleophilic oxidative addition of RX

So, here if you see I am considering a square planar complex and R—X bond is polarized. When it is polarized, what we have is R^+ and X^- and addition of R—X to the square planar complex is a slow step and also this is a rate determining step here. So, in this what would happen is now once bond is polarized. So, electron density moves and it becomes X^-, and then it becomes R^+.

When it is R^+ it attacks here we have this d_z^2 with two electrons. Now this attacks this one and generates a five coordinated species and now you can see here we have a positive charge. We have an empty orbital because the electrons are already given from metal to generate M—R bond, now you can see, this is an anionic ligand. So, oxidization is halfway through now.

So, now basically what happens this one attacks this position here and then the reaction is completed in the next step. So, that means this nucleophile is attacking here. Because of this one it is called nucleophilic oxidative addition reaction. So, this is the path followed by most of the polar molecules. So, how to assess this reaction, for example what are the factors that contribute to the rate of this reaction.

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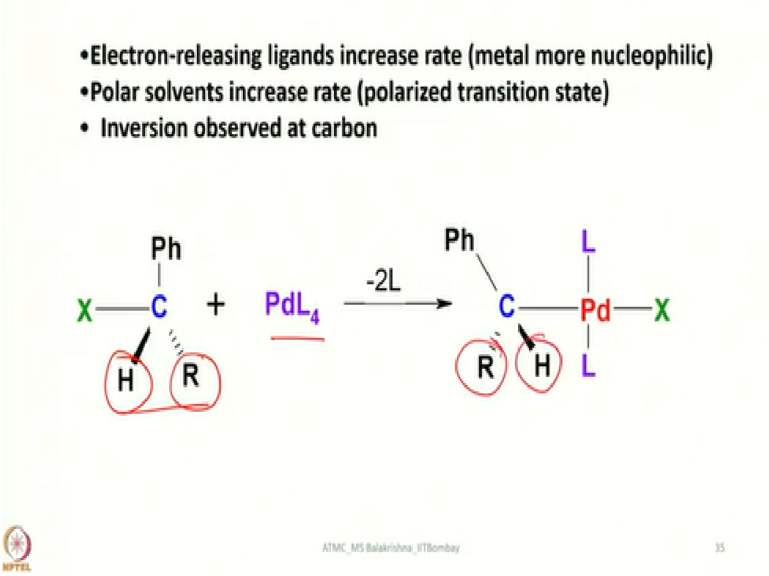

- Electron-releasing ligands increase rate (metal more nucleophilic)
- Polar solvents increase rate (polarized transition state)
- Inversion observed at carbon

So, electron releasing ligands that means electron rich metals which are in a position to readily lose a couple of electrons that means metal should be more nucleophilic in order to make it more nucleophilic. So, polar solvents, if you use, increases the rate because polarized transition state is there and inversion is observed at carbon, these three things are important. So, electron rich matter that is true in case of previous concerted addition also.

And then polar solvents should be used and then if you take a chiral molecule inversion is observed at carbon. You can see from this one, we are taking chiral compound here and you should focus here and now since it is added in a trans manner. So, this is how the addition takes place here. So, as a result what happens? The configuration is changed, so that means, inversion happens. If any substrate molecule is added which is chiral in nature, what happens?

In the oxidatively added product, inversion can be observed. So, now the third one radical pathways.

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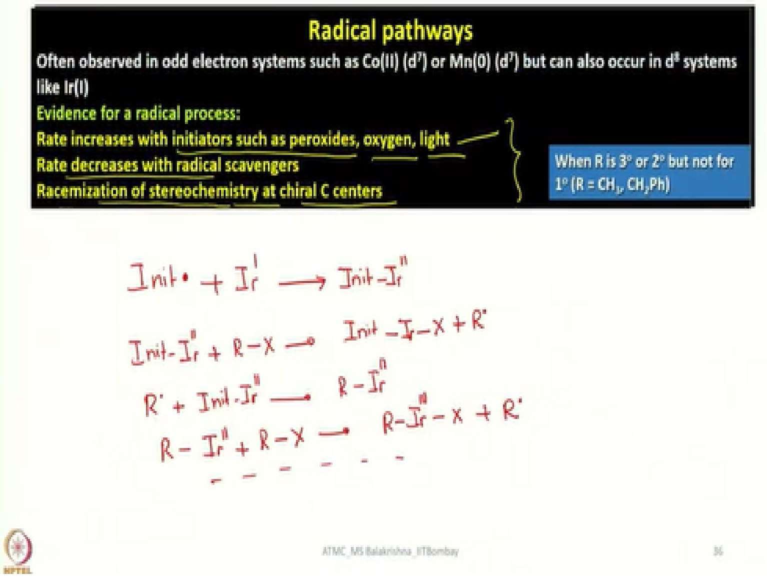

