Reactive Intermediates: Carbene and Nitrene

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Lecture – 12
Reaction of Carbene (Contd.)

Hello everybody, welcome to the course Reactive Intermediates Carbenes and Nitrenes. So, we are learning now different type of Reactions of the Carbene species. Up to the last class we have studied that different type of additions reactions; that mean the carbene species how does it react with olefin or alkine that we have studied and additionally we have studied various type of examples based on that particular concept.

Today what we will learn that insertion reactions, this is another type of reaction these carbene species generally goes through these type of reactions also when there is different type of nucleophiles are there, that can be inserted into the carbene species.

So, what is this insertion reaction?

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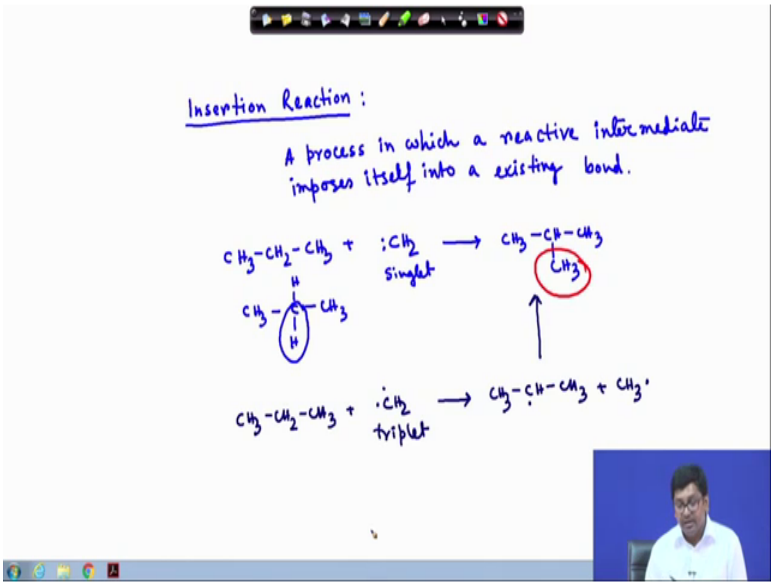

Insertion Reaction :

A process in which a reactive intermediate imposes itself into a existing bond.

So, insertion reactions is a process in which reactive intermediate that is here like a carbene imposes its itself into a existing bond ok. So, these process, so this is a process in which a reactive intermediate imposes itself into a existing bond ok. So, in general if there is a bond then if that reactive species inserted into it, then that is the insertion reaction.

And, as we know that carbenes are in general highly electron deficient;, so it wants a pair of electron to fill up it octet. So, that is why these type of reactions are very common with carbenes species. As per example it take this in propane with the carbene species. So, this is a singlet, then in these one step because in these case these are concerted type of reactions.

So, what it will give ok, so here if you see there are these bonds ok. So, one of this C H 2 singlet that has been inserted into this carbon hydrogen here this carbon hydrogen bond and that gives you this C H 3 group over here. Now, if we take similar substrate with triplet carbene ok. So we can think that is like triplet carbene again this is a stepwise process, but eventually after first step this will give this methyl radical and this radical species because this will pick up 1 H dot here and make this one methyl radical whereas, it will be here like a C H 3 C H dot C H 3. And obviously, after that hydrogen abstractions and recombination will give these 2 steps; first is this hydrogen abstraction followed by this recombination that gives the similar product ok.

Now, in these 2 step these 2 processes rather can give the same product whether it is singlet or triplet. Now as you know that singlet carbene will react in a concerted manner ok; that means, it can insert into a carbon hydrogen bond in single step. So, we will see now the orbital interaction during the insertion of a singlet carbene into carbon hydrogen bond ok. So, for that what we have see, we have to see the highest occupied molecular orbital or we have to consider it the highest occupied molecular orbital of carbon hydrogen bond and lowest unoccupied molecular orbital of carbene ok.

So, let us draw that. So, we will first see the now these orbital interactions.

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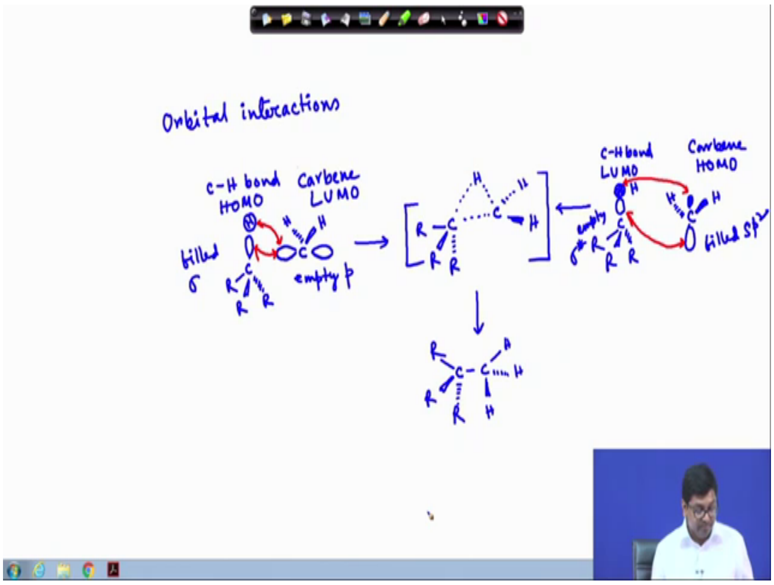

