Organic Photochemistry and Pericyclic Reactions

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Module No: # 01

Lecture No: # 30

Cycloaddition – Diels – Alder Reactions (Contd.)

Yes. So, we were discussing in the previous class about Diels Alder reactions. We saw some selectivity about Diels Alder reactions. Today, we will be talking about the reactivity of Diels Alder reactions and then we will be understanding much about intra molecular Diels Alder reactions.

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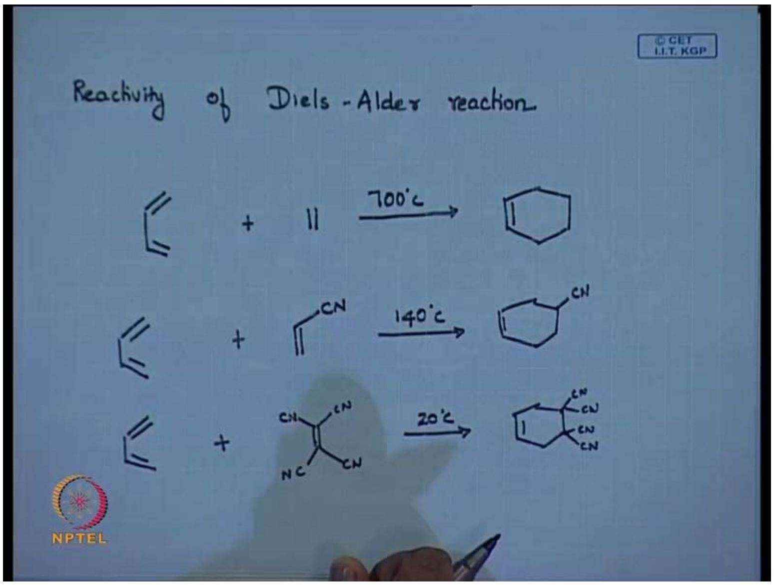

So, we will start with the reactivity of reactivity of Diels Alder reactions. For example, like I take a butadiene with a alkene and do this reaction. Normally, it takes 7000 degree Celsius to do this reaction and you end up with your Cyclohexene cyclohexene. So, you have your butadiene with alkene and you see it takes very very high temperature like 700 degree Celsius to do this reaction. But, if same, if I take my butadiene and if I make my alkene more electron poor by attaching electron withdrawing group like (( )) you see that, rate of the you see the reaction, 140 degree Celsius I get the same product.

See, there is a rapid degree in temperature, tremendous degrees in temperature. So, that initially it was 700 degree Celsius. Now, the reaction goes in one only 140 degree Celsius. Very another interesting fact is that, if I take the same Cyclobutadiene, but, with a very good Dienophile as a very poor like yeah four sides I know all electron withdrawing substituents, and you can see this this reaction goes in only twenty degree Celsius and you get this very interesting products.

See, like if I take my diene Dienophile and attach an electron withdrawing group; that means, I am making my Dienophile much electron poor poor. And you can see the temperature of the reaction its starts from seven hundred degree Celsius and you can take it to twenty degree Celsius. That much you can change the reactivity of your Diels Alder reaction by modifying your Dienophile.

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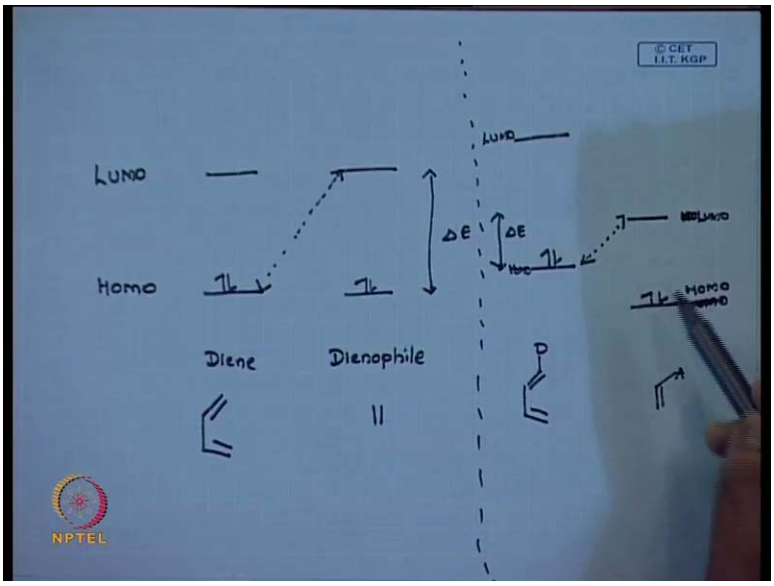

Even, you can play around with your diene also. If I have a reaction like aldehyde and this reaction if you see it is one sixty degree Celsius and it goes in one hour. I get my Diels Alder product fine. But, if an. So, how you make your diene much better for your Diels Alder reaction? You just you have to attach your electron donating in the case of electron dienophile. You use electron withdrawing, here you use your electron donating.

So, you have an for example, I take an methoxine and do the same reaction. You see that the reaction in hundred degree Celsius in two hours gives me my product.

So, So, the reactivity that is what the reactivity of Diels Alder. So, reactivity of your Diels Alder can be altered by altering your dienophile and diene. How it happens? Why it should happens basically? or How to understand it basically? You can get into your Lumo and Homo again. If I say, I will take the Lumo and Homo basically. I will take my regular diene without any substituent and a dienophile. So, this should be my Homo and this should be my Lumo and kind of (( )) this should be my. So, what I am talking about here, I am talking about the interaction of the Homo of your diene with the Lumo of you dienophile.

So, if you are saying this is the inter reaction I am talking about. This is your delta e. So, this is the energy difference we are talking about between your Homo of your diene and Lumo of your dienophile. But, in the same case, if I attach a donor and an electron withdrawing register acceptor (( )) what happens? My donor and my acceptor you see, what will happen with this Homo? This Homo, once I have a donar Homo will lifts up with this and same way your Lumo will come down. So, this is your Homo and this is your Lumo of your diene. This is the Lumo and this is the Homo of your sorry, this is your Lumo and this is your Homo. Now you are talking about the Homo and the Lumo right. You see now the energy difference.

In this case, this is your delta e. In this case this is your delta e. So, you can easily see now why the reactivity is. The initial case we had so big energy energy difference between your Homo of your diene and the Lumo of your dienophile. Here you can see once you have a donor, the Homo energy lifts up and if you have a acceptor, then the energy of the Lumo comes down. And now the energy gap is very small compared to the initial case and the reactivity of your Diels Alder is much more faster. If you if you watch this energy diagram much more careful carefully, you can end up in asking one question is that is, why cannot I can react the Homo of my dienophile with the Lumo of my diene?

