Introduction to Organometallic Chemistry
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Lecture - 19
Reductive Elimination Mechanism

Today, we will discuss reductive elimination, which is the simple reaction. It is the inverse of oxidative addition. So, during oxidative addition, we had an increase in the coordination number. The number of ligands coordinate it to the metal will also had a change in the oxidation state, which increased by 2 units or 1 unit. On the other hand, the reductive elimination involves the exact reverse of this particular reaction. So, it will involve a reduction in the oxidation number, the formal oxidation number of the metal.

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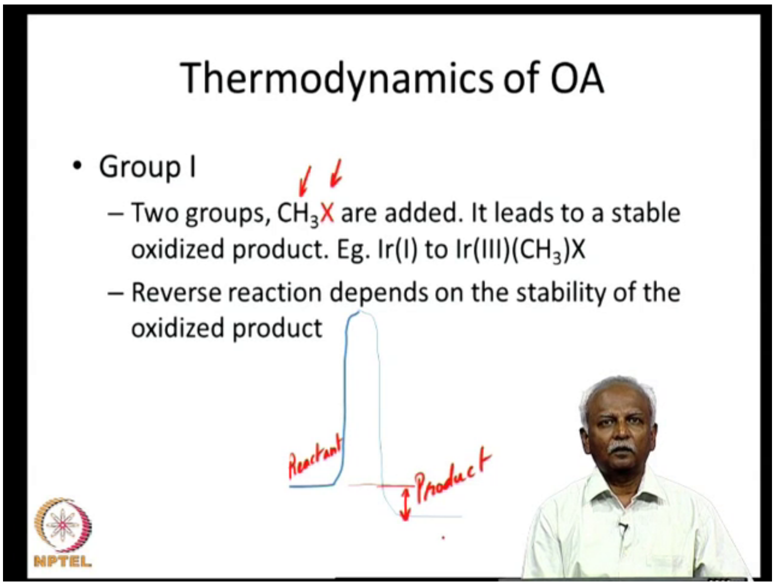

Thermodynamics of OA

- Group I
  - Two groups, CH_3X are added. It leads to a stable oxidized product. Eg. Ir(I) to Ir(III)(CH_3)X
  - Reverse reaction depends on the stability of the oxidized product

So, before we look at reductive elimination in detail, we should look at the thermodynamics of the oxidative addition. If you consider the 2 groups where oxidative addition happened, you will realise that group 1, you had the addition of 2 groups say CH3X. This is labelled in 2 different colours just to tell you that these are the 2 fragments, which are going to be added to the metal CH3 and X invariably ends up.

If 1 takes the example of iridium, it ends up in an increase in the coordination number by 2 and also in the oxidation state change of plus 2. So, the reverse reaction depends on the stability of the oxidised product. So, here, I have pictured an energy level diagram, where we have the reactants here, where the reactants and the product on this side. You will notice that there is a energy evacuation, but this reaction is exothermic by a certain amount.

The thermodynamic stability of the product will determine how exothermic this reaction is. If the reaction is very exothermic, we will have an extremely stable product. The reverse reaction that is the oxidative addition will become more difficult. So, when will this be more difficult or when will the oxidised product be more stable? In this particular example that I have given, I have added CH3 and X.

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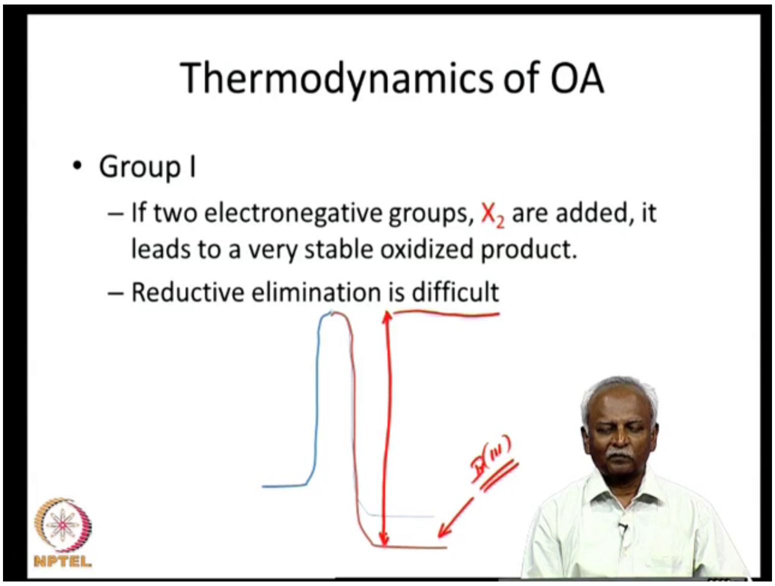

Thermodynamics of OA

- Group I
  - If two electronegative groups, X_2 are added, it leads to a very stable oxidized product.
  - Reductive elimination is difficult

Let us take another example where you have 2 more electronegative groups, say halogen is added to the metal. Then, the stability of the oxidised product is most. So, iridium 3 becomes more stable when you have 2 electronegative groups in the coordination sphere. So, the formal oxidation state of iridium as plus 3 becomes more stabilised when you have 2 electro negative groups. Then, reductive elimination is lot more difficult.

It is obvious from this energy level diagram that the energy of evacuation in this process is going to be greater. So, the energy of evacuation in this instance is going to be this large amount. So, this will become more difficult process compared to the reductive elimination of CH3X. So, this is just to illustrate the principles involved in the reductive elimination process. It is primarily dependent on how stable the oxidised product is. If the oxidation product is extremely stable, then reductive elimination will be a high energy process.

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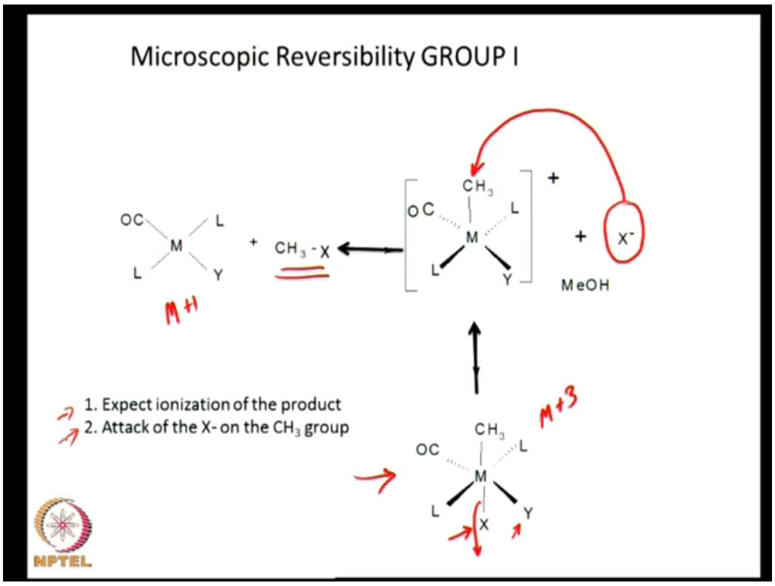

Microscopic Reversibility GROUP I

1. Expect ionization of the product
2. Attack of the X- on the CH_3 group

Let us now take the group 1 agenda. Let us try to explain how a reductive elimination might take place. The principle of microscopic reversibility suggests that if a reaction proceeds in a particular part, then the reverse reaction in this particular case, the reductive elimination part should involve, should retrace the steps which it took when it formed the oxidised product. So, we started with a metal in plus 1 oxidation state. We ended up in a metal in plus 3 oxidation state.

You will notice that the product, which is given here, if it has to lose 2 groups, can do so in a variety of ways. It can do so in a synchronous fashion, in a concerted fashion, but what happened in the oxidative addition was a step wise reaction. It was a s n 2 reaction between CH3 and X. So, in the reverse path, one can imagine loss of X. So, that is X here is lost from the coordination sphere of the metal. You form an ionised product.

So, X minus is formed. The metal complex positively charged metal complex is formed. So, this is basically an exit of this X. So, X has to be a good leaving group. You will immediately notice that there is a complication. Instead of X, there is the other group Y that can also leave. So, this group is Y that can also leave. So, let us take the next step. Now, X minus has to make an attack on CH3 in n s n 2 type of fashion. If it does that, CH3X will be formed. The original complex will be released. So, this is what is dictated by microscopic reversibility. So, you expect ionisation of the product. In the second step, you expect attack of X on the CH3 group.

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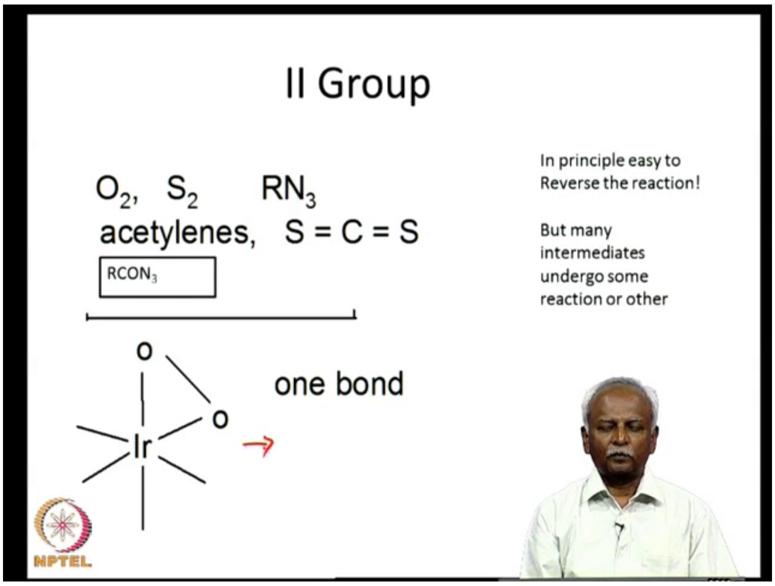

II Group

O_2, S_2 RN_3

acetylenes, S = C = S

$RCON_3$

one bond

In principle easy to Reverse the reaction!

But many intermediates undergo some reaction or other

So, if you take the second group of molecules, which carried out oxidative addition, you notice that there are some agenda like oxygen where 1 bond between the 2 atoms, which are adding on was retained. In fact, in group 2, all of them will retain 1 of the bonds. In the case of acetylene, there are 3 bonds. So, it will end up with a product, which had only 2 bonds.

But, invariably in the case of systems where you have an electro negative atom like oxygen, it is highly unlikely that the reverse reactions have been take place because the oxidised product will be extremely stable. It can undergo further reactions as in this particular instance. You have a di oxygen product, which will react with some other species and carry out a redox reaction of say the ligand or a substrate.

