Essentials of Oxidation, Reduction and C-C Bond Formation. Application in Organic Synthesis

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Lecture - 56
Further Synthetic Aspects of the Chemistry of Allylsilanes (Part 3)

Hello, welcome you all to today's lecture. As we saw in the last class that we looked at various aspects of the allylsilane chemistry particularly in an intramolecular fashion, where the major emphasis was on the stability of the beta carbocation.

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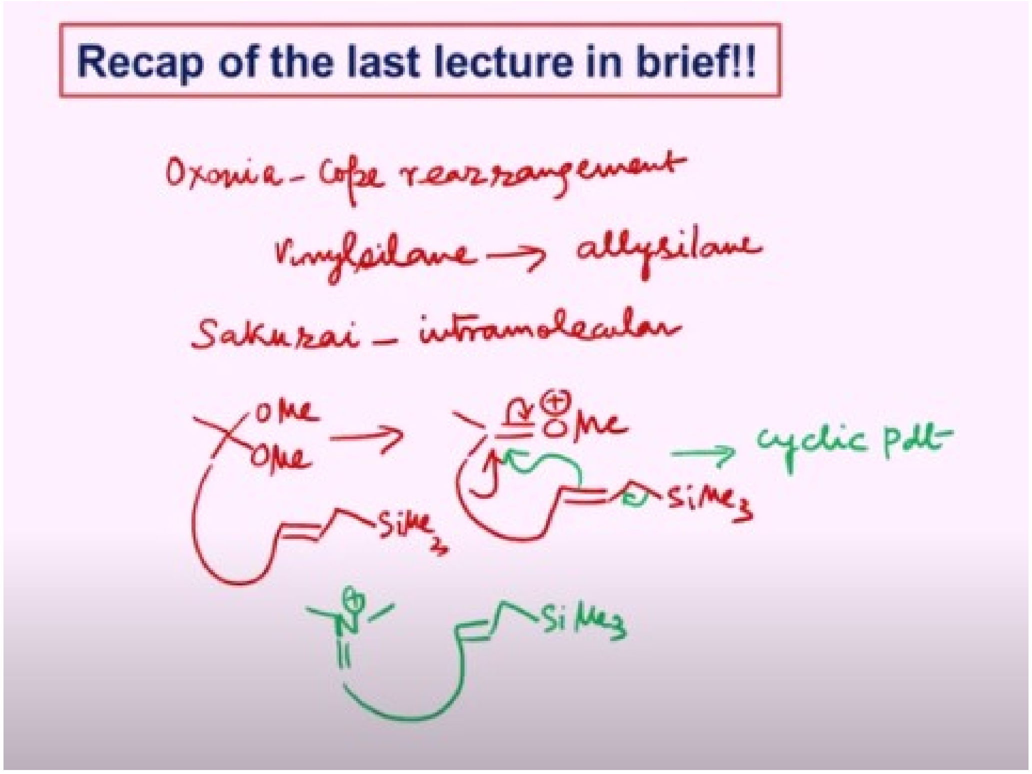

Recap of the last lecture in brief!!

Oxonia-Cope rearrangement

Vinylsilane → allysilane

Sakurai – intramolecular

And that allowed as we saw for the first time there was a multicomponent reaction, where we had the Oxonia-Cope rearrangement as one of the important steps where we were able to convert a vinylsilane to the corresponding allylsilane via a Cope rearrangement and then that undergoes the allylsilane based reaction in an intramolecular fashion to give the product after of cyclization.

In a similar fashion, we saw Sakurai reaction in an intramolecular fashion, Sakurai intramolecular fashion and that led to the conjugate addition and leading to bicyclic molecule. In a similar fashion, we saw different types of carbocations that can be formed especially say for example, the ketals that lead to upon reaction with a Lewis acid lead to the formation of this type of intermediate where this carbon is now electrophilic carbon.

And to which now in an intramolecular fashion the for example, if you have a substrate, allylsilane attached to this, then of course, we can think about that this allylsilane intramolecularly can react to allow the cyclization to take place in this fashion here. And then of course, we get the cyclic product. So you have a cyclic product form.

So like this we also saw the imonium ion to be formed and then imonium ion could be then reacted in an intermolecular fashion, where you have allylsilane in a way that led to the bicyclic products and then we saw two natural products, which we discussed in detail. Now we will see the remaining aspects of allylsilane based chemistry for some other interesting reactions.