So first we will see the HOMO of this carbon hydrogen bond, where these carbene is getting inserted, so that one we will see ok. So, let us grow that the filled sigma bond, sorry orbital. This filled sigma bond we will see and as you know that from our previous experience that how these carbene remove that is proceeding that is sideway approach. So, that will come like this way. In my previous one of my previous lecture I have explained; what is this side way approach. So, this is the empty p orbital and this is the filled sigma ok. Now if we see that the bonding interaction that can happen with this as well as with this ok.

So, this is the C H bond HOMO and this is the C H bond HOMO, sorry and this is the carbene LUMO ok. So, in this way the side way approach that can actually shows that how these singlet carbene can be inserted into a concerted manner ok. Now, once it is this one then what will be this, you can drawn in these way ok, overall that this transition state, so these could be the product ok.

So, these we can see that here this filled sigma bond and this empty p orbital they can nicely these highest occupied molecular orbital and the lowest unoccupied molecular orbital of carbene and HOMO of these each bond they can be nicely give bonding interactions ok. Overall that means these carbene C H 2 carbene that can be nicely inserted into the carbon hydrogen bond ok. Similar way we can see that this particular step can be obtained in opposite way. That means, if we consider now carbon hydrogen bond, LUMO that is the sigma empty sigma star this is the hydrogen.

So, this is the empty sigma star and if we take the carbene HOMO and there if we consider their sideway approach ok. So now, if we check its side way approach again that can nicely give these bonding interactions; so either you consider this carbon hydrogen bond HOMO and carbene LUMO or the carbon hydrogen bond LUMO and carbene HOMO in these both cases this will give in the bonding interactions. So, here it is empty sigma star and this one is filled S p 2 ok.

So, these are the orbital interactions that actually shows that how the singlet can be carbene can be inserted into a carbon hydrogen bond ok. Additionally this mechanism implied that the stereo chemistry that is the if where this diazo sorry; where this carbenes species inserting into the if it is a inserting into a stereo centre, then the retention of the configuration has been observed or it is predicted, because these reaction is going via concerted manner.

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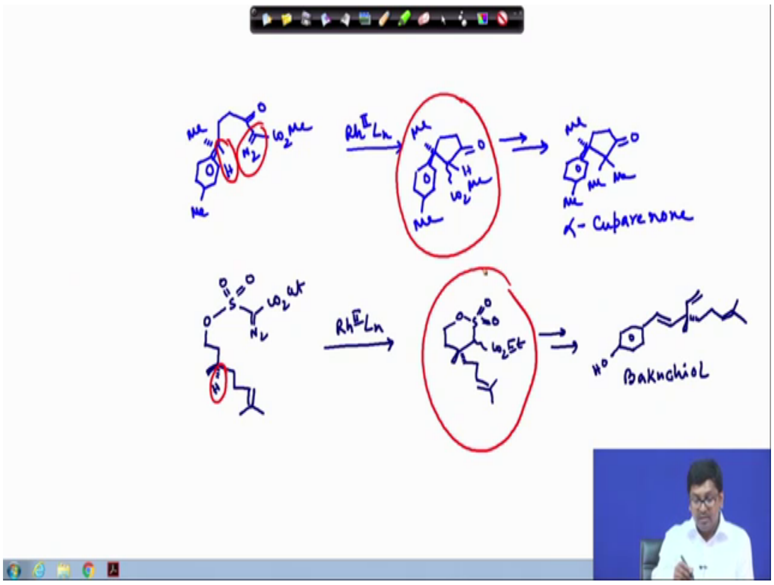

We will see now few of the examples where these carbene species has been inserted into a carbon hydrogen bond.

As per example if we take this particular diazo compound as a carbene precursor ok, now you see if we use these rhodium 2 acetate here, I am writing rhodium 2 catalyst then what will happened that first here writing ln here, so in these case it will generate the corresponding metallocarbene over here and give you the metallocarbene species and once it will generate what it will give? It will give you the corresponding 5 memebered cyclopentane type of ring, because if you consider 1, 2, 3, 4, 5, so there are 5 membered ring that will form ok.

