Organic Photochemistry and Pericyclic Reactions

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Module No. # 01
Lecture No. #32
1,3 Dipolar Cycloaddition – I

Yes. So, for couple of classes we were discussing about cycloaddition reactions right. In that, we were trying to understand Diels Alder reactions. We covered them and we moved towards your Alder Ene reaction. That was previous class, we discussed about that. Today's class what we are going to do is, to take one more important reaction. That is, your 1 3 dipolar cycloaddition which falls in your four plus two cycloaddition reactions.

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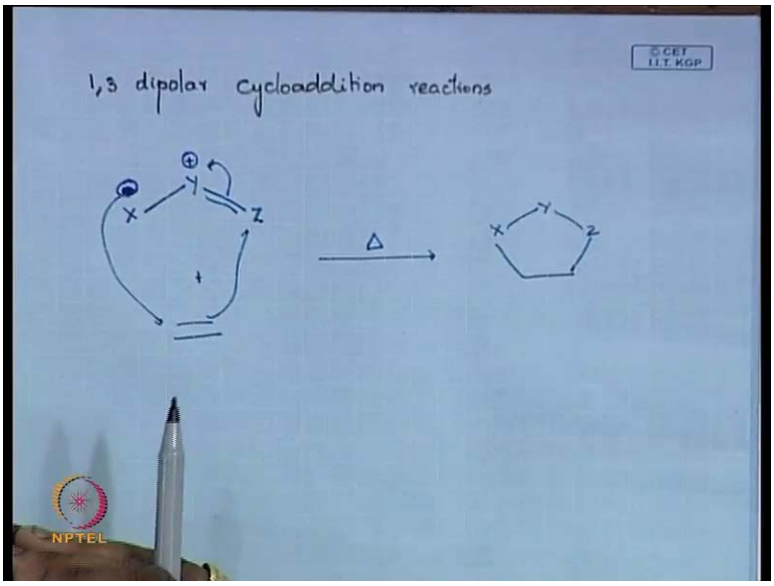

So, we will start discussing 1 3 dipolar cycloaddition reactions. Yes, I will just shortly brief you in yesterday's class about your 1 3 dipolar cycloaddition. I will just remind you one more time.

So, what is that? You have an you can take X minus, you have, you can take a substrate and then you have a two substrates like this fine. And the reaction can be initiated if you have a double bond to give you a very nice five member ring this. So, called beauty of your 1 3 dipolar cycloaddition. Normally, if you do your Diels alder reactions you end up with your six member ring right. In 1 3 dipolar cycloaddition you end up with your five membered heterocyclic rings. So, you can think if you have want to make five members heterocyclic reaction compounds, I think 1 3 cycloaddition comes first in your mind.

And this reaction goes by heating. So, you have basically, you have taken two substrates which on heating ended up giving your five membered heterocyclic rings. Now, we will take we will try to understand all this substrates individually and the conditions and then of course we have to find out whether it is supra facial or antara facial right.

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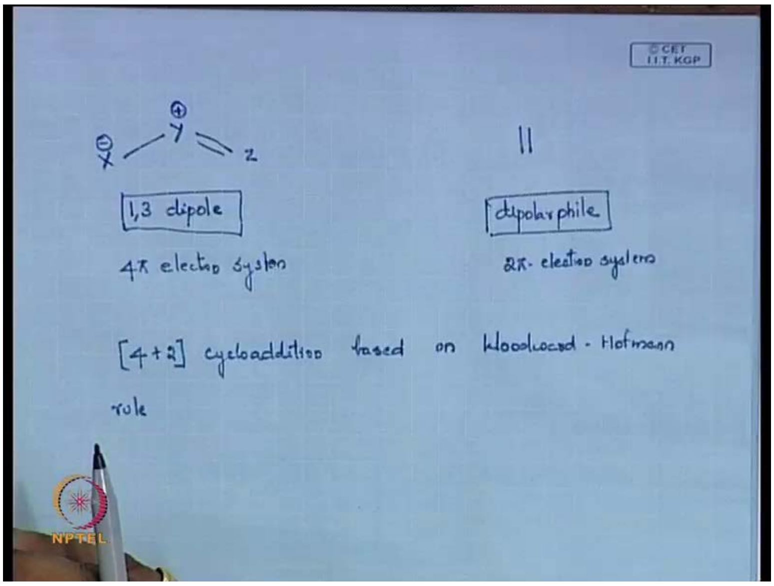

1,3 dipole

4π electron system

dipolarphile

2π- electron systems

[4+2] cycloaddition based on Woodward - Hofmann rule

So, first we will take the substrates and try to understand how we call call them. We have this X minus Y plus Z. You have one this substrate. Another, you have this basically, you call this as 1 3 dipole and this is if you want to see the similarities with your Diels Alder reactions. This is your diene.

And this is your now 1 3 dipole and this and this has your five pi electron system, 4 pi electron system fine. Now, you have an alkene here right. In Diels Alder reactions, you you say this is your dine and this is your dienophile. But, in this case since it is a dipole since one of the substrate is dipole you call them as dipolarophile. This is your dipolarophile and and this was 2 pi electron system and if you see the reaction it is nothing, but, it is 4 plus 2 cycloaddition based on Woodward Hoffmann rule fine. Now, understanding more about your 1 3 dipolar and dipolar phile is very important to fix your dipolar cycloaddition reaction. You should know in detail how this 1 3 dipole looks and how your dipolar phile should be to understand your dipolar cycloaddition. So, what we will do is that, now we will talk, we will put some focus on 1 3 dipole.