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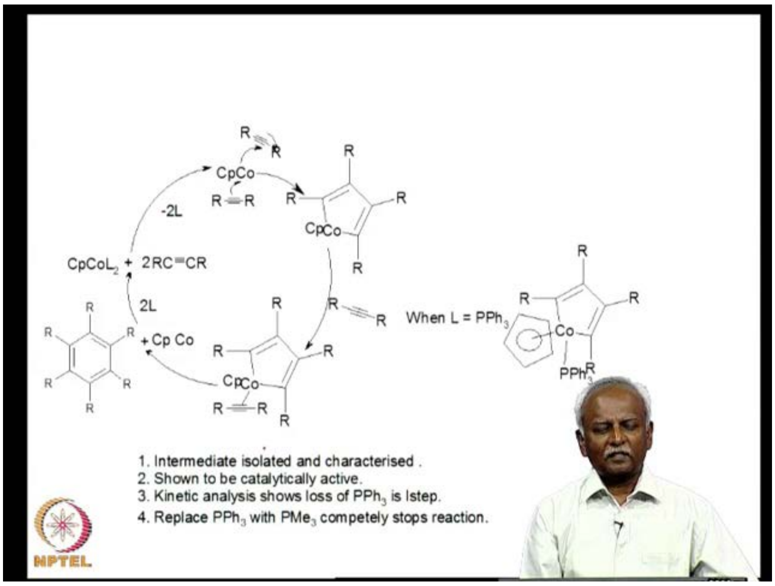

1. Intermediate isolated and characterised .
2. Shown to be catalytically active.
3. Kinetic analysis shows loss of PPh$_3$ is Istep.
4. Replace PPh$_3$ with PMe$_3$ competely stops reaction.

We also notice that in the case of acetylenes, you have after oxidative addition, which involved 2 acetylenes. For example, in the cyclic catalytic cycle that I have written here, you will have a second substrate coming in. So, you can do an insertion reaction and then eliminate say an arene. So, elimination of arene in the final step, which is indicated here, elimination of arene turns out to be a thermodynamically very favourable process. So, you take acetylenes and convert them into arenes after performing an oxidative addition. What we have achieved is oxidative addition with 1 substrate. Subsequently, through insertion reactions, we carried out the transformation of that substrate into a very different molecule, in this case, an arene.

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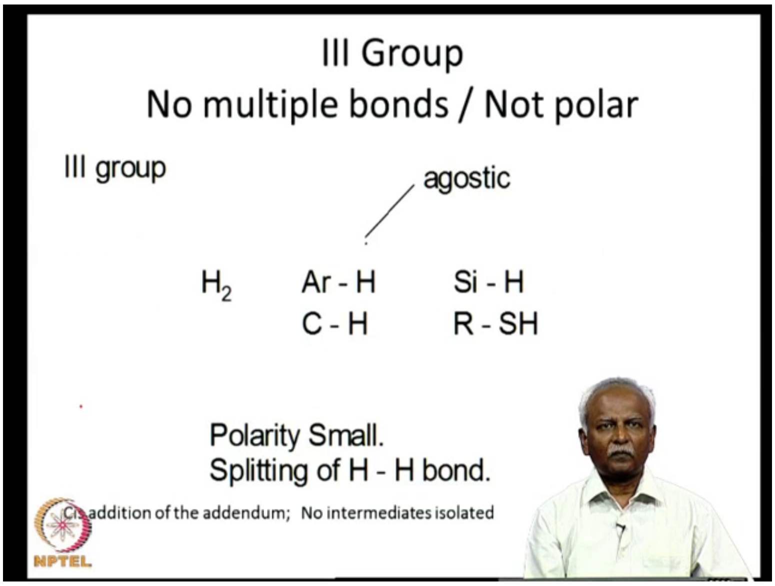

III Group

No multiple bonds / Not polar

III group

agostic

H_2 Ar - H Si - H

C - H R - SH

Polarity Small.

Splitting of H - H bond.

Cis addition of the addendum; No intermediates isolated

So, in the third group, we have no multiple bonds nor we have polar groups. In the first group, we had polar groups. In the second group, we had multiple bonds. Within the third group, we have neither polar group nor we have multiple bonds. This is typified by hydrogen or aromatic CH or Si H bond. Here, the polarity is typically very small. So, let us take a look at how these molecules will undergo reduction reaction.

If you remember what we said in the beginning of this lecture, if you have 2 electro negative substrates, oxidative addition becomes favourable. Here, we have substrates, which are not very electro negative. So, the redox, the reductive elimination or the reverse reaction would be an extremely facile process. In fact, it is very difficult to carry out oxidative addition in the substrates and the reverse reaction is always favourable.

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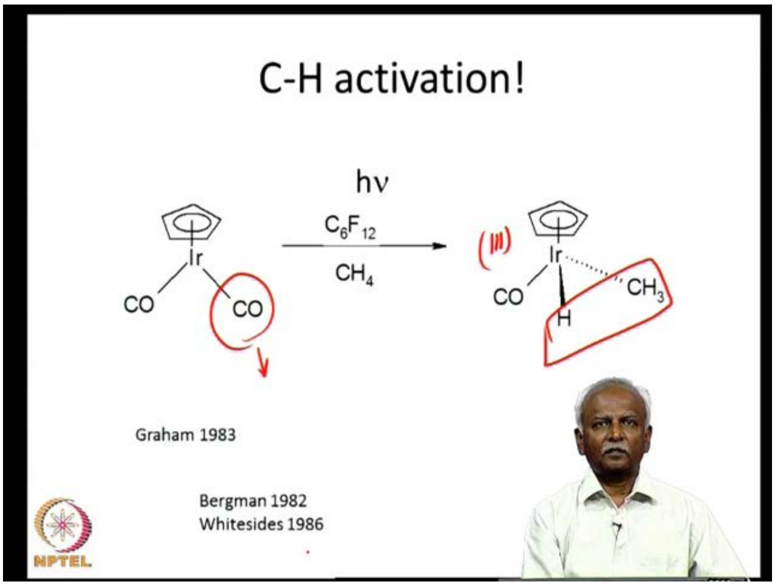

C-H activation!

Graham 1983

Bergman 1982
Whitesides 1986

For example, we took this case where you can photolyse a carbon monoxide complex. Photolysis leads to elimination of 1 carbon monoxide from the coordination sphere of the metal. It leads you iridium 1 species, which is coordinative unsaturated. Coordinative unsaturated species can add on methane. If it adds on methane such that hydrogen and methyl group are added to the iridium, you end up with an iridium 3 species.

So, this is an iridium 3 species and this oxidised product will readily undergo reductive elimination. In many cases, it will reductive eliminate the 2 agenda that it added on or 2 different species. That is what leads to useful reactions. If it just eliminates methane in this case just needs to reverse of the forward reaction, that is also reductive elimination, but it is not a productive reaction. Several examples are known. We had noticed this. In the beginning of 1980s, it started with a variety of CH activation reactions. Now, this has become fairly common, but it is still a particular challenge.

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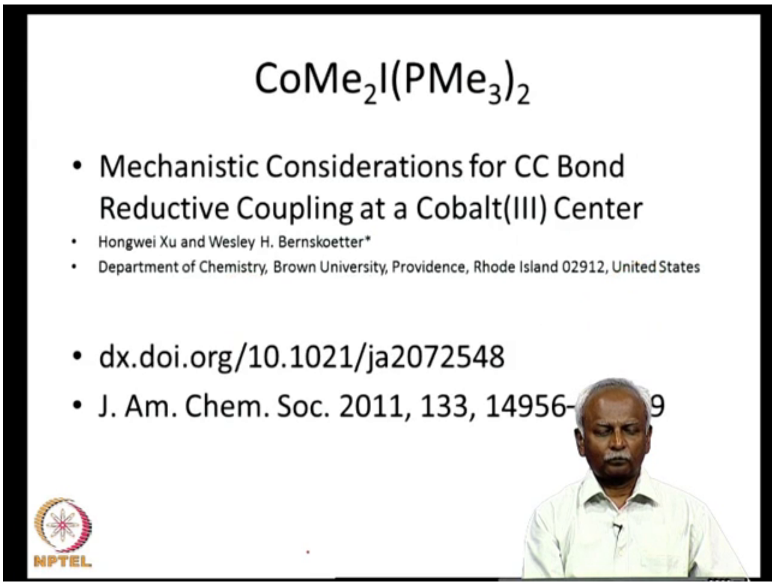

$CoMe_2I(PMe_3)_2$

- Mechanistic Considerations for CC Bond Reductive Coupling at a Cobalt(III) Center
  - Hongwei Xu and Wesley H. Bernskoetter*
  - Department of Chemistry, Brown University, Providence, Rhode Island 02912, United States
- dx.doi.org/10.1021/ja2072548
- J. Am. Chem. Soc. 2011, 133, 14956- 9

Today, we are going to talk about 2 or 3 different reductive elimination reactions. We will take some specific examples where these principles that we have dealt with can be discussed. The first example that I have taken is an example from the recent literature of 2011 where a cobalt 3 complex was synthesised. The synthesis itself was known for a long time. It is an old synthesis, but the reductive elimination was studied in detail. Some very important principles regarding reductive elimination could be obtained by looking at these reactions. So, the reference, the detailed references given here the d o i and the journal references given here for your information. You could read this paper in detail if you would like more information.

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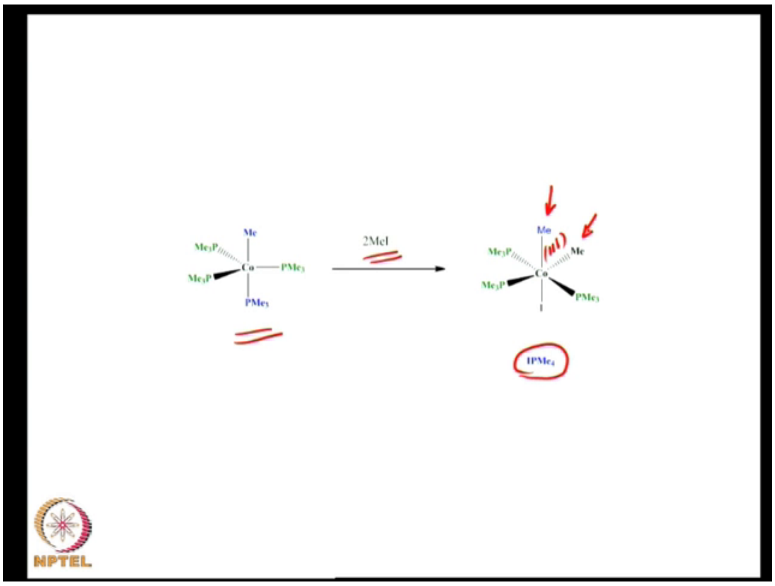

The substrate and question is a cobalt 3 complex, which was formed. The cobalt 3 complex could very simply be generated by taking a methyl cobalt complex. That is given here. This PMe3 complex was synthesised, and then treated with methyl iodide. Notice that methyl iodide added will do an oxidative addition, but during this process, PMe3 is generated. The PMe3 reacts with methyl iodide that is present.

So, you need to keep 2 equivalents of methyl iodide so that the reaction can be pushed to one direction. In other words, PMe3 is removed as it is formed. It forms this PMe4 plus I minus salt here, which is indicated here; this cobalt 3, formally cobalt 3 species, which has 2 methyl groups on it. Notice that this molecule can now reductively eliminate in different ways.

As I told you before, the elimination of methyl iodide will lead to a non productive reaction, but this molecule has the option of removing 2 methyl groups in the coordination sphere. Cobalt 1 is this, which is labelled in blue and the other which is labelled in black. So, these 2 molecules, which are cis related are not very polar. So, they can undergo reductive elimination in asynchronous fashion, in a concerted fashion and eliminate ethane.