And think about that. And these can be converted into a natural product in further steps and these name of these natural product is alpha cupare none. So, what we have done here we have taken a diazo a carbene precursor that is the daizo keto ester compound. That means, this diazo is flanked with 2 electron withdrawing group and then with the treatment of rhodium 2 catalyst we can generate the carbene metallocarbene and now these carbon hydrogen bond that is over here this one in these the diazo the diazo ester keto compound. That means the precursor of the carbene that can be inserted now into this carbon hydrogen bond to form these particular five membered species ok.

And if you see here interesting thing is that this stereo center that is the retention of configuration is happening ok. So, in similar way we can see another example where the sulfone type sulfonyl has been used as the carbene precursor. So, the diazo is flanked with ester and the sulfone moiety. Now if it is again under rhodium 2 catalyst.

So, in that case these can be fused as to generate the metallocarbene and to provide the corresponding cyclic product after the carbon hydrogen insertion. Here interesting thing is that here in these ok. So, these will insert that metallocarbene that will insert into this particular carbon hydrogen bond.

So, overall the product will be here ok, here interesting this is that even though there is a olefin, but the carbene that is not giving any addition product or not giving the addition product as a major rather it is going through the c h insertion reactions because here it is forming the 6 membered ring ok. And these again this particular substrate which we have synthesize from these precursor through the rhodium 2 catalyzed C H insertion reactions that can be converted into another natural product in fewer step that is this one and the name of this is bakuchiol ok.

So, you can see how much important this ch insertion reaction is because using these particular technique there are several important reactions that can be carried out and which can be the advanced intermediate of various important biologically active natural products ok.

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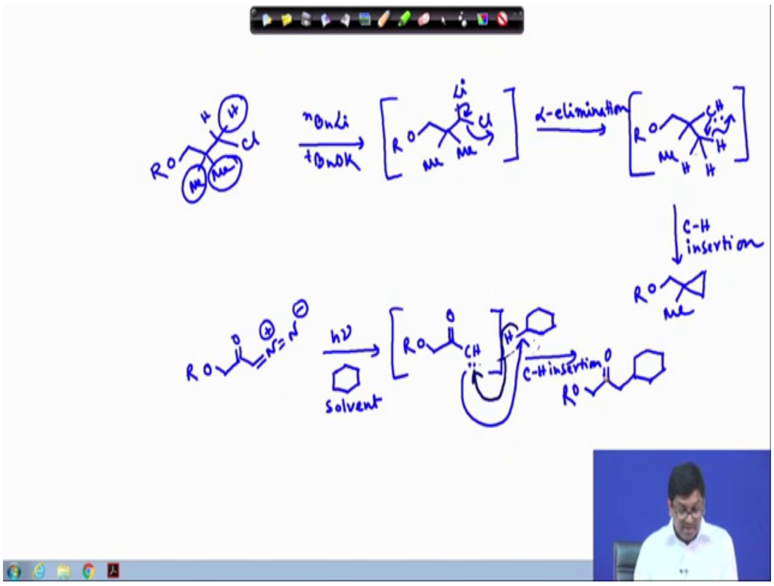

Next we will see another type of reactions where this CH insertion reaction will give us the cyclopropane moiety. Earlier what we have seen that the carbenes that can be inserted or that can be reacting with the olefins to (Refer Slide Time: 18:38) the cyclopropane ring cyclopropane ring whereas, here we will see that the carbenes how that is by CH insertion is giving the cyclopropane ring.

As per example we can take this substrate, where there is no beta hydrogen. Now if we use one of the schlossers base ok, so that proton will be abstracted from here and give us the lithiated salt this ok. So, once we have this species then by alpha elimination these will give the corresponding carbenes species ok. So now, you see this methyl that is having three hydrogen; we can draw in these way ok.

Now, the CH insertion will happen to give us the corresponding cyclopropane derivative ok. So, here what is happening? Here the CH insertion is happening. So, in this case by CH insertion we are getting three membered ring, because there is no beta hydrogen present here and once there is no beta hydrogen. So that means, that is force to getting this alpha elimination. And once this alpha elimination is happening then the carbene species is forming. And once this carbene species formed then it is forced to go to this CH insertion to give the product with cyclo propane ring ok.

In these cases this type of insertion CH is insertion reaction it has been found even the carbene species is, so much eager it is having so much eager to get the electrons that it will even react with the solvent. As per example if there is solvent like cyclohexane that will be inserted into the carbon hydrogen bond of cyclo hexane and give the corresponding product. So, if we have this type of diazo compound as the carbene precursor then if the cyclohexane is solvent here ok.