You see it is possible see. So, far we are talking about the Homo of your diene and Lumo of your dienophile. If I can change this energy difference, can you can always say. So, I can lift this up and lift it down. So, the Homo of my dienophile, yes it is any possible to react with Lumo of dienophile. Yes you have such type of Diels Alder reaction and we call as inverse electron demand Diels Alder reactions. That is what we are going to do now.

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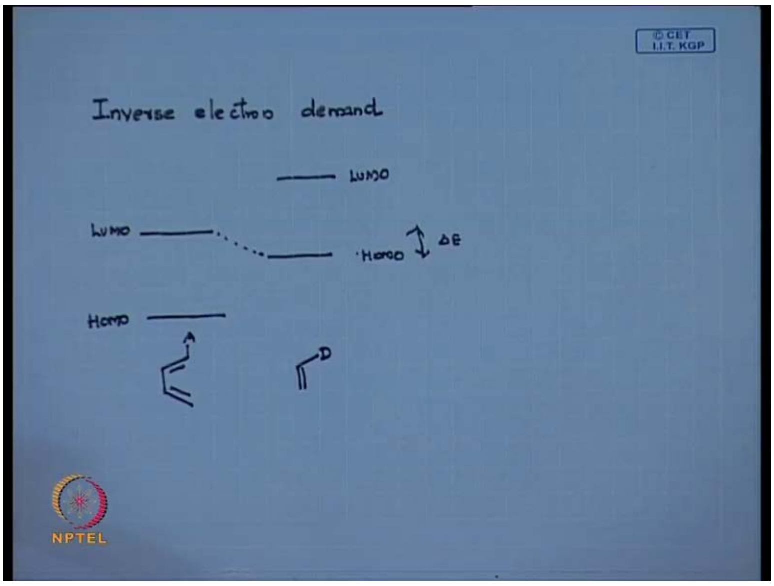

You can call them as inverse electron demand. Basically, what we are talking about is, I have a Lumo, I have a Homo. This is a diene with an acceptor molecule and if I have a dienophile with a donor which is completely reverse; now I can talk about this interaction this the Homo and this is the Lumo and this is your delta e. So, then it is possible. So, I will be talking about the interaction between Homo of my dienophile and Lumo of my diene always. So, far we were talking about the Homo of your diene and Lumo of your dienophile now, it is entirely inverse. So, this these type of reactions are allowed. You can see many Diels Alder reactions by energy diagram it is looks to be fine. Now, now we will see that whether it is orbitally allowed. Because, that we should keep in mind ok.

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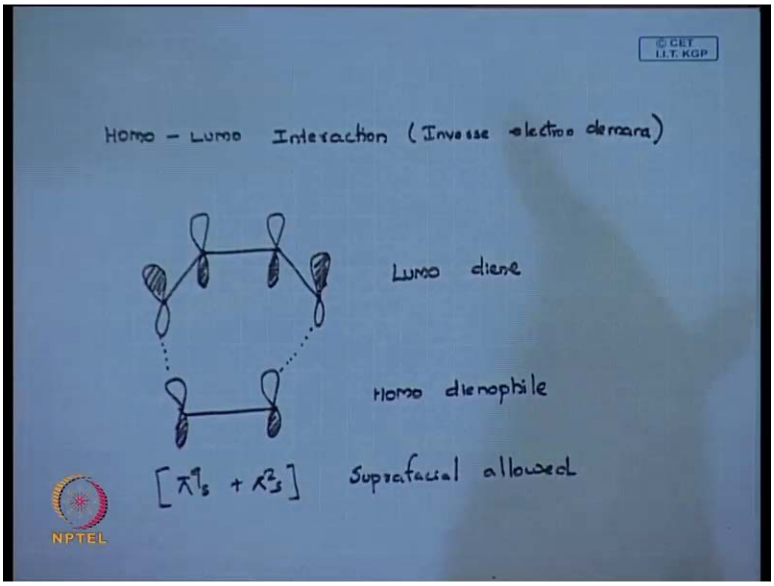

Homo - Lumo Interaction (Inverse electron demand)

Lumo diene

Homo dienophile

$[\pi^4_s + \pi^2_s]$ Suprafacial allowed

So, if you do the again, Homo Lumo interaction for inverse electron demand or you can people call it as photochemical also fine. Right now we will call it as fine right now you can call it as inverse electron demand. You were talking about the Lumo, we were talking about the Lumo of our diene, this is the Lumo of your diene. If I have my Homo of my dienophile, now you can you can see, again it is allowed suprafacially it can again have a pi 4 S plus pi 2 s. So, we have suprafacial allowed. So, what it says? Basically it says that yes, the inverse electron demand by energetically it is favored and by if you do orbitally and it also allowed. So, if you take the Lumo and Homo dienophile again it is suprafacially allowed just similar to your earlier normal Diels Alder reactions.

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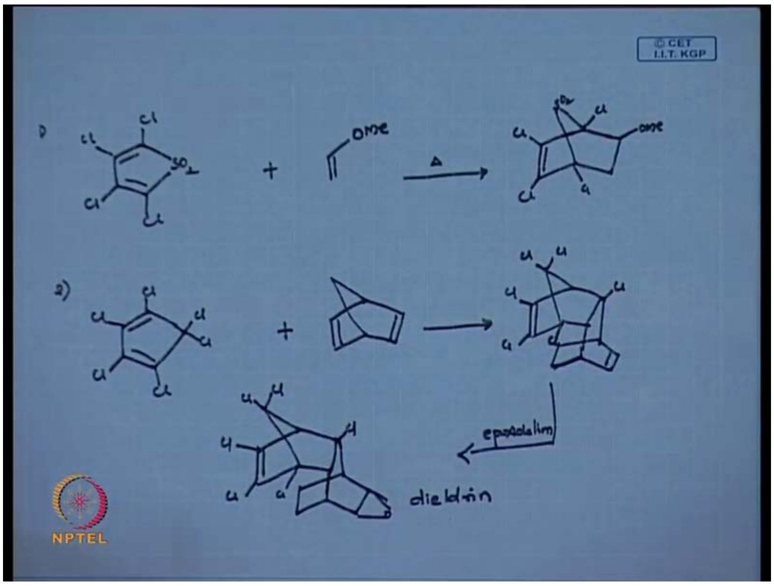

So, we will see some quiet interesting reactions of of inverse electron demand. Some examples of an inverse electron demand. I can have your type of systems (( )) systems like this with your, now your dienophile has an electron donating substituent. If you just read this reaction you end up with that (( )). All the sides of reactions you can get this product. Even I there are there are reactions where it has been used. You have been heard about dieldrin type of pesticides, you can synthesis using this inverse electron demand reactions.