Radical pathways

Often observed in odd electron systems such as Co(II) (d^7) or Mn(0) (d^7) but can also occur in d^8 systems like Ir(I)

Evidence for a radical process:

Rate increases with initiators such as peroxides, oxygen, light

Rate decreases with radical scavengers

Racemization of stereochemistry at chiral C centers

When R is 3° or 2° but not for 1° (R = CH_3, CH_2Ph)

$$Init^{\bullet} + Ir^{I} \longrightarrow Init{-}Ir^{II}$$

$$Init{-}Ir^{II} + R{-}X \longrightarrow Init{-}Ir{-}X + R^{\bullet}$$

$$R^{\bullet} + Init{-}Ir^{II} \longrightarrow R{-}Ir^{II}$$

$$R{-}Ir^{II} + R{-}X \longrightarrow R{-}Ir^{III}{-}X + R^{\bullet}$$

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Radical pathways is always followed by metals where we have odd electron systems such as cobalt (II) a d^7 system or manganese(0) a d^7 system exclusively follow radical pathway mechanism. It does not mean that other electronic configurations having even number of electrons do not fall, it is not true. Even a d^8 system can also follow sometime radical pathways. So, that means only thing is we should assess to know whether a radical pathway is followed or a concerted method is followed or nucleophilic oxidative addition method is followed of course distinguishing between concentrated addition and nucleophilic addition would be very easy.

Because the moment we look into substrate molecule we can tell whether it is a polar molecule or non-polar molecule. If it is polar yes, it is it follows nucleophilic oxidative addition, if it is non-polar, it follows concerted method. So, that means between radical and nucleophilic addition we have to follow certain tests.

That means, if the reaction shows ambiguity about the pathway that is followed, we have to do the following experiments. What we have to see is we have to see whether the rate increases with initiators such as peroxides oxygen or light. And in case if we add radical scavengers, then the rate should decrease and of course if the reaction follows radical pathway, we can exclusively see racemization of stereochemistry at chiral carbon centre.

If we consider any chiral carbon substrate then there will be a racemization. So, these three would tell us about the path followed by a particular polar molecule. So, then what are the steps that are involved in a typical radical process? Let us look into it. Initially we have to use an initiator I, Init and then this interacts with iridium, d^8 system, to begin with, we have a plus one species, in the next step it interacts with substrate molecule RX and generates a radical.

And this radical reacts with iridium(II) to form Ir(III) species. Now a radical is coming to Ir(II) species. And now iridium(II) species further reacts with another molecule to have plus so it continues. So, these are the few steps that are followed and they are very similar to a typical radical reaction we come across in inorganic chemistry. When R is tertiary or secondary, but not for primary.

So, you should remember this radical pathway is favoured for or a tertiary carbon or secondary carbon but not for a primary carbon that means if you have CH_3CH_2X, no.

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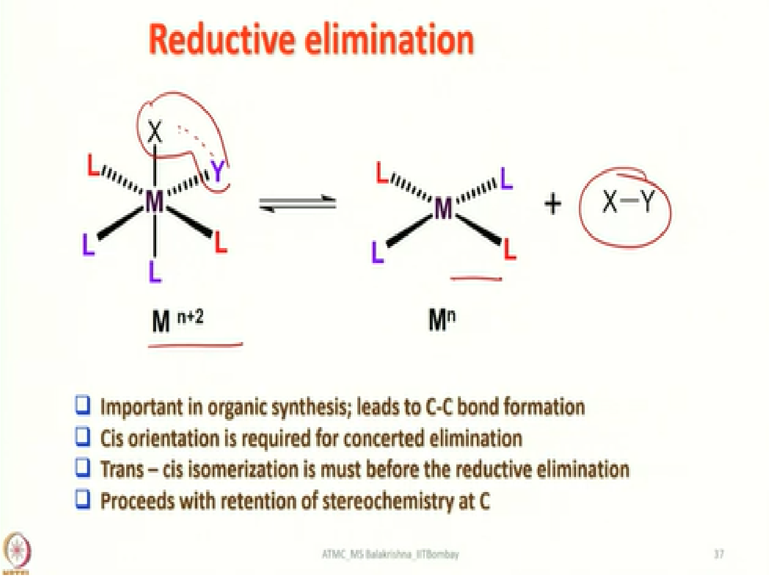

