## Reactive Intermediates: Carbene and Nitrene Prof. Rajarshi Samanta Department of Chemistry Indian Institute of Technology, Kharagpur

## Lecture – 09 Reaction of Carbene (Contd.)

Hello, everybody. Welcome to Reactive Intermediates Carbene and Nitrene. In our last class we have discussed that how the carbenes can react and what are their reactions.

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Cart	ene's reaction:	
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as per example we have started the different type of reactions first is that addition reactions. So, carbenes reactions rather addition reactions. Number -2, is various insertion reaction and finally, we will learn different rearrangement.

Now, in our last class we already started about this addition reactions. There what we have studied that when the carbene can add to the olefin that can generate the cyclopropane. So, this method is very important and this is one of the most used method to prepare the cyclopropane ring. So, in general what you can make that the cyclopropane ring from the olefin, ok. So, this is the additions reactions we have started to learn, then we have understood from there that how the singlet carbene can react with the olefin; that means, if the singlet is the carbene is singlet, then how it react in concerted way and if the carbene is triplet then how it reacts in stepwise manner.

Basically, we have understood the electronic nature of this carbene can be verified through these different experimental results. Apart from the spectroscopic method we can measure the nature of these carbenes through this addition reactions through singlet we can get only one product. But, if it is triplet then due to stepwise reaction it will give more than one product.

So, now today during the addition reaction we will learn another very important reactions in this topic for the cyclopropane synthesis that is called Simmons-Smith reactions. So, this is also another reactions where you can make the olefin into it is cyclopropane ring mostly, ok. So, unsaturated bond can be prepared to the corresponding three member ring, ok.

So, now what is this Simmons-Smith reaction that we will learn. It was discovered in 1958. So, this is discovered in 1958 by two chemist and these two chemist professor Simmons and Smith. So, and this is one of the best method to prepare cyclopropane from alkene, ok. So, now, you will learn that what are the reagents, that they used to do this reaction.

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So, what they have taken? They have taken these I CH 2 I that is methylene iodide and in presence of zinc-copper couple that gives iodomethyl zinc iodide, ok, then it will be in equilibrium with it another zinc species plus zinc iodide, ok. So, this is the iodomethyl zinc iodide, and this is this iodomethyl zinc, ok.

So, now this complex zinc complex will act as the active reagent. Though there is a certain discussion and lot of investigations about this reagent has been carried out and there are lot of lot of different different experiments were carried out with these to understand exactly structure though there are certain discussion about these are already in the literature, but this is the more acceptable way that people have represented this reagent.

So, now this is we can think about that is like a zinc carbenoid. We have already studied what is called carbenoid, ok. So, you know already what is called carbenoid you know that also acts or that also behaves like a carbene, but it is associated with some other metals, like here it is associated with zinc.

So, now, if we take one olefin as per example here it is cyclohexane. So, in presence of Simmons-Smith reagent that is the CH 2 I 2 and zinc copper couple. So, this is called Simmons-Smith reagent. So, now, if we use that one, so, what we will get? We will get nicely from olefin to the corresponding cyclopropane, ok. So, this is the basic fundamental reaction for the Simmons-Smith reagent, ok. So, this is called Simmons-Smith reagent. So, this is called Simmons-Smith reagent, ok. Now, once this reaction is going next question is that how this reaction is happening, what is what could be the probable mechanism that we will learned. Let us see that how this reactions can proceed.

So, we will take the starting material that is the cyclohexane. Now, as we have already seen that this methylene iodide and zinc-copper couple can generate this iodomethyl zinc iodide. So, that could be the active species for this reaction. So, we can write like this now these reactions can happen in the concerted manner to give the desired cyclopropane ring. So, the transition state could be like this, ok. Next this is the 2 hydrogen that is over here, ok.

Now, this is the corresponding active species, ok. So, this could be the probable transition state. So, this could be the transition state, ok. So, through it these reactions can happen actually this reaction is going via concerted way, ok. So, I have written this transition state now this can finally, give the desired cyclopropane ring, ok. So, this is the concerted way that can dictate up to this product, ok. Now, this zinc carbenoid actually here behaving like a singlet carbene, that is why this can react as a in a concerted manner.



So, next we will what we will see, we will check some of the example for these Simmons-Smith reactions. We have seen that normal olefin how it can give the corresponding cyclopropane. Now, is very interesting if there is some allylic alcohol, ok. This kind of allylic alcohol is there, then actually what happen in presence of this Simmons-Smith reagent, this reaction is giving only one diastereomer, ok. So, this is highly stereospecific reaction, ok. So, the overall diastereomeric is that this diastereomer is more than 99 percent yield, ok. So, much selective reactions here, this is regioselective as well as this is highly this particular diastereomer is forming.

So, now, why this reaction is only giving this product? Ok. So, here actually the reason probable reason behind this selectivity is the coordination between this heteroatom here it is the let us say this oxygen is here. So, coordination between these zinc atom and this hydroxylic group in the transition state explain this faster these stereo selectivity, ok.

So, these hydroxilic group here or if it is some other heteroatom that can coordinate with this zinc carbenoid and that dictates as here it is this particular one isomer. So, that actually dictates from which phase this cyclopropane ring will generate, ok. So, here this coordination between this zinc atom and this hydroxilic group is very important, ok. So, let us see how the probable transition state can be.