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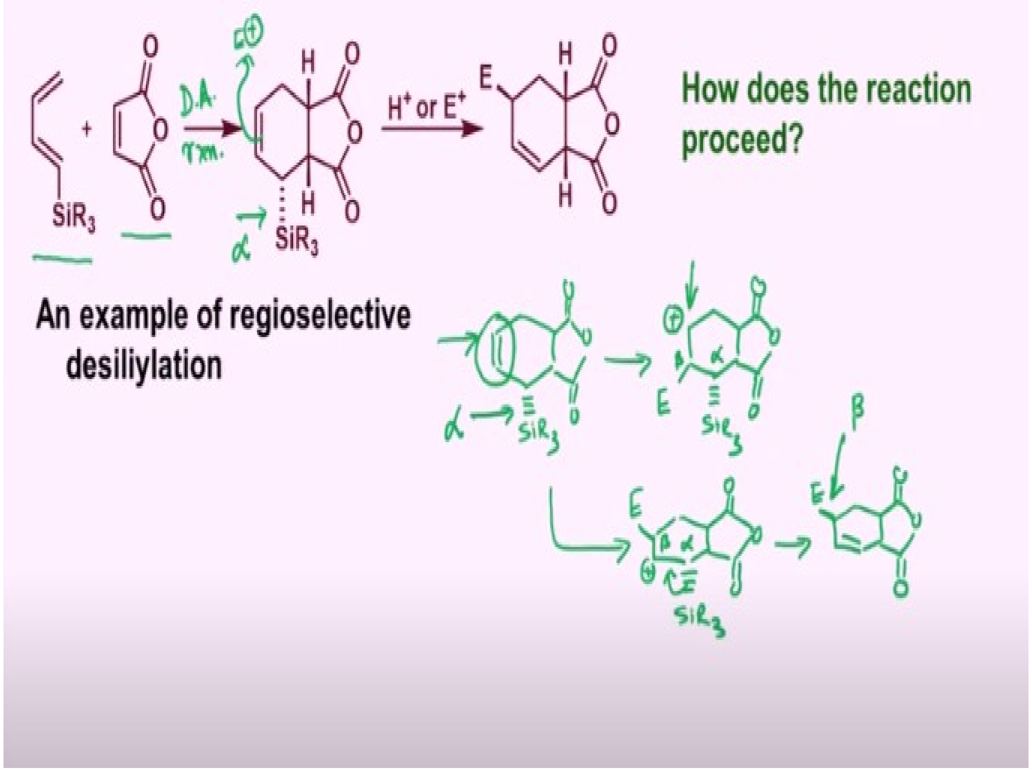

How does the reaction proceed?

An example of regioselective desiliylation

For example, if we take a diene of this type where the silicon carbon bond is attached at the end of the diene and if we take a dienophile like this, then as you know that a diene and a dienophile undergo Diels-Alder reactions. And so this is basically a Diels-Alder reaction which Diels-Alder reaction. Now the dienophile is symetrical dienophile. This particular dienophile is symetrical dienophile.

So it does not really matter which way the diene is oriented. And once the reaction occurs, then of course, as you can see, that you have here the carbon silicon bond, which is now alpha oriented. When this reacts with a proton or an electrophile, then of course the electrophile reacts with this particular double bond. And there are two possibilities. The possibilities are that whether the double bond reacts.

Supposing we simply say that this is the part of the product that is here. Without worrying as far as the stereochemistry is concerned right now, there are two possibilities this double bond can react. One is that it gives the electrophile attachment at this particular end of the double bond here. So if this is the electrophile that is going to attach, then of course silicon will be here and the positive charge will be here.

Now this positive charge is very far off and therefore, there is no specific reason why this carbocation will be stabilized. On the other hand, if the electrophile attaches on to this end of the double bond, so if we have the attachment of the electrophile here, then you generate a beta, a cation like this, where now as you can easily appreciate that this is alpha position and this is the beta position and therefore, there is a beta carbocation stability.

So this particular carbocation is here, where you have a beta carbocation stability leading to the product that as we have seen it here. So now as we can see that the electrophile attaches opposite to the carbon silicon bond as we have discussed it last time also that the attachment takes place on the opposite face.