Reductive elimination

- ☐ Important in organic synthesis; leads to C-C bond formation
- ☐ Cis orientation is required for concerted elimination
- ☐ Trans – cis isomerization is must before the reductive elimination
- ☐ Proceeds with retention of stereochemistry at C

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Now let us look into the reductive elimination. So, far we discussed about oxidative addition and two type of oxidative addition we saw. Now let us look into the reductive elimination. So, this is a typical reductive elimination process. To begin with we have n+2 state and six coordination is there, and it may be 18 electron species. Now after reductive elimination what happens?

So, slowly, these two entities are brought close to each other, they start interacting and a bond is established and then eventually this will be eliminated. And then now it gains two electrons and also it loses two ligands. So, coordination number decreases, oxidation state decreases and we get back the starting compound, prior to the oxidative addition, what we had, this one.

And if the rate at which oxidative addition happens and reductive elimination also happens then we can say this called microscopic reversibility. For example, if XY is added and if the XY is eliminated and the rate in both the cases are very similar, then it is called microscopic reversibility. Because this is exactly opposite of oxidative addition reaction. This reductive elimination is very important in organic synthesis.

Especially when we are doing cross coupling reactions, cis orientation is required for concerted elimination, cis orientation. The two leaving groups should be cis to each other on a metal centre and this is because whether it follows initially concerted addition or nucleophilic addition reductive elimination is always a three bond concerted process. As a result, cis orientation is very important. In case, due to some reason, if we get a trans position, two moieties that are supposed to be get eliminated should find a way to undergo isomerization.

So, that trans to cis isomerization happens prior to reductive elimination and always proceeds with retention of stereochemistry at carbon. Only in case of nucleophilic oxidative addition, inversion takes place and then whatever the configuration we have at the end of reductive elimination, configuration is retained. Let us look into the stereo chemistry of reductive elimination here.

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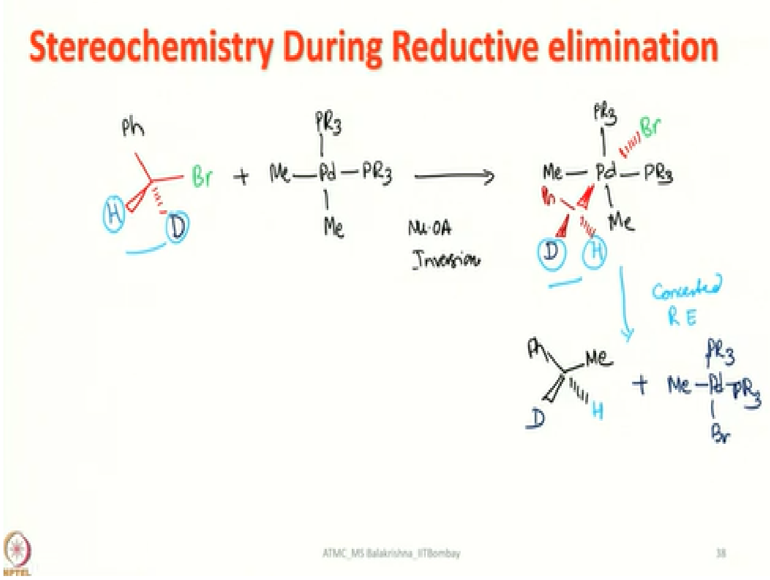

Stereochemistry During Reductive elimination

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So, a chiral compound is chosen along with a metal having two methyl groups and two tertiary phosphines. So, here palladium is in +2 state. So, here nucleophilic oxidative addition has taken place. So, inversion has happened already. So, now you should remember this is polar. So, nucleophilic oxidation means they will be added to the trans positions. What we have here is bromide so now oxidative addition is completed.

Now we are talking about concerted reductive elimination. So, now it should not change, already you can see the configuration has changed now configuration has changed. Inversion has already happened now; this inversion is retained in the next step, that is, during concerted reductive elimination. What we get is, methyl group is coming here, H will be here and D will be here, and of course plus what we get is, you can see here.