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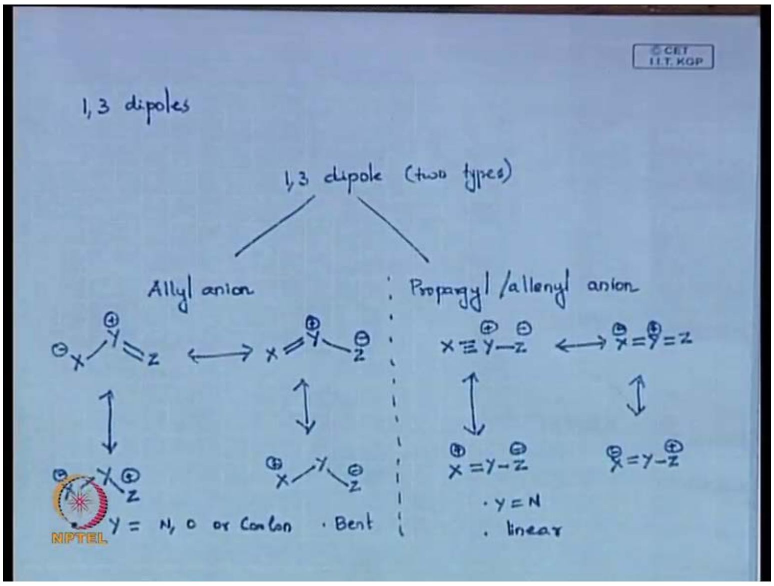

If you see, if you take 1 3 dipoles they can be broadly classified in two types. You can classify them in two types; 1 3 dipole; one you call them as allyl anion, one will be allyl anion type, another will be your propargyl or you can also call them as allenyl anion. So, that is how you can broadly classify your 1 3 dipoles. One will be your allyl anion, another will be your propargyl. If you want to see, I have the general structure. We can have an X minus we will have Y plus fine.

This, I can this can be in equilibrium. You can write other forms, not other resonance forms for this. You can write like this. For this you can write X minus Z plus you can write for this, X plus Z minus. So, you can write resonance structure for this allyl anion and you can see their dipoles 1 3 position. That is why, we call them as a 1 3 dipole. So, what he says, it mostly says that this dipole can be nucleophilic as well as electrophilic right. If you take allyl anion is. So, your Y can be most of the time your Y can be nitrogen, oxygen or carbon right. And your allyl anion should will be bent in structure because if you see the structure there they will be bent in nature because they are respective.

When you look your propargyl, in that case propargyl will be more like a linear linear; you can have a propargyl anion which dine will be more in linear linear in structure. yes Even I can write a nice regional structure for them, X minus Y plus and Z. (( )) Again you have your linear structure your Y can be here, nitrogen in this case it will be linear. So, so that is how your 1 3 dipolar. You can, as two types; one allyl anion, another is propargyl anion and allyl anion here, more like a bent structure and your propargyl anion is more like a linear structure. This was is the two major type of your 1 3 dipole.

Now, we will see, there are there are many classifications of allyl anion and they are many good classifications of your propargyl anions. I will just take you some important classifications of allyl anions.

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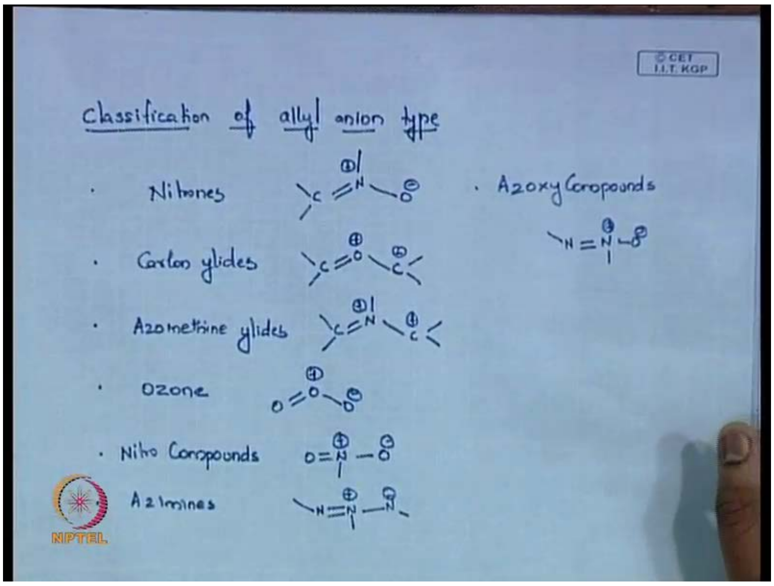

Classification of allyl anion type

- Nitrones
- Carbon ylides
- Azomethine ylides
- Ozone
- Nitro Compounds
- Azimines
- Azoxy Compounds

Then, we did some main classifications which you see, dipoles of allyl anion type. Not taking to all the classification, are many classification. can I am just taking you towards some important classifications of allyl anion.

Can you think about any? You have your nitrones, they are they are very important type which you can see many reactions of 1 3 dipolar additions taking place with nitrone substrate right. You can think about your carbon ylides right. Have your carbon ylides then, you can even have your azomethine ylides. Any And you have your ozone right because ozone ozone arlises you know ozone axis acts a very good 1 3 dipolar, 1 3 dipolar cycloaddition ozone.

