Organic Photochemistry and Pericyclic Reactions

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Lecture No # 20

Singlet Oxygen Chemistry

So before getting into singlet oxygen chemistry, we will see one small rearrangement, then once we finish that, then we will get into singlet oxygen chemistry.

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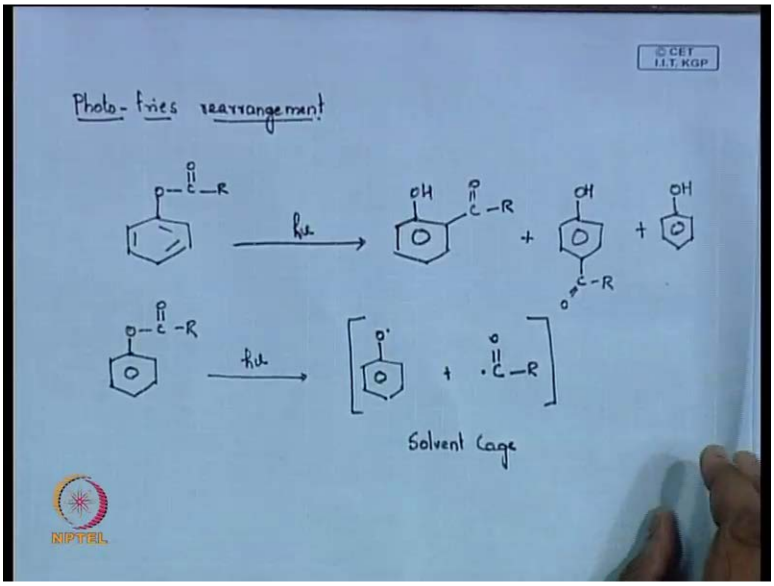

That is your photo-fries rearrangement. This you have studied fries-rearrangement you know for sure. Normally if you take fries-rearrangement, what happens? Any idea? I will just write the molecule that you will just you can recollect it. What happens? You just take this, and if put aluminum chloride, you have studied right yes aluminum chloride you will see your aisle moving towards your ortho and para right that here. In that case you will generate what? You get what? Carbocation, that is very important. You will you will generate an aisle carbocation, that is your regular fries rearrangement.

But in photo fries rearrangement is other way round. If you do the photo photolysis, same way you end up your ortho, and you will end up with your para; similar to your fries-rearrangement, but next you get one more product which tells something. You get a type of phenol which you do not see in your fries-rearrangement. You get these three products. Any idea what you suggest? Yes, decarbonization happens. It does not happen like that intra molecular intermolecular no.

So only thing is that this whole chemistry goes in radical. How it works is that if you take your and if you fertilize this? In regular one, you get an aisle carbocation and fries-rearrangement, but in this case you will get a free radical chemistry. Now this is in solving cage. That is more important. This is call as solvent cage. That is why I will always I talk about diffusion and these are very important when you talk about diffusion. See I will just write this molecule here for one more time.

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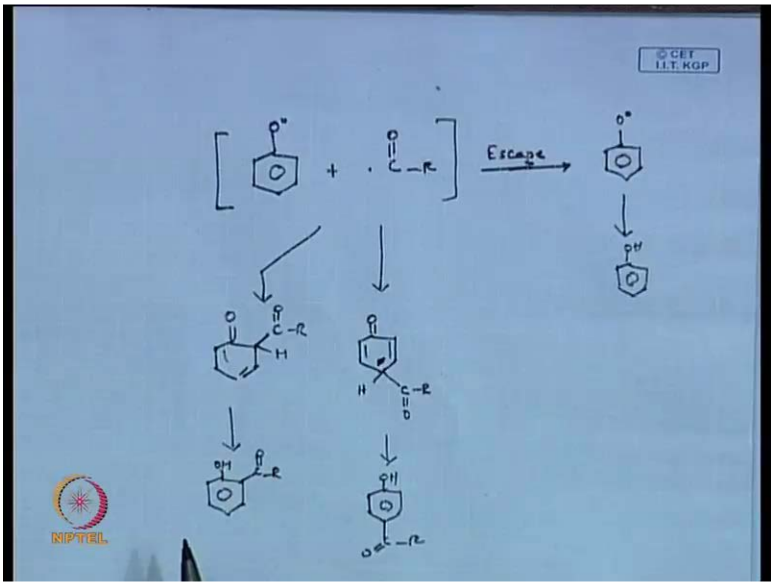

These two molecules, these two radicals can diffuse. Diffusion is faster. Before diffusion if they recombine, then you can see some sort of rearrangement happening does not need that it had to recombine there it recombine here. It can also recombine your para portion, but if it escapes then what happens you get your phenoxyl radical which can abstract hydrogen from the solvent to give you phenol. That is how you get, if it can have here if they recombine. If it is escapes from if it is escape from the solvent, escape from the cage, then you will get this type of radical. This then can give you the only thing is you have to remember is that this whole chemistry goes by radical. That is all. Previous case, it was carbocation and this is the radical chemistry. So do not think like there is no photo fries-rearrangement.

Just to say you that this type of rearrangement are also there in photo chemistry. Basically we have studied rearrangements die pie enone systems, die none systems and photo fries-rearrangement. Thus that is most of the important rearrangements you cover it. That is all for rearrangements.

Now what we will do is that we will see another important chemistry that is your singlet Oxygen chemistry. Most of the time when you do photo chemistry. You here you have to degasify if you are looking for some other products.

