Organic photochemistry and Pericyclic Reactions

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Module No. # 01
Lecture No. # 29

Cycloaddition- Diels – Alder Reactions

For the last couple of classes, we were trying to discuss about the cyclo addition reactions. We said like two unsaturated molecules can undergo a additional reactions to give you cyclic unsaturated products and based on cyclo addition reactions, we said that cyclo addition reactions can be broadly classified based on their numbers of electrons which are interacting. We broadly classified them as 2 plus 2 cyclo additions and 4 plus 2 cyclo additions and we said that we will be discussing that in the coming classes.

So, we started with 2 plus 2 cyclo addition reactions. We said that 2 plus 2 cyclo addition reactions on photo chemical activations is suprafacially allowed and then, if you do a thermal activation, we get an anterafacial addition. In the case of anterafacial, we said that there is a limitation and that is the geometry of the molecules. If it is favored, then you end up with the anterafacial reactions. We said if we take a simple cyclo, simple alkene system and do photo chemical activation, you end up with the suprafacial 2 plus 2 cyclo additional reactions, but when you do the same reactions in thermal, you do not end up with any product.

So, we we did some, we saw some good examples where we can get 2 plus 2 cyclo addition reactions on photo chemical activation and they go by a suprafacial additions. When we went for anterafacial, we took in ketene molecules and we saw the ketene geometry was nice. It under goes a 2 plus 2 anterafacial cyclo additional reactions and we did many synthetic utility of your ketene chemistry. We try to react with an alkene and we saw that we can think about getting cyclo ketone systems. Then, we did reactions with your aldehydes and we end up with beta lactones and then, we carried out reactions with your amines and we got beta lactum systems.

So, we studied in general how 2 plus 2 reactions occurs. Then, we said we will now, what we will do is we will concentrate on our 4 plus 2 cyclo addition reactions. Now, the first reaction comes into your mind about 4 plus 2 cyclo additional is your famous Diels-Alder reactions. So, that is what we are going to concentrate in this class.

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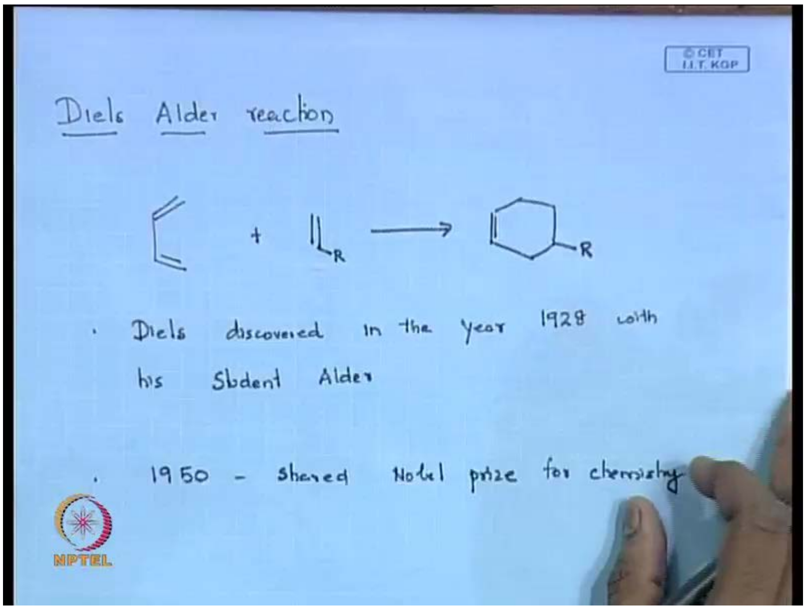

Diels Alder reaction

- Diels discovered in the year 1928 with his Sbdent Alder
- 1950 - shared Nobel prize for chemistry

So, this is your Diels-Alder reaction. So, you can have a 4 pi electron system and you can and there is a 2 pi electron system. Your alkene and this, your diene-butadiene with your alkene forms a nice cyclic product. It can have a substituent end up with a substituent here. So, this is your simple Diels-Alder reaction. Basically, Diels-Alder reactions, Diels discovered this reaction in the year 1928 with his student Alder. I think this is the first reaction which has been kept based on the scientist name who has invented, who has discovered this reaction and this, your Diels-Alder reaction in the year 1950; they shared Nobel Prize for chemistry.

They got Nobel Prize for chemistry in the year 1950 for Diels-Alder reactions. Diels-Alder reactions are very like many important synthetic utility this reaction has. So, what we will do initially is we will try to see the mechanism of the reactions and try to understand different components. How diene should be, how dienophile, your dienophile should be, what condition favors these reactions and all these things we will do in all detail, right.

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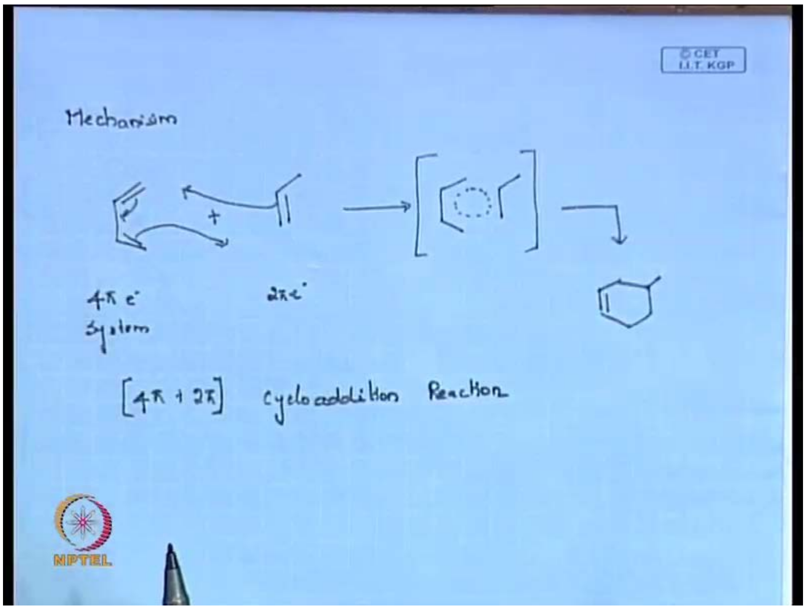

So, the first thing we will get into is his mechanism. It is nothing, but a simple, you take a diene system having an alkene. So, you get a sort of transition state, six member’s transition state. I think about this transition state very nicely and this will give you a final product. If you carefully watch your diene, your diene is 4 pi electron systems and your dienophile is 2 pi electrons.