So, that means during reductive elimination, retention one can see, if you are using chiral molecule.

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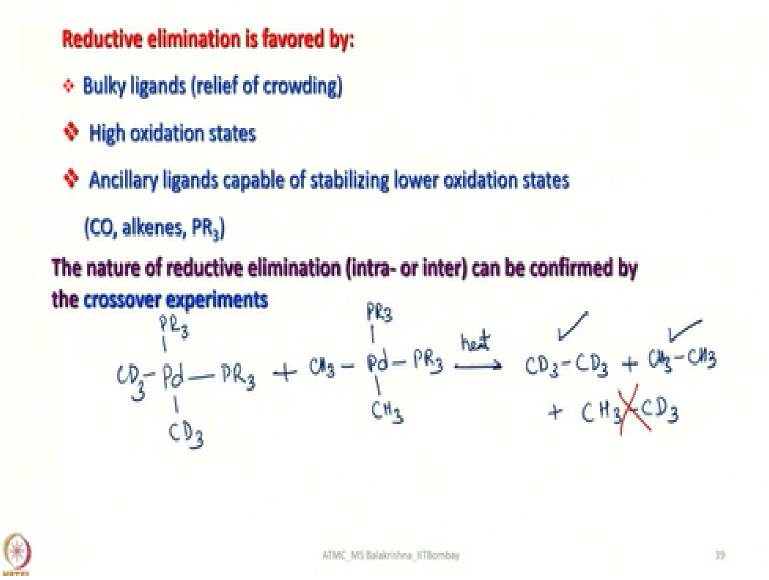

Reductive elimination is favored by:

- Bulky ligands (relief of crowding)
- High oxidation states
- Ancillary ligands capable of stabilizing lower oxidation states (CO, alkenes, PR_3)

The nature of reductive elimination (intra- or inter) can be confirmed by the crossover experiments

$$CD_3-\underset{CD_3}{\overset{PR_3}{Pd}}-PR_3 + CH_3-\underset{CH_3}{\overset{PR_3}{Pd}}-PR_3 \xrightarrow{heat} \overset{\checkmark}{CD_3-CD_3} + \overset{\checkmark}{CH_3-CH_3} + \cancel{CH_3-CD_3}$$

Under what circumstances one can perform reductive elimination very easily, can be seen here. If you have bulky ligands, due to the steric crowding, what happens reductive elimination will be very facile and of course if the metal is in higher oxidation state, it will try to get reduced, as a result again reductive elimination will be very facile, and besides these things, what is important is, what kind of ancillary ligands, we are using on the metal.

So, called silent spectator ligands or ancillary ligands, they have a role very, important role. So, that means ancillary ligands capable of stabilizing lower oxidation states is what important that means we should have ligands which are non-classical in nature. That means we should have ligands which are capable of functioning as sigma donors as well as pi acceptors. You should remember when the reductive elimination happens metal will be coordinatively unsaturated and then more electrons will be there.

In that case, what happens, there can be interelectronic repulsion that will try to destabilize the metal. In that case what happens we should have sufficient ligands having back bonding capacity. So, that they can release some of the repulsion by taking electrons to their appropriate back bonding orbitals. In that context, carbon monoxide, alkenes and a variety of phosphines play an important role. So, this is about reductive elimination.

And then the nature of reductive elimination can be again assessed whether it is intra reductive elimination or intermolecular reductive elimination through some crossover experiments. What happens? For example, if C-C bond formation is there, not necessarily both the carbon atoms should come from the same metal in cis fashion or they can come from two adjacent metal atoms also. That means although we know, we have to confirm from further experiments.

For that one, what we call it as cross over experiments, are ideal and how to perform this crossover experiment. Let me show you, let us consider two species. Again, I am considering this tertiary phosphine having two methyl groups deuterated and another case it is simple methyl groups. So, what we will do is we will take a 1:1 mixture of these two complexes and heat it.

When we heat it, let us not worry about what happens to the metal centre, let us look into what kind of organic products we can get from this reaction. Three possibilities are there, one is CD_3 coupling to give deuterated ethane, another one is simple ethane and third possibility is CH_3CD_3. So, when we analyse the products obtained in this reaction, we can account for this one, we can account for this one, but this would be missing.

