Reactive Intermediates: Carbene and Nitrene
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Lecture – 10
Reaction of Carbene (Contd.)

Welcome, everybody. Welcome to our next topic in Reactive Intermediates Carbene and Nitrene that is the Simmons-Smith reactions continuation. We are already discussing about the Simmons-Smith reaction. Last class, we have discussed about what is the reagent, necessary for this particular reaction and how the reaction goes through; that means, the mechanism of this reaction and after that we have studied few examples with different type of olefin, how that will convert into the corresponding cyclopropanes and we have seen that how the allene that type of molecule also can be converted into its cyclopropane derivative.

So, today we will learn different variations in Simmons-Smith reagent little bit of that and after that we will proceed with different additions reaction with various carbenes generated with the help of transition metals, ok.

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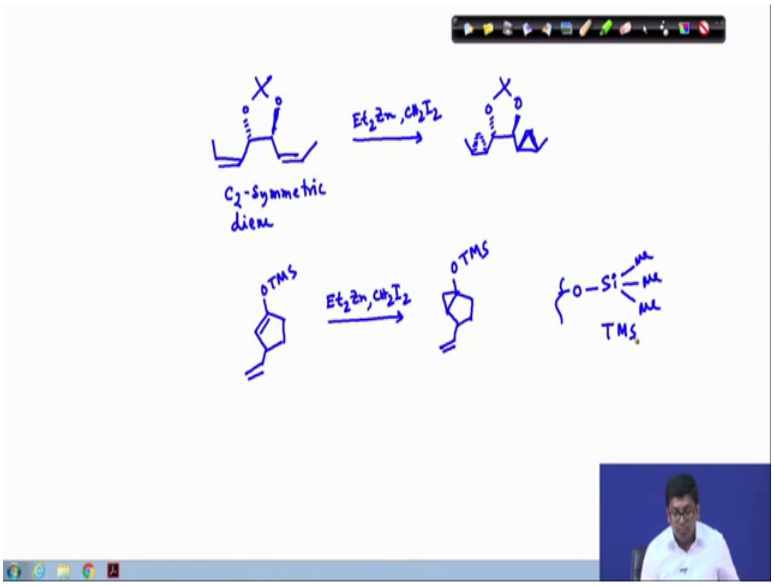

So, now, the variations in different Simmons-Smith reagent as per example we will see let us say we have these protected diol, ok. This is a C 2 symmetric diene, ok. So, these diene if it is exposed under modified Simmons-Smith reagent here what they have used diethyl zinc and the methylene iodide, for the generations of these modified Simmons-Smith reagent and once it has been generated then it gives the corresponding cyclopropane ring that is in this case what you will get sorry this bond will be bolt so, what it will get and here the cyclopropane ring is this, ok.

So, you can easily understand that due to presence of these heteroatom, how these heteroatom here it is oxygen is guiding the stereochemistry of the cyclopropane in this case it is a beautiful example you see there are two hydroxy groups with different stereochemistry and they are actually guiding that what will be the stereochemistry of the product cyclopropane product.

Now, in another example where it has been used vinyl silyl ether as the starting material in presence of diethyl zinc and methylene iodide, as for the suppose it is as a modified Simmons-Smith reagent and the product is again the corresponding cyclopropane, having these TMS ether, ok. TMS means here O-silyl group trimethylsilyl. So, I am not drawing the rest of the part. So, this is the corresponding TMS or O-trimethylsilyl, ok. This is a one hydroxyl protecting group.

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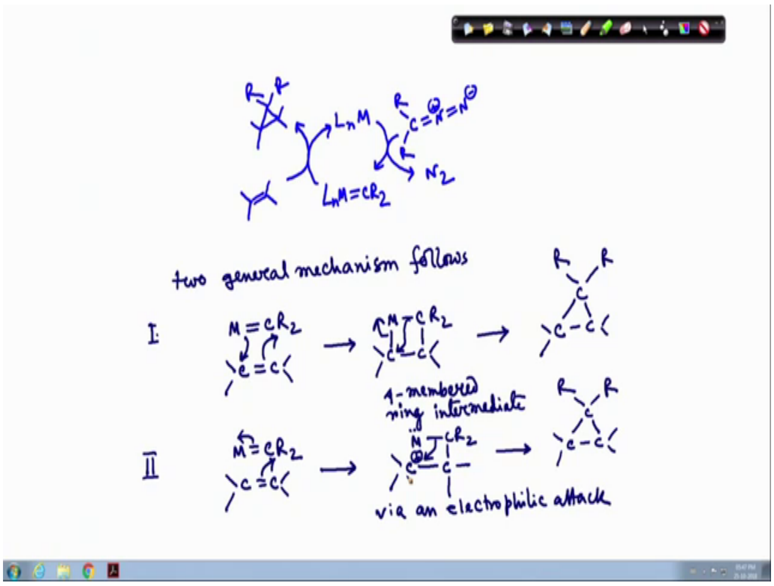