So, that is why we call this reaction as 4 pi plus 2 pi cyclo addition reaction. This is the simplest mechanism of Diels-Alder reaction. Just you take a diene which is your 4 pi electron system and you have a dienophile which is your 2 pi electro system. They form a type of cyclic transition state and this cyclic transition state, then gives your product. They just clearly obey your pericyclic principles. This reaction, now what we will do, we will see your diene. How your diene should be for the reactions, Diels-Alder reaction, how your (( )) should be favoring your Diels-Alder reaction, how it should be to favor your Diels-Alder, how your dienophile should be? So, we will do in detail. Now, we will start with your diene.

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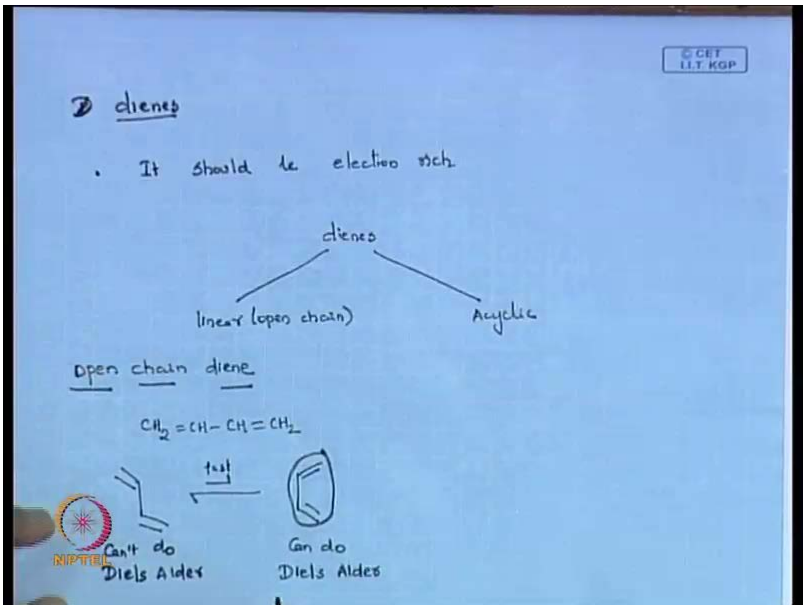

D dienes

- It should be electron rich

dienes

linear (open chain)

Acyclic

open chain diene

$CH_2=CH-CH=CH_2$

Take your dienes. The first condition your dienes should be if you want the proper diene for carrying out a Diels-Alder reaction is that it should be electron rich. That should be first condition that if a diene which is good electron rich will make your reaction nice, will favor your reaction, Diels-Alder reaction very nicely. The second important thing about diene is that diene should have a perfect geometry to carry out a Diels-Alder reaction. For example, if I take your dienes, I can classify them as open chain system like linear one or we can call it has open chain or you can think about having an acyclic. So, how it should be if consider an open chain diene?

For example, your buta will take a open chain diene system. So, in open chain diene, if I take your butadiene, for example like this. So, this is the simplest way of your butadiene. How it exists normally, you can write in two ways, right. So, butadiene can exist like your transoid form and sisoid form. So, which should be, which geometry it should do a Diels-Alder reaction? See this is a preferred one to do a Diels-Alder reaction. It should be in sisoid form, in transoid form that is a limitation. If you talk about diene, see the major limitation that it should be in the cis configuration or sisoid configuration to carry out your Diels-Alder reaction apart being an electron rich. If it is in a transoid form, in our get this type of Diels-Alder reaction. Since, it is a linear, you always have a equilibrium which when your sisoid to transoid. If you have your transoid, you end up with a sisoid which under goes a Diels-Alder reaction, not this one.

So, we cannot do Diels-Alder. This can do Diels-Alder reaction that is the more important point of your open chain. So, first we say that diene should be electron rich. After the second point, we are talking about that the diene should be in cis configuration to do the reaction. You call as S-CIS, right. Sisoid if it see in the case of linear, you have always an opportunity of your transoid and sisoid and your sisoid ends up doing the Diels-Alder reaction, but once we go to acyclic system for example, if I take an acyclic dienes, we take two cases like you will have a cyclo pentadiene, furan, a cyclo hexadiene one of type.

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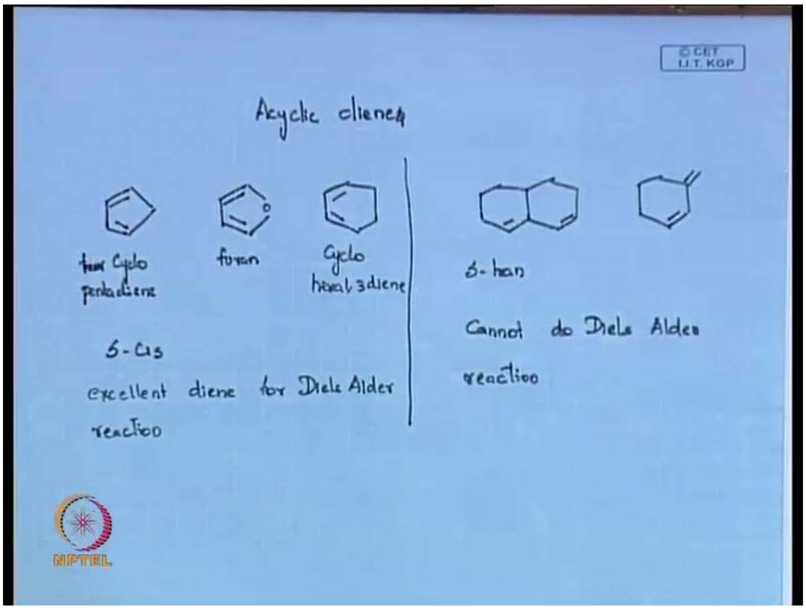

Acyclic dienes

Cyclo pentadiene

furan

Cyclo hexa1 3diene

S-cis

excellent diene for Diels Alder reaction

S-tran

Cannot do Diels Alder reaction

Another class you were talking, we can talk about this your type of (( )) system. If you see this class of dienes, that is your cyclo pentadiene, furon and you have a cyclohexa 1 3 diene, this is your furan, sorry cyclo pentadiene, furon, cyclo hexa 1 3 diene. See this type of dienes if you see, their conformation is locked. All these guys are S-CIS and they vary and they are excellent diene for Diels-Alder reaction, but if you come to this class of diene (( )), they are S-trans. Your conformation is locked in S-trans. They cannot go for your sisoid form, so their conformation is properly locked and they are the S-trans. They cannot do Diels-Alder reaction. They are not good diene for Diels-Alder reaction. So, that is the thing about your diene.