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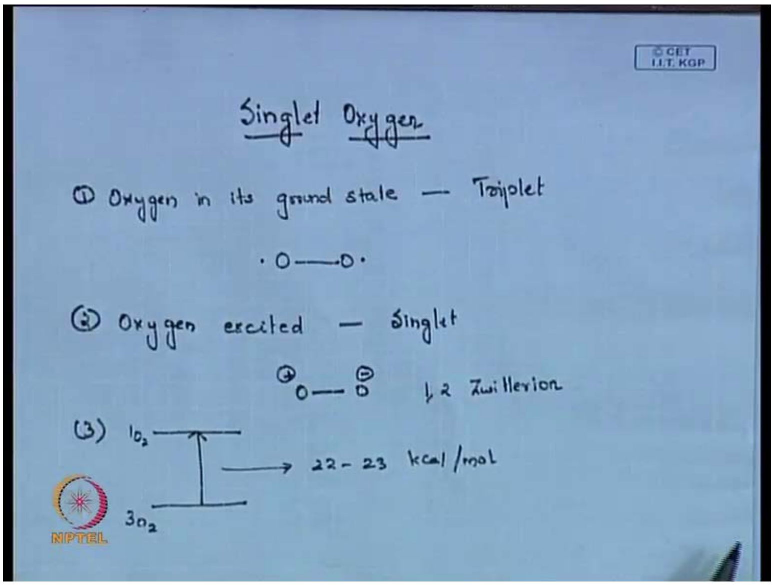

Singlet Oxygen

① Oxygen in its ground state — Triplet

$\cdot O - O \cdot$

② Oxygen excited — Singlet

$\overset{\oplus}{O} - \overset{\ominus}{O}$ 1,2 Zwitterion

(3) $^1O_2$ → 22 - 23 kcal/mol $^3O_2$

So you degasify propylene organ for at least 10 to 15 minutes then you do the photo chemistry; otherwise what happens? Oxidation happens or any other general terms otherwise, photoxation any other thing. Oxygen basically, you have to remove when you do photo chemistry. When you looking for some other important photo chemistry. Why? Because once if you do a ketone; if you excite the ketone; what happens? It goes to singlet then it gets to triplet right. Your triplet exited ketone can be easily quenched by your oxygen because oxygen is in properly triplet state. You have one of the system; very rare system to see in triplet. That is your oxygen

You try to excite your ketone and you want that keytone to do some other chemistry like alpha cleavage. But instead of doing that it will react with your oxygen because oxygen is there dissolved oxygen is there in the solution. So immediately the reaction goes off.

Type of clinches all your process because oxygen is in the triplet state that I ask most of the time this question in the viva. What state oxygen is? Oxygen in its ground state. This is I think one of the main molecule which in ground state exist in triplet. Its normally you can write that I am I am not writing any m o theory or something I am just I can say oxygen if it is in triplet, I always think them as a radical. For chemistry, but if oxygen is if you excite this oxygen, it gets to singlet. Singlet of oxygen normally exists like this. So this you can call as one two zwitterion. These are very good findings do you think what will be the energy gap between this triplet oxygen and singlet oxygen. Any idea? Whether no this will tell an idea like whether what process it is a very hard process or it is a simple process to do it.

It is only 22 to 23 kilo calories per mol energy is so less. This you know why it is important when I take the application you will understand so basically oxygen is ground status triplet, do not forget that. Once you excite it becomes singlet that acts more like 1 2 zwitterion the energy gap between your singlet and triplet is roughly around 20 to 23 kilo calories per mol.

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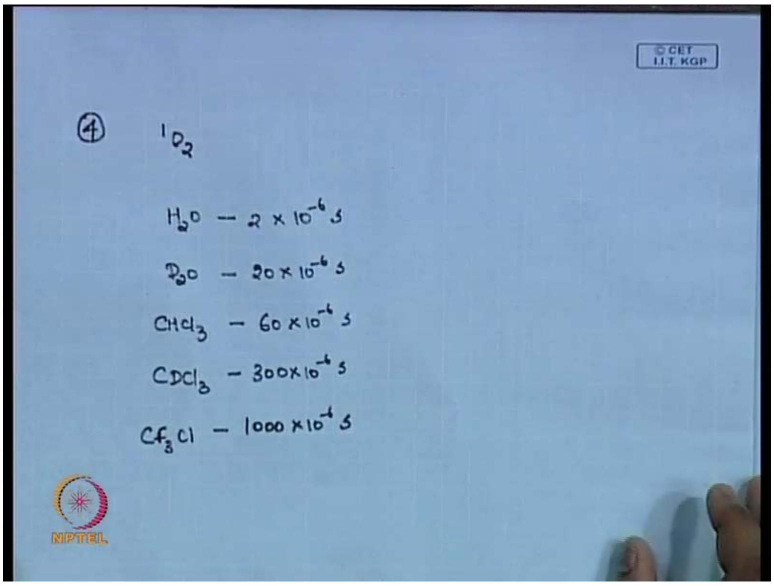

④ $^1O_2$

H_2O – 2×10^{-6} s

D_2O – 20×10^{-6} s

$CHCl_3$ – 60×10^{-6} s

$CDCl_3$ – 300×10^{-6} s

CF_3Cl – 1000×10^{-6} s

Another important thing which you have to know about singlet oxygen is their life time. Because any species you want to know their life time that is more important. How much life time it is there? See singlet oxygen lifetime is more solvent dependent, it depends on the solvent lot

But approximately it stays 10 to the power minus 6 seconds, but if it is in water, it has a life prime of 2 into 10 to the power of minus 6 second, but if it is in D 2 O, it increases 20 into 10 to the power minus 6. If it is in chloroform, it gets 60; if it is in CDCl3, 300 into 10 to the power minus 6 second; it if it is CF3Cl, its 1000 into 10 to the power minus 6 second. So it is highly solvent dependent, but it works around 10 to the power of minus 6 seconds more of the time. It is always nice to know the lifetime of your species so that you can think of many good chemistry like reactions. This has some basic aspect of your oxygen. So triplet singlet energy gap is 22 life time is around 10 to the power minus 6 seconds some physical aspects.