For example, if you take, you have a system like this and then I (( )) system and if I do this reaction, end up with a, and your chlorines. See this this product is interesting in one sense like, you can, it is used as a nice pesticide. So, if you epoxidize this, epoxidation get a very nice product.

So you get this product and this is called as dieldrin which is a good pesticide. So, you can use, using your inverse electron demand chemistry Diels Alder reactions you can do the step of Diels Alder reactions fine. Now, what we do is that, we will see some examples of heteroatom Diels Alder reactions which also important one case like we call as you can do that reactions. we will.

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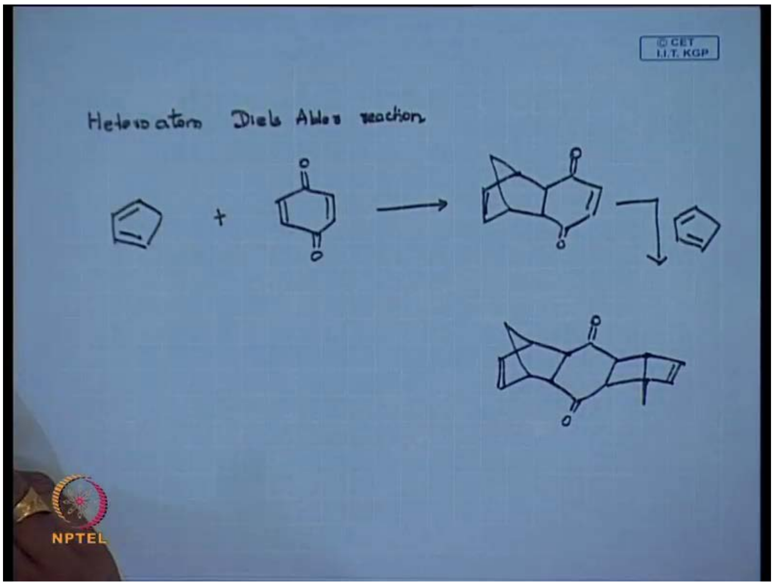

Heteroatom Diels Alder reactions where, you can have like, we were talking about dienophiles all with the carbon systems right. So, we can think about having that dienophiles of oxygen and all this type of systems. Slowly, you know this reactions nice favorite reaction like, yeah we can start with this initially with your oxygen type of systems. This you have known because, you get a very nice product here. Again I can do my second thing, a double bond here. So, I get like two Diels Alder reactions are happening. Two types of Diels Alder reactions if I look for here in this case, this is called as hetero atoms Diels Alder reactions like this. This is not exactly hetero atom, but, you can think about oxygen in this these systems. But, we will see now the exact hetero atom Diels Alder reactions which are like if I have a.

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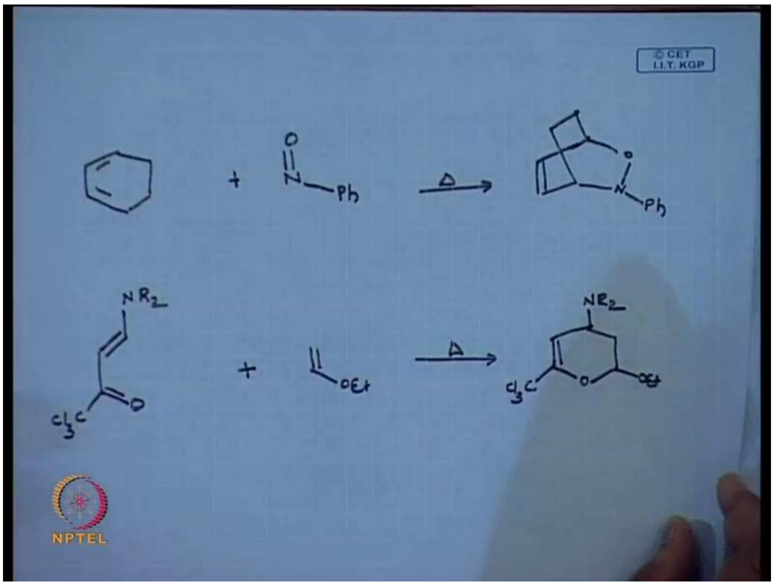

This is a proper example for you hetero atom Diels Alder right, very good class example. So, if you have this type of systems, what is the product you look for? This will be your dienophile and diene and so, you can look for right. So, I can look for this type of product. I can have my hetero atom on the other side of my diene that also I can take for example, I can take a system which is like ketone and my C C L 3 (( )) and I have this type of systems.

And it can have my Oet, this also undergo nice hetero atom. If I have an o yes S you make a type of pyrans type of rings structure. yeah This reaction goes in it very nicely. These are like, two good examples of your hetero Diels Alder. We have one more nice example which, you have studied on hetero atoms Diels Alder reactions is using your danishefsky dienes alright.

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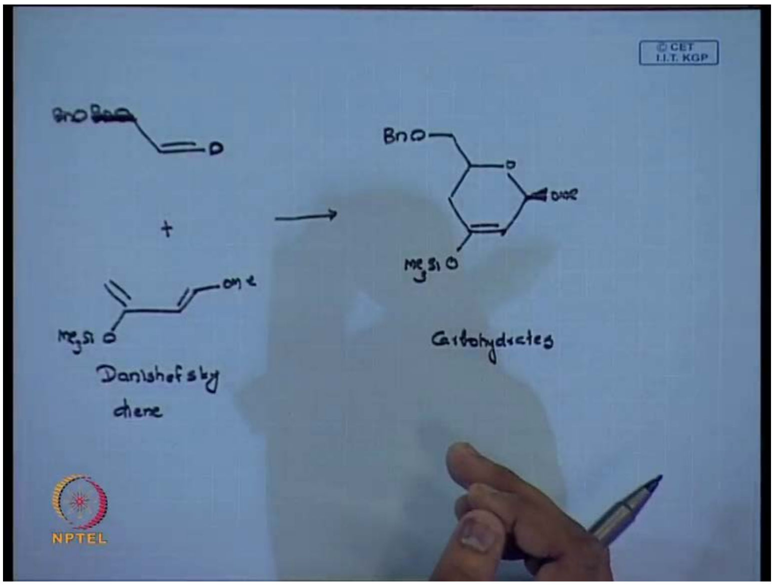