Your nitro compounds. Nitro compounds, any other thing? Azimines, azimines because you have three nitrogen’s in azimines. You can even think about your azoxy compounds with two nitrogen’s, more like a bent structure. All are more bent structure if am linear is it bent structure. That is what allyl anion type is. You have other classes also, but, this these are like more important classes is. You keep on saying when you do reactions, nitrones you see many reactions with your nitrones.

We are going to talk about nitrones. Then we can talk about ozone some reactions on some ylides and so on. But, you can, this these reactions are very common which are this are very common allyl anions, which you see in 1 3 dipolar cycloaddition.

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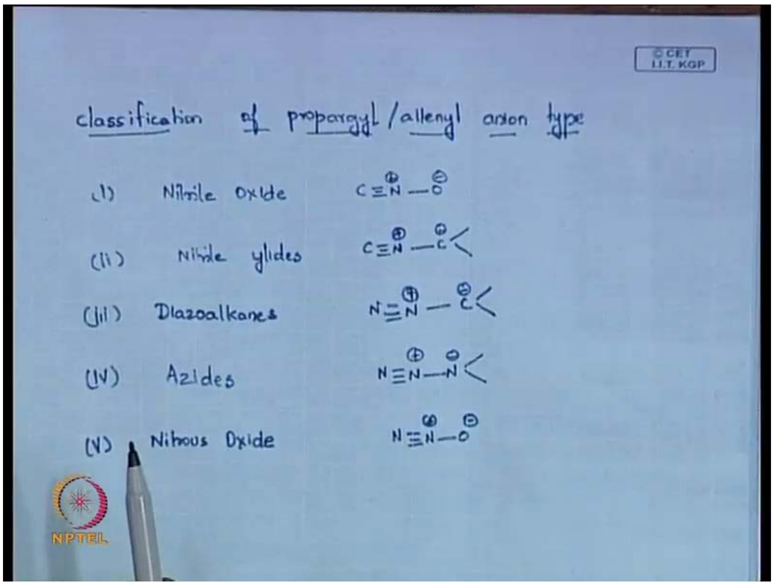

classification of propargyl / allenyl anion type

(i) Nitrile oxide $C\equiv\overset{\oplus}{N}-\overset{\ominus}{O}$

(ii) Nitrile ylides $C\equiv\overset{\oplus}{N}-\overset{\ominus}{C}<$

(iii) Diazoalkanes $N\equiv\overset{\oplus}{N}-\overset{\ominus}{C}<$

(iv) Azides $N\equiv\overset{\oplus}{N}-\overset{\ominus}{N}<$

(v) Nitrous Oxide $N\equiv\overset{\oplus}{N}-\overset{\ominus}{O}$

So, then we will see some other classifications of propargyl anion type because, that also we have to study on propargyl or you can call as allenyl anion type. Any thing comes in your mind? Any compound when I talk about propargyl? nitral oxides because na you can do many things with nitrile oxides. they any There are many reactions you have studied in nitrile oxides. Then nitrile ylides, think about nitrile ylides. Diazo alkenes with three nitrogen’s you have studied that right. What is that azides? Click chemistry because azides undergoes nice 1 3 dipolar cycloadditions; very good examples your click then nitrous oxide. So, this these are some main classification of your propargyl anion type.

So,. So, what we will do is that, we will take each type of allyl 2 or 3 examples of allyl anion type, see how they do 1 3 dipolar cycloaddition. Same way we can take some examples of propargyl and see how they undergoes cycloaddition reaction fine.

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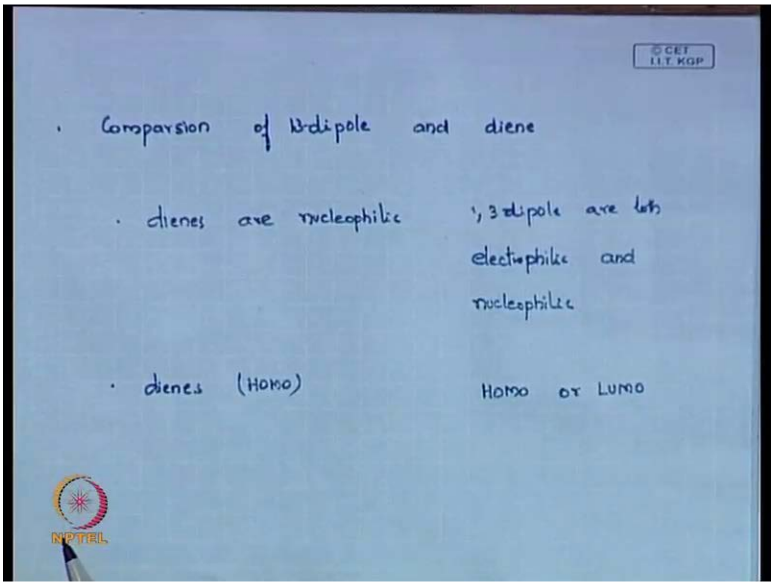

- Comparsion of 1,3-dipole and diene
  - dienes are nucleophilic — 1,3 dipole are both electrophilic and nucleophilic
  - dienes (Homo) — Homo or Lumo

Now, we will see like, how we can comparison of 1 3 dipole and diene. Can you just diene, we talk about more diene systems right, when we talk about Diels Alder reaction. In this case, it is more like 1 3 diene. So, is there is any comparisons we can think about normally how your dienes are in Diels Alder reaction, how the diene should be more like an nucleon? It should be nucleophilic right, fine. But, in 1 3 dipolar, 1 3 dipole how they should be? They are both, they are 1 3 dipolar, electrophilic and nucleophilic. See normal cases, if you take dienes normally, if you take dienes of in Diels Alder reactions what they use mostly?