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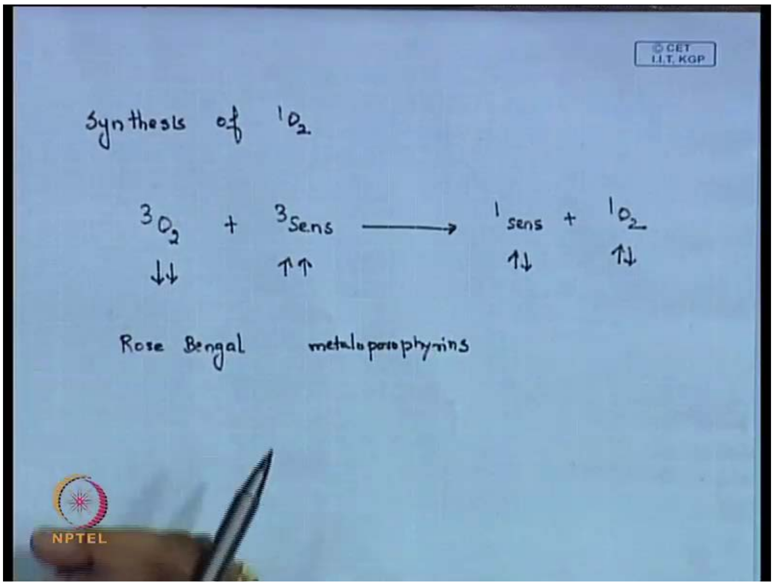

Synthesis of $^1O_2$

$$\underset{\downarrow\downarrow}{^3O_2} + \underset{\uparrow\uparrow}{^3\mathrm{Sens}} \longrightarrow \underset{\uparrow\downarrow}{^1\mathrm{sens}} + \underset{\uparrow\downarrow}{^1O_2}$$

Rose Bengal metaloporophyrins

Now we will see how we can synthesize singlet oxygen how people synthesize singlet oxygen. Any other any method synthesis of singlet oxygen? It takes your triplet oxygen. You can use rose Bengal. You can use a commonly triplet sensitizer. You get a singlet sensitizer plus singlet oxygen. Basically if you want to look into a electron view, you can just look like this. You can rose use rose Bengal any other which you can think because you guys are studying bio and organic chemistry lot. Any other guy who can think about which you studied you studied lot in biology.

Any metalloporphyrins, you can do nice chemistry with metalloporphyrins. People are doing like you can take alkene; you can take your ground oxygen; you put light and you put a metalloporphyrins. You end up with a Diels alder reaction. This is one common which is we call is photosensitization by which you can generate your singlet oxygen using sensitizers. Nothing big just you have to take system with an oxygen, just put your rose Bengal keep it in the light you get singlet oxygen. That is all. Nothing more to do on that.

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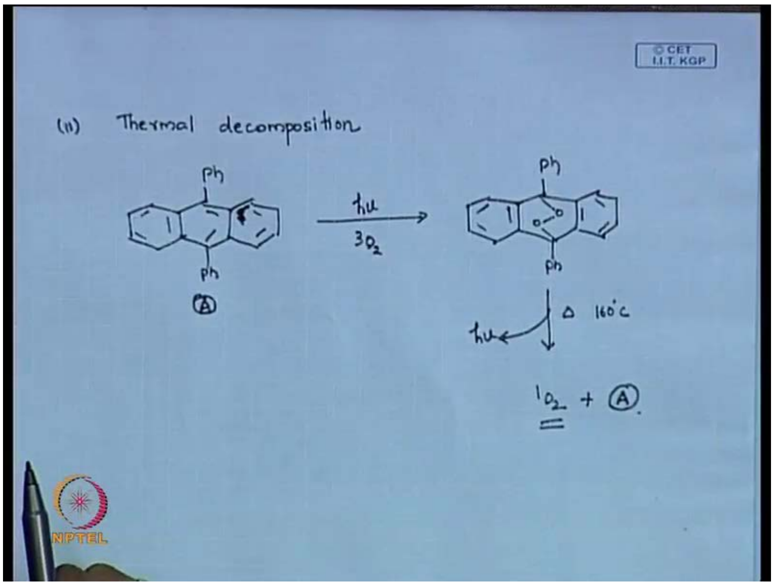

Another method which people use people do is that heard about chemiluminescence. You call this as thermal decomposition method, but you can call them as chemiluminescence. Heard about luminescence? What is luminescence? Just simply say or where you observe this luminescence process in nature (( )). You will see luminescence process anywhere in the nature? Your fire flies best example. See there are many chemistry has been done lot of I think research groups in Japan work on luminescence. They found out the enzymes which are which can make this light, but still they are struggling to find out how this colour transformation takes place. Sometime it gives yellow, blue, green. That is very important. What type of protein? It is trying to do that. That is lots of research are going on that area.

But we will take some synthetic way of doing, it take a proper anthracene type of system with a phenyl when you fertilize this. Just think you have an oxygen in the system. You get a nice type. This what happens if you heat this like 160 degree Celsius? It gives out your singlet oxygen nicely with your starting material. That you call it as a it gives you singlet oxygen plus a and the interesting part is that. This also gives light. This reaction once you heat you get your light also out from this. That is how it does luminescence. Basically takes the light then after sometime gives the light back and that is how people are generating singlet oxygen. But normally if you want to do in lab you use your photosensitization method.