And therefore, the since the carbon silicon bond is alpha oriented here, it is alpha oriented and therefore, the electrophile attaches from the beta face. And of course, the junction and all that is decided by the rules of the Diels-Alder based reaction.

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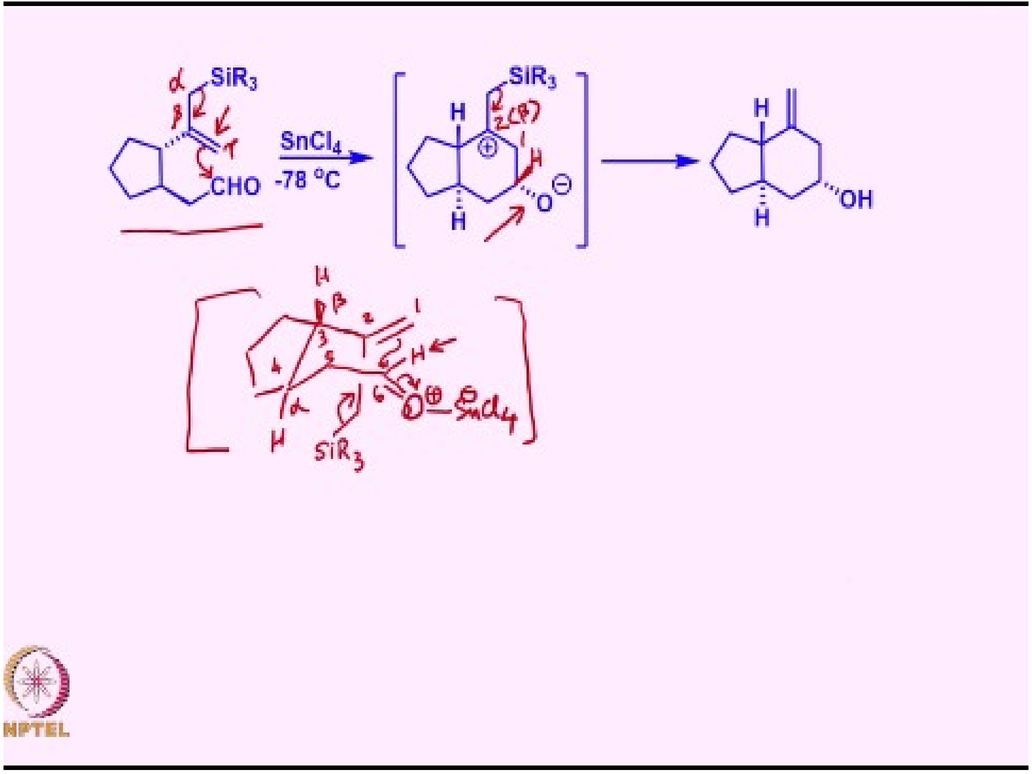

Now we can also take another example in which there is a very interesting cyclization of this kind where the allylsilane is inbuilt as you can see it from here and then that leads after the aldehyde chelates or coordinates with the tin tetrachloride it forms an intermediate which will be then attached by the gamma carbon here. This is gamma, this is beta and this is the alpha.

And therefore the attachment takes place from this side in this fashion and via this carbocation here. Now how does this reaction occur? We can try and see that how this particular part undergoes as cyclization here. So we can think about that we have here something like this. So you have a 5-membered ring here, where there is a hydrogen and then of course, we have this here, there is a hydrogen here.

So this is the alpha hydrogen, this is the beta hydrogen and this is what the silicon based things come. So once the Lewis acid coordinates here, so you have a $SnCl_4$ for example here. You have a positive charge and the negative charge here. And then this is position number 1 here, position number 2, 3, 4, 5, and 6. So this is the 6-member transition state which we can write it here.

So now when the reaction occurs, you have this is what is coming here and this is what is happening here. Now this is the intermediate that is formed. As you can see that when the reaction occurs between this one carbon atom number 1 and the carbon atom number 6, the carbonyl group is oriented below which is what is alpha oriented here and the hydrogen is beta oriented. So this is what is the hydrogen, which is correct.