Diene systems; Homo or Lumo. yes normally we can see dienes will be having this homo for the reactions. But, other way inverse electron demand you have seen, but, otherwise dienes is most of the time. Homo and you have seen you can use Lumo of your diene. But, it is inverse electron (( )) in similarly, 1 3 dipole also Homo or you can have Lumo depending upon your dipolarphile. If you have an electron deficient dipolarphile or you have an electron rich dipolarphile, they try to change.

Then some time you can uses Homo and other cases you will be using the Lumo. We will be seeing that in detail when it is going to use the Homo. And when it is do same way. Your dienes see, like that you can try to understand both of them. And both are 4 pi electron system. You can count 4 pi electron from your diene as well as your 1 3 dipole. This is more about your dipole, one of the substrate.

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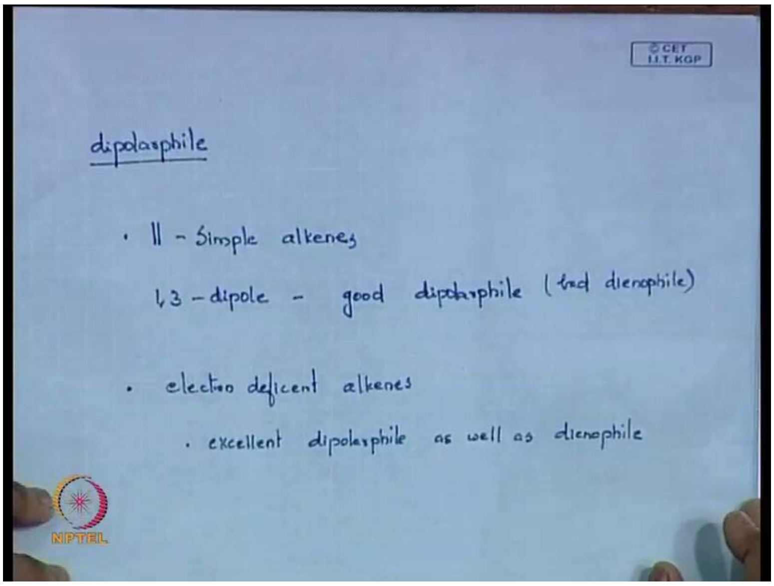

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dipolarphile

- ‖ - Simple alkenes

  1,3 - dipole - good dipolarphile (bad dienophile)

- electron deficent alkenes
  - excellent dipolarphile as well as dienophile

Then, we will be talking about little bit about your dipolar phile. See, if you take a simple alkene for example, I will take an simple alkene. Take a simple alkene. How how this, if it is, if you take a simple alkene and do a Diels alder reaction is this is a good dieno phile, dienophile? Simple alkenes are not good dienophile. But, in 1 3 dipole in the case of 1 3 dipole, they are very good, they are good dipolephile. They are, they are I can say they are bad dienophile. Simple alkene, simple alkenes are good dipolarphile. That means, you can do your 1 3 dipolar cycloaddition reactions with your simple alkenes. But, it is not that good dienophile when you think about Diels Alder reaction. See, if you having a electron deficient alkene If you have an electron deficient alkenes yes they are excellent in both the cases, excellent dipolarphile as well as they can be a very good dienophile right. That is fine because it becomes a electron deficient. Yes. it can be act as a good dipolarphile as well as it can be a good dienophile. But, in the case of simple alkene, it is good dipolarphile. But, is not good a dienophile, that is about your dipolar phile. So, basically you want your dipolarphile to be electron deficient. If you want, you can (( )). So, that is about your two substrates; one your 1 3 dipole and another is your dipolar phile.

Now, what you will do is that, just depending upon the Homo and Lumo interactions your Diels alder reactions 1 3 sorry 1 3 cycloaddition, dipolar cycloadditions can be classified into three types depending upon the Homo Lumo interactions that is based on your f m o theory. Just we will see how they are classified.

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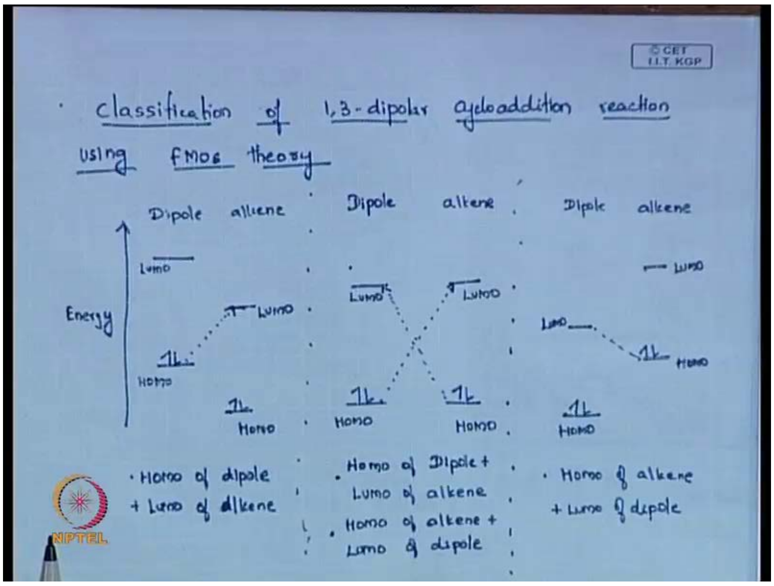

- Classification of 1,3-dipolar cycloaddition reaction using fMOs theory

- Homo of dipole + Lumo of alkene

- Homo of Dipole + Lumo of alkene
- Homo of alkene + Lumo of dipole

- Homo of alkene + Lumo of dipole

How you can classify that 1 3 dipolar cycloaddition reactions using f m o s theory? Just I have a case of, I will just have an energy here. So, I will take first case or I will take one case where, I have a dipole and I have an alkene system. So, this will be my, this is the Homo and this is the Lumo.