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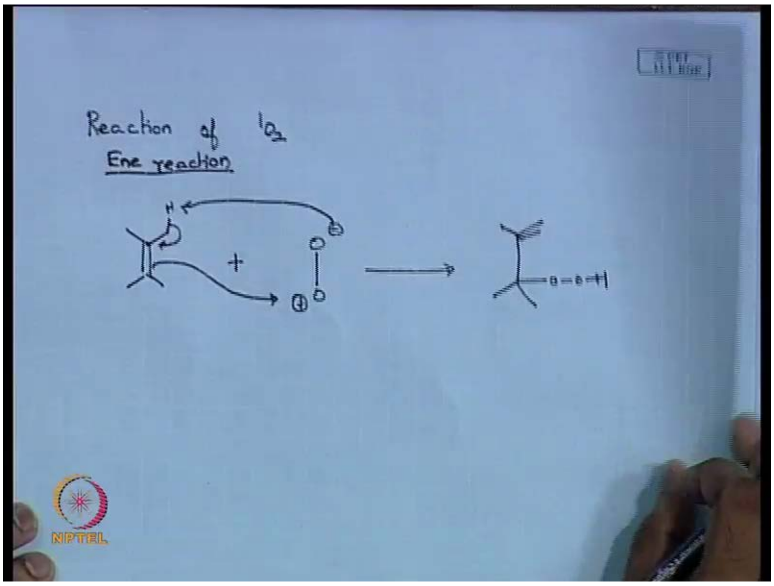

So these are the two importants two ways by which you synthesize. Now we will see the reactions of singlet oxygen. What are the reaction singlet oxygen does? Any idea? What reaction singlet oxygen can do? It does Diels alder 4 plus 2 cycloaddition. Then it does 2 plus 2. One more important reaction it does. What is this?

If you have an alkene like this system, I can write my singlet oxygen like this and think I am generated a singlet oxygen. What it does? See hydrogen see what it does is nice it exerts hydrogen? This can become O H immediately or like theta, but you can isolate O O H. What this reaction is? Ene reaction. This is the first reaction. You can see lot of Ene reactions happening with singlet oxygen. Very good examples for Ene reactions. There are many examples; there are lots of examples where singlet oxygen does Ene reactions.

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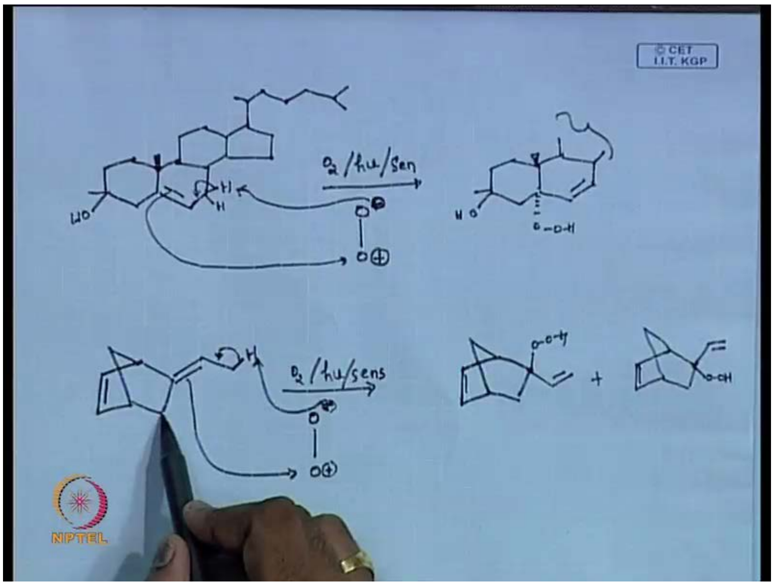

We will take some good examples and see what happens? Again do not scold me since; I am doing with natural products. Now I just want you to know about this writing this terpineol structures. Now I take this use my oxygen photolysis in the presence of sensitizer triplet sensitizer rose bengal. What do you expect? What happens? Epoxidation happens; ethoxylation. See you can think about your nice Ene reaction ergoline allylic hydrogen that is what I say you have a nice allylic hydrogen there. So you can you think like your generator system O minus and plus so you can come across this. Now I will ask you so you will get, it can be O O H which then breaks down to O H. Whether the stereo chemistry will be preserved like, it is a stereo specific reaction or it is non-stereo specific.

It should be stereo specific because I am not talking any radical here. It is a very good example of doing with natural. Because people call this type of reactions remote funtionalization. It is very hard to functionalize this type of molecules with an O H if you think like you can make only O H. It is very hard to do that you have to make an epoxide, then break it up then other side is there. This just an Ene reaction and its very stereo specific also and those if you think about company point of view no nothing you have just you are using oxygen. So they will also be happy fine.

Now we will take tell me what product you can think off? Can I give a clue the reaction gives me three product? Once I fertilize this in oxygen the presence of h mu sensitizer. I get a type of three products. Shall we write? So one case you have your O plus O minus and your O plus so you say that you can pick this hydrogen which is allylic. You can take this up get double bond and take this up. This can be in two ways it can be in upward direction giving you a O O H like this or you can write it like this alnow write like this also fine.