So, that indicates if this is missing means the process the reductive elimination has proceeded via intramolecular process not intermolecular. So, that information comes if it is inter, then they would have very nicely combined, so that product is not obtained. So, this is called crossover experiment. In many other reactions also one can think of this kind of experiment to consolidate our claim about the type of product formed in a particular reaction.

So, now let us look into bimolecular reactions and of course already I discussed in the beginning a few bimolecular reactions.

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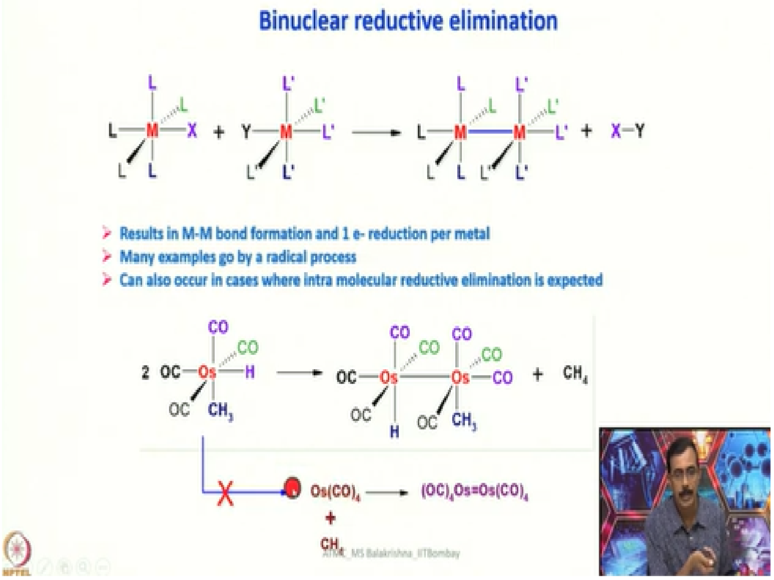

Binuclear reductive elimination

- Results in M-M bond formation and 1 e- reduction per metal
- Many examples go by a radical process
- Can also occur in cases where intra molecular reductive elimination is expected

A typical bimolecular reaction I have shown here. So, metals which do not have two accessible oxidation states with a difference of two electrons possibly. On the other hand, if they have two accessible oxidation states with a difference of one electron for example copper(I), copper(II), cobalt(II), cobalt(III), iron(II), iron(III), in such cases one can anticipate binuclear reductive elimination. How that happens?

For example, you take a molecule like this where we have a substrate X is there and another one, we have a substrate Y is there and what we are doing is reductive elimination. So, in this process, through the establishment of a metal-metal bond they will come close to each other and X—Y is eliminated. This is a typical binuclear reductive elimination and of course if we take this molecule and add this one, we can get these two species that is by nuclear oxidative addition.

That I had already showed you in one of the previous lectures. So, this is how one can imagine a binuclear reactive elimination that is happening with species where we have metals which have a difference of one electron having two accessible oxidation states. So, results in M-M bond formation and this is one electron reduction per metal. And of course, these kind of binuclear species, unless these substrate molecules are capable of cleaving this, M-M bond to add oxidatively, you cannot use it in catalysis.

As I mentioned, if the species is capable of splitting this one reversibly then only, we can use a binocular process. Of course, there are quite a bit of metal complexes used in catalysis which follow binuclear reaction mechanism. So, this results in a new M-M bond formation and this is one electron reduction per metal. Many examples go by radical process. In these things as I mentioned, where one electron process is there most of them follow radical mechanism and intra molecular reductive elimination is expected.

So, that means, in some cases where intra molecular reductive elimination is expected also can follow binuclear method. So, for example, if you consider this one here, let us take two such species having H and CH_3 here like this and as I mentioned they can form something like this and methane can be eliminated. And of course, here it does not follow this mechanism to give this complex.

So, that means basically, what you can see is if this is formed one can think that yes, it is following a binuclear radical mechanism. Otherwise, what happens we would have ended up with osmium tetracarbonyl complex. So, that means this shows that it follows binuclear method.