So, two things you have to keep in mind when you are thinking about your diene. One is that your diene make its electron rich. How you make a diene electron rich? Any idea?

You can have your how you make your diene? Yeah. You can just attach your donor donor substituent to diene like methoxy like that substituent. If you attach your substituent to your diene, then it becomes like more electron rich. Once they are more electron rich, yeah you can do the reaction nice. You can be a very good diene to the Diels-Alder reaction. That is the first point. It should be electron rich.

The second important point to be remembered in your about your diene in Diels-Alder reaction is it should be S-CIS, that is sisoid in configuration, sisoid confirmation. Otherwise, if it is in a transformation, you will never get your Diels-Alder reaction in acyclic system. Yes, you know that there in sisoid and transoid. So, in acyclic system, you get Diels-Alder reaction, but in cyclic system, sorry in linear system, but in acyclic system the conformations are locked. If you have like trans, it never gives your Diels-Alder reaction, but in linear, you always have an equilibrium. So, you can think about Diels-Alder reaction. Clear?

So, two points are electron rich, another is your sisoid conformation. These are the two things you have to remember when you talk about dienes in Diels-Alder reaction. So, we are clear with this. Now, what will do is we slowly move to the next (( )), that is your dienophile. How a dienophile looks in Diels-Alder reaction? It should look as I said first. Dienophile should be electron, just opposite your diene.

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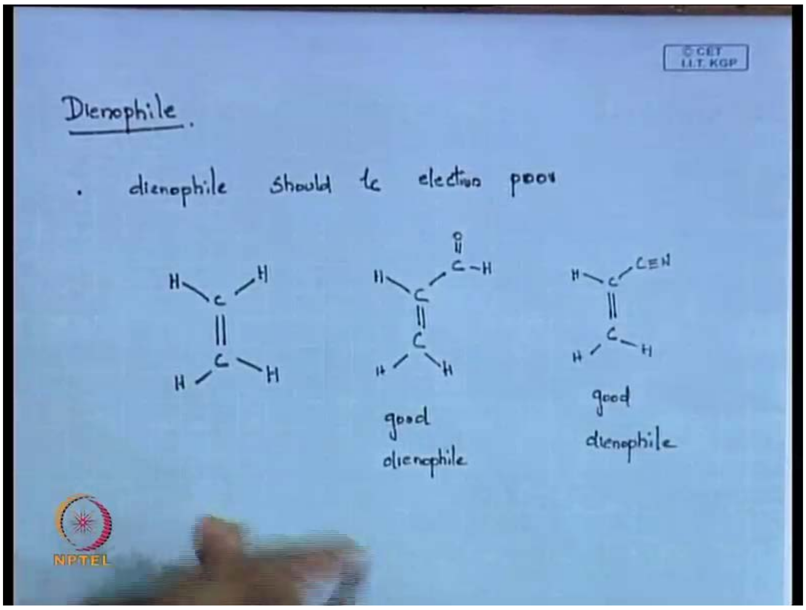

Dienophile

- dienophile should be electron poor

So, your dienophile should be electron poor in nature. They have considered to be very good dienophile for your Diels-Alder reaction. For example, if I take an alkene and alkene system, this is a dienophile which acts for a Diels-Alder reaction, but I can make this as a better dienophile just making it much more electron poor. You can do that. Yeah, in case of diene what we did? You just attach your electron donor our substituent, so that it becomes electron rich. In case of dienophile, you just go for your electron withdrawing substituent and think about your drawing electron. This is a very good dienophile. Even you can think about this type of systems. We have very nice that your nitride, accrual nitride, this type of systems are very good dienophile. These are all good dienophile, right.

So, this is the important thing about your diene and dienophile. So, I said that in Diels-Alder reaction, if you take your Diels-Alder reaction, what you have? You should first understand about your diene. So, we said that it should be an electron rich; it should be in S-CIS confirmation. Then, we should understand about our dienophile. We should know that it should be electron poor and now, we are going to talk about the condition. Which condition will favor Diels-Alder reaction much better?

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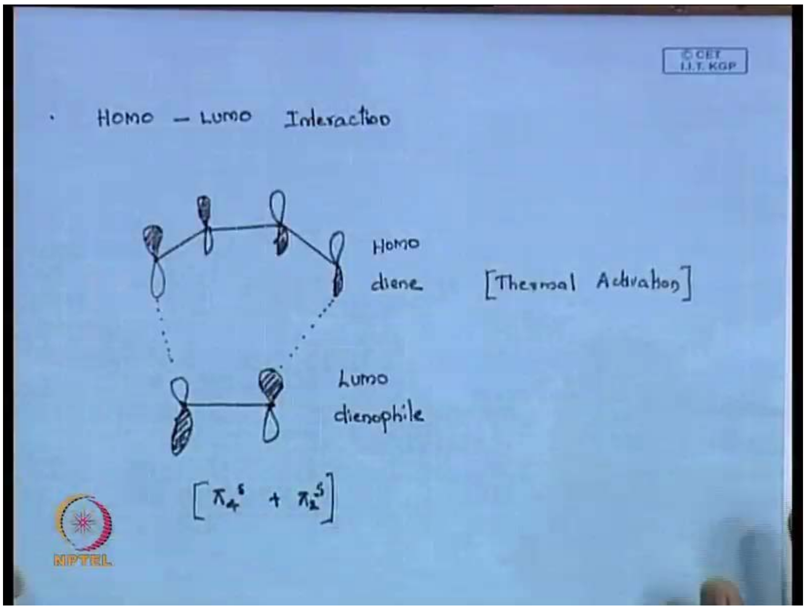
- Homo – Lumo Interaction

So, to understand the condition of Diels-Alder reaction, we can get into the homo theory, that is your homo lumo interactions by knowing the homo lumo interactions. By knowing the homo lumo interactions, we can see which condition is much more in favor.