So, for example, I have like (( )) system. I have my, this is my dienophile I am talking about. This diene you have studied where you have, o S I m I 3. We call this as what? Danishefsky diene. It has lot of synthetic utility, has been done across this. You can end up with type of like very nice carbohydrates using this chemistry Diels Alder chemistry. You get this is your oxygen, you can synthesize very few reactions in which Diels Alder. You come across carbohydrates synthesis. This is one of, one among them. Danishefsky you use and you see you are going to end up if you see the product you are going to end up. is It will be because, again it gives you selectivity sorry just just there is a change in the dienophile it should be o B n. There is a C S 2 fine. So, you will have a B n o.

With a nice carbohydrate, a very normal approach for synthesis of carbohydrates and you know it has a selectivity. You can select this this part stereo chemistry will be selected because of the dienophile. So, it is an it is a very novel approach for your carbohydrates. So, that is what you have to, that is why this is very like specifically important. That is why I am taking it um.

So, these are all some, you and you and you can call these as some scope of Diels Alder reactions, very good scope of Diels Alder reactions. You are talking about like making first example, you were talking about making a two types of Diels Alder reactions then you have an pyran system and nitrogen based ring systems you are creating. Now you are creating about your carbohydrate systems. You can call as a scope of Diels Alder reactions. these are all It has lot of scope.

Now, what we will do is, that them we will slowly get into the understanding the hetero atoms Diels Alder reaction. That is all much more good Diels Alder reactions like you show to should know that intra molecular, now hetero atom you have seen in.

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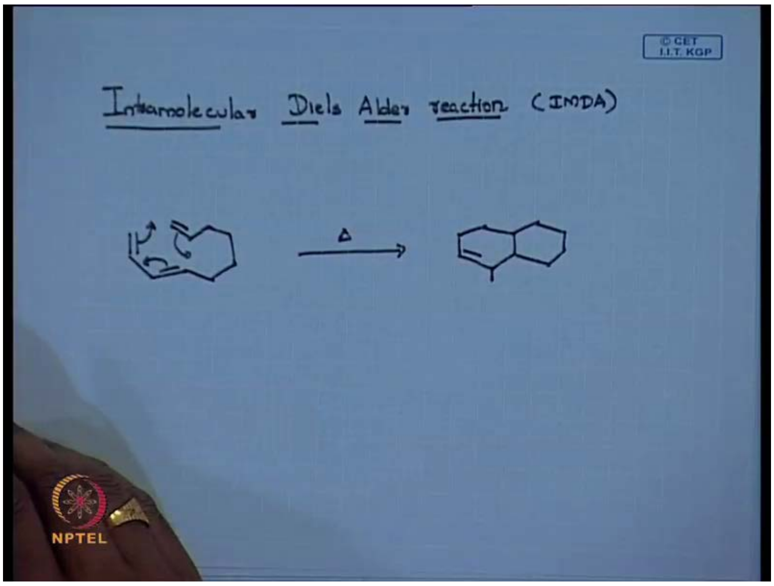

Intramolecular Diels Alder reaction (IMDA)

Now, we will see this, intra molecular Diels Alder reactions. We call this as simply I M D A, intra molecular Diels Alder reactions. For example, we will take the simplest substrate and try to understand them in detail. I take, first we will see what happens here. Do not worry about the stereo chemistry right now. First we will see how the reaction goes. So, its again, this will be your diene, this is your two pi electron system and this is your four pi electron system. This is your diene and this is your dienophile; two pie and this is your 4 pi system. If you heat this, you can you can get your cyclic ring system like your (( )) type of systems all right. This is your simplest Diels Alder reactions. So, you have a diene, you have a dienophile within the system and you heat it, you get your Diels Alder reactions. This stereo chemistry is really interesting because you are trying to fuse a ring right. So, now, you can think about whether it is a Trans ring junction or it is a sis ring junction, which it is which it is going to favor.

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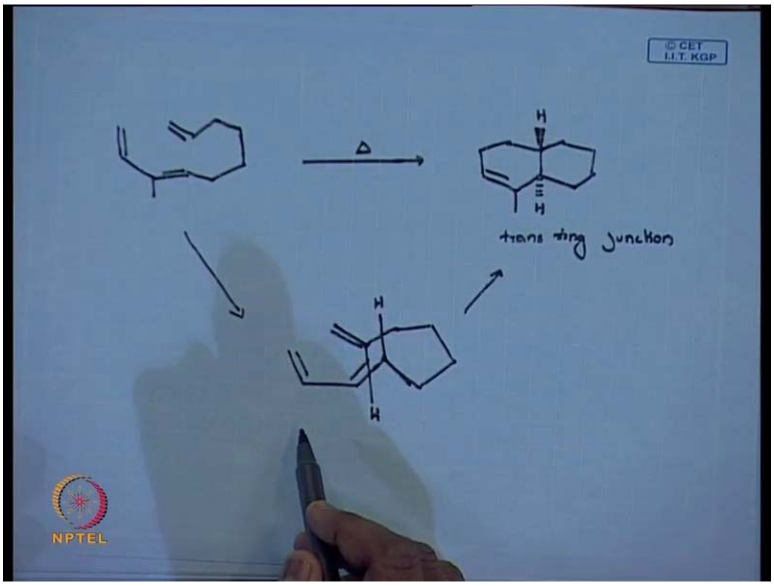

So, this stereo chemistry part is very important in understanding this same reaction. If I take the same product, if I take the same taking the same product now, if I do the heating and I will say that the product that which we get is a trans ring junction. One, this you end up with sort of trans ring junction one. yeah o sorry sorry right in the previous example also. So, you end up with a trans ring junction. I can call this, see how to understand this guy. How to understand that is giving a trans ring junction. See basically when you are talking about intra molecular Diels Alder reactions sometimes, you consider more stearic than your endo rules. Stearic, you have to take into consideration. If I dram draw the, how it in transition state how it looks like; not transition state exactly, stearic in bitch which way you can avoid much stearic interaction. If I draw this properly I can say that.