Now, we will see the transition metal carbene complex in cyclopropane synthesis. So far we have seen that how Simmons-Smith reagent or it is modified version has changed the olefin into it is cyclopropane ring or the allene to corresponding cyclopropane. Now, we will see that how transition metals or transition metal complexes they can generate the carbenoid type species for the cyclopropane synthesis. So, overall mechanism that we can predict from here, so, if we have this metal complex and if we have this carbene precursor let us say here it is diazo group.

Now this can easily liberate the nitrogen, and if it liberates nitrogen what it will form, ok. Now this can again go back to here, but obviously, the olefin becomes the cyclopropane, ok. So, we have started this corresponding diazo compound. So, in presence of metal it will transition metal it will liberate the nitrogen will form it will form the metalocarbene and the olefin will be converted to its cyclopropane ring, ok.

Now, this reaction that is from the olefin to cyclopropane that can goes via two different way, ok. So, what I mean that when this transition metal carbene complex has been used in cyclopropane synthesis then that follows two general mechanism. So, this transition metal carbene guided cyclopropane synthesis rather follows two general mechanism. Two general mechanism it follows follows ok. So, what are the two general mechanism? Number – 1 is that it can goes via a 4-member ring intermediate.

So, if we have we have this type of complex now we have olefin. So, now it can form these 4-member intermediate ok. So, this is the ok. So, once it generated, then this 4-membered ring that can decompose to the corresponding cyclopropane ring. So, this will be ok. So, what will be the next one? So, the next general mechanism could be via stepwise; that means, that if there is some electrophilic type of attack to this carbene as we have said that carbenes are generally like electrophilic in nature, so, via an electrophilic attack to form a polar species, ok. So, to form a polar species which finally, goes 1, 3 bond migrations and give the corresponding cyclopropane. Let us see how does it work.

So, if you have this metalocarbon then you have this olefin now it can attack like a electrophile like this olefin is attacking to the electrophile then ok. So, it is having something like this, then now these polar species which can undergoes this 1, 3 bond formation and that gives ok. So, this is via an electrophilic attack, ok. Here we have to keep in our mind that as this type of cyclopropane synthesis are stereo specific in general, so, if the mechanism two is responsible then the product formation state that should be more rapid than that of single bond rotation.

Otherwise if this step these bond formation step is not fast enough then there will be chance to rotate among this carbon-carbon single bond around this carbon-carbon single bond overall the stereo specificity will not be maintained, but we found that in these reactions generally are highly stereo specific, ok.

So, in this case the transition metal carbenes that can form the cyclopropane through these two general mechanisms, ok. Now, we will see some of the example through these methods.

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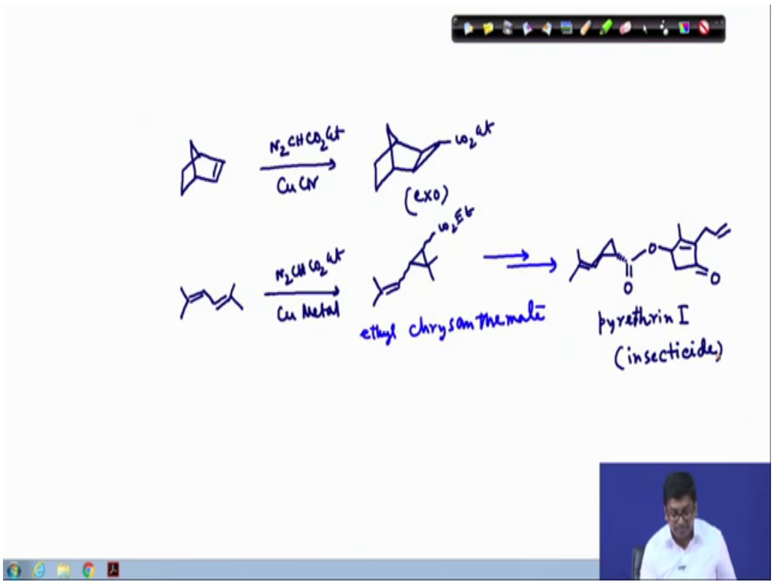