Whether you can do thermal activations or you can carry out your photo chemical activation.

First, we will see that in normal thermal activation, whether this reaction is favored or not. For that, we do that, you basically take your homo of your diene. So, this is homo of your diene. Then, we can consider the lumo of your dienophile. So, we have seen the homo of diene and lumo of your dienophile. Now, they try to interact and you can see that orbitally, it is nicely favored. So, this is a thermal activation. So, on thermal activation, you can see that this reaction is. How you write this? You can write as 4 pi s plus pi 2 s. So, it is thermal activation. It is sacrificially allowed Diels-Alder reaction. So, that is that, else this reaction on heating it is suprafacial and it is allowed and the reaction goes very nice because it is geometrically as well as orbitally favored. The homo lumo interaction tells that. So, on heating we get nice suprafacial to get our nice Diels-Alder reaction.

These are the three important things we should know on the Diels-Alder reaction, that is your character of your diene which we studied and then, we studied how dienophile should be. Now, we are just seeing the condition of the reaction. The interesting part of Diels-Alder reaction is the selectivity. Diels-Alder reaction gives lot of selectivity like we can talk about facial selectivity. In Diels-Alder reaction, we can talk about exo-endo selectivity; we can talk about regioselectivity of our Diels-Alder reaction. So, we will do what? One by one selectivity and we will try to understand them in detail.

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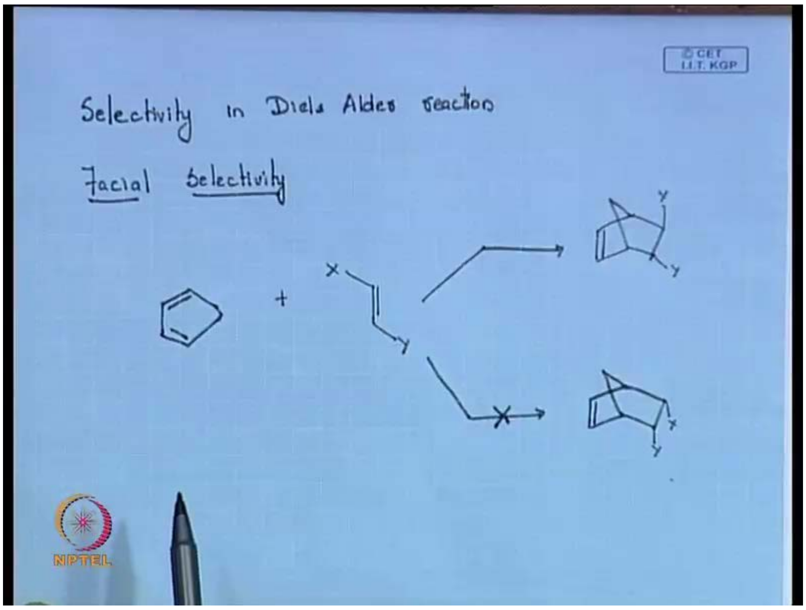

Selectivity in Diels Alder reaction

Facial selectivity

So, once you get into your selectivity in Diels-Alder reaction, so the first part will be talking about is the facial selectivity. If you take a cyclo pentadiene with trans alkene, I can think about two products. One I can say, where your excess up and another case, I can talk about both in the same phase. Correct? So, you can get, you think about two products if we talk about facial selectivity, but in a Diels-Alder, the reaction is selective. So, you do not end up with this product. You end up with only the one in this. So, how to understand that part? We can see this reaction in two ways like we can see them in front approach or side approach and see how they make things to selective, how it gives selectivity.

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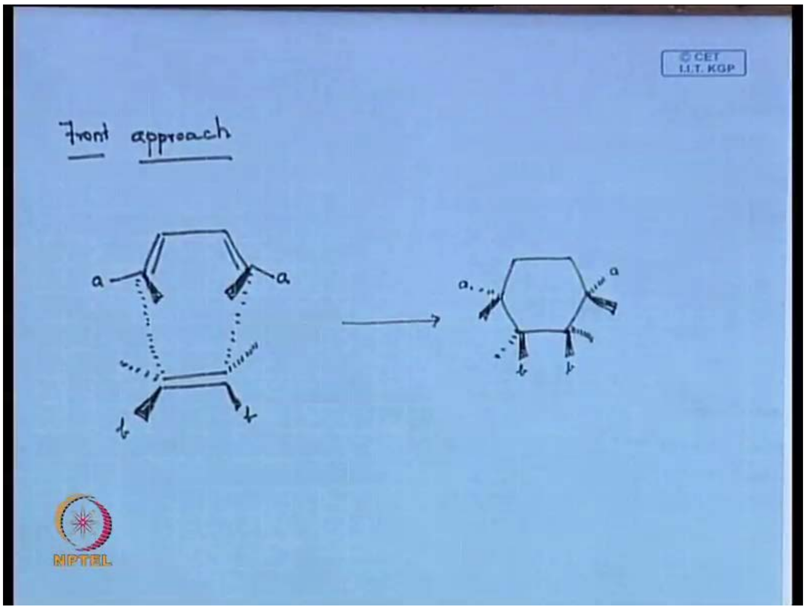

Front approach

So, we will just see the front approach. See how we can look this. For example, I am taking a diene, a substituent, another substituent. Now, I can think about my alkene. Now, if you just watch, if this is the front approach, now what happens, it has only one way your methyl comes up. These two methyl’s and in this case, two metals goes away. There is only one behalf orbital aligning together. So, you can end up and writing product. The methyl on direction we can write this d on. So, you can look in this way and the front approach like how they come together. So, there is no change in chemistry.