And once this carbon number 1 and carbon number 6, they interact with each other as a positive charge at the carbon number 2, this is the carbon number 2, this is the carbon number 1. So this is carbon number 1, this is carbon number 2, which is beta to the silicon and therefore there is an orientation between the carbon silicon sigma bond and the p orbital they have such an orientation that they can easily overlap.

And then they can stabilize the beta carbocation. And that leads to the product formation like this.

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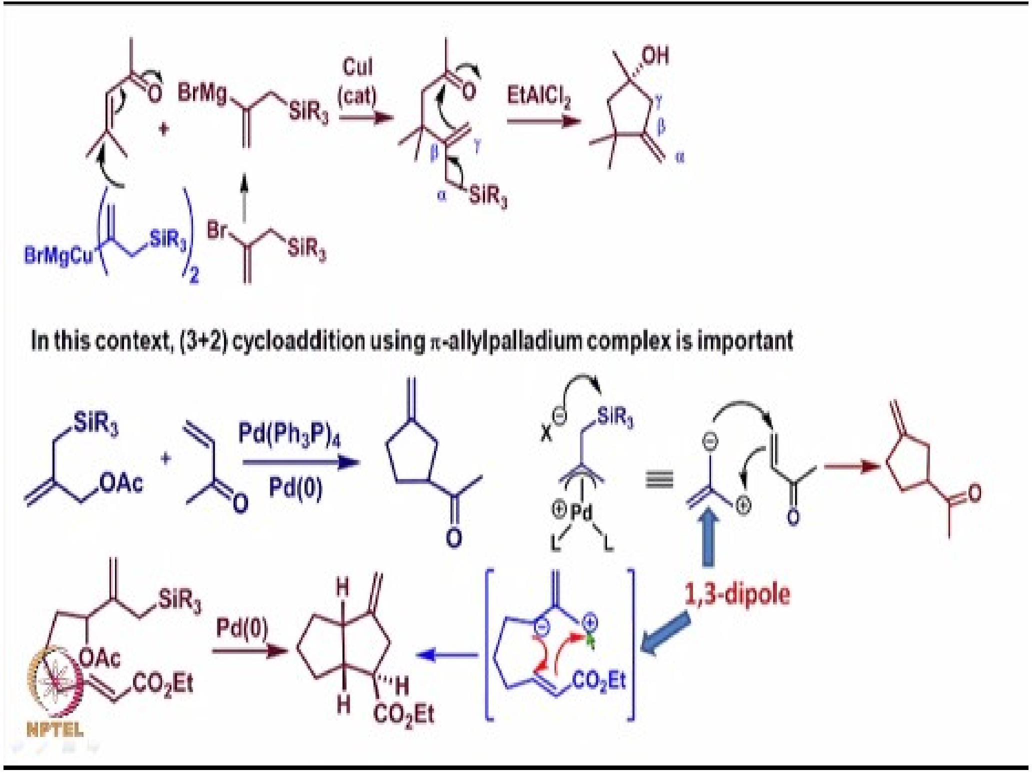

In this context, (3+2) cycloaddition using π-allylpalladium complex is important

Now we can also do one thing that we can start with a molecule of this type and react with an alpha, beta unsaturated ketone in the presence of cuprous iodide to form this intermediate which upon treatment with the Lewis acid leads to the formation of the cyclopentane derivative. This Grignard reagent can be prepared from this vinyl bromide upon treatment with a magnesium.

And then when this Grignard reagent react with cuprous iodide this cuprate is formed. This cuprate then reacts with the alpha, beta unsaturated ketone in a Michael addition fashion to form this intermediate. And when this intermediate reacts with a Lewis acid like this, the Lewis acid interacts with the oxygen making this carbon electrophilic.

Then double bond reacts with this particular carbon atom from the gamma end. Because then a cation will form at the beta position which is beta to the silicon and thus there is a beta silicon effect that is driving this reaction to eventually make this particular cyclopentane derivative. Now formation of this kind of cyclopentane molecules reminds of the 3+2 cycloaddition strategy using allylpalladium complex.

Now we take a compound like this instead of a Grignard reagent and this particular molecule has an allyl acetate part as well as allylsilane part and when this is reacted with an alpha, beta unsaturated ketone in the presence of palladium (0) like this, then of course we get a product like this. Now we can understand that in case this particular starting material is reacted with palladium (0), then acetate acts as a leaving group and the palladium (0) forms a what is called as a pi-allyl palladium complex.