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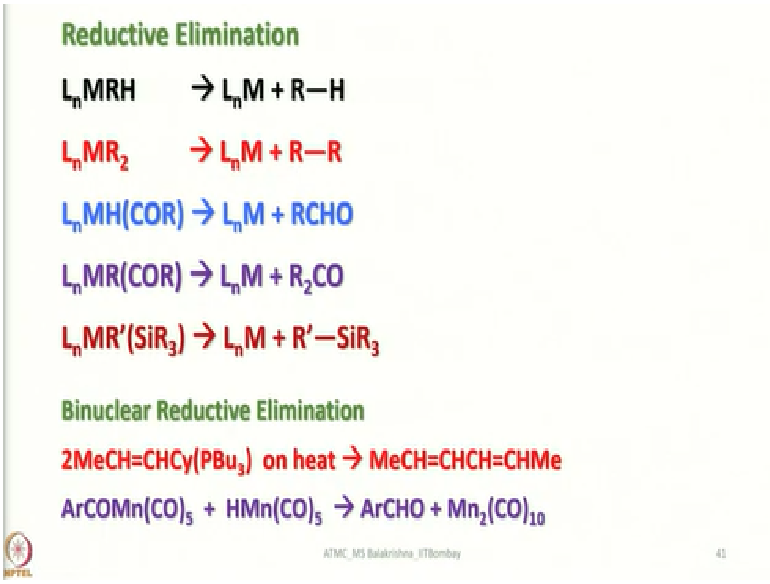

Reductive Elimination

$L_nMRH \rightarrow L_nM + R{-}H$

$L_nMR_2 \rightarrow L_nM + R{-}R$

$L_nMH(COR) \rightarrow L_nM + RCHO$

$L_nMR(COR) \rightarrow L_nM + R_2CO$

$L_nMR'(SiR_3) \rightarrow L_nM + R'{-}SiR_3$

Binuclear Reductive Elimination

$2MeCH{=}CHCy(PBu_3)$ on heat $\rightarrow MeCH{=}CHCH{=}CHMe$

$ArCOMn(CO)_5 + HMn(CO)_5 \rightarrow ArCHO + Mn_2(CO)_{10}$

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And what are the types of reductive elimination we come across. You can see here RH, CH coupling can be seen and CC coupling can be seen and again here CH coupling can be seen and here CC coupling can be seen and here you can see carbon to silicon bond formation can be seen.

And by nuclear reductive elimination for example you take this molecule here so take this molecule on heating it can generate a species something like this.

If you take a manganese compound like this with benzoyl group ArCO and with combining with another metal hydride you can see this is a typical binuclear reductive process. In this one you can see this species is coming out through the formation of $Mn_2(CO)_{10}$. Let me show you couple of more reactions here to make you familiar with this oscillatory additional elimination process.

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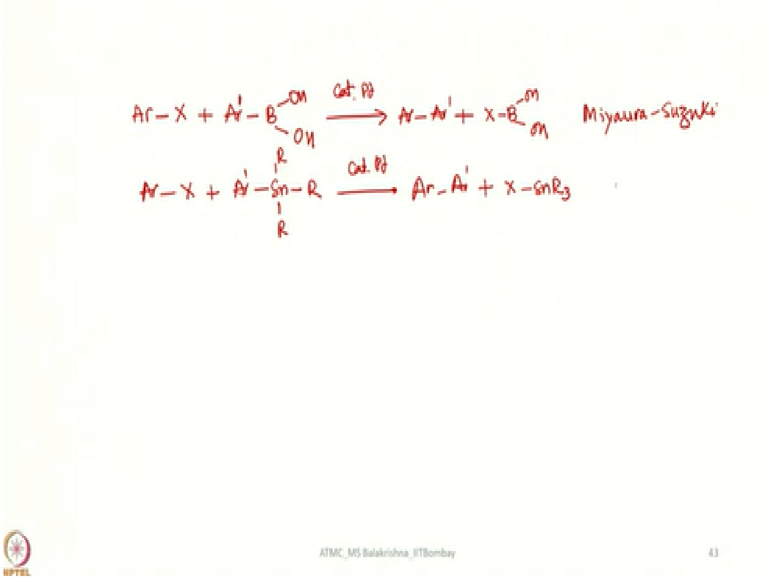