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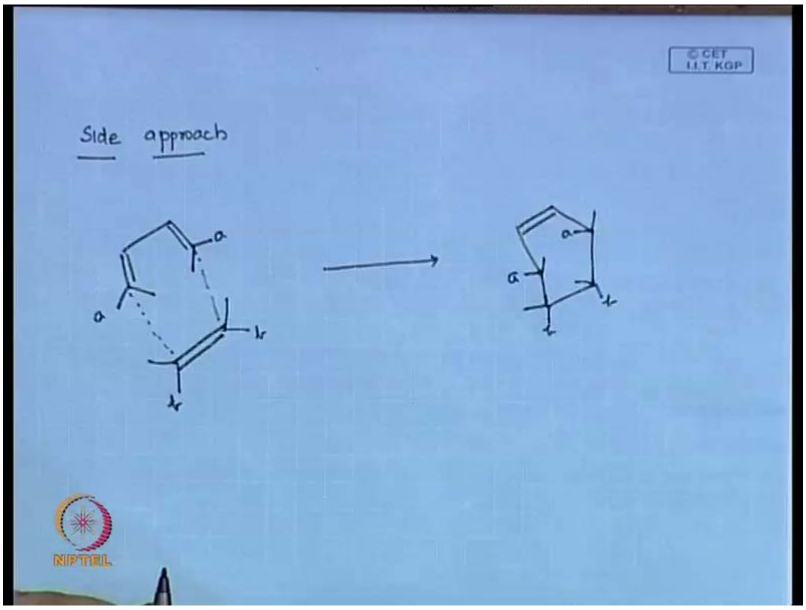

So, that is why they gave much selectivity. You can see that in the side approach also, your side way some it is easy for seeing that in some problems. It will be easy to see the side approach side view you have here and it is your substituent. You have same substituent and on outside, this is one behind it looking to it and you have an alkene methyl and you have big another substituent because this type of approaches will help you out in doing intra molecular Diels-Alder reaction. That time you you can use this type of approaches. So, now, what happens is that you can draw like that. So, your a will be outside and your b will be a. In this case, your a will be a and b will be b.

This way also you can look this. So, you can see in two ways. One you can see in the front approach, another by side approach. That is all. Because of this alignment, we get selectivity in Diels-Alder reaction and this is your facial selectivity. We will see some examples.

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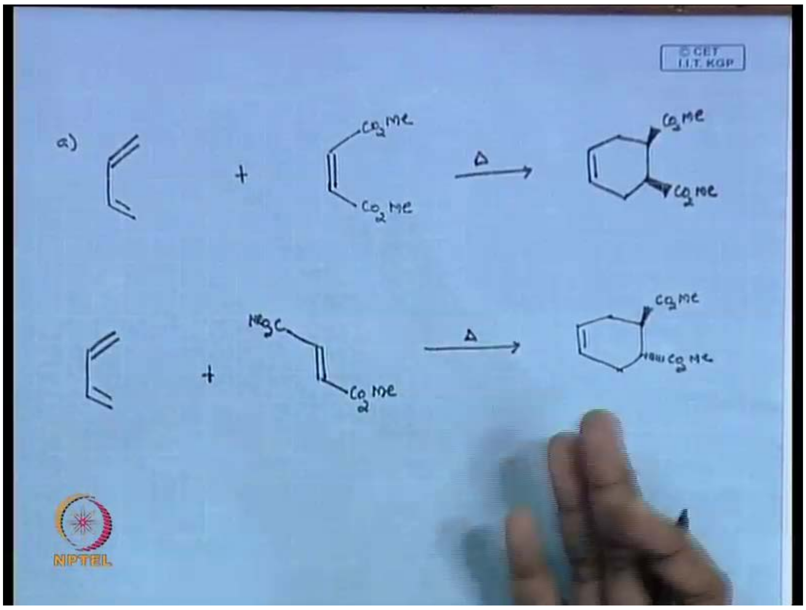

So, we will see one or two examples. See how the selectivity is there if I take diene plus dienophile, so this reaction on heating. So, you should think about the facial selectivity when you draw the product. So, you might end up with get a nice product like this. If same way, if I take the same diene and treat it instead of cis if I treat the trans, so again you have selectivity. So, you end up getting see this. That is why it is very important that you think about the facial selectivity when you write Diels-Alder reaction reactions, very stereo specific, right. So, you get like one type of products that is your first selectivity about your Diels-Alder reaction facial selectivity. Now, what will do that is slowly we will be getting into a second selectivity that is your exo-endo selectivity.

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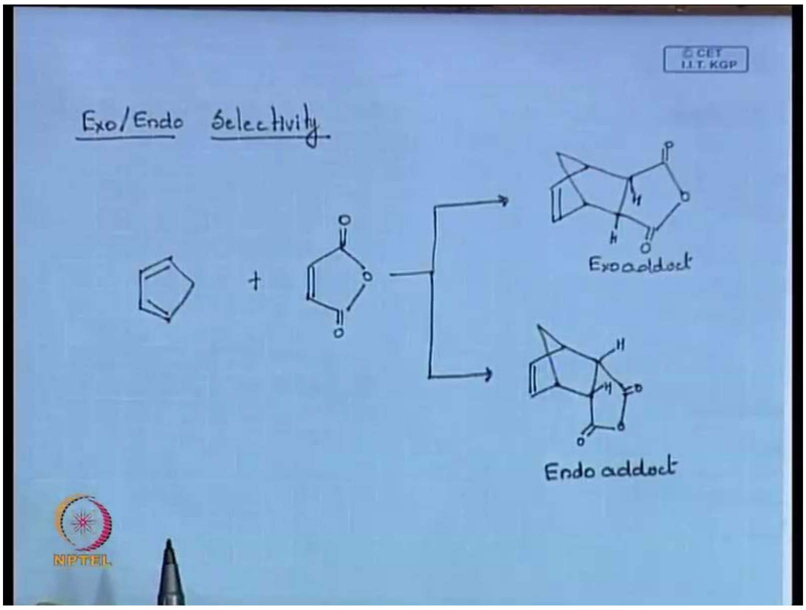

Exo/Endo Selectivity

So, I can take same way a cyclo pentadiene and treat it with your anhydride, right. I can again think of writing two products. One case, I can have my anhydride away. Be careful with your hydrogen. That is only it is the thing very nice.