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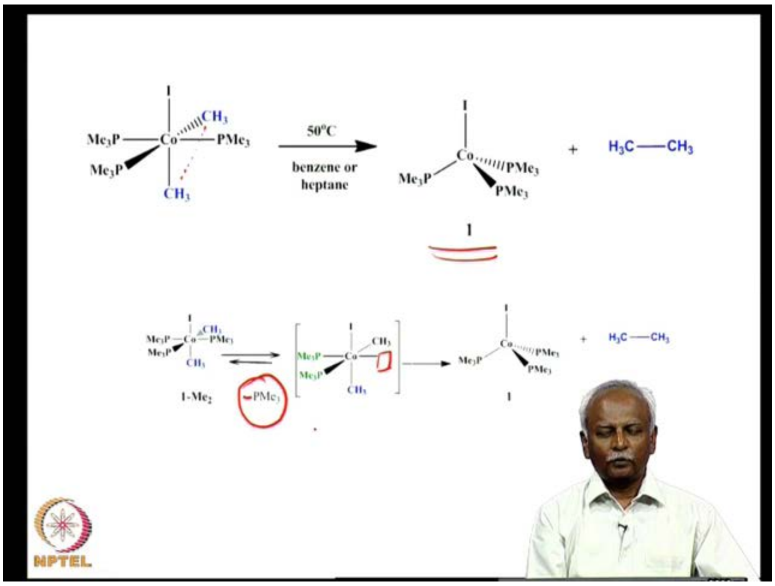

In fact, this is exactly what happens if you slightly warm the reaction mixture. In many cases, if the reaction can be carried out at slightly elevated temperatures, it allows you to characterise the reactant very well. In this particular case, the cobalt 3 complex is stable at room temperature, but if you heat it, it eliminates methane. The colour coding is purely to tell you what the groups, which are being eliminated, are. Here, there are 2 methyl groups, which are going to be excluded.

It is not methyl iodide which comes out, but it is 2 methyl groups which come out. That makes it a favourable reaction. So, then you end up with a cobalt 1 complex, which is not an iodo ligand. It is stabilised by these 3PMe groups. That is labelled as the compound 1. Now, if you think about this reaction, it could be done in a concerted manner. 2 methyl groups can come together methyl-methyl bond can be formed. The elimination can take place, but because we talked about microscopic reversibility, there are different possibilities. In fact, these workers examined this reaction in detail.

What they found was a first step required dissociation of PMe3. So, if you have excess of PMe3 solution, if you do try to do this reaction in the presence of PMe3, this reductive elimination is hindered. In other words, when you heat this reaction mixture, the first step is loss of PMe3. So, loss of PMe3 is there. A vacant coordination side is generated. So, this is a vacant coordination side and that is essential for the reaction to happen. This is in fact strange. In the previous instance, we said that of the 2 groups, which are reductively eliminating, 1 group comes out first and leaves a vacant coordination sphere.

That was what we learnt from microscopic reversibility. But, in these cases, it is the third group, the one which is not added. Methyl iodide was added. PMe3, which is a spectator ligand, has to leave the coordination sphere of the metal and generate a 5 coordinated intermediate. Remember that the reductive elimination involves reduction in the number of ligands coordinate to the metal.

Surprisingly, for the reduction in the number of ligands, you need to generate a vacant coordination side. This turns out to be a paradox, which is there in organometallic chemistry and especially in reductive elimination. Why you need a vacant coordination sphere before you can generate more vacancies on the metal? So, this is a mystery which needs to be solved. Now, this is the first step of the reaction. There are more interesting things to follow.

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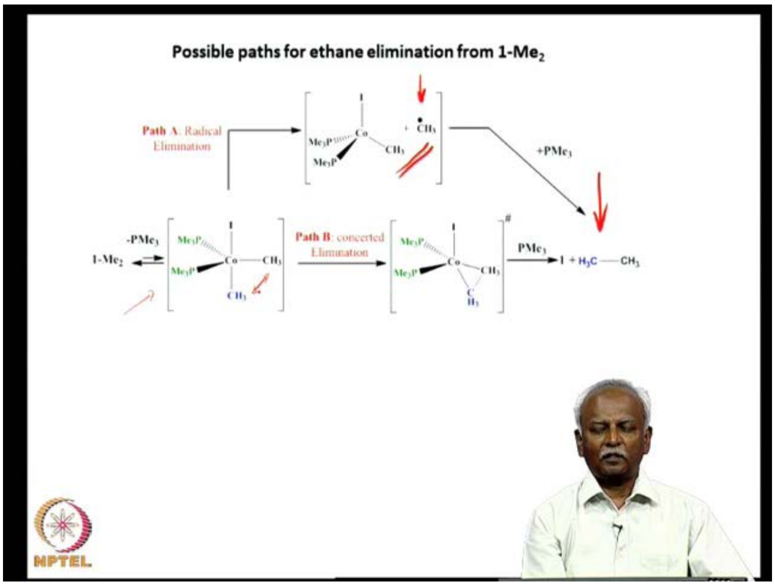

Possible paths for ethane elimination from 1-Me$_2$

If you take the second possibility after generating a vacant coordination sight by loss of PMe3 that is indicated here in the first step on your left side, top you have these 5 coordinated intermediates. That is what is generated in the first step. If you remember the coordination chemistry 5 coordinate complexes are extremely fluxional, which means they are labile. They will change the coordination side according to the need and that leads to very interesting reactions.

Now, there are two possibilities which the authors considered. One is to dissociate a methyl group, generate a methyl radical. So, this is a methyl radical, which is generated. A cobalt 2 species, a formally cobalt 2 species is generated. If you remember, we said generation of methyl anion is difficult. Iodo anion would have been possible, but that leads to non productive reaction. Here, we are generating a methyl radical, which means cobalt 2 complex or formally cobalt 2 complex is generated. This methyl radical could be in a cage. It could react with the methyl species, which is still attached to the metal.

The combination of these 2 could lead to elimination of the dying methyl group or the ethane. So, this is the group, which is eliminated from the coordination sphere of the metal. So, you have ethane elimination from this intermediate. Surprisingly, this is not the part that is favoured. It is also possible that you have a concerted elimination after you form the high coordinate intermediate.

Now, that will give you a species where the 2 methyl groups have a cis coordinated. As I told you because of trigonal bi pyramidal species being fractional, you can have rearrangements that will lead to cis arrangement of the 2 methyl groups and elimination. Concerted elimination can give you ethane.

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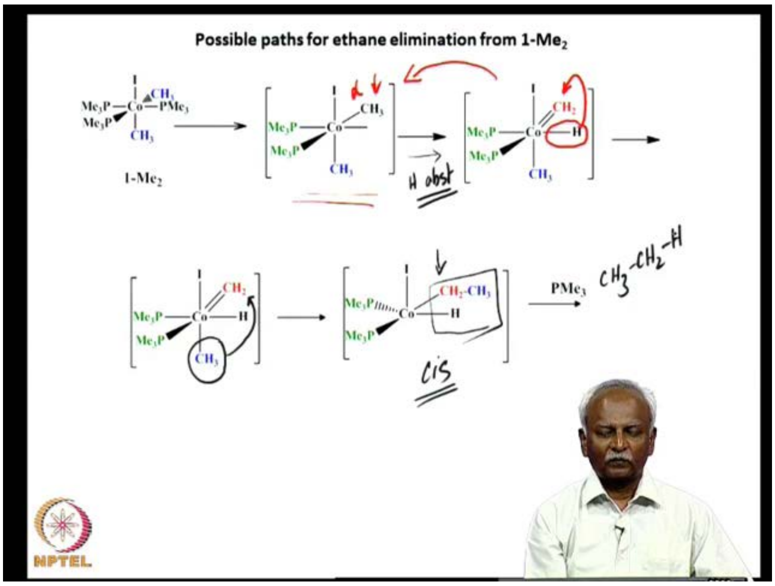
Possible paths for ethane elimination from 1-Me$_2$

A third possibility was also considered by these workers. That involved both reductive elimination and also insertion reaction. Considering the fact that you require a vacant coordination sphere on the metal, let us generate it with this 5 coordinated intermediate.

Having generated a 5 coordinated intermediate, you could in principle generate from this methyl group. You have 3 hydrogens on this methyl group. 3 hydrogens are there in this methyl group. You could generate a cobalt hydride species that would correspond to a abstraction of hydrogen from the methyl alpha hydrogen abstraction. This is the alpha group alpha carbon. If you abstract 1 hydrogen from there, then you would end up with methylene unit along with a hydride.

This is not an unreasonable reaction to write considering the fact that this is just reverse of a migratory insertion of a hydride unit. This is the hydride unit. If this migrates onto the CH 2 group, you would end up with a reverse reaction that is a methyl group formation. So, this is basically just a hydrogen abstraction from the alpha position. You can think of this as a nucleophilic attack of a hydride onto a neutral methylene group. So, this is migratory insertion and its reverse. What we are talking about in the black in the forward reaction is actually the forward reaction is actually the hydrogen abstraction. This is the hydrogen abstraction reaction.

Now, having formed this methylene group, you could have a second step in which the methyl group which is again cis to the methylene. This can now carry out a nucleophilic substrate, nucleophilic attack on the methylene group. So, that is a migratory insertion of the methyl. If that happens, this is a migratory insertion of a methyl onto the methylene; you would end up with a ethyl maleate on the cobalt. You will notice that these are colour coded, the migrating methyl group, the anionic group is the one which migrates to the neutral group.

So, that is what we have written. It is a migratory insertion. So, the methyl group attacks the methylene unit. Then, ethyl maleate is formed. It is generated on the cobalt. If you eliminate ethane, you can very easily generate CH3CH2H by eliminating these 2 units together. So, you can just eliminate these 2 units. So, both the units are cis related. They are cis related. It can have a reductive elimination to have CH3CH2H.

So, this is another alternative mechanism. What the researchers carried out was to do isotopic labelling in order to figure out whether this reaction was happening or not. In fact, they showed that they are not happening in the reaction during the course of the reaction.