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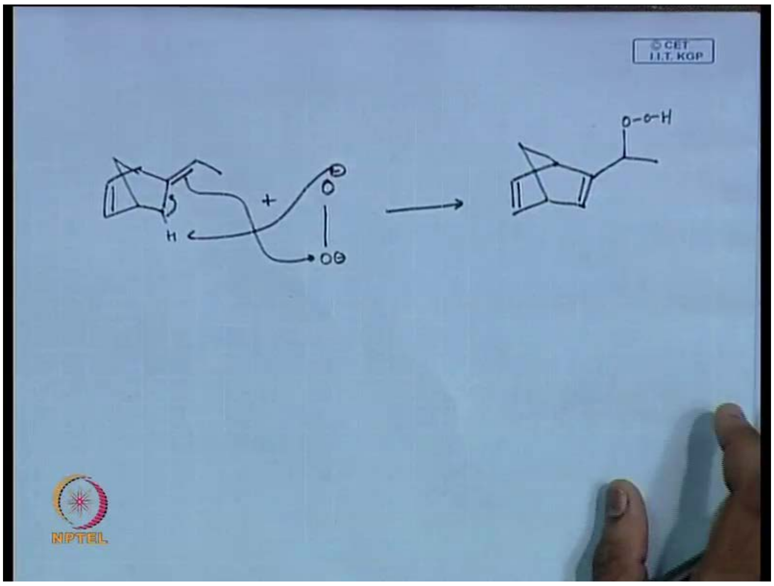

Another product that you can look for. What is the another product? You can think off. I can pick an hydrogen from this. This is also allylic. See I am just writing O O H, just you should remember that it can be O O H immediately, because normally when people give you this and give you O O H. You should you should think that it is an type of Ene reaction do not look for O O H all the time. This O O H can easily break and become O O H. Your Ene reaction should come. You get three products nicely. This is one type of reaction of first reaction of your singlet oxygen Ene reaction. Singlet oxygen does nice Ene reaction. We will see the next type of reaction which is singlet oxygen does that you call as diels-Alder reaction or you can call as four plus two cycloaddition.

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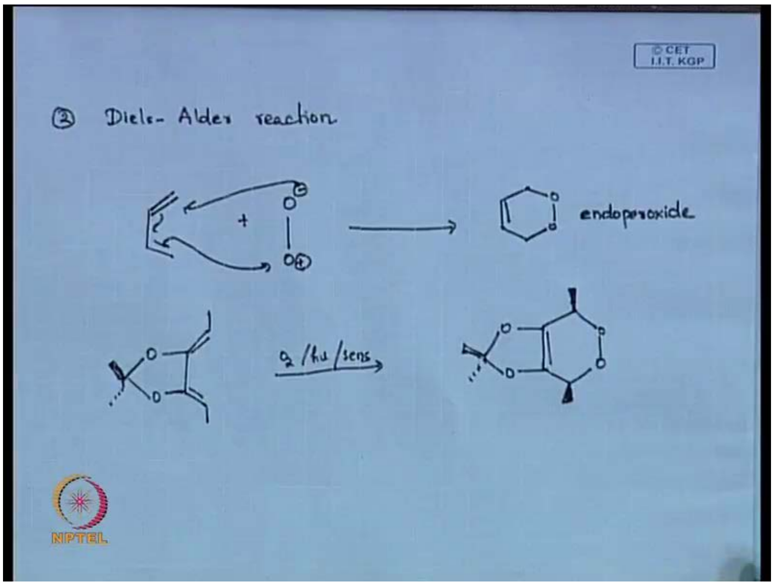

I can generate a singlet oxygen. I can do my nice Diels-Alder. You call this as endoperoxide. If you take this product because just want to check about what do you get. Now I am why I am writing this just to check up the stereo chemistry because this is a Diels-Alder then it reaction is type of very stereo specific. I am just worried how you write that metal that what this example is all about. Just to show that this reaction is very stereo specific highly stereo specific. Now we will take another very good example which you can see how Diels-Alder works. Finish.

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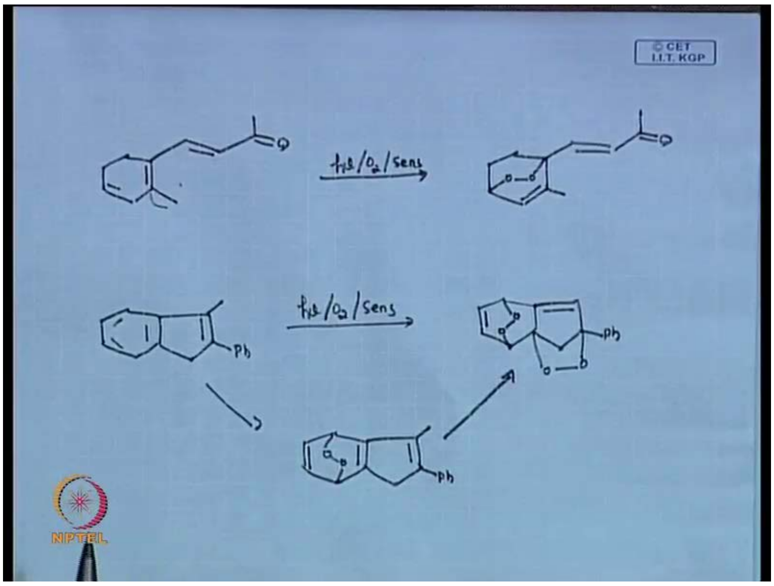

It is better that you do lot of problems that will help you out write the problem. You wrote a correct. You were thinking about this one. That is the interesting part you can see what happens this guy started flipping. It can around cis and trans and all those things happen. Does not allow you to come like this to make a O O bond. There are examples which I will show. But this is easy this cannot do anything. Oxygen can sit nicely inside and make a Diels-Alder there. No if you are thinking like this it is not wrong. It is right. Do not think that you are completely wrong, you are thinking rightly, if you are doing that also.