Can I have a system? I can think about. I have my hydrogen here, this is the hydrogen I am talking about see. I can think about drawing this in this way fine to have a less crowding. So, now, you can see when it is fused this hydrogen's on that way and this is the other way. So, you end up with a Trans ring junction. That is why you end up with a Trans ring. It is its not more about your endo rule, its more about your stearic. So, I have taken, I have drawn there is a minimum stearic crowding interaction fine. So, you get a nice Trans ring junction now.

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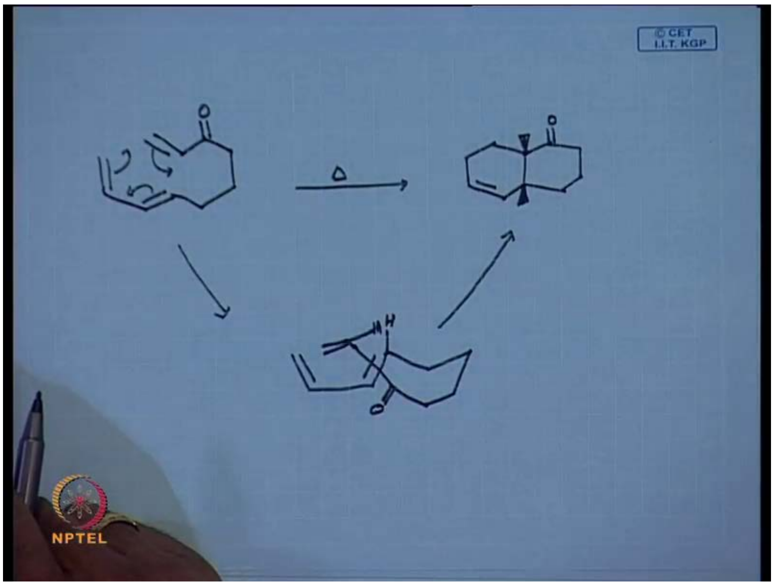

Clear? This whole chemistry becomes little more bit interesting once you have a carbon (()). Same system, same Diels Alder, if I have carbon here, same substrate, I have taking the same substrate now. So, the same substrate I was talking in the earlier case, now, I just have a carbonyl here. Now if you say that, if you do this reaction yeah you know what product you are going to get. So, that is no problem. So, you might but, what junction you are going to talk about here? Interestingly what happens is that, I get a sis ring junction. See in the earlier cases, I have in the earlier case where it was without a carbon here, just a system. I was getting a trans ring junction. In this case when there is a carbonyl, I am thinking of I am getting a sis ring junction. This also you can get into it. You can understand again by the same stearic and orbital corroding is that. So, again if I think to draw this system, but, much in this in this case in the both lecture form.

This is the hydrogen I was talking in the earlier case. This is my alkene and this is my hydrogen. Now what happens? My hydrogen is same in both the phase right and why this happens? This happens because, this carbonyl now have a overlapping with your alkene backside overlapping. That is why it takes this phase and it ends up giving up a trans sis ring junction because of your carbonyl can now overlap with diene taking this system. That is very nice if you see your now alkene inter molecular Diels Alder reaction, you end up with a trans ring junction. If you have a carbon in the system you end up with a sis type of ring junction fine.

We can make it still looks to be much more interesting inane in one sense like if you are taking, see now you have a double bond, I can take a sis olefin or I can take trans olefin and we will see what happens in that cases like.

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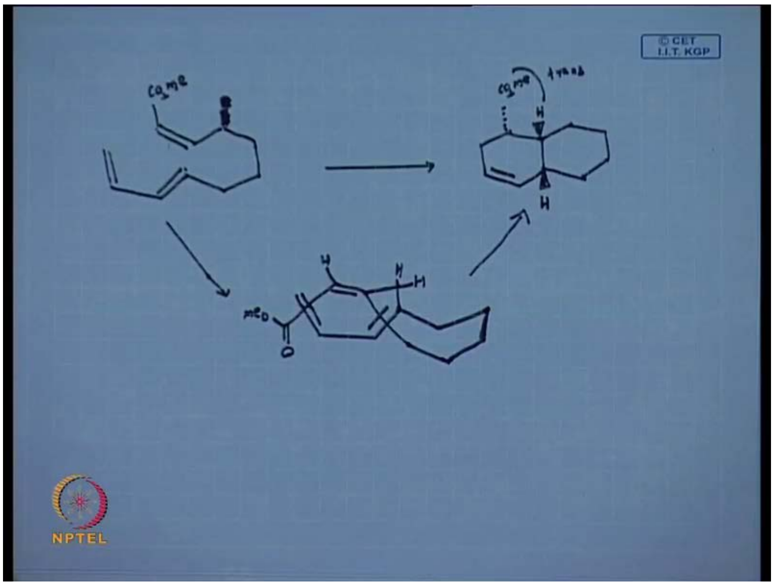

If I have taken this olefin, which is like more like a trans bond na (( )). We are taking because hydrogen is, hydrogen yeah sis olefin we are taking out and see what happens in this case; once we do this reaction we get the we get a product.

Yeah what we have studied that, if you are talking about this system should be sis ring junction. But, very interestingly you have a c o 2 me, that this and this are Trans right. So, you get this type of products. So, you know, you this you can explain with your endo (( )). We have a, I have just and I have a double bond here yes c o double bond o sorry sorry carbonyl is missing there. No we will take a system without carbon sorry sorry just without carbonyl and see what happens.

Um a. So, how to go about now? Just same way you can understand this if you can think about the endo folding of this. So, I can write my, I have my o me here. Now I can put my hydrogen and see whether my I am right. See you get this interactions and you end up with your trans because, of your carbonyl on the other way to your hydrogen. That is why you can look this, much more better to give your product.