Fine, this will be the Homo of your dipole 1 3 dipole and this will be your alkene, the energy. If both are in the same energy, then we will be talking about the interactions of your Homo of your dipole with the Lumo of your alkene or otherwise we will be talking other way round when the energies are same. So, basically what we are talking, you will be Homo of your dipole plus Lumo of alkene or you can say Homo of your alkene plus Lumo of dipole. So, you can think about two combinations here right.

This is one type; we can think of another type where they there, I have another case where I am going to have the Lumo and Homo right. So, in this type we will be considering the Homo of your dipole with the Lumo of your alkene. So, you do not have other case now, you cannot have your Homo of your alkene with the Lumo of dienophile that is possible. So, it will be Homo of dipole with the Lumo of alkene or dipolar phile right. Same way you can think about other way round right. That is, can have energy down still.

The Homo of dipole and Lumo of alkene, this is Homo. So, in this case what happens? You are talking about the Homo of alkene with the Lumo of dipole 1 3 dipole. So, that means, basically we have like three types right. would I gave a You are talking about three types now. This is your type one; where you are talking about the interaction between the Homo of dipole with your Lumo of your alkene. You have type two, where you can have both the possibilities. In type 3, you are talking about the Homo of your alkene with the Lumo of dipole right. So, you have. So, that is how you can classify your 1 3 dipolar cycloaddition using f m O s theory. We will see some examples based on this. That will be much interesting how this Homo and Lumo you are talking about. That, we will see some examples. In that, you will understand, I take you one example how you can talk with the Homo and Lumo differently.

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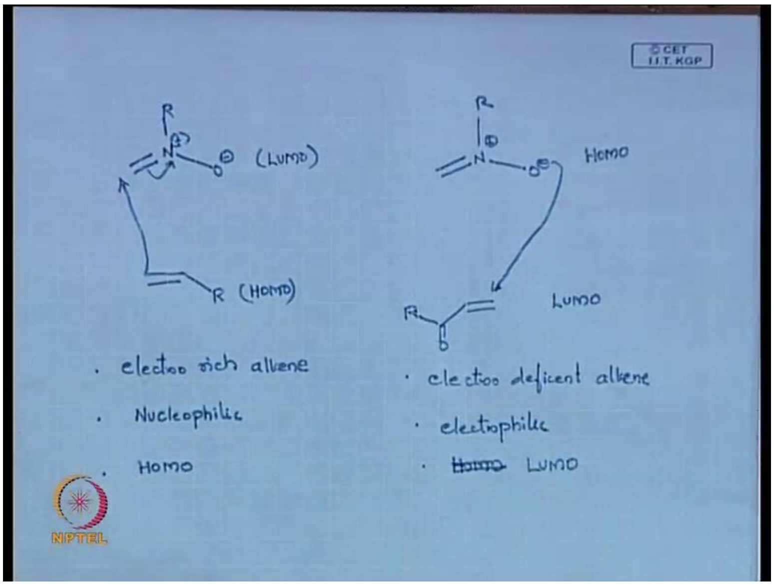

For example, for instance we will take a nitrone system, I will take a nitrone. One case, I am taking nitrone and reacting with an alkene. Same same nitrone I am talking (( )) similar structure.

Now, we have to think about this type; one type to system of things where it falls and how to understand them. And so, first point what is this? Alkene, it is an electron rich alkene right. So, if it is electron rich alkene so, it should be what more nucleophilic right. So, that means, this is see try to understand; that means, this is basically, this is initiating the reactions I can take this part fine.

So, now you can think. So, which will be the Homo and which will be the Lumo because this is initiating the reactions because its more nucleophilic. So, that means, you are talking the Homo about your dipolarphile like this, your alkene. So, na because this is in the Homo and this will be your Lumo. That is how you classify.

See, if I again bring this O minus, see it will do a cycloaddition. But, I do not want to do that otherwise, you do not know where it will be started, the whole reaction. when it. When you take your second case it is an electron deficient alkene. So, it will be more electrophilic right. So, then what I can think the reaction this right, this will be initiative. So, then I am talking about the Homo of this and the Lumo of. So, that is why we say this dipolarphile where it is different from your diene same dipolarphile. Now, one case it acts as an nucleophilic; another case it acts as an electrophilic. It uses the Lumo one case, it uses the Homo. It depends more about your dipolar phile if it, if your dipolarphile is electric un rich. Then you are talking about the Lumo of your 1 3 dipole. If your dipolarphile is electron deficient then you talk about the 1 3 dipole. See that is why this classification of 1 3 dipolar cycloaddition is very important. Clear? um

In this case, oh sorry sorry sorry I write Homo, oh yes it should be Lumo. thanks If I take this classification again back, which we have done if I take this classification. If I add Lewis acid then you know what will happen? The energy gap will become smaller and the reaction rate will be faster just like your Diels Alder reaction. Just to remind to you that point that, more about your introduction, about your 1 3 dipolar cycloaddition.