If we take this normodyne type of system and in presence of the carbene precursor here the diazo ester and the transition metal complex is this Cu Cn here then the product is the corresponding cyclopropane. But, here one interesting thing is that there is a possibility of two different stereo isomers, ok; one could be exo and another one is endo. Interestingly here only one stereoisomer has been formed and that is the exo one; obviously, this exo product is thermodynamically more stable and there is less stereo interaction or less stereo hindrance that is why this product is stable and this product is sole product here, or may be the major product here.

Next, if we take the diene as per example this one, ok. So, with the corresponding diazo ester as the carbene precursor and with the copper metal then again the product is the mono cyclo propane one. Interestingly here the diene is more nucleophilic then the mono then it is mono olefin, ok. So, what happens when the diene is there that can readily attack and after formation of one cyclopropane ring the reaction stopped. So, in this way you can actually control the mono cyclo propanation, ok. So, these will generate this is called ethyl chrysanthemate, ok. So, these can be further leads to one natural product that is called pyrethrin I, this is one insecticide, ok. This name is pyrethrin I ok. So, this is one insecticide ok.

So, in this way actually this diene can react with the carbene metalo carbene and give this monocyclopropane and this fragment has been used for further protosynthesis.

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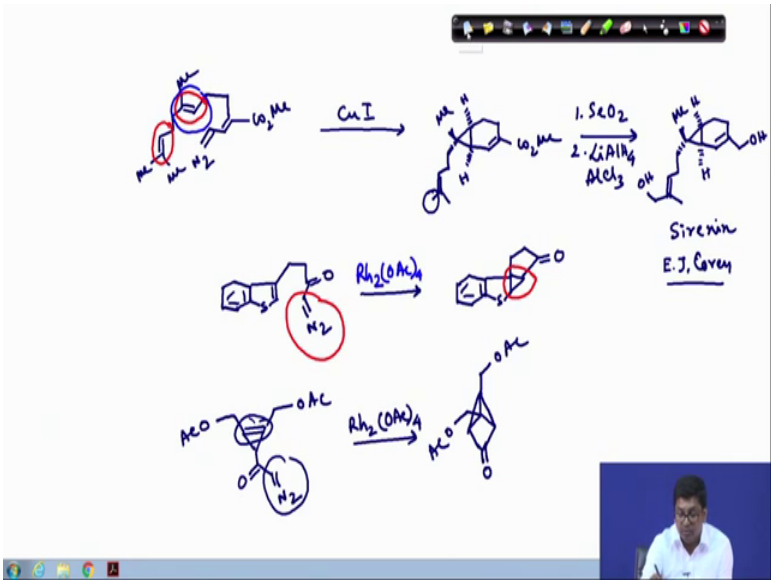

In another example we will see that the molecule contains the corresponding diazo part and the olefin part both are in one molecule, ok. So, they are methyl methyl methyl. So, in this case what will happen? Previous cases we have seen that the metalo carbene and the olefin they have reacted in inter molecular way. But, in this case we have seen the precursor for the carbene and the olefinic part both are present in one single molecule. So, this is a beautiful case where the carbene can react intramolecularly, ok. Let us see how does it react.

Now, in presence of these cui what will happen that copper iodide then there are actually two different olefins are there , but in presence of these metal iodide what will happen that the form metalo carbene will selectively react with only one double bond, ok. If you see here both the double both the olefins that are tri substituted, ok. So, but the product what they found that is the 6 and 3 member ring that is the cyclopropane few cyclohexene ok.

So, if you see that only this double bond only this double bond reacted. Why? Because when the carbene insert into this double bond or when this addition is happening that gives 6-member ring if it reacts with this double bond. So, that you will get this stable 6-member ring, otherwise in this case it will form very large member ring rather than forming 6-member is much more easier. So, it reacts or the carbene metalo carbene that add to this olefin, ok.