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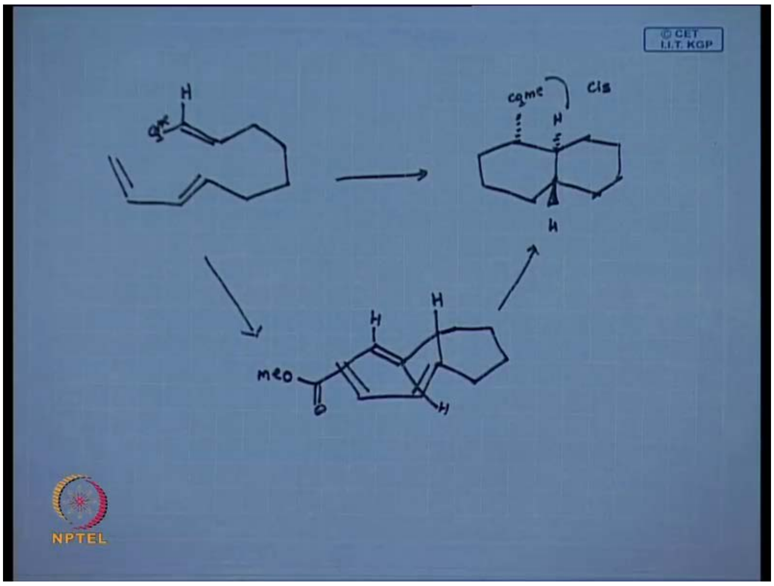

Now, if you do the same chemistry using your trans form, your alkene, a two m e plus my hydrogen. So, this is c o 2 m e. So, if I do this reaction, you see nicely you end up otherwise geometry hydrogen. So, I getting a sis type of thing. You know how to draw sis? Because you have seen that, in sis case how we folded it. Trans case we tried to use a chair like conformation. n a sis case we were using different way. That is how we taught about sis ways like pentyne type of molecule I am talking about. I have a alkene here, I will talk about my carbon here, o me and my hydrogen will be this way. See this way you can fold up, endo folding to give your this product fine. So, that is that is what you can think about like when you are doing intra molecular Diels Alder reactions like, if you have a diene. It has to selectivity if you have a diene type of systems you have to when you are fusing a ring, you have to see whether it is a sis junction or trans junction. You can use folding, but, you have to keep in consideration your stearic. That also should be into taken into consideration fine.

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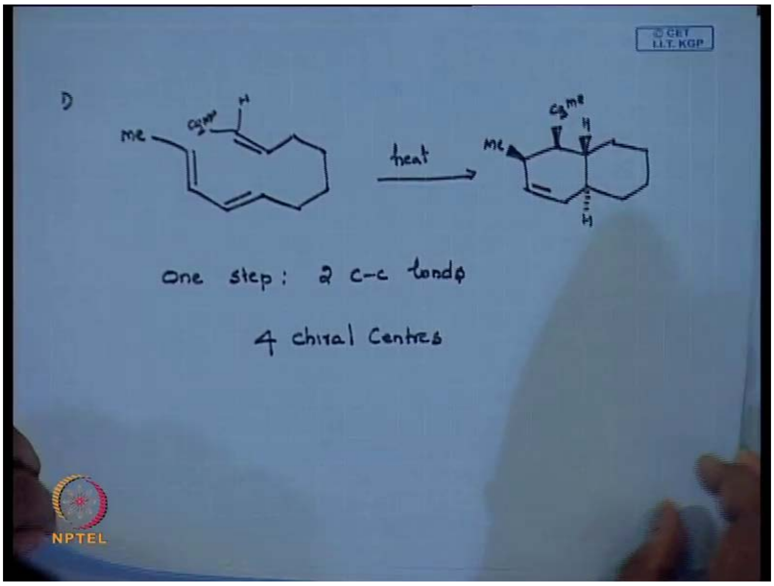

One step : 2 c–c bonds

4 chiral Centres

So, that is the thing about your intra molecular Diels Alder reaction. We will we will do some examples on that. See how intra molecular Diels Alder reaction works. We will take the first reaction. One methyl, same example one way yeah, but, we will just try to see whether we can trigger the product out of this. We have done this, but, with the methyl. I want, can you write the products c o 2 m e, heat. just You have this, I want you to heat this. So, can you think about writing the product?

See what you are going to do? This, if you just slowly look into this reaction, you are you are creating a two c-c bond right and you are ending up with four chiral centres. yes yeah. So, that is where that this particular example is really interesting. So, what we talked about, if you have a trans type of systems like, you can have the same geometry right, if I have an hydrogen this way, then my c o two m e also, should be the same. That is what we have studied in our earlier example right. So, we have a c o 2 m e both will both should be sis. n a When you have a system like this and this junction should be trans and your methyl should be the same direction of your c o 2 m e. Now, we have a four chiral centres now. So, this reaction is a one step. Very nice reaction, it is a one step where you had making two c-c bonds and then you are ending up with a four chiral centres.

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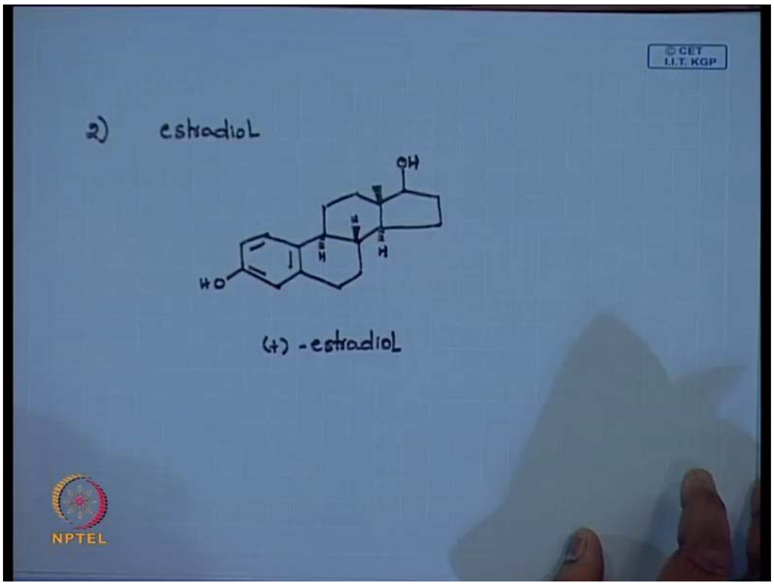

2) estradiol

(+) -estradiol

So that is that is very interesting that part. We will take another important, another good synthetic application of your Diels Alder reactions. Have you studied this extra diol synthesis? You have studies this extra? Have you seen this component? Extra extra are there. You have studied this x, this is the structure. If you want, this is your extra, see the thing is that, it has nice chiral carbon centres and it is always nice for you. In organic chemistry you look for chiral centres. right This is called as plus extra estradiol, this compound.

If you want to synthesize this compound, there are n number of good ways to do that. We will start our, there is one electro cyclic reaction. Anyhow I will teach you that.