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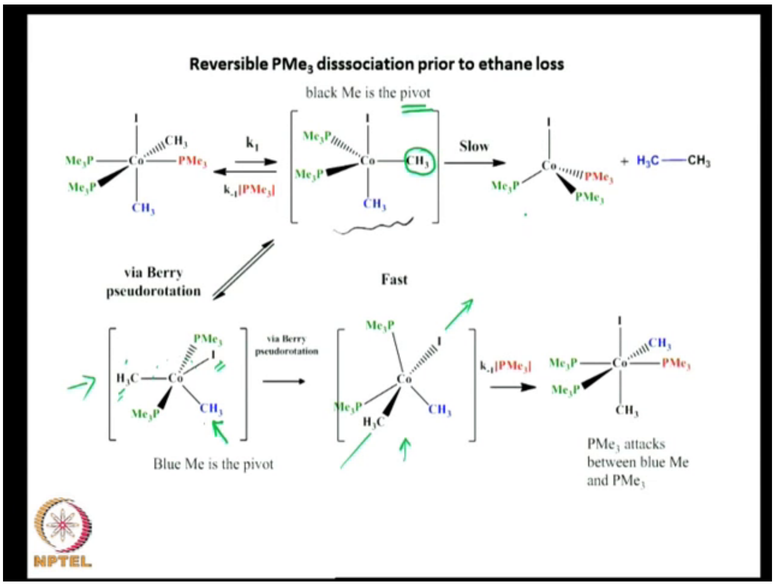

Reversible PMe$_3$ disssociation prior to ethane loss

black Me is the pivot

Slow

via Berry pseudorotation

Fast

via Berry pseudorotation

Blue Me is the pivot

PMe$_3$ attacks between blue Me and PMe$_3$

So, they considered 3 reactions. Based on their results, they concluded that part where you have a concerted elimination. This is path b concerted elimination. It is the most favourable path way and alpha elimination to give a series of migratory insertions and alpha abstractions is not happening. So, in other words, this is not happening, this part is not happening. The radical elimination was also not happening. It is in fact, the formation of a coordinative unsaturated intermediate from which a concerted elimination of 2 methyl groups happened. You have the reductive elimination.

So, the various paths that the molecule can take because of the 5 coordinated intermediate are listed here. We can start with the 5 coordinated intermediate, which is here. Then, we can carry out very pseudo rotation, which is basically a reaction in which the 2 equatorial groups become axial. 1 equatorial group remains stationary. That is called the pivot atom. So, if the black methyl is a pivot, which means, this is the pivot. Let me colour it for you in a different colour. So, if the pivot atom is this, if this is the pivot atom, then we will move the equatorial groups, the 2 green equatorial PMe3 units and make them axial.

You would end up with an intermediate like this and this intermediate, which will be a slightly higher energy. This intermediate can undergo another berry pseudo rotation. That can be carried out this time. You take the 3 equatorial groups are the methyl, the methyl, the iodo group and another methyl group. So, you can know. Notice that the 2 methyl groups can be interchanged through this very berry pseudo rotation process. You can end up with a second intermediate, which is listed here, which is the intermediate here through another berry pseudo rotation this time.

The blue methyl is a pivot. So, that means, we keep this constant. We carry out a berry pseudo rotation in such a fashion that the methyl and the iodo units, which are labelled in black, become axial groups. So, this is the axial group. Now, this is the axial group. So, this angle contracts, this angle between the methyl cobalt and the iodo group contracts. The PMe3 units come together to form a berry pseudo rotation product, which is listed here. Now, you can see how the 2 methyl groups can interchange very easily during the course of this reaction. You can have elimination of methane resulting in the formation of a product, which is cobalt 1 process, cobalt 1 compound.

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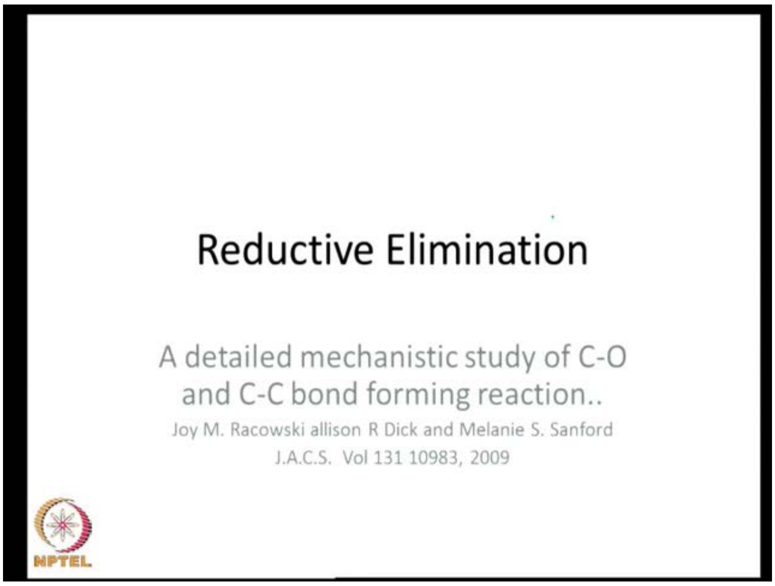

Reductive Elimination

A detailed mechanistic study of C-O and C-C bond forming reaction..

Joy M. Racowski allison R Dick and Melanie S. Sanford

J.A.C.S. Vol 131 10983, 2009

So, reductive elimination is a fairly complex process. Recently, more detailed investigations are being carried out. In this particular study, which brings out some very important principles, it has been possible to figure out how palladium 3 compound and palladium 4 compounds can undergo reductive elimination. In the example that I am going to first discuss, it is primarily a palladium 4 compound, which is again a mononuclear intermediate. It is formed and it undergoes reductive elimination to give you a CO coupling.

As I mentioned to you, if there is a possibility for CC coupling and CO coupling, reductive elimination might very often favour CC coupling. But, in this particular instance because of considerations that are steric in nature and also serial electronic in nature, basically you end up with elimination of 2 cis groups, which are C and O. You have only a CC elimination product. CC elimination product is not favoured. CO elimination is favoured. The research has been focused on how we can make CC couple products.

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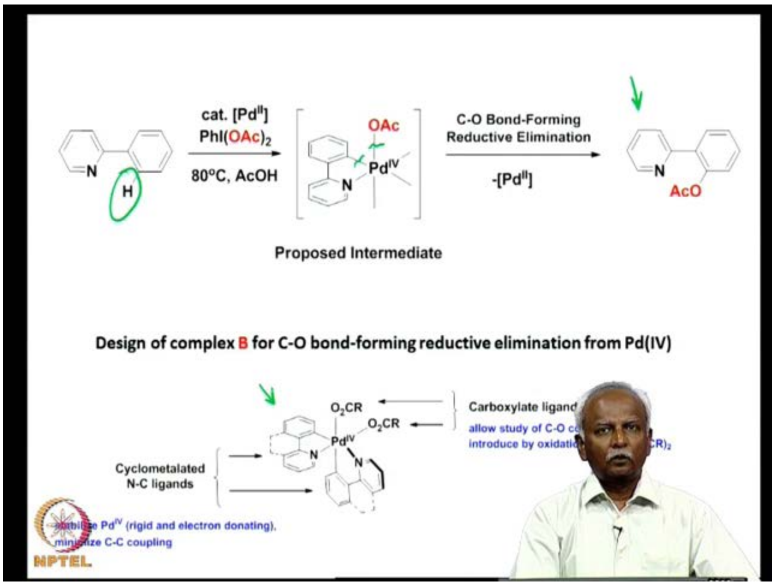

Design of complex B for C-O bond-forming reductive elimination from Pd(IV)

allow study of C-O c
introduce by oxidati
CR)$_2$

e Pd^{IV} (rigid and electron donating),
ze C-C coupling

So, let us take a look at this reaction in detail which will help us to understand some very important principles. If you take a species, which is palladium 2, you can have a palladium 4 intermediate through an oxidative addition of a CH bond. In this particular instance, the CH bond that is oxidative added is given here. This is the CH bond, which is going to be oxidative added. It forms the bond with palladium and 1 of the acetate groups leaves with the hydrogen, which is present on the arene. So, you have an intermediate, which is a palladium carbon product leading carbon bonded product.

You will notice that from palladium 2, you have changed the oxidation state to palladium 4. So, in this palladium 4 intermediate, which had 2 acetates to start with, you end up with acetate and HO Ac has been removed. HO Ac has been removed. So, this proposed intermediate can undergo reductive elimination. This time it undergoes reductive elimination. Again, the elimination happens in a cis fashion. So, these 2 bonds are broken. The 2 bonds that I have marked in green are broken. An acetate aromatic ring bond is formed. The product is the acetate functionalised aromatic phenyl pyridine.

So, this product is formed exclusively and the intermediate is supposed to be a palladium 4 intermediate. What makes this study very interesting is the fact that you can generate the palladium 4 intermediate. You can make it in a stoichiometric fashion and study the chemistry of it. Palladium 4 intermediate that could be formed in this particular instance is listed here.

It has got a very stable palladium 4 coordination geometry octahedral geometry, which is very stable for palladium 4. Because of the cyclamate relations, it leads to very rigid geometry. That is illustrated in this particular picture, which I have given here. The carboxylate ligands, the 2 acetate ligands which are present in the coordination sphere of the metal are the ones which allow for reductive elimination. It can be introduced via oxidation with phenyl iodo acetate.

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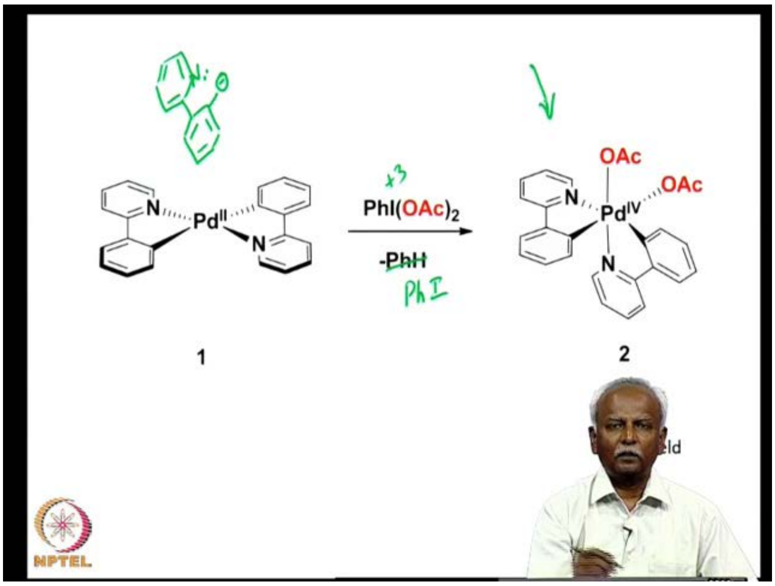

So, let us just take a look at this reaction. If you take the best cyclo metalated product, which is again palladium 2 formally because these are anionic ligands. So, if you look at this ligand, you have a pair on the nitrogen, which is coordinated to the metal. Then, you have anionic centre, which is coordinated to the metal. So, let us take a look at these. These are the 2 species, so because this is anionic and you have 2 of them have a palladium 2 centre, you can oxidise this species with phenyl iodo acetate, which is an oxidising agent. It has got iron in the plus 3 oxidation state.

If you select treat this molecule with phenyl iodo acetate, you will end up with removal of the Ph I. This is actually minus Ph I and O Ac is added onto the palladium. So, palladium 4 complex is formed. This is formed in good yield. This allows you to characterise this intermediate very well and then study the reductive elimination.