And the X- basically it is an acetate ion, which has come out from here then reacts with the silicon and generating a carbon ion here. So maybe we can consider this particular species when x- removes the silicon to be equivalent to this kind of 1,3 dipole. Because there is a double bond and of course there is a positive charge because the acetate has gone. Therefore, this can be considered to be as an allyl cation.

And this silicon carbon bond is broken, therefore we can consider this as an anion. So basically this particular part represents as a 1,3 dipole which adds on to alpha, beta unsaturated ketone in this particular fashion to form this cyclopentane derivative. In a similar fashion if we take an inbuilt allyl acetate and allylsilane and of course, an alpha, beta unsaturated system like this and if we treat with palladium (0), then we get this kind of bicyclic molecule.

Already there is a enough number of carbons to make a cyclopentane on the left hand side and the right hand side part anyway leads to the formation of a cyclopentane derivative. And thus we get a bicyclic molecule like this having two cyclopentane rings. We can imagine that this particular part of the molecule here can upon treatment with palladium (0) leads to this 1,3 dipole the way we have shown it here.

And thus the negative charge then attacks onto this alpha, beta unsaturated system and eventually it closes to form the 5 member ring.

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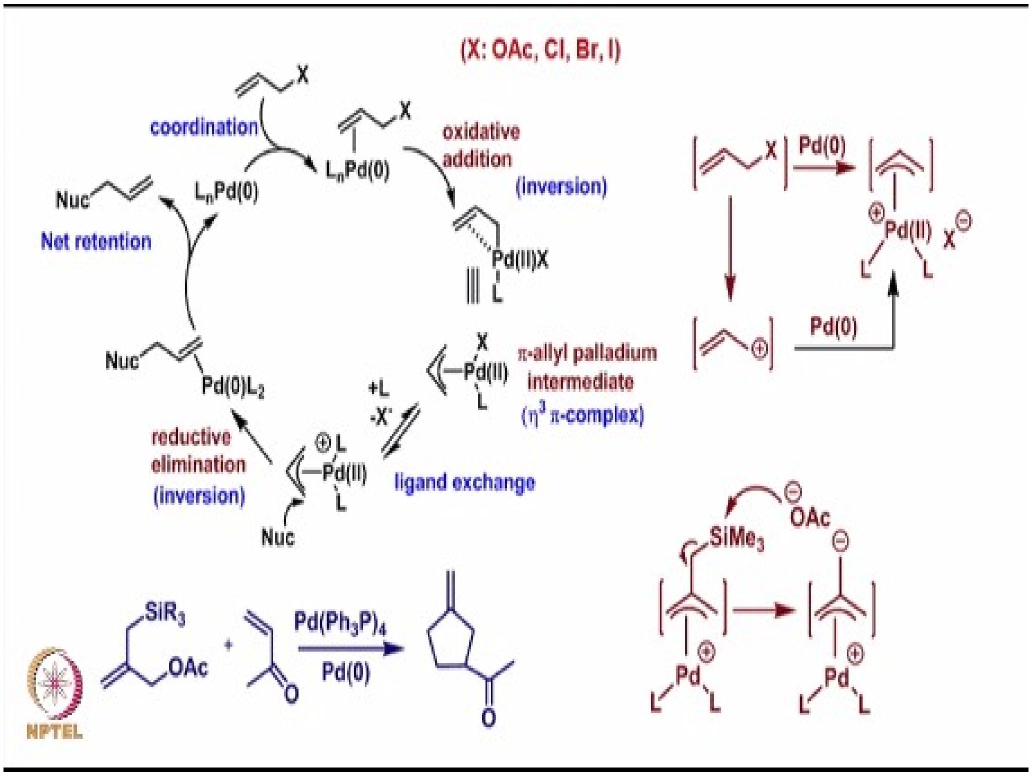

Now how does the pi-allyl palladium complex formation occur? When we have an allyl compound of this kind which has a leaving group like X. X can be an acetate, chlorine, bromine or iodine. And when palladium (0)interacts with this kind of allyl compound, there is coordination as the first step. That means the double bond interacts with the palladium to form this kind of pi complex or the coordinated molecule.