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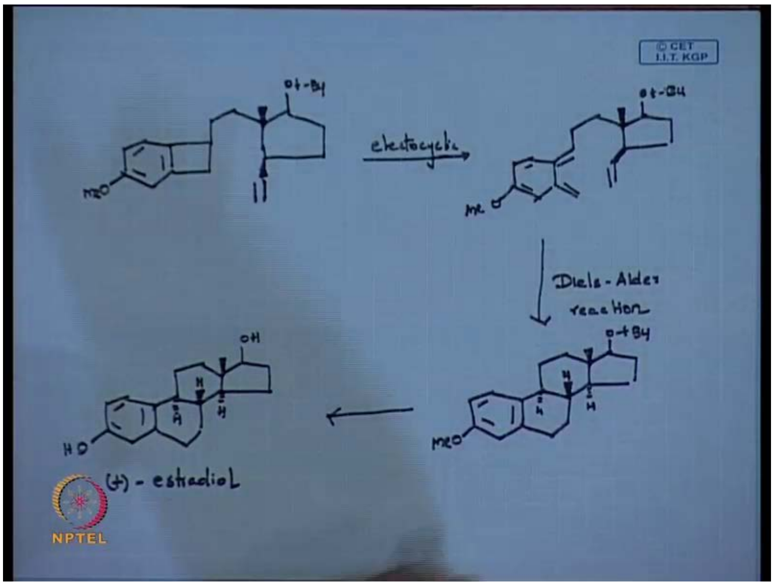

So, if we can take this step for example, this particular molecule o m e, what has to be attached? See this. What we are going to study? This electrocyclic reactions in this after Diels Alder reaction, after cyclo additions. But, anyhow it has known about electro cyclic already right. What what happens? Any idea? like Electrocyclic reactions, if I take this and ring closure or ring opening yeah. So, you end up with a nice ring opening. yeah I will explain when we go there. We will study why it is con dies all these things, but, just right now we can say that ring opens.

(( )) Now you can see see see. You have a system, now which can undergo a type of Diels Alder right because you have a very good diene system here. And you have a dienophile. It can undergo nice Diels Alder reaction. So, what you end up? Now you have to fix your stereo chemistry. Also, when you are doing Diels Alder reactions that is why much more important n a.

That is why your pericyclic reactions are more important because like it tells you to get your stereo chemistry in a right way (( )) yeah here. So, you have a ring closure here. So, I have a system like hydrogen outside. Think about this. So, this you have, then you can always, you can de methylate, this to your hydroxyl group. That is your estradiol.

So, you can also have this, O H here. You can also have O H here because you can have an hydrogen. That is why Diels Alder, there are the there are many applications which you can think about doing Diels Alder reactions and very very well known synthetic applications are known you see like Diels Alder reactions.

So, these are some synthetic applications of your Diels Alder reactions which you have seen. So, what and exactly to wrap out your Diels Alder is that, because that is more important to summarize. These are what we did in the Diels Alder. just I will just summarize what all we studied in Diels Alder um.

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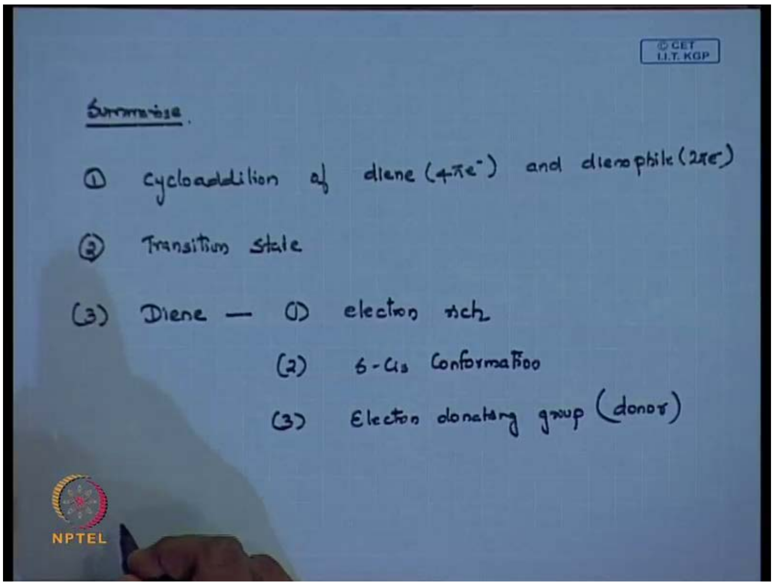

Summarise.

① cycloaddition of diene ($4\pi e^-$) and dienophile ($2\pi e^-$)

② Transition state

(3) Diene — (1) electron rich

(2) S-Cis Conformation

(3) Electron donating group (donor)

First, we studied, it is a nothing but, it undergoes cycloaddition of diene which is your four pi electron system and dienophile which is your two pie electron system. That is what we said it is a cyclo addition. And it goes to a transition state. And fine, that is what we studied and what we did is that, we went to the third important part. We understood is, about your diene; we set up two conditions; we found two conditions necessary for diene to Diels Alder reaction. One it should be electron rich r and another thing which we talked about is it should be in S-cis conformation.

See in case of cyclic, cyclic acyclic dienes you have like conformation law. One, it should be sis or it should be either Trans. So, one can be an excellent diene; another case cannot be a diene. But, in linear system we always have an equilibrium. Like, if you take a butadiene, it moves from S-cis to S-trans, you have all these things. So, that that case your S transform reacts, S sis form reacts. So, these are the two important addition, electron rich and S. So, that means, what I am saying, diene should have electron

electron donors or electron donating groups. That is your donor molecules. There, it is nice. That is about your diene.

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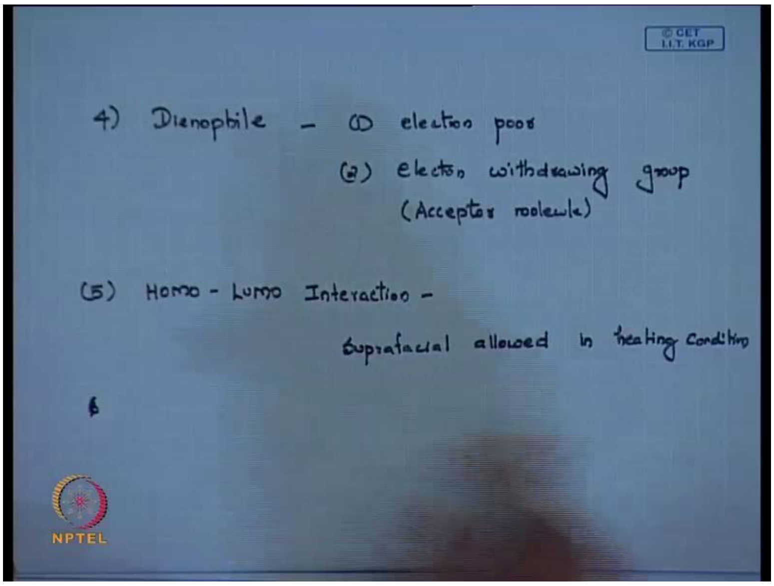