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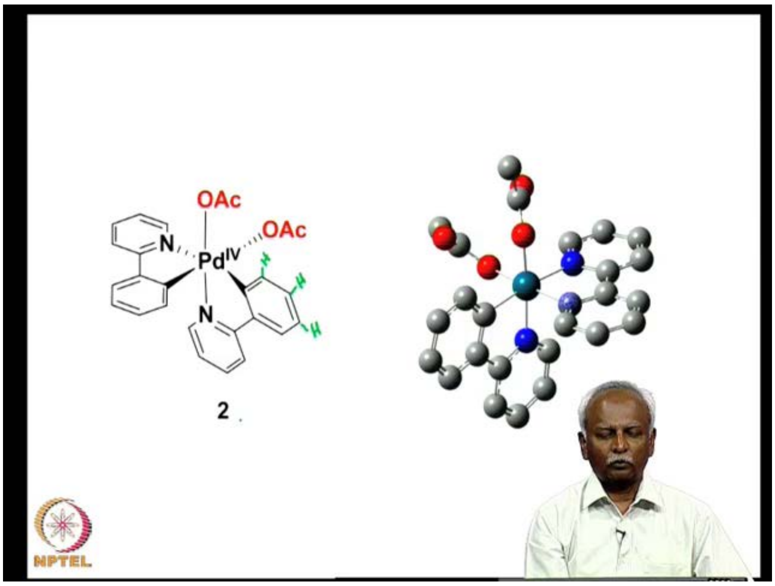

Here is a crystal structure of the palladium 4 complex. It is interesting that this type of a geometry coordination leads to 16 different CH signals. Each one of this hydrogen is unique and gives you a different signal in a m r spectrum because the environment around them is different. So, you have 16 of this hydrogen on both rings. All of them have a different environment. Since, this is not particularly a spectroscopic class; we will not discuss the spectroscopy of it. That allows them to characterise the structure of these molecules very well.

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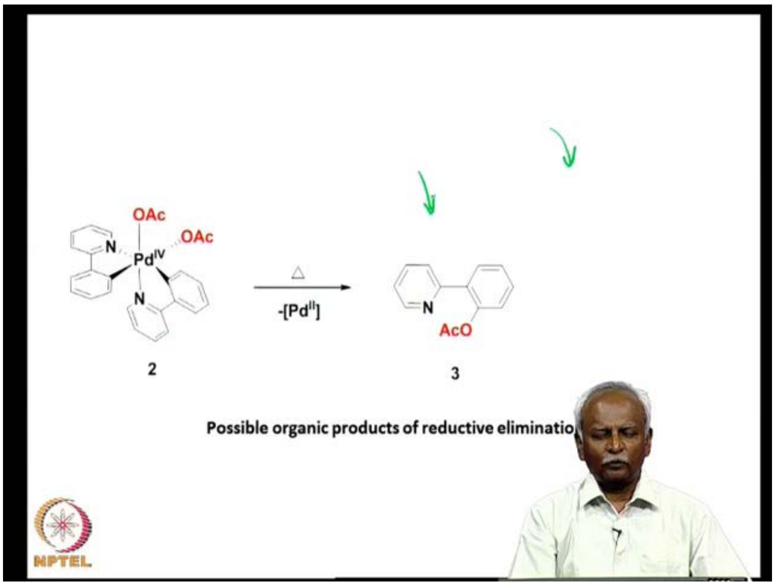

Possible organic products of reductive eliminatio

If you heat this molecule, you have the possibility of forming both carbon-carbon couple product. You can have a carbon-carbon coupling happening. That will give you this particular molecule where you have the 2 phenyl pyridines coupled together. You can have the acetoxy compound. As I mentioned earlier, although 2 products are possible during the reaction, only the acetoxy product 3 is formed, when you heat it.

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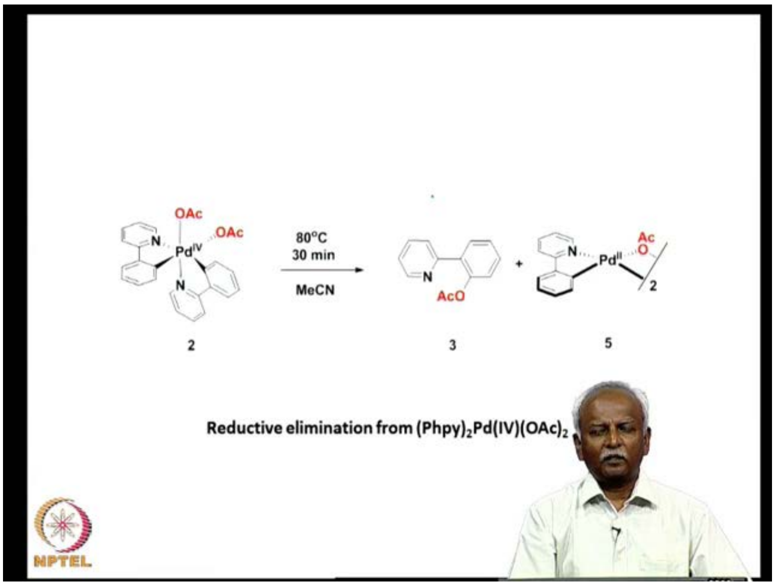

Reductive elimination from (Phpy)$_2$Pd(IV)(OAc)$_2$

So, we would like to understand how exactly this whole reaction is happening. The reaction is carried out by heating at 80 degrees and in aceto nitride. This leads to formation of 3 and the other metal containing product is the aceto acetate bridge palladium 2 pyridine.

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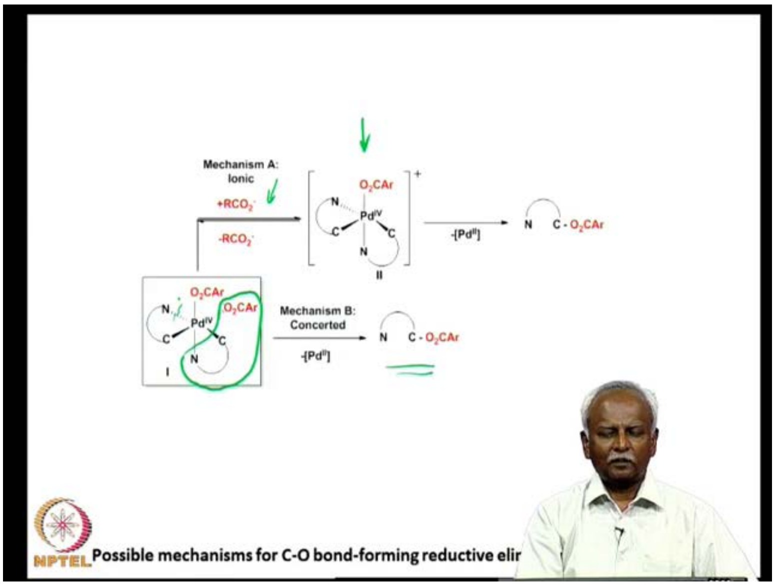

Possible mechanisms for C-O bond-forming reductive elir

Now, the question is how exactly is a reductive elimination happening because we know from several other examples that reductive elimination, although it is paradoxical, it requires a vacant coordination site. The first thing that they examined was what would happen if you have added acetate ions.

Suppose that you have acetate, an aromatic acid. If you add the anion, then it should suppress the equilibrium, which is given here. If this equilibrium is suppressed, then you would have only the penta coordinate intermediate. This penta coordinate intermediate is presumably the place from which reductive elimination happens. So, you could have a concerted mechanism in which the 2 groups, which need to be eliminated, which is what I am going to mark up in green here; these are the 2 groups that need to be eliminated.

These can be eliminated in a concerted fashion and could give you a palladium 2 compound with the organic material which is listed here. So, these are 2 possibilities. Initial studies in fact suggested that there is no effect of added acetate or the carboxylate anion, which means, whether you suppress this formation of the intermediate or not, the reaction was happening.

This was in fact very surprising because 1 normally has the formation of a vacant coordination sphere. Elimination of 1 of these bonds would be highly unlikely because you would have to generate a chelated compound, breaking 1 of its bonds and forming an mono coordinated species which is highly unlikely, but nevertheless, that has also been considered for this mechanism.

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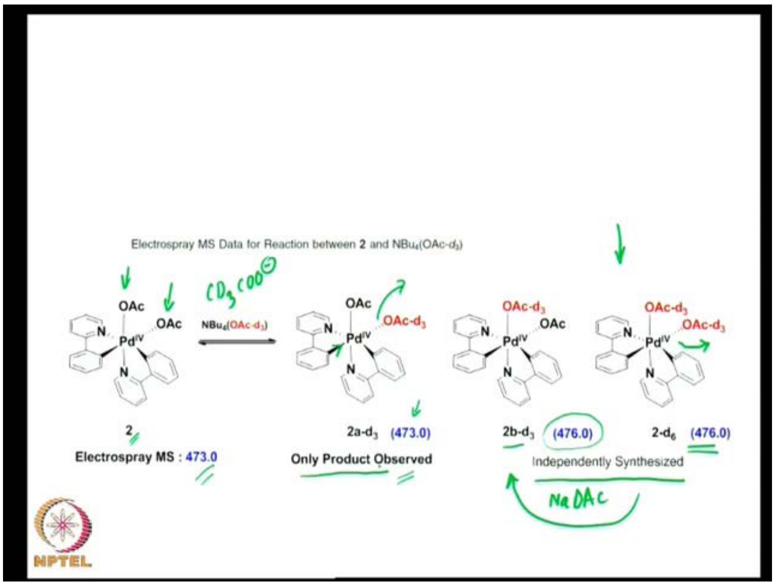

Electrospray MS Data for Reaction between **2** and $NBu_4(OAc\text{-}d_3)$

2 Electrospray MS : 473.0

2a-d_3 (473.0) Only Product Observed

2b-d_3 (476.0)

2-d_6 (476.0)

Independently Synthesized

The third possibility was another mechanism where you would have some rearrangements. We will come to that. Before that, let us just see how these compounds can be detected. For this particular example, we used electro spray mass spectrometry to study the reductive elimination. They found that if you equilibrated the system with labelled acetate, which means it is CD3COO minus, this is the labelled acetate where deuterium labelled acetate was used. They could exchange 1 of the acetate groups. There are 2 acetate groups; 2 acetate groups here, but only 1 of them underwent exchange.

They identified this using mass spectrometry and the combination of crystallography of a differently labelled carboxylate. In the mass spectrometry experiments, they could show that loss of acetate from the palladium 4 species was readily happening from this position that means opposite the carbon. This is because carbon was having a large trans effect. This group was very label and even if you have the labelled acetate, you would end up with the mass of 473; M by S value of 473.

If you took the unlabelled acetate, then also you ended up with a mass of 473. If you took the labelled acetate generated using acetate, which was added externally, then also you ended up with 473. On the other hand, if you independently synthecised doubly labelled acetate, which could of course, be carried out by taking the iodo acetate which is rebuilt, then you can generate this fragment. This gave you a mass of 476.

This 476 is coming from the species, which would be generated by loss of this 1 acetate group. But, because of the second acetate is labelled, you have an increase of 3 a m u. Even if you take an acetate, which is only a di acetate molecule, palladium 4 di acetate molecule as 2 b d 3, if you take this molecule, which can be generated by taking 2 d 6 and treating it with Na O Ac in excess.

If you treat it with sodium acetate with excess, which is un labelled to generate 2 b d 3, this molecule also gives 476 as the mass. So, using mass spectrometry, they were able to show that in fact, the only species which was being formed in solution was immediately 2 a d 3. So, this tells you that 1 acetate atom is labile in the reaction in the film because of reaction.