Now, further it has been converted into the another natural product that is called sirenin using two steps that is first selenium dioxide mediated allylic oxidations of this allylic methyle will be oxidized, this part will be oxidized, ok. So, this part will be oxidized and after that reductions. So, that will eventually give this natural product and in presence of lithium aluminium hydride the reductions will occur also finally, and give the ester to corresponding alcohol, and here and this is the name is sirenin, ok.

So, here in selenium selenium dioxide mediated allylic oxidation followed by reductions in presence of lithium aluminium hydride gives this natural products sirenin this has been done by Professor E. J. Corey. So, this is one beautiful example where these cyclopropane synthesis via the addition of this metellocarbenes to the olefin leads to the natural product.

Next we will see if we have another hetero cycle this is called the bingo thiophene derivative and it is intramolecular carbene insertions into the corresponding double bond here what it will give in presence of rhodium complex that will give this product, ok. So, basically after forming the carbene here after performing the carbene here that will make the cyclopropane here, ok. So, overall these intramolecular reactions will generate cyclopropane ring.

In another example if we take this cyclopropene system ok, this is also precursor for carbine. Now, again under rhodium complex, this will generate the metallocarbene and overall the product will be the insertion of this metallocarbene into this double bond and eventually that will give the product, ok. So, after addition of these metallocarbene into this corresponding double bond that generates this product. So, this is the transition metal based metallocarbene added to the olefins and that gives the different type of cyclopropane rings.

Next we will see other different type of addition reactions using various carbenes.

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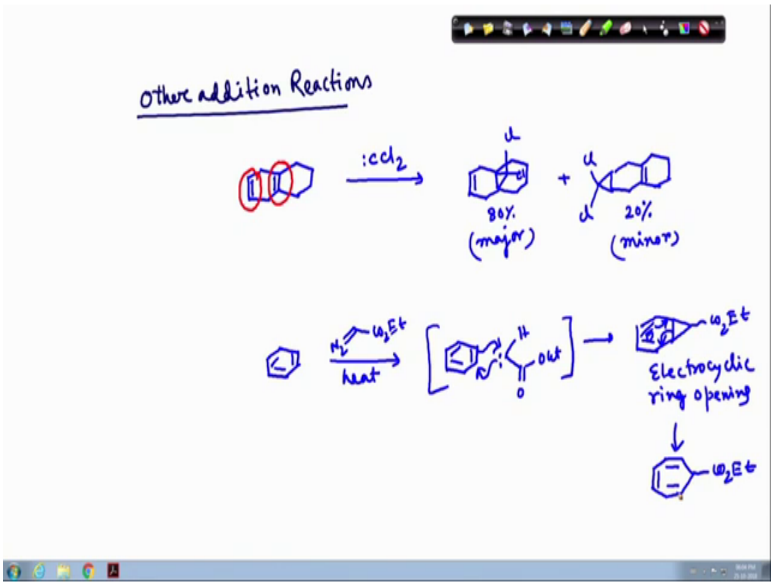

Other addition Reactions

So, other addition reaction. As per example if we take this system you see here there are two double bond one is tetra substituted another one is di-substituted. Now, if we use this dichloro carbene as the reactive intermediate or reactive carbene here then what will be the product? Ok, in this case what will happen that first there are two possibility that it can react here or it can react here as you have seen these double bond is highly substituted and more electron rich so, it will react with the electron deficient carbene and first give as a major product, and the minor product will be ok.

So, in this case it is obvious that as this double bond is not that much electron rich so, this is giving the minor product whereas, these double bond is more electron rich so, this is giving the major product. Similarly, if we take only benzene what will happen if only benzene, then we will take the diazo ester as the carbene precursor then under heating conditions this will generate the carbene and what it will form, ok. So, this hielo electrophilic electrophilic carbene will generate the cyclopropane ring.

Now, electrocyclic ring opening this is one type of peri cyclic reactions, the electrocyclic ring opening that will give this 7-member ring, ok. So, after forming of the cyclopropane ring, it goes via the electrocyclic ring opening and gives this stable 7-member compound and that is one type of reactions where after formation of cyclopropane, it rearranges to another product and gives the 7-member ring containing ester product.

Thank you, very much.