In another case, I can think about inside mostly like. So, I can write basically two products. One, this is which is like away from ring which call as exo addoct. Inside we call that as an endo addoct and if you see, if you carry out the Diels-Alder reaction, most of the time you have selectivity across your endo product and then, your exo. So, we will find out, we will just look why why it is, why u get selectivity over endo.

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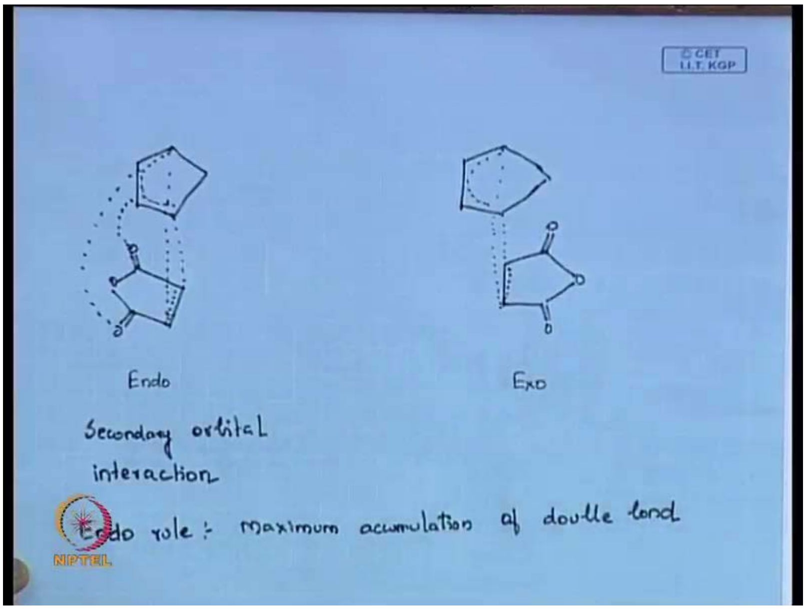

Secondary orbital interaction

Endo rule :- maximum acumulation of double bond

Just you can think about the transition states of these reactions like, I will just draw the transition state for my endo I can think (( )). So, I have interactions basically ways or writing it and just we have best way of writing that as cyclo pentadiene. So, it should be this. It will be this. It will be a better way of facing down. So, I can have a link here because if you see your double bond is here and if you think about the cyclic transition, what happens is you can think about like you will have a bonding here, right. So, you have transition state across this and you have here this how you can look your endo, right, but if same way if you look your exo also, if I draw my exo, so both the ways, you can say that it has been bonded, but the advantage in the case of endo across a exo is that this is more the transmission states here.

You have this secondary orbital interaction of your carbonyl with your alkene system. This is very important. You have a secondary orbital interaction and this reduces the stabilizer that this stabilizer your transition state. In this case, you cannot write. That is why we say that the endo is as selectivity across your exo. When u talk about the Diels-Alder reaction, endo is much more favored because of the secondary orbital interaction. You call this endo rule also. Yeah. You can call endo rule. What endo rule says? It says maximum accumulation of double bond on one side, all right. It is not maximum accumulation of double bond. So, you can view in the case of secondary orbital interaction or you can sometime you go with your endo rule which says maximum accumulation of your double bond of one side.

So, that is what your exo-endo selectivity is. So, when you take an exo-endo, when you come across two products like exo adduct as well as endo adduct, endo adduct is much more selective because of the secondary orbital interaction and governs by the endo rule. Clear?

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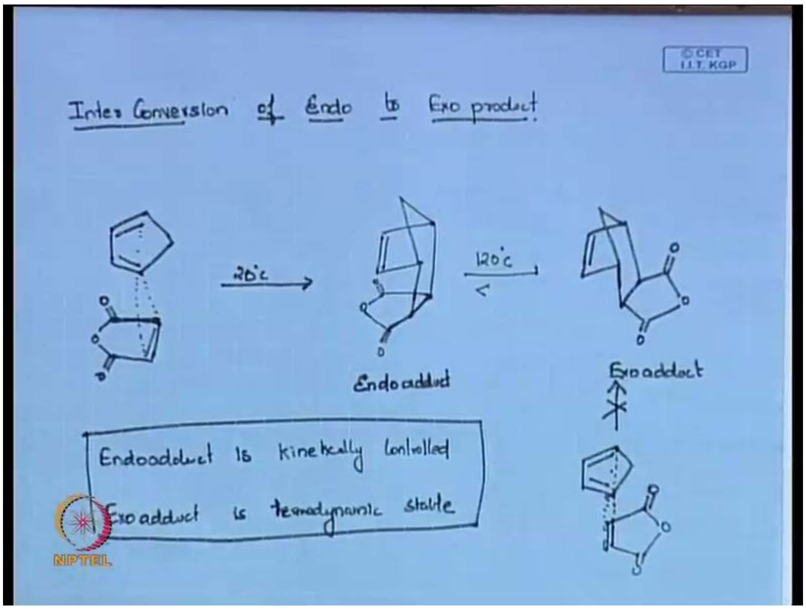

Inter Conversion of Endo to Exo product

Endoadduct is kinetically controlled

Exo adduct is termodynamic stable

So, now we will get into another. Before getting to another selectivity, we will just see inter conversion of your endo to exo product. This is very interesting one inter conversion of your endo to exo product. So, what will you do is that will take our system which we have been discussing that is your cyclo. Similar system will get cyclo pentadiene. Same systems you can have your interactions here. If you want, just try to think about interactions. So, if I normally, if you heat this reaction at 20 degree Celsius, just take your thing and do it in 20 degree. I am writing this way like you have a bond here and you have a bond here, 20 degree Celsius what product you can really think about is.