Then there is an oxidative addition between this carbon X bond to form this species in which the inversion occurs. That means, the carbon palladium bond forms from the opposite side to this carbon X bond leading to the formation of this kind of species, where the palladium is now in palladium (II) oxidation state. Now we can write this particular species in this kind of pi-allyl palladium intermediate type where the complex is of eta III type.

Now there is a ligand exchange. X goes as X- making the palladium as positively charged and of course a neutral ligand like L, which is a triphenylphosphine in many of these cases, then eventually forms this pi-allyl palladium complex like this with a positive charge on the palladium and also palladium being in oxidation state of II. Now nucleophile then adds from the opposite side in such a way that again inversion occurs accompanied by reductive elimination.

So eventually what happens is that, the carbon X bond which has gone is then substituted by a carbon nucleophile either on the same carbon or on the other side depending on the structure of the molecule eventually leading to another inversion. That means in all there is a retention of configuration overall. So there is a net retention as we can see it here.

Now during this reductive elimination process, then of course the palladium (0)comes off and of course that will have a coordination with the double bond as we had in the beginning. And then the final product is released and along with the regeneration of palladium (0.)

Now we can imagine that although this all involves a highly stereoselective transformation, but we can say that in nutshell what is happening is that this allyl X moiety which has X as a leaving group eventually forms a cation to which palladium (0) interacts to form this pi-allyl palladium complex. And then of course, the nucleophile adds on to this pi-allyl palladium complex.

But the main process that takes place is as shown here. Now if we take a molecule like this, as we discussed earlier, then of course, we can imagine that this pi-allyl palladium complex formation occurs just the way I have shown here or the way we have seen it here. Then of course, we get this pi-allyl palladium complex.

And then the acetate ion which has come out in the case of allyl acetate then takes the silicon from here generating this kind of anion. And of course, that undergoes 2 + 3 cycloaddition. So this is how the reaction occurs.

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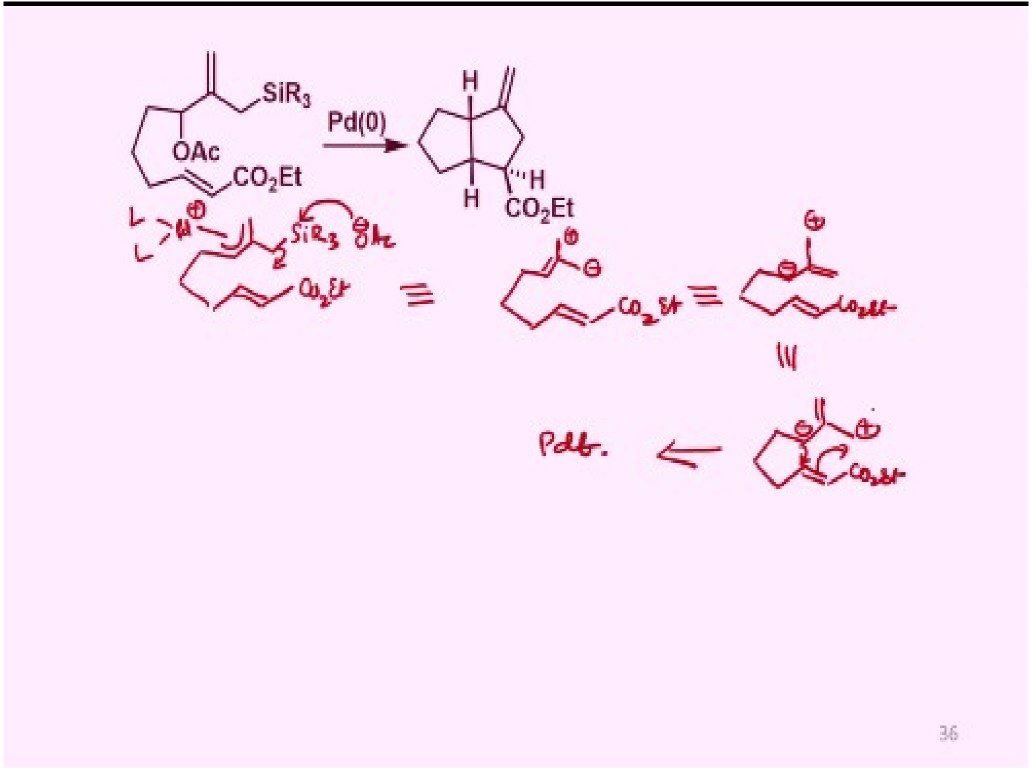

And of course in this particular case, as we discussed that the positive charge of course can keep on shifting or the negative charge keep on shifting. So you have a pi-allyl palladium complex, say you have a pi-allyl palladium complex here and this can be written up equal to something of this kind. So you have a negative charge here and a positive charge here.