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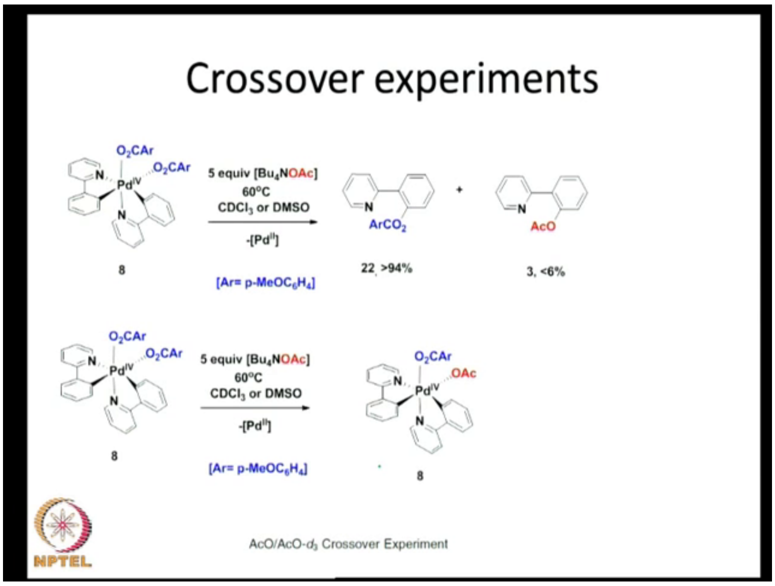

Crossover experiments

AcO/AcO-d_3 Crossover Experiment

The palladium 4 complex has got 1 acetate atom, which can be removed and replaced, but surprisingly, that was not helping the reaction. So, they also showed that the acetate, which was left behind, which was not exchanging was the one which was doing that carbon oxygen coupling. So, here is a crossover experiment taken out.

They took 2 aromatic carboxylates. These aromatic carboxylate were added onto the palladium 4. Now, after exchanging with acetate, they carried out the reductive elimination. If reductive elimination is carried out from these species because you have 5 equivalents of the acetate, this carboxylate would now be replaced by acetate. In spite of that, you have only 1 product being formed. That is being generated by a combination of the aromatic carboxylate and phenyl pyridine. This is the only product, which is formed during the course of this reaction.

That is because of the way in which the species, which is exchanging is not the one which is undergoing reduction elimination. So, in the first step, they showed that only 1 acetate atom is exchanging and that is the group, which is trans to the carbon. That is the one which is present here, which I have labelled in green. This is the one that is undergoing exchange. In the second step, they showed that even if you exchange that acetate, it is a carboxylate which is left behind intact on the palladium 4. That is the one, which undergoes reductive elimination.

So, 94 percent of this product was formed in spite of removing the carboxylate, which is trans to the carbon. It is a clear indication that it is not this carboxylate, which is going out, which is carrying out a nucleophilic attack on the ligand and carrying out reductive elimination as we had seen in the group 1 chemistry group 1 oxidative additions. So, one more experiment they showed. This is very clear that even if you carry out this exchange without carrying out the reductive elimination, you end up with acetate labelled in position 8.

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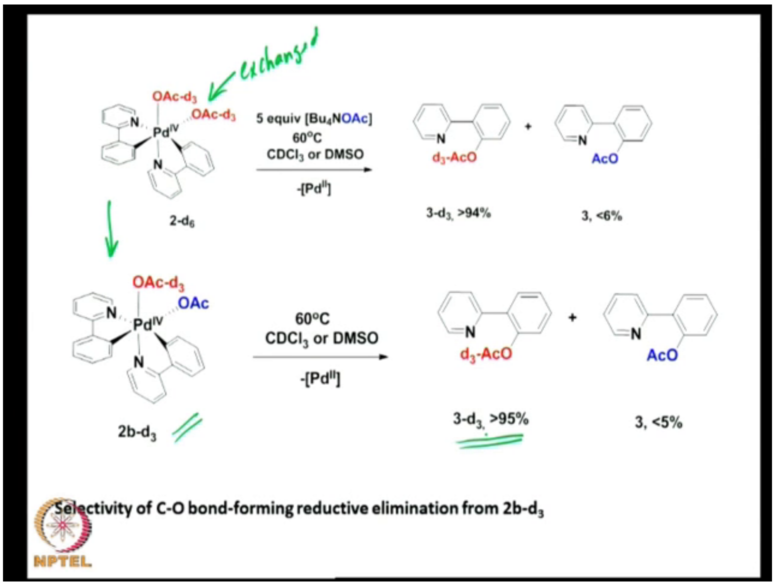

Selectivity of C-O bond-forming reductive elimination from 2b-d_3

So, now we have 2 sets of experiments which are listed here. So, with all with labelled compounds, which I told you could be independently synthesised, they confirmed very clearly that it is only the labelled acetate, which is left behind on the palladium. It is reductively eliminated. Now, this is very clear. If you treat this with unlabelled acetate, you would end up with only this product 2 b d 3.

So, we should treat this with sodium acetate, which is not labelled. You would end up 2 b d 3. This molecule would only give you this as a compound because only this acetate is exchangeable, but this can be exchanged. This other acetate is not exchanged. If you heat this compound, only 1 product is formed and that compound is got to label. So, two things have been established very clearly. The acetate, which leaves the coordination sphere, is not the one which is attached to the carbon at the end of the reaction. Only 1 acetate atom is exchangeable.

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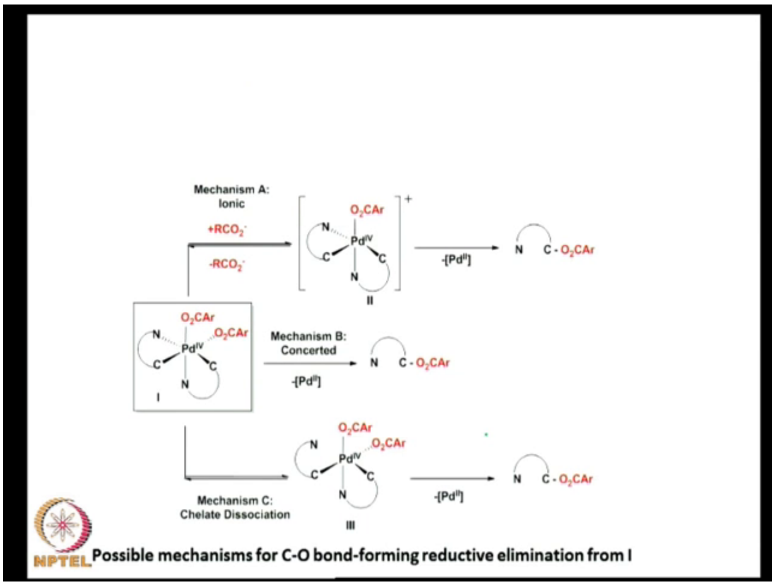

Possible mechanisms for C-O bond-forming reductive elimination from I

So, the third possibility, which I told you, will require this chelate ring breakage. It was also considered, but this requires that you have speculating, which is not coordinated. It is highly unlikely and through a series of experiments, where we tied up the 2 chelate rings is showed that this is highly unlikely to happen. So, the concerted mechanism part is probably the one that is happening from the coordinative unsaturated intermediate that is formed.

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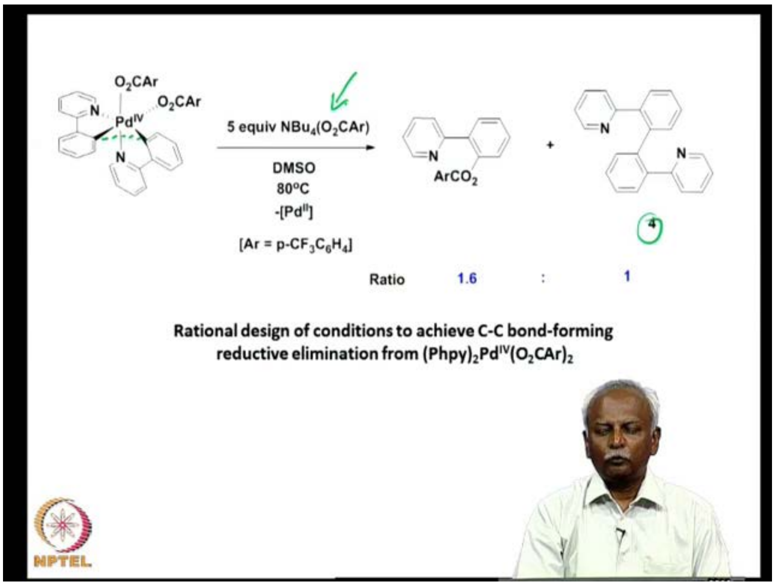

5 equiv $NBu_4(O_2CAr)$

DMSO

80°C

$-[Pd^{II}]$

[Ar = $p\text{-}CF_3C_6H_4$]

Ratio 1.6 : 1

Rational design of conditions to achieve C-C bond-forming reductive elimination from $(Phpy)_2Pd^{IV}(O_2CAr)_2$

So, rational design for carbon carbon coupling is one thing that we talked about. Now, how would we make this carbon carbon coupling happen? In this case, if you use a large amount of a carboxylate carboxylate that is coming out, if you use a large amount of the carboxylate, then what would happen is the ionisation of this intermediate is suppressed.

When you heat the reaction mixture, this stops the unsaturated intermediate being generated. Now, if you have reductive elimination, it turns out that carbon carbon coupling can happen. These 2 carbon bonds are cis related. So, in principle, it is possible to have reductive elimination by forming a bond between these 2 carbons. So, these are the 2 carbons, which need to be bonded together in order to form the carbon carbon coupled product, which is marked as 4 here.

You will remember that if you do not have this added carboxylate aromatic carboxylate, then you have 96 percent of the C O coupling. C O coupling is formed in 96 percent and only 4 percent of the carbon carbon coupled product is formed. By adding a large amount of the carboxylate, you suppress the reaction the ionisation. Then, a concerted reaction happens. This time, you will have only a carbon carbon coupling.

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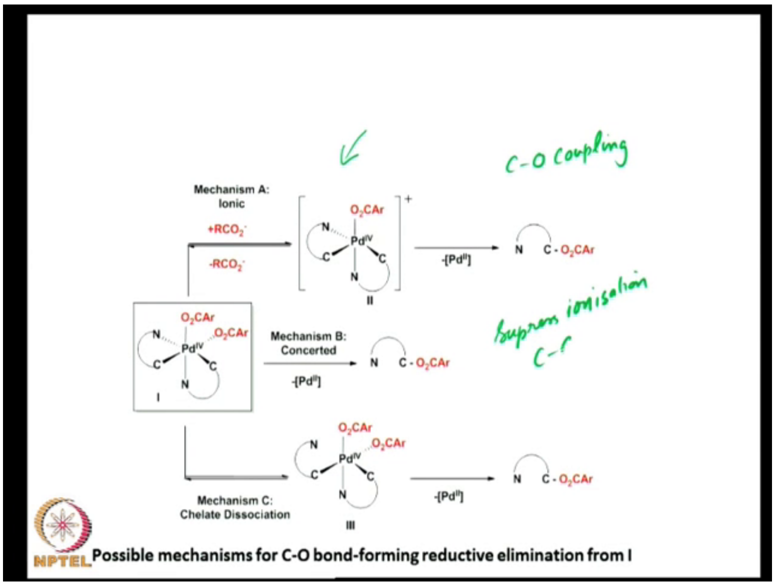

Possible mechanisms for C-O bond-forming reductive elimination from I

So, if you go back to this general scheme, you notice that the first step is in fact, generation of a coordinative unsaturated intermediate. Then, you have C O coupling. Then, you have C O coupling. If you suppress the ionisation, then you end up with C C coupling. If you suppress ionisation, then you end up with C C coupling.