So, I can get an endo product, right. If I take this reaction and just do it in 20 degree Celsius, earlier case say that we have a second orbital interaction. So, the reaction will give me the endo product. Now, what happens is that once you get an endo product, if you take the product and heat it to 120 degree Celsius, the interesting fact occurs that you end up with an exo now. So, you have an endo adduct and this endo adduct if you heat it, converts itself into exo adduct. It is very interesting, but the same reaction. For example, if I take my cyclo pentadiene, I do not get this product. If I take my cyclo pentadiene with my anidride (( )), I do the reaction. I never get my exo adduct, but if I take the reaction and do it by 20 degree Celsius, I end up with my endo adduct, but if I take my endo adduct and heat it, I end up with my exo product.

So, what this says? This says very clearly that the endo adduct is kinetically controlled because that is preferred once you do the reaction kinetically controlled one, where as the exo is thermo dynamical stable. See that is a very interesting point to know about your exo and endo. So, endo is that it is kinetically favored because the transition state stabilizes. So, the reaction wants to give you the endo, but once you heat, endo gets flipped to your exo saying that exo is thermo diametrically stable one. Clear? So, that is more important part of your exo and endo. So, we have seen selectivity. Now, we will see the inter conversion of endo to exo.

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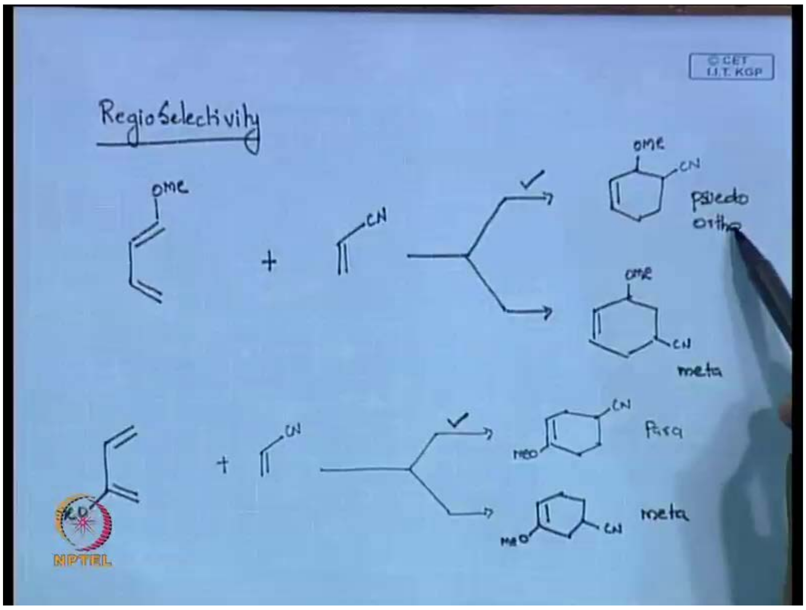

Now, another selectivity which we are going to talk about is your regioselectivity which is very, which also occurs in Diels-Alder reaction. So, what happens is that I take a diene butadiene with my methoxy substituent. In the case I take with the electron beta in dienophile with the sign of substituent, now I can write two products again in this way. So, one see if this is going to form like this Diels-Alder reaction. I have my sign here or if it is inverted dienophile have sign. See we call them because it is not an aromatic system still. That is why we call them as a pseudo ortho. We can call as pseudo ortho.

In this case, we can call them as a pseudo meta because aromatic system only we used the word ortho and meta. Since, anyhow for understanding, we can call them as ortho, this ortho substituent and in this case, it is a metal substituent. You can think about both, but if you do the reaction, you have selectivity across your ortho. You have selectivity over this. Same way, if I take a methoxy with a similar system, you sign on ok(( )), again I can think about writing two products. For this one case, you get para and in other case, you end up with meta, right. So, if I do this reaction, the selectivity is over para. So, when you do regioselectivity, that is if you take this reaction, you end up with a pseudo ortho and meta or you end up with the pseudo para and meta.

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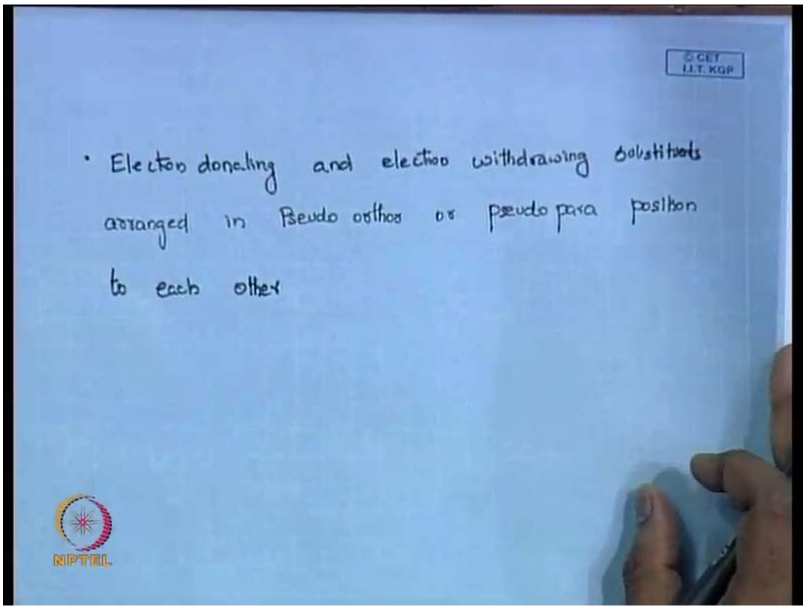

- Electron donating and electron withdrawing substituents arranged in pseudo orthos or pseudo para position to each other

If you generalize it, you can come to a statement saying that electron donating and electron withdrawing substituents with respect to the product, electron donating and electron withdrawing substituents arranged prefers to arrange in pseudo ortho or pseudo para position to each other, so that you can do this generalization. So, your electron donating and electron withdrawing substituent in the product. What I am meaning is that the electron donating and electron withdrawing substituent, most of the time the product prefers to be in the either ortho or para. You never get, yeah. You have selectivity over these two over metals. So, that is what I said the electro donating and electro withdrawing substituent arranged in pseudo ortho or pseudo para position to each other. Now, you will understand how it happens, why these things happen? It is very easy. You can see from the mesomeric structure of this, you can understand them.