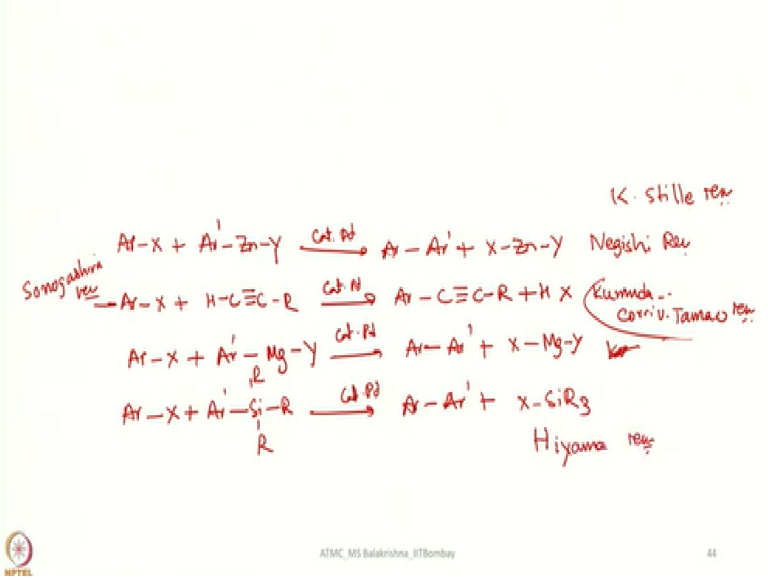
$$Ar{-}X + Ar'{-}B(OH)_2 \xrightarrow{\text{Cat. Pd}} Ar{-}Ar' + X{-}B(OH)_2$$

$$Ar{-}X + Ar'{-}SnR_3 \xrightarrow{\text{Cat. Pd}} Ar{-}Ar' + X{-}SnR_3$$

Let us consider this $Na_2[Fe(CO)_4]$. On several locations when question is asked whether this molecule can undergo oxidative addition or not. This can undergo oxidative addition despite, it is an 18-electron species, but I also showed you enough examples, where an 18 electron species undergoes oxidative addition reaction. So, for example you take this one and treat with halide, alkyl halide or aryl halide, it forms in this fashion, this can undergo oxidative addition.

And of course, here Fe was in -2 state and here if you see a Fe is in zero state. So, one electron is given one electron is taken here so zero state. And here it was 18 electron here also it is 18 electron species. Let us try to see catalytically important reactions, of course, catalyst is needed, the moment I write these two substrate molecules and reagent, you know what kind of reaction this is.

So, this is called Miyaura Suzuki coupling reaction. And if you take again Ar-X and add a tin species again of course in all these reactions without saying it goes that we are using a typical palladium complex or something this is Stille a reaction. **(Refer Slide Time: 24:39)**



K. Stille rex

$$Ar{-}X + Ar'{-}Zn{-}Y \xrightarrow{Cat.\,Pd} Ar{-}Ar' + X{-}Zn{-}Y$$ Negishi Rex

Sonogashira rex

$$Ar{-}X + H{-}C{\equiv}C{-}R \xrightarrow{Cat.\,Pd} Ar{-}C{\equiv}C{-}R + HX$$

Kumada.. Corriu. Tamao rex

$$Ar{-}X + Ar'{-}Mg{-}Y \xrightarrow{Cat.\,Pd} Ar{-}Ar' + X{-}Mg{-}Y$$

$$Ar{-}X + Ar'{-}SiR_3 \xrightarrow{Cat.\,Pd} Ar{-}Ar' + X{-}SiR_3$$

Hiyama rex

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This is called Negishi reaction and of course you are familiar with this reaction as well. I would say reaction of an alkyl halide with an alkyne, catalyst is there even if I do not write you understand that you assume that there is a catalyst. This is called Sonogashira reaction, it is always good to write all the names of discoverers involved in this one. It is not right to say simply Suzuki reaction, we should tell always Miyaura-Suzuki reaction and also a Heck reaction, i.e. Mizoroki-Heck reaction. Couple of other reactions I would write quickly.

So, reaction of an alkyl halide with Grignard reagent. This is called Kumuda reaction. This is addition of an alkyl halide to acetylene and in the last one in the series I am going to write Hiyama reaction. We are using a silyl reagent called Hiyama. So, I think whatever I have discussed so far under these two topics oxidative addition, reductive elimination would be enough to get some clear idea and understanding of these two reactions.

Of course, one can always go to text books to see similar reactions to understand in a better way at some point of time, if you want to do some catalysis. This is an ideal beginning to learn these things. With this let me stop the discussion. In my next lecture I should start discussion on another important topic inorganic reaction mechanism. So, until then have an excellent time reading chemistry, thank you for your kind attention.