The next is that you have to see why it is wrong. And this I am this is interesting one because this has been a recently done this work. We will check how many has written the right one for this. I want the product for this. Looks to be very simple molecule, nothing big there. Can you give me the final product? Have you written the product? Just simply your Diels-Alder. That is all. Benzene ring; any other? That not wrong. See if you basically have stopped from there. It is not wrong, but you get a benzene plus you get one more cycle that you have not thought about it. See what happens? Your first step is what? Thus, molecule thinks nice than us. Now again you have a system which is ready for Diels-Alder. That again can give you this form. Basically if you not stop that. These are good examples we have showed and learn about doing things Diels-Alder reactions.

I will see Diels-Alder reaction of oxygen in heterocyclic systems very famous. You can it is used for many synthetic utilities like see there are there are few reactions which you which you can for example, I have furan. I want to do funtionalization here here here here.

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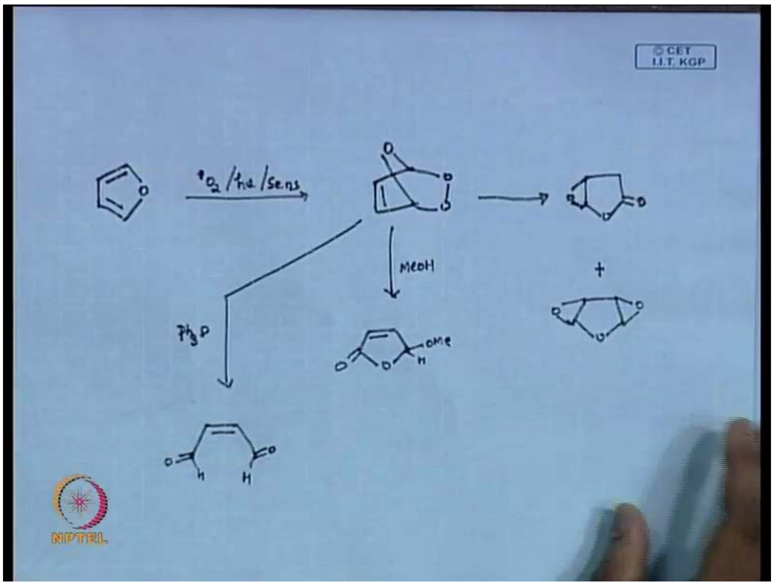

You can do by using this is normally done in even synthetic labs. This you can do because these reactions are normally done easy. Even if you are doing in your project you can think of doing that you can come to my lab. There are I think previous year also some projects student did. This reaction they came to my lab and did this reaction. Very simple. In one sense you get this correct once you do it through Diels-Alder. If you slightly warm this once you take it out and slightly warm it immediately. You can get these products then you can break this epoxide to give you a O H.

Concat this. These two products basically you can get opening upon both the sides and making epoxide or you can get a keytone with an epoxide. While warming if you warm it using methnol slightly if you warm it metenol then you end up with the keytone get this product while if you want to warm it with methanol slowly. You can functionalize your keytones. There are some more reactions if you want to warm using little bit triphenyl Phosphene then you get nice Die-Aldiates. You get you take because furans are cheaper take furan do a singlet oxygen put lightly warm it with triphenyl phosphine you get Die-Aldiates. Then you can do us take or whatever you want you can extend the chain. Even you have reactions with thiophenes you can do with thiophenes also. Not only with pureons. You can do with thiophenes; you can same way you can get sulfer and the same products. These are all like important reactions of your singlet oxygen in Diels-Alder.

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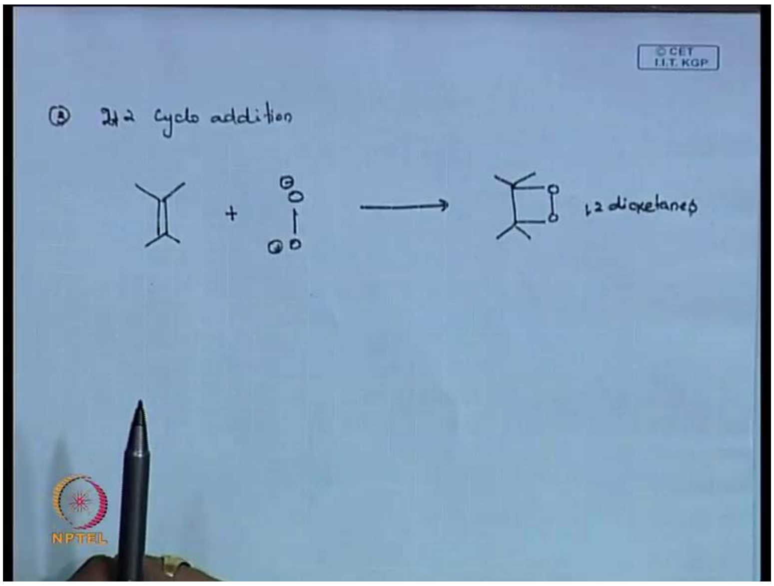

Now we will see the third one that you know by yourself like that is your 2 plus 2 cyclo addition. This is just for previously you have seen 4 plus 2 cyclo addition which is your Diels-Alder. Singlet oxygen does also 2 plus 2 you get 1 2 dioxetanes molecules.

You have studied basically three reactions in singlet oxygen. One you have studied ene reaction, another Diels-Alder and another is 2 plus 2 cyclo addition. Now I will give you one simple example and ask you how to see what you can take this molecule like.