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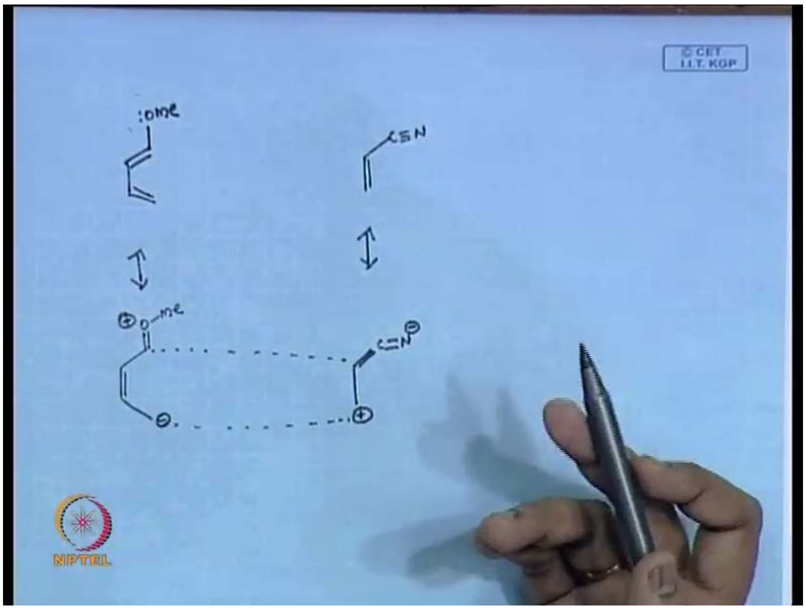

For example, I have the system. Just we can write the mesomeric form of it minus you can end up like this structure. So, this should be your positive minus positive, yeah. Now, you can have these nice interactions, right. So, you can just have your flow of electrons. The mesomeric structure this side, this is an electron withdrawing and this is electron donating. So, you get a nice type of structures and based on this, you can think that it goes for the, it prefers to be in the ortho position compared to meta.

Just by drawing the mesomeric structure, you can find out and that helps the reset, yeah. There is more about selectivity. You get the products when you do reactions of Diels-Alder. You always end up with the 75-25, but 75 will be your ortho and 25 will be your meta. It is not like specific. You do not get only one product, you get both the products, but selectivity is across ortho or para, fine.

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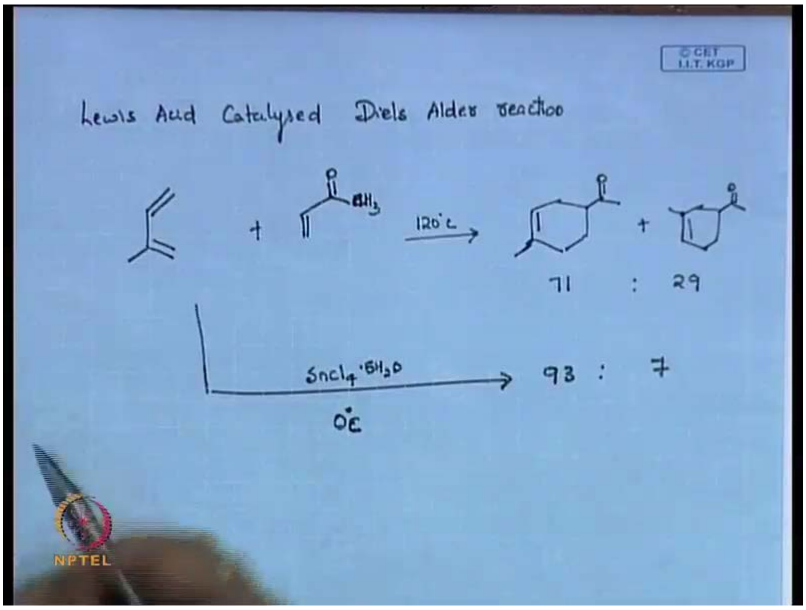

Similar to the extension of this, if you see we have Lewis acid if you do a Lewis acid catalyzed Diels-Alder reaction. So, basically like if you take a reaction of a diene like this with aldehydes, oh sorry, it can be an acetone. If you do this reaction, you should get two products, right if you take the regioselectivity you are talking about. So, I should get one should be in the para position and one should be in your meta. So, I should think about two products and if you do this reaction, yes exactly. If you do it at 120 degree Celsius, just you put these two and heat it, you end up with two products, but if you see the selectivity, it is 71 is to 29.

Same reaction if you do it in thin chloride for example, the same reaction if I do it in Sncl 4, yeah sorry Sncl 4 (( )) any Lewis acid Sncl 4 sorry at 0 degree, just at 0 degree Celsius, you end up with 93 is to 7. So, you have an increase in the selectivity, yeah. You can easily understand why it happens because like you in the case of your dienophile now, your Lewis acid goes on binds with your dienophile. So, it can withdraw the electron much better than earlier case. So, you end up with the nice increase in selectivity. That is just because of your binding of your Lewis acid to the dienophile and makes it stronger electron with drawing group. That is why the selectivity is increased. It is very important when you do Lewis acid catalyzed by Diels-Alder reaction.

So, what we did is that, so we took Diels-Alder reaction. We said that dienes are very important, diene is important. So, we said how the diene should be electron rich one and your diene should have S-CIS confirmation to do a proper Diels-Alder reaction. Then, we went to dienophile. We said your dienophile should be electron poor if does an electron withdrawing group, it is well, good becomes a very good dienophile. Then, we slowly went to the condition and by using your homo lumo interactions, we said that by thermal activation, it is supra allowed and the reaction goes nicely. Then, we saw three selectivity's. We studied facial selectivity and we went to exo-endo selectivity. We said endo selectivity is good because of its secondary orbital interactions. Then, finally, we went to the regioselectivity. We said that the ortho, the electron withdrawing and the electron donating substitution should be in the pseudo ortho or pseudo para. Those products are much more favored to compare to the meta one.

So, that is about your Diels-Alder reactions. We will try to study Diels-Alder reaction, about the reactivates of dienophile dines and then, intra molecular Diels-Alder reactions in the next class.