4) Dienophile – (1) electron poor

(2) electron withdrawing group
(Acceptor molecule)

(5) Homo - Lumo Interaction –

Suprafacial allowed in heating Condition

6

Then, we slowly went to your dienophile. So, first thing we said that, it should be electron poor right. If it is electron poor, what it essentially means that, you should have electron withdrawing group. That is, your acceptor molecules, this can be your aldehydes nitrides right. These are all very good for that your dienophile, that is how we made your diene and dienophile. The fifth thing we thought about is your Homo Lumo interaction and we studied that it should be suprafacial allowed in heating condition under thermal activation or heating condition. So, if you thermally activate, suprafacially it is allowed. So, that is why these are the Diels Alder reactions goes very nice. That is your, that is your about your, Homo Lumo interaction.

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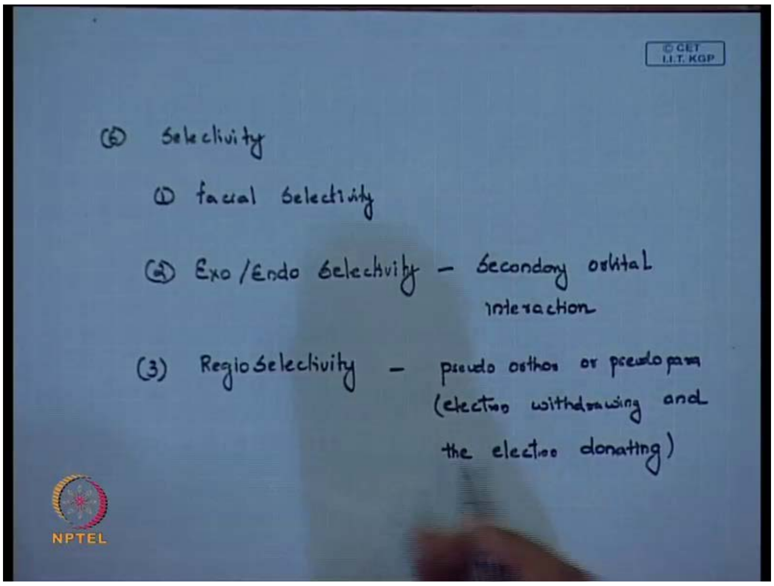

(6) Selectivity

(1) facial Selectivity

(2) Exo / Endo Selectivity – Secondary orbital interaction

(3) Regio Selectivity – pseudo orthos or pseudo para (electron withdrawing and the electron donating)

Then, we went down to the important part that is, about your selectivity right. We first, we studied about your facial selectivity. It is more like specific right, the facial selectivity. It is more like very specific reactions. There we we said that, we can see in the front approach as well as side approach the whole reactions. After that we worked on our Exo/Endo selectivity. So, in Exo/Endo selectivity we said that, Endo will be favored because of its secondary orbital interaction. Then, we went to Regio selectivity and we talked that, the electron withdrawing and electron donating substituent's in the product should be either pseudo ortho or pseudo para. This electron withdrawing or electron donating electron withdrawing and electron donating electron withdrawing and electron donating if you see the product, it should be either pseudo ortho or pseudo para in position. that is. So, that will be Reigo selectivity. And you can explain thus, based on your isomeric structures that is, we saw about the selectivity.

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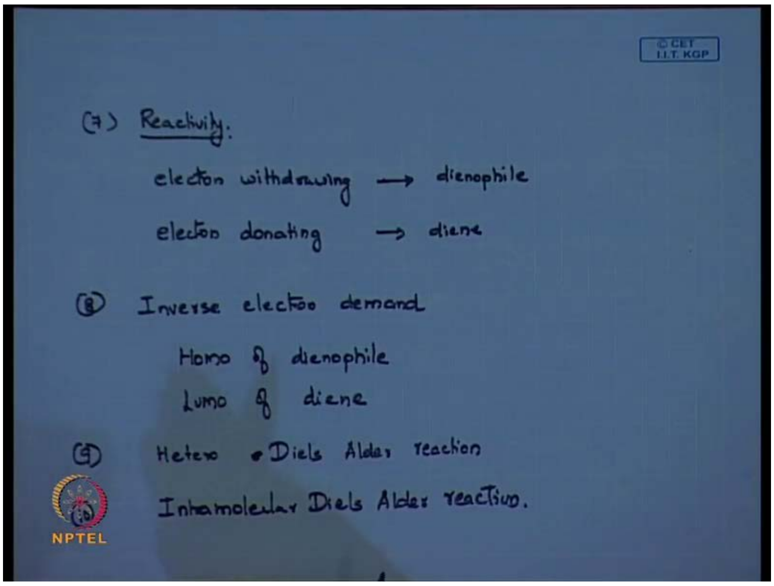

(7) Reactivity.

electron withdrawing → dienophile

electron donating → diene

⑧ Inverse electron demand

Homo of dienophile

Lumo of diene

⑨ Hetero Diels Alder reaction

Intramolecular Diels Alder reaction.

Once we finished our selectivity, then we went about the seventh part the reactivity and we say that, if we can change your diene, if you put an electron donor on your diene, and electron accepter on your dienophile, the reactivity of the reaction tremendously increased. And we studied that, based on your energy gap correct. So, yeah electron withdrawing; if you have a electron withdrawing in dienophile, it is good. Electron donating on diene is good for reactivity. So, that the energy gap will become less and you can have a nice reaction going on. So, that is about the reactivity we talked about. the then Then we called that as a scope or then went back and studied the inverse electron demand and which is very important. In all the cases you were talking about, Homo of your diene and Lumo of your dienophile. In this case you are talking about the Homo of your dienophile and Lumo of diene. So, it is basically Homo of dienophile with Lumo of diene.

Once we did our inverse electron demand, then we moved across the scope hetero Diels Alder reaction. Then finally, we ended up with talking about the intra molecular Diels Alder reaction fine. So, this is the, (( )) just the these are the areas where we covered on Diels Alder reaction.

When we cone next class, we will be talking about Alder ene reaction fine. That is how we That is how we end this class.