After the acetate has taken away the carbon, the carbon silicon bond being broken and something like this is form and the positive charge is here. This can also be written up as though equal to negative charge being here. The negative charge being here and the positive charge here. And of course, we can also think about CO$_2$Et here. Or this can be written up equal to and then negative charge here and here.

This is what undergoes in cyclization forming the final product. So basically it is nothing but, and all these cases the allyl cation is stabilized by the palladium (0) or the palladium species which is formed.

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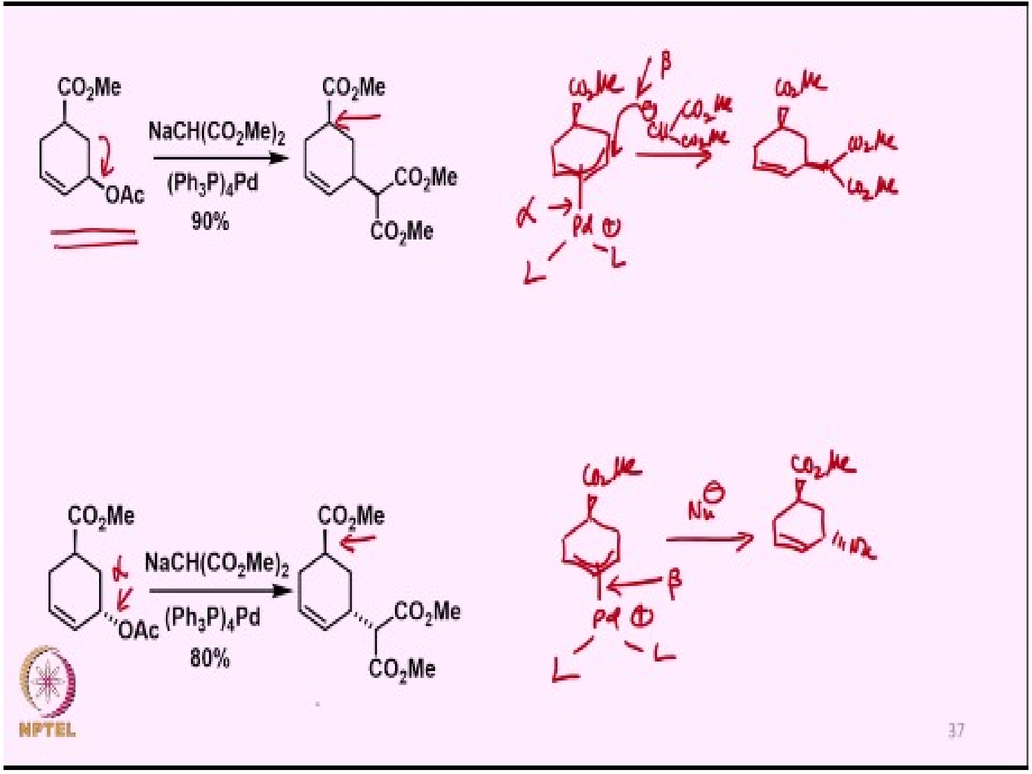

Now it is also seen that the palladium reactions can also be quite useful in C-C bond formation in a slightly different way. For example, if you can start with a substrate like this, which does not have any silicon but the only reason I am mentioning about it is that it can allow C-C bond formation using the same concept of pi-allyl palladium complex as you can see it here that the acetate is beta oriented.

And therefore, the pi-allyl palladium complex forms from the alpha side. So you have here the ester group which is present here and the pi-allyl palladium complex formation will occur from the alpha side, alpha oriented and then to that the nucleophile which is nothing but this particular nucleophile, this attacks from opposite to the alpha side, that is from the beta side and that leads to the formation of the product.