So, if we here that if this is our heteroatom, then actually these active species that can coordinate with this hydroxyl group and give this kind of transition state from which

actually the cyclopropane can form from only one phase and give only this particular diastereomer, ok. So, this diastereomer will be more than 99 percent this diastereomer.

Another very interesting aspect of this reaction is that these reaction in much more faster almost 100 times faster than it is unfunctionalized precursor. So, if we think or if we compare between these two cyclopropanation of these two derivative, under similar condition then actually what the experimental result says that, the reactions of these alcohol these allylic alcohol this reaction is very faster, reaction is very faster very fast, then its unfunctionalized precursor, ok.

So, what could be the reason that again the reason is same that due to presence of this hydroxyl group so, it can easily coordinate with the reactive zinc carbenoid and that facilitates this reaction rate, ok. So, this is the reason that is why this reaction is almost 100 times faster than on normal cyclohexane, ok. Interestingly here I would like to mention that if we take any achiral olefin, and we wanted to do its cyclopropanation using the Simmons-Smith reagent. In that case if we use as a menthol as a chiral alcohol menthol is a alcohol which can be found as racemic as well as a it is particular one an isomer.

So, if we take one particular an isomer during the reactions with the Simmons-Smith reagent, then the product that we will get the cyclopropane that we will get that contains optical activity, ok. So, this shows that during the reactions when these active iodomethyl zinc iodide is forming there this menthol is reacting with that and generating the chirality so, that it can give finally, the optically active cyclopropane ring. So, this is another example where we can show that even though achiral alkene we are using, but that can give finally, optically active alkene, ok.

Next, we will see that another example that ok. So, if we take these cyclopentene alcohol, ok; now, if it is treated with the Simmons-Smith reagent, again in this case also this reaction is highly stereo specific, ok. So, this will also give only one cyclopropane product, ok. So, this starting material this olefin also in presence of Simmons-Smith reagent will give this particular stereoisomer, ok.

Similarly, in another example, if we take this allylic alcohol again, ok, here also if you see very interesting because in this case also under Simmons-Smith condition the

product that we will get again the heteroatom guided product here the hydroxyl guided product that is this one.

You see here even though this bulky methyl group is there in the ring junction, but still the cyclopropane ring is forming in that phase. Like here it is upbond, but here cyclopropane also forming with that particular stereoisomers even that is not sterically inhibiting, this formations rather this hydroxyl group which is actually coordinating with these Simmons-Smith reagent or zinc carbenoid that actually guiding that in through which phase these cyclopropane ring is going to form, ok. So, in this case that is why this example is very interesting, ok.

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Next we will see another interesting example that is this one where the olefin is highly substituted and it is again having some ester group here, ok. If you see in ester group also that is having some heteroatom like here it is the oxygen, ok. If you now treat with the under Simmons-Smith reagent I am not. So, CH 2 I 2 and zinc-copper couple what will be the product if you take little excess of this Simmons-Smith reagent then the product will be ok, fine.

So, in this case this ester is directly affecting about the stereoselectivity of this cyclopropane ring, ok. So, this is actually this ester group is guiding that in through which phase this cyclopropane ring is going to form, ok. So, this is very interesting. So, that is why these highly substituted olefins became the cyclopropane ring through the

corresponding ester guidance, ok. But, if we see that if there is nothing to guide I mean there is no heteroatom or no such kind of guiding group is there then what will be the consequence?

Let us see you have this is the olefin corresponding olefin and if you have taken this olefin, this carbene then actually the product is that is generating, ok. If you see here these two cyclopropane ring actually trans whether here these two cyclopropane ring if you see they are same. But, here they are trans because here the guiding group is this ester group, this is the corresponding guiding group or this is directing, that from which phase this cyclopropane will form. Here the as there is no such type of heteroatom or no such type of guiding group that is why here these two cyclopropane ring that are trans to each other, ok.

Next what we will see another example where we have the olefin as a exocyclic exocyclic olefin like this, ok. So, we have this exocyclic olefin. Now, little bit modified Simmons-Smith reagent or little bit I can say that modified Simmons-Smith reaction that there in not we are not here they have use the methylene iodide rather they have used a ethylene bromide as the corresponding reagent in presence of zinc-copper couple. So, what that has given that has given this product that exocyclic double bond becomes the corresponding cyclopropane ring.

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Now, next what we will learn that what will happen if these carbenes or these rather the Simmons-Smith reagent if that adds to the corresponding allenes. So, addition to allenes, ok. So, you know what is allenes? Ok. Allenes are something like this I am not going to detail of its structure, how they are all might have stays and all those things, but this is some kind of structure of allene. So, now, there are also double bonds, so, if you take the carbenes or the Simmons-Smith reagent how that is going to react with the allene, ok

We take one example just I will show here as per example here we take this one. In presence of the Simmons-Smith reagent, ok, the product is you see here under the Simmons-Smith reagent only this double bond become cyclopropane, ok. This one, why because again if you see this is near about one heteroatom is there and that is guiding that in through which double bond is going to be cyclopropanated additionally this is more substituted also this side.

So, overall the product is this one this cyclopropane ring with this exocyclic double bond. Finally, this one has been converted into natural product that is the hypoglycin a I have shown previously also. This is a very important natural product ok. So, this is the corresponding a racemic hyperglycin A. So, using this technique or using these reactions Simmons-Smith reaction these allenes can be converted into the another cyclopropane derivative which further leads to the natural product that is racemic hypoglycin A.

Thank you.