So, basically you talked about your 1 3 dipole. It should be allyl anion type or it should be propargyl type. Allyl type should be your bent one and your propargyl will be linear and then we slowly moved to a dipolarphile. We said even simple alkene can do that this 1 3 dipolar cycloadditions. And then, we slowly moved the classification. You have seen 3 types based on their Homo Lumo interactions fine. So, that is more about that. Now, we will take individual dipoles and try to understand the chemistry of your dipolar cycloadditions.

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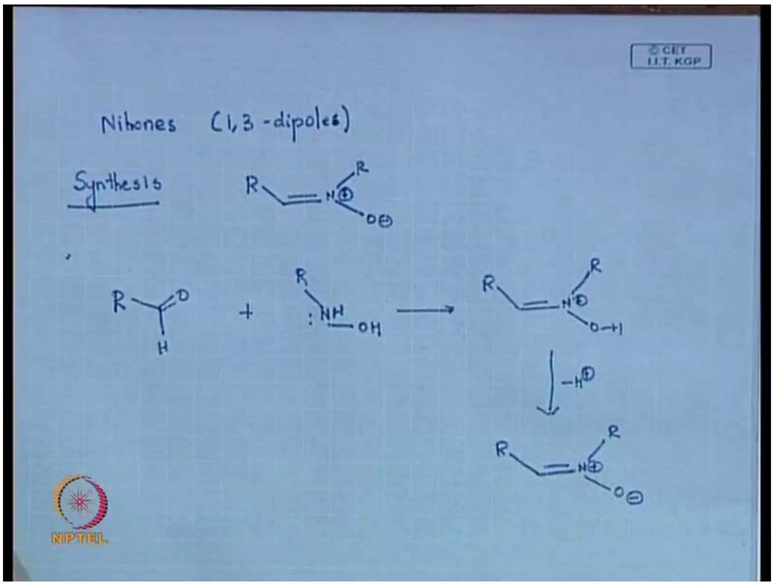

We will start with your famous dipole that is your nitrones. So, nitrones will take, in this case first we will try to do the synthesis of nitrones. Any idea how how we can synthesis nitrones? ah.

See, if I have, if you want to synthesis synthesize for example, I am doing this, I want to synthesis this nitrone. yes It can take your simple aldehyde because it is sort of imine. na You think, you have to think more like an imine system. How to make the imine of this then? You can get up; you can easily remove the hydrogen. So, it can create an O minus. So, mostly if I have O H here, then it will be more like an imine system right. So, think in that now, what we can do if it is an you want to create an imine. Just you take an aldehyde right and treated treat it with your, you can think of my amine system. I can get my nicely get this. Then you can pull out your H plus. Then, make like this your nitrones. Simple ways, a very simple way to make this nitrone.

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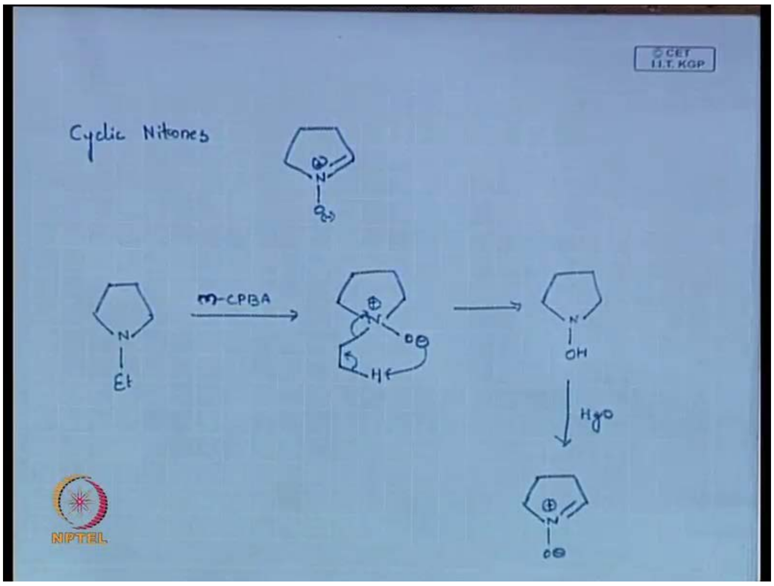

Another thing, there is another interesting nitrones which is cyclic one right, cyclic nitrones and see how to synthesis cyclic nitrones. See, this type of, can talk about this type of nitrones, cyclic nitrones. If you want to synthesis cyclo nitrone, you can you can have your nice hector cyclic five membered hector cyclic reactions. You can take n ethyl. Just you have to make n oxide, you can use m-C P B A sorry small m if you take m-C P B A. So, you have your ethyl. just for You can create your O minus right n oxide just m-C P B N oxide. You do then. What happens this O minus fix your H? So, your ethane can go out giving an N O H. This, if you put in mercury oxide you get your nice cyclic nitrones right. These This are some synthesis of your, like this are many ways if you want to have your acyclic nitrones. You can synthesis some, you can synthesis cyclic nitrones. You can even, even there are many chiral cyclic nitrones and thiral acyclic nitrones you can synthesis. So, that is more. fine.

Now, before getting into this these reactions; how this cyclic nitrones is going to react with your dipolar phile? We should understand whether this these additions are supra facial or antara facial right.