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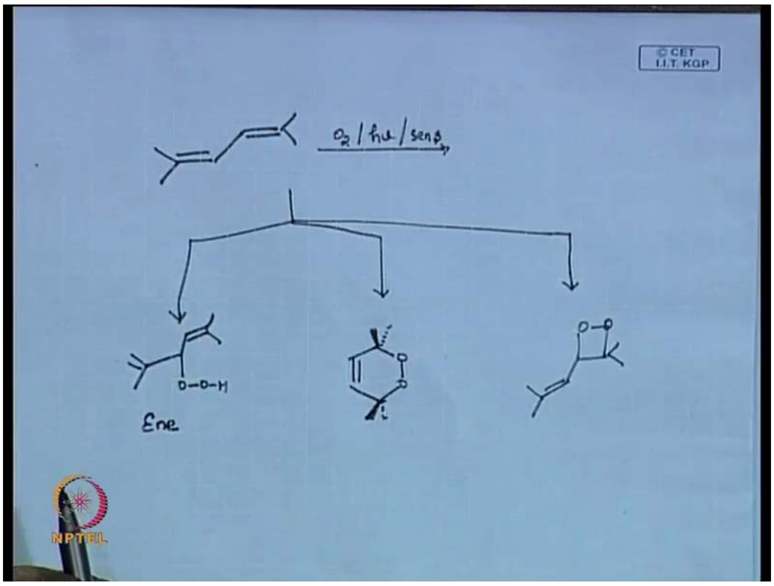

Tell me what products you can think off? I am taking a type of diene system; I am using oxygen photolysis in presence of sensitizer. What you can think in this reaction? What products this can give you? All three very good. You get all three of your reactions, here you get ene reaction you can think about 4 plus 2 you can think about your 2 plus 2 very good example for this very good.

So you get all three. Can you write the product? This you can get from your ene. I can take this hydrogen from this product. Am I right? I can get this product then I can think about nice 4 plus 2 cyclo addition. I can get my 2 plus 2 cyclo addition. These are very good examples to understand about your chemistry.

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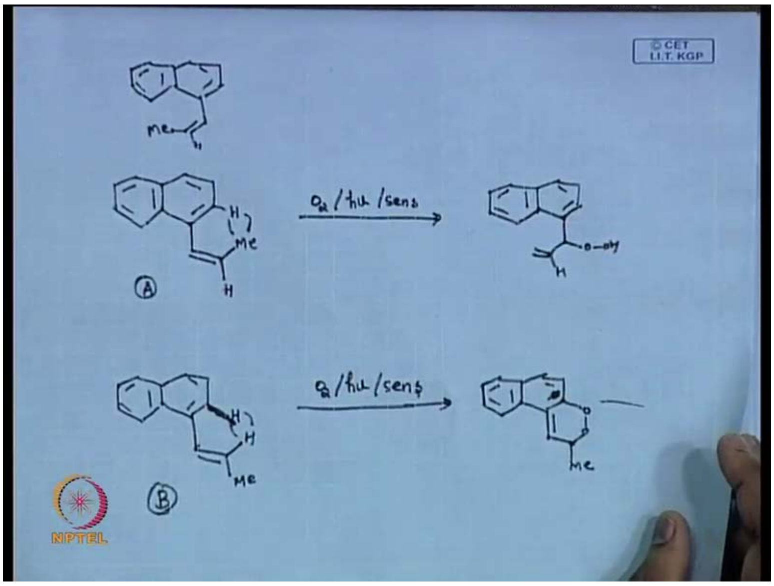

I will take another same type of molecule. See I am just giving you a molecule. I have molecule like this. This is the other way round. One I have a methyl hydrogen another I have hydrogen methyl, it is just a (( )). I am doing oxygen photolysis sensitizer same condition I am following for this. Same molecule I am taking I am following the same condition. So in which what will happen? In which case you are thinking about ene reaction and in which case you are thinking about 4 plus 2 cyclo addition.

See this gives among this two molecule one give. Only ene reaction another molecule gives only 4 plus 2 cyclo addition. Anyone can tell you want you say? We call it as a and be so that we do not get confused. You say a as ene reaction. Why? Any idea?

See you just see here this hydrogen is there. The interaction of this hydrogen and methyl this interaction of this hydrogen and hydrogen. Which is more? This is greater. What happens? It does not want to stay there just flip across. It goes down and flip across so you get a structures. I will just say similar to a structure facing this direction, it moves away. With a hydrogen and methyl this direction which is completely away it goes flips around. In this case it does not happen. Now this is not facile for doing a 4 plus 2. It can do only ene reaction. In this case you can think about nice 4 plus 2 cyclo addition because it will be on that side. So oxygen can come and bind and give you a nice 4 plus 2 cyclo addition.

In this case if I write the product, I can get this product can get this product fine. More about the like substrate also has more control in which the reaction wants ene or 2 plus 2 or 4 plus 2. In some places you see all this three reaction happening in some place two for example, if you take this type of systems.