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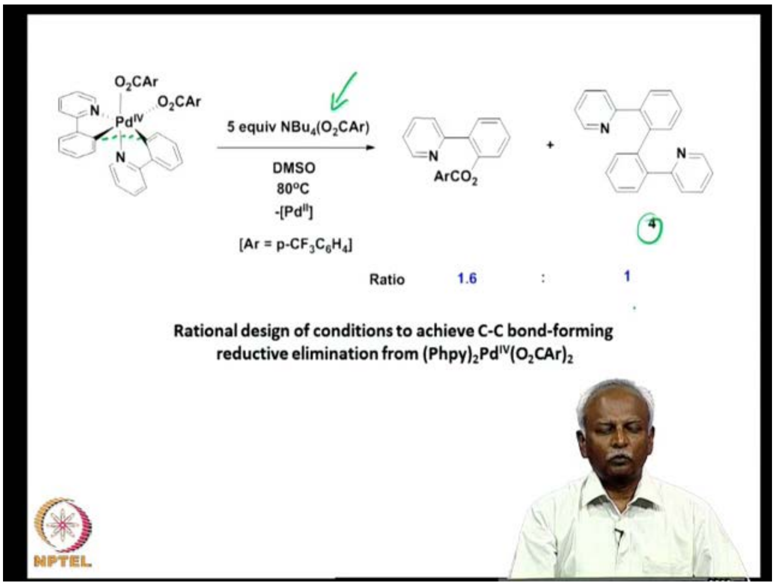

5 equiv NBu$_4$(O$_2$CAr)

DMSO
80°C
-[Pd^{II}]

[Ar = p-CF$_3$C$_6$H$_4$]

Ratio 1.6 : 1

Rational design of conditions to achieve C-C bond-forming reductive elimination from (Phpy)$_2$Pd^{IV}(O$_2$CAr)$_2$

So, this is the first time where both C C and C O coupling in a reaction have been studied. It is also a rational way by which you can bias the reaction towards the 1 product that has been achieved. This is being done through the formation of a palladium 4 mono nuclear intermediate.

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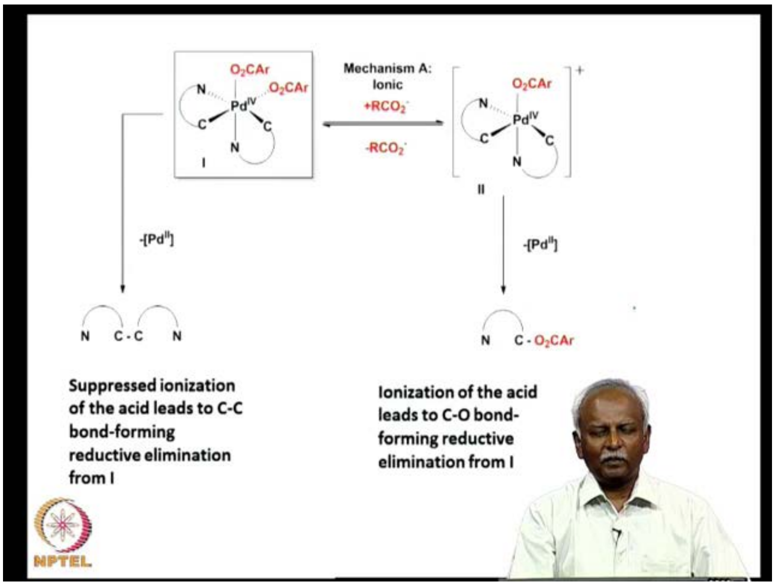

Mechanism A:
Ionic
+RCO$_2^-$
-RCO$_2^-$

-[Pd^{II}]

-[Pd^{II}]

Suppressed ionization of the acid leads to C-C bond-forming reductive elimination from I

Ionization of the acid leads to C-O bond-forming reductive elimination from I

In the same year surprisingly, there was another reaction, which was also studied. We will come to this reaction after summarising what I had just told you. So, what I have told just now is that suppress ionisation of the acid leads to C C bond formation and the

C C couple product. If you have ionisation of the acid, it will leads to C O coupling of the product.

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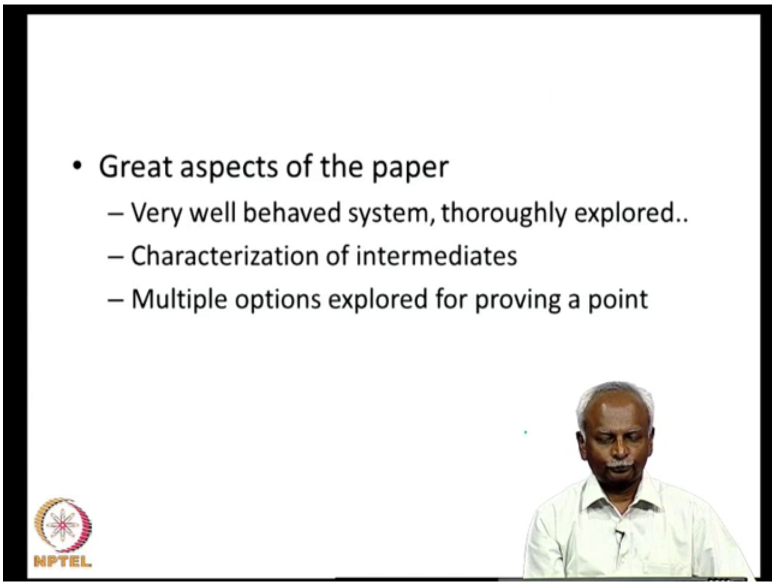

- Great aspects of the paper
  - Very well behaved system, thoroughly explored..
  - Characterization of intermediates
  - Multiple options explored for proving a point

The nice aspect about this paper is that we have studied a very well behaved system. It could be thoroughly explored. They have also characterise the intermediaries that are involved using mass spectrometry and in mass spectrometry spectroscopy. They were also used in a variety of other tools to like x ray crystallography to show the intermediates that are involved. It is important to note that multiple options have been explored to prove exactly what was going on in the reaction.

Now, before we go to the next step, we have to briefly review some literature that was prior to the 2010. It was known that reductive elimination could involve these concerted reactions. That is labelled as 1 here in this projection. You have 1, which is a concerted elimination. You could also have the formation of a di nuclear intermediate, where you could eliminate X and Y in a bimolecular after undergoing a bi molecular reaction.

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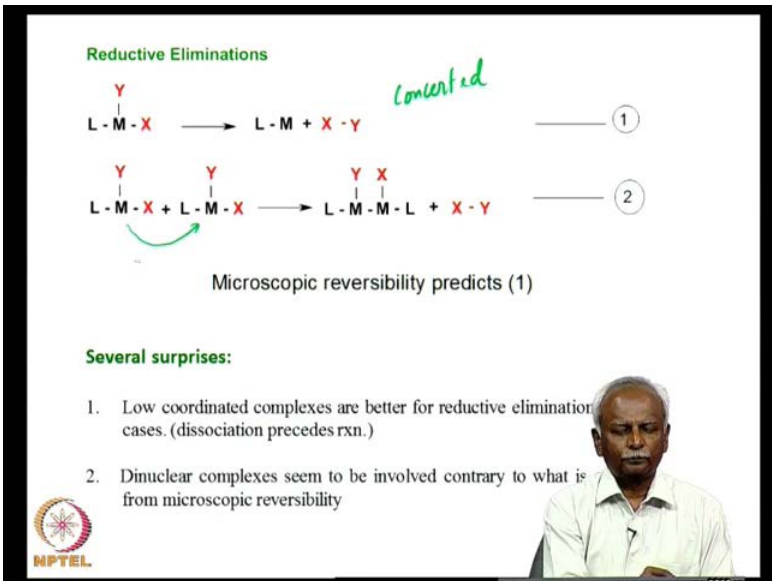

Reductive Eliminations

$L-\overset{Y}{\overset{|}{M}}-X \longrightarrow L-M + X-Y$ Concerted ——— ①

$L-\overset{Y}{\overset{|}{M}}-X + L-\overset{Y}{\overset{|}{M}}-X \longrightarrow L-\overset{Y}{\overset{|}{M}}-\overset{X}{\overset{|}{M}}-L + X-Y$ ——— ②

Microscopic reversibility predicts (1)

Several surprises:

1. Low coordinated complexes are better for reductive elimination
   cases. (dissociation precedes rxn.)
2. Dinuclear complexes seem to be involved contrary to what is
   from microscopic reversibility

In other words, these 2 react together; form may be a bond or bridged intermediate. In this bridge, intermediate X and Y are reductively eliminated. Microscopic reversibility favours the first possibility, but as I told you, there are several surprises in reductive elimination, several paradoxes. One of them is the fact that you need low coordinated complexes. They undergo reductive elimination much better than the coordinative saturated intermediates. Second surprise is the fact the di nuclear complexes seem to be involved. This is contrary to what is expected from microscopic reversibility.

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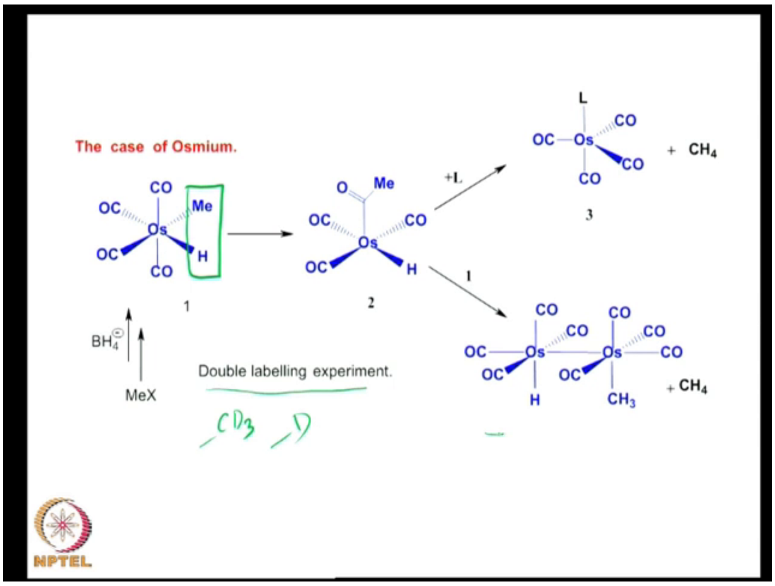

The case of Osmium.

Double labelling experiment.

So, one particular example that needs to be talked about is the case of osmium. Osmium2 intermediates undergo reductive elimination of methane. They can also undergo carbonyl insertion. What is shown here is carbonyl insertion; during the course of this insertion, you can also have 1 of the products is elimination of methane. It could have in principle come from a concerted elimination of Me and H from a single intermediate.