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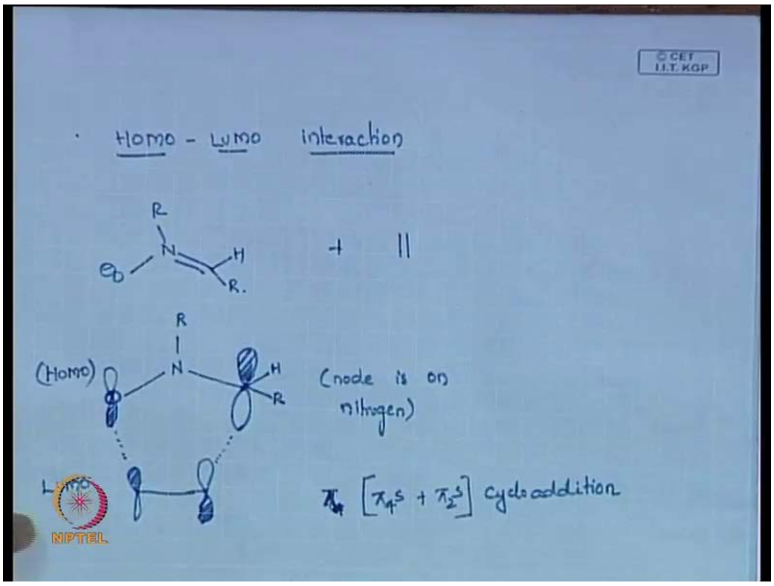

So, what we will do? We will see the whether the Homo Lumo interactions and will see how this reaction goes; Homo, Lumo interaction between your dipolar 1 3 dipole and dipolar phile. For example, I am taking a system where I have my N R O minus with the (( )). This type of system I am talking about with my an alkene. So, all this addition should go. All this all this orbital should go, interact with each other. So, if I draw them. So, we are talking about the Homo of this with Lumo of your alkene. So, it is a lone 3. So, can we draw the Homo of this? It is more like your allyl system.

This is your oxygen nitrogen R. So, basically the node is no nitrogen. Now, that is we are talking about. So, that node is on nitrogen because we are talking about 1 3 right. So, now, we will do. So, this is your Homo. So, now we will draw the Lumo of your dipolarphile. So, you can see now the interactions more like a supra facial. That is why, this 1 3 dipolar cycloaddition reactions goes very nice when you do the thermal activation where thermal activation supra facially it is allowed. Just like a Diels alder reaction it goes nicely. See we said, Diels Alder reaction is nothing, but, how to represent them pi 4 s plus pi 2 s. But, when you talk about Ene reaction, it is more like a pi 2 s plus pi 2 s plus sigma 2 s because in Ene reaction, we are talking about one sigma bond. So, it will be pi 2 s plus pi 2 s plus sigma 2 s.

See, if you if you want to talk about 1 3 dipolar addition, it is similar like your Diels Alder. It is pi. So, it is pi 4 s plus pi 2 s cycloaddition. So, it is it is more like a supra facial allowed right.

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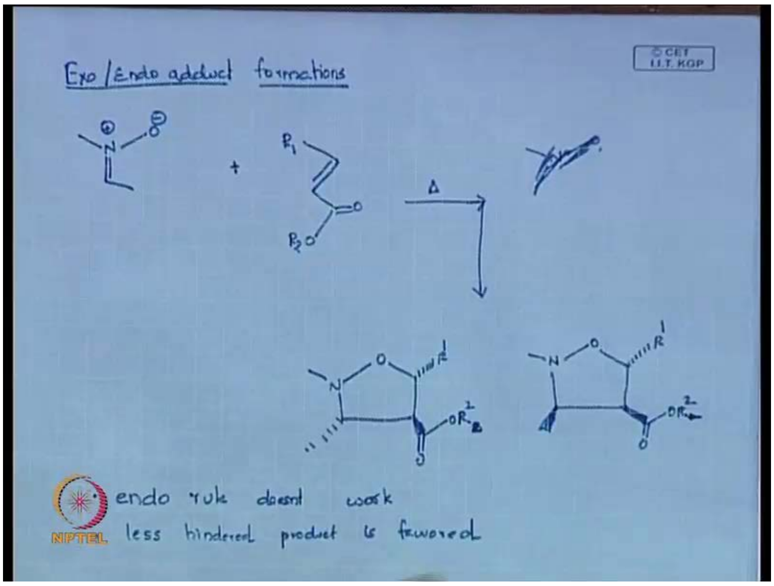

Exo / Endo adduct formations

endo rule doesn't work

less hindered product is favored

Now, we will be will see the reactions how it gets? For example, I take a nitrone and treat with a system like here. Two systems like this. Now, you have to carry out your, I just heat it, thermally activate it. So, what product you get? So, this will be your dipole, 1 3 dipole and this is your dipolarphile. So, just you have to attack your O minus. na

So, here then you have your thing, you you can think about just I can write here. So, that I can when I fix my steroid chemistry, this is the interesting part of this reaction. I can think about one product like this, fine another product also which I can believe that.

This is R two then, this will be your R 2 talking about right. So, you can think about two products now. If I take this nitrone with your alkene system, which is no the electron with drawing one electron deficient, then I can think about this two products. See, if you if your carefully watch this product one as we we will see, but, before that one has been formed by Endo approach and another has been formed by Exo approach, what you studied in Diels alder reactions Diels Alder reactions? What it says?

Which will be more preferable, Exo or Endo in Diels Alder? Not here. In Diels Alder reaction, we studied Endo is more favorable. That is, your Endo rule right. Endo rule says that Endo product it is more favorable compared to your Exo because, in Endo you will see the secondary orbital interaction. Can we use the same here? But, if you see the product and if your find out the Exo will be more more favorable about when compared to Endo. That means, what it what I am trying to say is that your Endo rule does not apply much here when you talk about 1 3 dipolar cycloaddition. It is more about your, the product which is formed by less steric, it is in the less, indeed way is much more favored. So, ah.