So, this will give the corresponding carbene and once it will form then this is highly electron deficient. Now it can nicely insert into a carbon hydrogen bond of cyclohexane ok. So, once it will go like this sorry we will draw in this way ok. So, if it reacts with this carbon hydrogen bond of cyclohexane of this carbene species finally, what will be the product? So, the product will be the corresponding inserted product ok. So, here what is happening? Here also CH insertion is happening fine.

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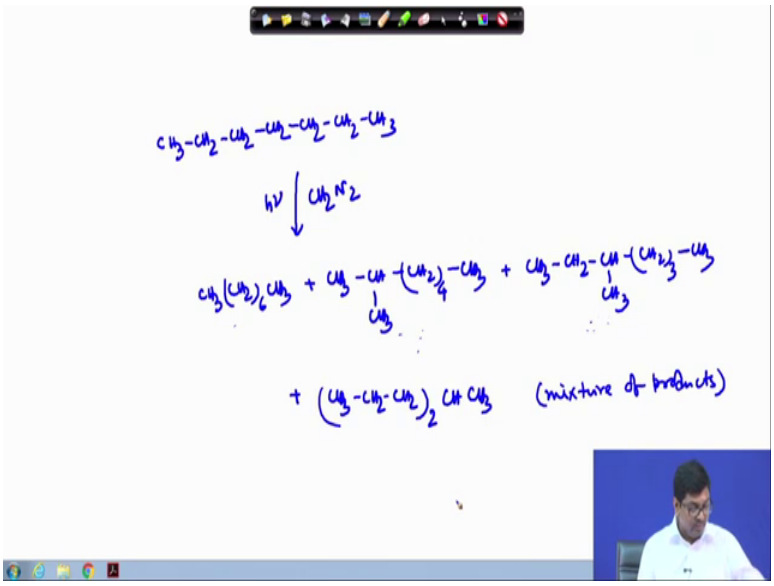

Now as we mentioned that carbene species are highly reactive. And if it is very much reactive, then there is a high chance of getting less selectivity and in as per example if we take that heptane and under the diazo methane in photolytic photolysis condition, so this will give various carbon hydrogen bond insertions you will see that in various positions of these heptane the CH 3 group CH 2 carbene that has been inserted and over all it will give this is as 38 percent whereas, this one will give 25 percent and another isomer is 24 percent ok, so this will also form certain amount.

So, these are the thing that we have to understand that how these carbene species become so much reactive that it can be inserted into various position of this heptane to give many products ok. So, this I will rather remove this percentage of this products we can say that these are the mixture of the products that we will get from this particular reactions; so mixture of products ok.

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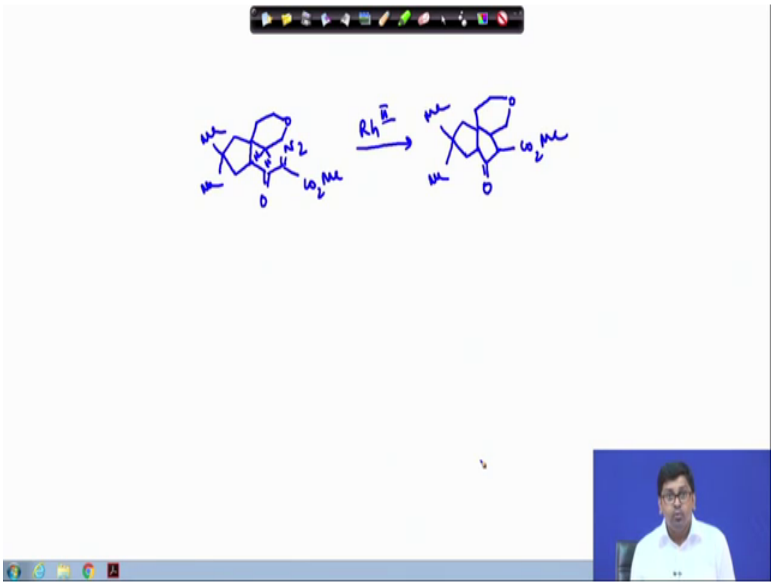

Finally if we see, another example where again diazo compound is the precursor for the corresponding carbine, so in presence of rhodium 2 catalyst again the CH insertion will happen from here there are 2 hydrogen. And if we see 1, 2, 3, 4, 5, so 5 membered ring can form and overall the product will be the corresponding 5 membered fused product.

So, in that all way whatever we have shown, we can understand that this carbene species nicely can be inserted into the different type of carbon hydrogen bonds specially as this carbenes are highly electron deficient, it prefers to insert into a electron rich, carbon hydrogen bonds, and even though there are not that much electron rich they are also it can be inserted. So, these are the specialty of the carbene species to react with various types of carbon hydrogen bonds with different type of electronic properties.

Thank you.