Using double labelling, they were able to show double labelling basically means that you make another molecule, where you have CD3 and deuterium instead of methyl and hydrogen. So, if you mix the 2, then you can see whether it is only methane, which is coming out or if you are getting CD3H or Me D. The observance of Me D and CD3H clearly tells you that you have bi nuclear intermediates and was possible that elimination is happening from a bi nuclear intermediate.

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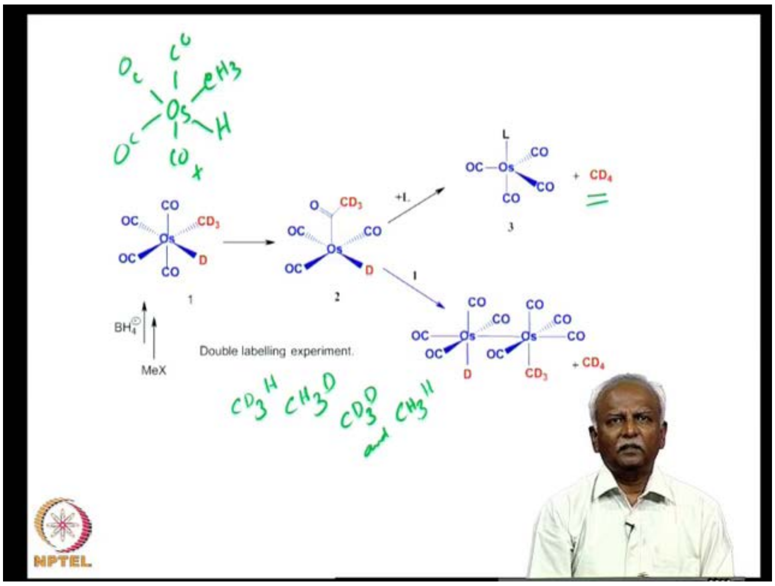

Double labelling experiment.

So, these 2 were considered. Both CD3D and CH3H species were mixed together. If indeed only the mono nuclear intermediate is formed, you would only have the possibility of CD4. But, because you have both CD3H CH3D CD3D and CH3H, when you start with the mixture, we will write this down here.

Now, this is the osmium compound have COCOCH3H. If you take a mixture of these 2 and then paralyse the mixture reaction, you would get only CH3H and CD4; if a mono nuclear intermediate was involved. If a di nuclear intermediate was involved, then you would end up with all 4 possibilities. In fact, this was observed. This tells you very clearly that the di nuclear elimination is happening from a di nuclear intermediate. It is possible that species like this are involved.

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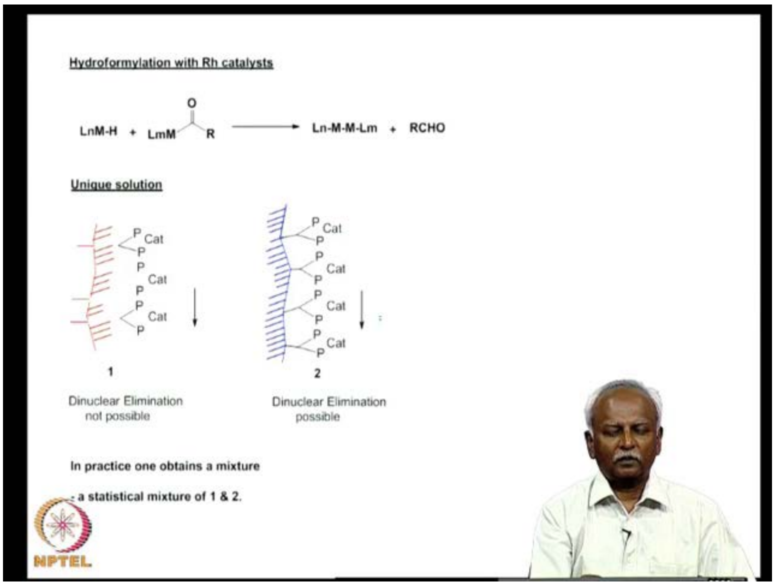

Hydroformylation with Rh catalysts

$$\mathrm{LnM\text{-}H} + \mathrm{LmM}\overset{O}{C}\mathrm{R} \longrightarrow \mathrm{Ln\text{-}M\text{-}M\text{-}Lm} + \mathrm{RCHO}$$

Unique solution

1 Dinuclear Elimination not possible

2 Dinuclear Elimination possible

In practice one obtains a mixture

- a statistical mixture of 1 & 2.

How the elimination was happening? One more possibility is to look at species, which are heterogeneously functionalised. This was carried out this was the study, which was carried out by hedges who showed that you can localise the molecules on a silica gel surface. Then, you can prevent di nuclear elimination. If they are sufficiently well separated, you could have elimination. If they are close by, then if the concentration of the catalyst is very high, loading level is very high, then the probability of di nuclear elimination will keep increasing.

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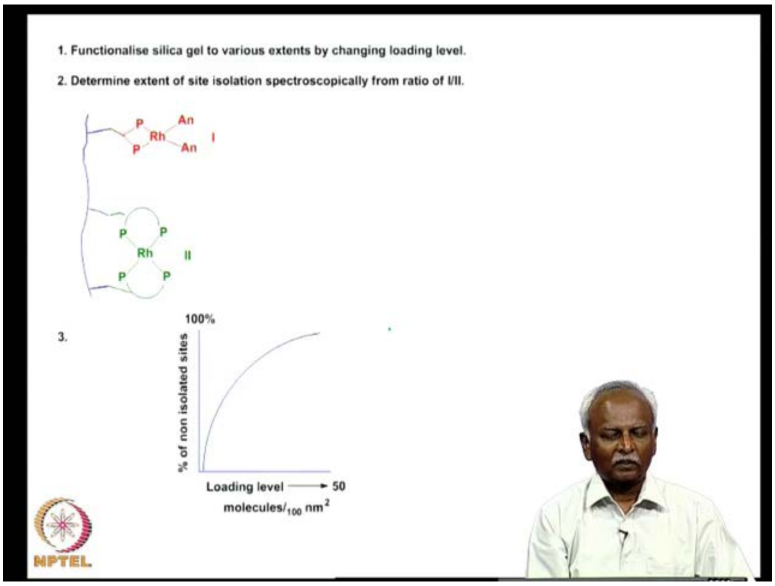

1. Functionalise silica gel to various extents by changing loading level.

2. Determine extent of site isolation spectroscopically from ratio of I/II.

3.

They showed by a carrying out this functionalization to different extents that the loading level was correlated with a number of non isolated sides. So, if you load the catalyst to a very large extent, then the percentage of non isolated sides will be increasing. That means the percentage of di nuclear species is increasing as you increase the loading level. Based on some spectroscopic features, they were able to distinguish the 2 systems. Subsequently, they showed that elimination was in fact happening from a di nuclear intermediate.

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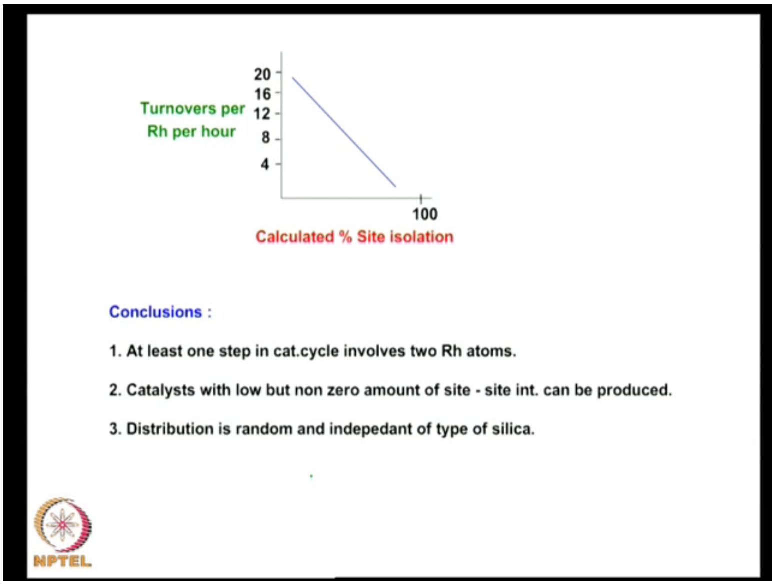

Conclusions :

1. At least one step in cat.cycle involves two Rh atoms.

2. Catalysts with low but non zero amount of site - site int. can be produced.

3. Distribution is random and indepedant of type of silica.

So, the turnovers of di nuclear elimination decreased with amount of site isolation. If you increase the amount of site isolation, only mono nuclear species are formed. If mono nuclear species are formed, then reductive elimination is unfavourable. In fact, that is what is showed here by plotting percentage of site isolation with turnover number. So, there is very clear indication. So, there was very clear indication that the elimination was happening in a di nuclear intermediate. Now, we will conclude today’s lecture by just briefly looking at what we have studied.

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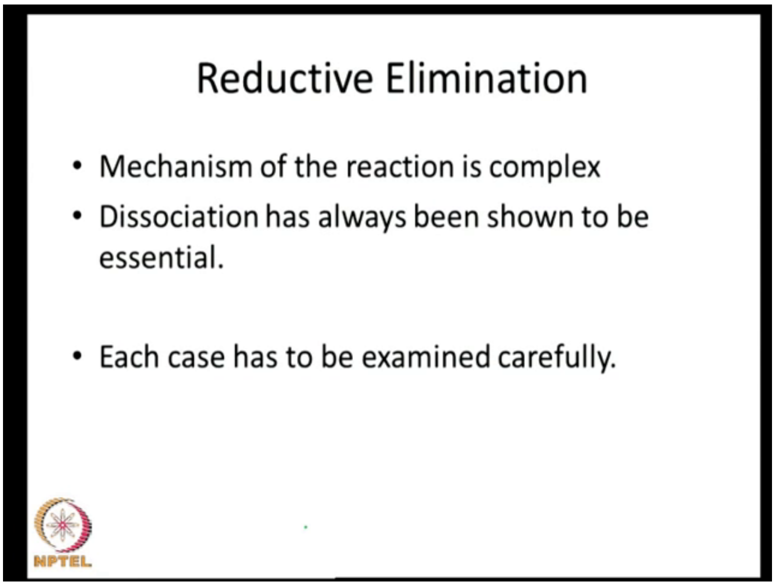

Reductive Elimination

- Mechanism of the reaction is complex
- Dissociation has always been shown to be essential.
- Each case has to be examined carefully.

What we have seen is that reductive elimination happens in a variety of ways. The mechanism of the reaction is fairly complex. We have also seen the dissociation is essential. This turns out to be a very important and paradoxical factor. Dissociation is essential before reductive elimination can be carried out.

We had also seen that the different compounds, whether it is cobalt or osmium or palladium reaction, mechanism has to be examined in detail in each case before one can conclude that the reaction is happening by a particular path. The only thing that can be told for sure is that dissociation of 1 ligand is needed. In all, probability is the 6 th groups will be reductively eliminated in a concerted fashion. So, we will consider some other complicated examples in the future lecture.