We will see why it is why it is Endo rule is not, it is not favored here. Endo rule basically, you cannot apply. You can say Endo rule does not work the way you look into it. You have to look less indeed products or less steric hinderer is favored. See that is, that is very important when you look about your, that we also, people say like Exo Endo adduct. Exo Endo adduct for formation when you when you particularly when you talking about 1 3 dipolar cycloaddition reactions. Your Endo rule is not much obeyed. It is more about your less steric interaction. We will see why why it is?

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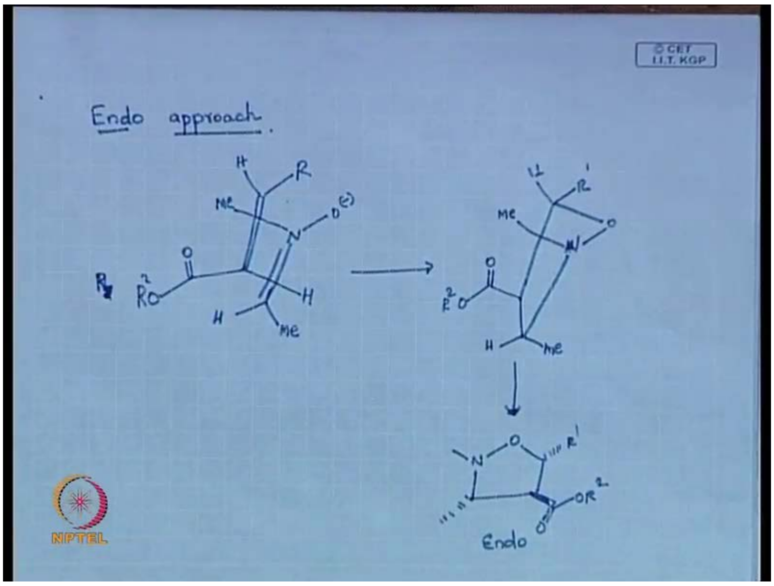

So, if we take this and try to understand the way Endo approach and Exo approach, same reaction will say how they, how it is. We will do an Endo approach for this reaction. So, we will write for this the endo way and it is my R 2 O right. Carbon here, just for your understanding I am drawing double one bigger.

So, this might be my, this is what this is my dipolarphile right. Now, my 1 3 dipole gets in, can have nitrogen metal. I have a metal here fine which as an O minus fine. If you see this is the Endo, it should come now. If you see, once the bond is formed you can understand nicely (( )). I want to draw this nitrogen then, have your hydrogen R. This is your nitrogen. Have your metal, now see in which side this n oxide is forming? O oxygen it is its more Exo right, and more Endo inside overlapping.

If you just open the structure, you see you will be getting a product just similar. I am just open that is all. You does need not not to do anything. This is your R 1, I am talking about. So, you end up with an Endo product right. Your R 1 is a way in other plain and we are talking about this N method fine. So, so you can see that, by Endo way, this if you show now, what you can do is that, you can slowly take it in the Exo approach and see how it works.

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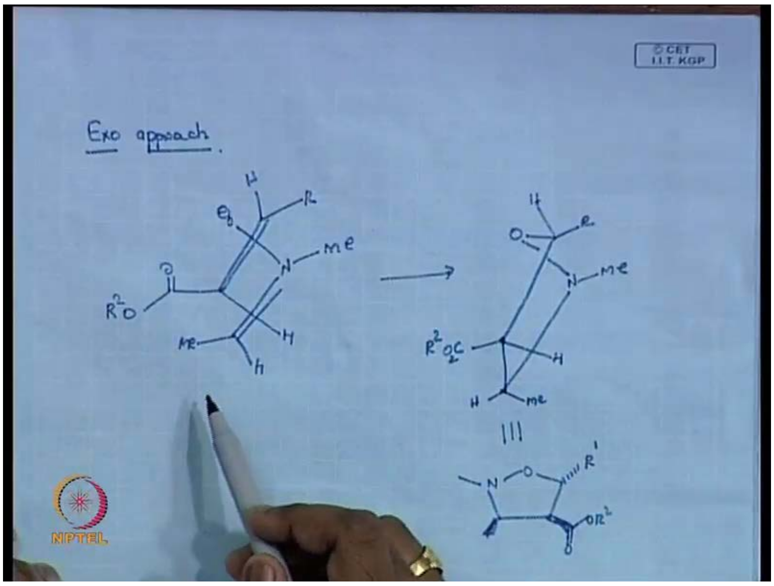

Same thing, if you can draw in Exo, we have a carbon here. My hydrogen, I am doing the Exo way. This with my nitrogen, just clipping around now, your O minus in this way and I have my metal. Just take the other way round and just for your Endo opposite. Now, your O minus in this way. So, if you write the structure, now I have 2 R c O 2 R (( )). See this is the main part where you have to understand them oxygen now.

If you open this up you get this part. So, if you look the Exo up it is less steric. Indeed right. This O hydrogen and you see, they are less steric indeed. But, if you take the endo approach, see in this case you have a metal in. For example, I will take an Endo approach; you have a methyl, but, if I have a tertiary butyl type of system then, you have an interaction more. So, in the Exo case, it is less steric and that is why it is more favored. Clear?

So, what we will do is that, in the next class we will see that, now we we said that by steric, Exo is much more favored. We will see that, why Endo rule is not applied here. What happen to your orbital interaction? Why it is not favoring you? That we will see in the next class. That is good. So, that is the end of this class ah.