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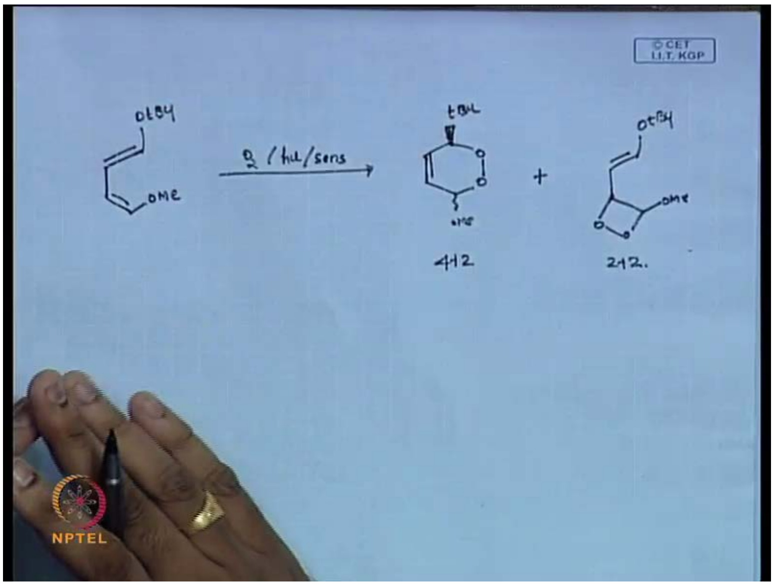

What you can think in this case? Oxygen photolysis sensitizer (( )). What do you expect in this case? You expect 4 plus 2. That means I have to write the structure like you expect this. Why cannot I write the structure like this? Which will be much more easier for me? I can think about writing like this 2 plus 2. You can think of writing like this anything wrong in this. Whether this undergoes so it undergoes both 4 plus 2 and 2 plus 2 that. That is the only thing in these reactions. Can see 4 plus 2 as plus 2 plus 2 see there are that is why I am saying there are many good examples where you can see all three reactions happening, in some cases two happening, in some cases its very selective for one reactions. But you should remember that if you have an singlet oxygen you think about ene Diels-Alder and 2 plus 2.

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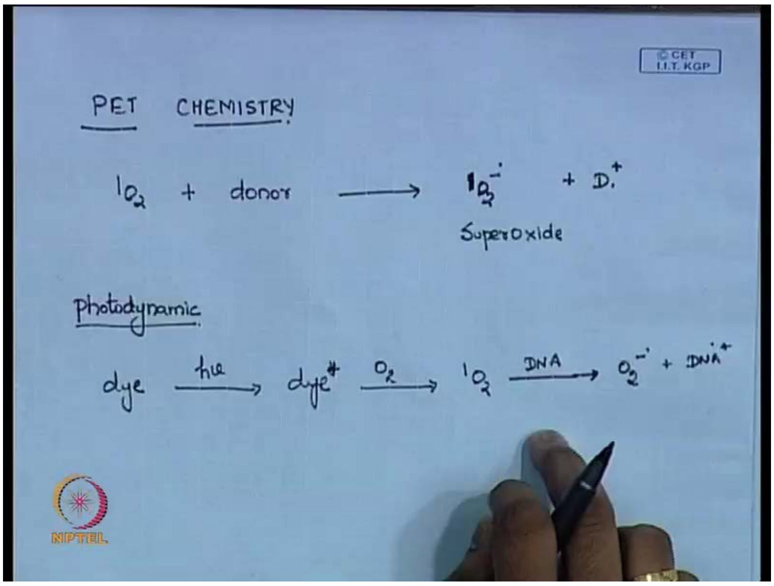

Now the last reaction of your singlet oxygen which is now well explored and people are using for lot of big applications. The last application which we are talking about is PET CHEMISTRY. If see this is this has been this application, this particular reaction application has been taken now, it is in basically in hospitals. They have been directly taken into our now people are using it. Singlet oxygen plus if you have a donor, you generate singlet oxygen. You have an donor so what happens? That donor can give an electron that is your PET chemistry; you get singlet plus D dot plus. I will just take this out this one O 2. What you call this? Very famous component. This is superoxide, highly reactive species. Just you take singlet oxygen plus your donor, you get your superoxide.

Now, I want to ask this where this chemistry is used; you have studied this chemistry lot of application it has. This particular superoxide. Anyone?

(( ))

More than that. What is photodynamic therapy? Heard about this, photodynamic therapy? You guys know about like how to kill cancer cells. Cancer therapy, how they will normally do? Normally in hospital, if you have a cancer, what they will do? Radiation therapy; radiation, because what is the big drawback of radiation? It kills your good cells also, and as a result of that, you might end up with some other problems. But in this photodynamic therapy, it is so nice that what happens is that. For example, you have a you have a cancer here and you want to kill only that area. What you do you take a dye inject that dye into that particular cell and then cover your whole area by black cloth or whatever, and make a small hole there where you have the cancer. Then shine light, what happens? Your dye gets excited.

This exited dye will be then interacting with your oxygen, because that is there in your body entacts with an oxygen to give you singlet oxygen. This singlet oxygen then react with your DNA or protein whatever comes into its part, and this DNA acts more like a donor; generating you O dot O 2 minus dot plus DNA plus dot. And this superoxide, ionii will just start killing the cells. It kills all the unwanted cells in that particular area, because your dye is not other reflect. The dye is only on that area. So it just kills all the unwanted cells that is called photo dynamic therapy. That is now started using in field.

But the only drawback of this system is that it is more in the leg skin cancer like peripheral region. If you have something inside like kidney or liver wherever it is, then this does not work that is the only drawback, but if you have a on the peripheral region this is a best thing you just because it is more target oriented and just you take that die inject on the particular area, and just then that is all; just shine your life; that is enough. Then you get your unwanted cells killed; and many schools have been started, centers only on photodynamic therapies. Bowling green state university is there are university of Leeds and many other universities they have started only center where they are doing only photo dynamic therapies. So that is the four important reactions of your singlet oxygen; so the chemistry of singlet oxygen is that. So we have seen what singlet oxygen, their synthesis, and we have seen their four important reactions. That is good. So ending our class with this.