That means, it is like retention of the stereochemistry where the acetate had attached. And opposite of that is in this case since the acetate is from the alpha side the palladium attaches from the beta side and then the nucleophile again comes opposite to the carbon palladium bond. So that is basically a retention of configuration. So here you have the stereochemistry being now in a similar fashion here.

But now what you have is a beta orientation of the carbon palladium bond. And that leads to the formation of the say nucleophile here that leads to the formation of the nucleophile being here. So it is not the geometry of this particular ester group is important. What is important is the orientation of the allyl acetate in both the cases.

And as you can see that the reaction of the palladium (0) is highly stereospecific because it is an SN_2 prime type of reaction eventually.

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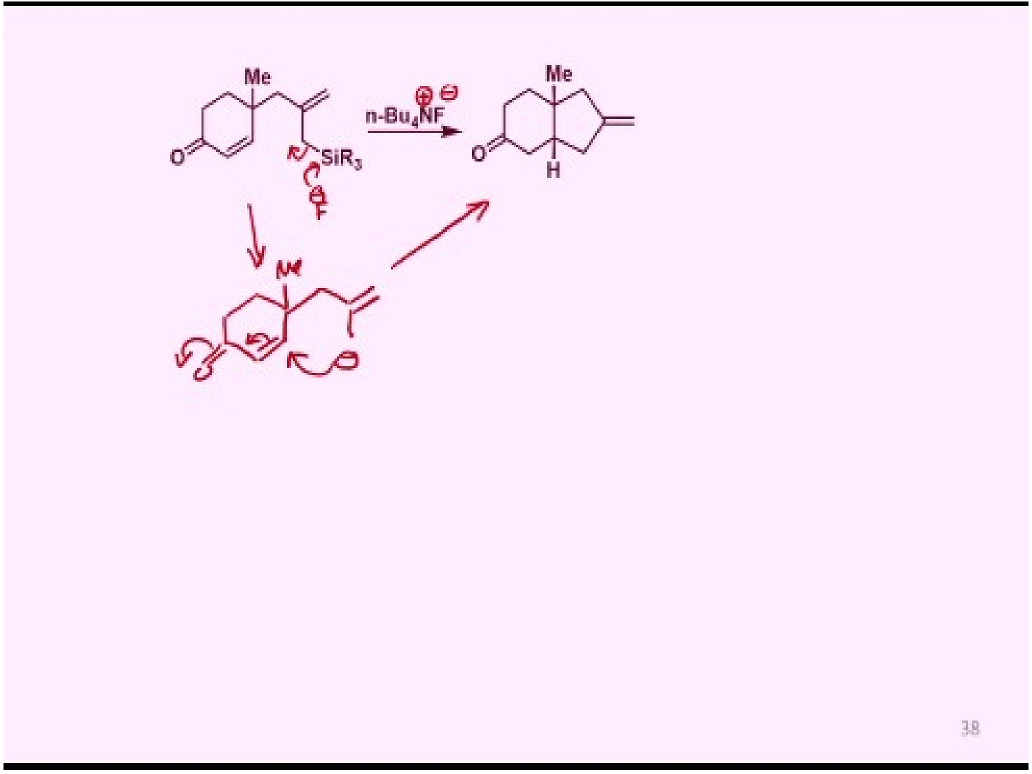

Now we can also see that we can react the allylsilane in a nucleophilic fashion also. Not only allylsilane reacts with an electrophile but also in the Lewis acid medium, but also we can make the reaction to undergo if you use fluoride ion. So you have a F- and a positive charge here. So F- takes the carbon silicon bond breaks and generates the anion here. So it is the chemistry of anion, not cation.

So now what you have is a enone of this type where you have now oriented an allyl anion. Because the silicon fluorine bond strength is quite high, therefore fluoride ion immediately reacts with the silicon and silicon carbon bond breaks because fluorine silicone bond strength is much higher than the carbon silicon bond.

And once this happens, then you have an intramolecular cyclization that leads to the formation of this particular pi cyclic intermediate. Now we will stop it at this particular stage and take up the silicon based chemistry, particularly vinylsilane based chemistry in the next class.

Till then you can go over whatever I have discussed it today and then we will look at the other aspects of silicon based chemistry in the next class. Till then, bye and take care. Thank you.