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

# Lecture – 11 Reaction of Carbene (Contd.)

Welcome everybody, welcome to the course of Reactive Intermediates Carbenes and Nitrenes. So, far we are learning the Reactions of Carbene. We have started the first type of the reactions in carbene that is called addition reaction. Today we are still continuing that addition reaction on that means, the addition of the carbene moiety to various unsaturated bond mostly these double bonds and triple bonds. Today we will see that how these carbenes will react with various type of double bonds including the double bonds that is inside the heterocycles.

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Let us start with the heterocycles first. As for example, if we have this pyrrole moiety, this is one 5 membered nitrogen containing aromatic heterocycles. Now if we treat this one with these ccl 2 carbene, then first it will form 1 cyclopropane ring containing 5 membered derivative that is these bicyclic compound ok. Once these has found then, the ring will open and eventually the expansion of this 5 membered ring to the 6 membered ring will happen to provide another 6 membered nitrogen containing heterocycle that is called the pyridine derivative ok.

So, here from nitrogen containing 5 membered ring to another nitrogen containing 6 membered ring can be formed by just additions of the carbene moiety. Similarly another heterocycle that is called indole, that also can react with the carbene moiety to provide its ring expanded heterocyclic moiety; that is called quinoline moiety. So, here we have taken the 3 substituted, 3 positions methyl substituted indole moiety. Now if we take this methyl lithium as base and the carbene precursor as dichloromethane ok.

So, now if we treat it under these conditions, then what will happen? Then actually it will form as per the expectation these fused ring system, where it have this cyclopropane ring and once this will form, the ring expansion will happen through this way ok, to provide the quinoline moiety ok. So, starting from indole moiety we are getting another very important nitrogen containing heterocycle that is called quinoline moiety. Interestingly if these particular substrates treated with another carbene allene type of carbene that is this one, this can be generated from the 3 chloro 3 methyl 1 butane from there we can generate these in presence of base this will give this type of allene type of carbenes and once we will treat this allene type of carbene with the 3 substituted indole, then immediately this will form like previous way ok.

So, it will also form and once it will generate then similar way these ring expansion will happen and this will pick up the proton from the reaction medium and overall this will again provide the ring expanded this quinolin moiety and it will give these type of quinolin derivative having 1 by 9 group with its ok. Here in the previous case when we have used this dichloromethane in presence of methyl lithium actually it will generate the carbene that is that c h c l dot carbine, so here it will be c h c l.

So, overall this will give these 4 methyl substituted quinolin whereas, here these in presence of these allene type of carbene this will give the vinyl and methyl substituted quinolin ok. So, starting from one heterocycles, we are getting another class of heterocycle just by using the carbene as a reactive intermediate ok.

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Next what we will see that what will happen if we use different type of naphthalene methoxy naphthalene type of compound; that means, what I am saying here that if we take that beta methoxy naphthalene and alpha methoxy naphthalene in presence of the carbene dichlorocarbene what will happen.

So, let us take this, so this is the beta methoxy naphthalene. Now if we treat this with dichlorocarbene ok, so what it will form? This will react with this double bond ok. So, this is obvious because this is having this lone pair so; obviously, this becomes this place become reactive more and once it will generate the cyclopropane ring ok, so this will form the corresponding cyclopropane ok.

And once this will form, this OMe group oxygen is having its lone pair, now these ring can expand ok. So, once it will expand then actually we will get that hello benzo tropone type of derivative; that means, starting from 6 membered ring here we are going to 7 membered ring. So, the end product will be these are nothing, but hello benzo tropone type of derivative.

So, we have started 6 6; that means, naphthalene ring and we ended up with 6 7 ok. So, this is nothing, but benzo tropone type of derivative. Fine now what will happen if we use the alpha methoxy naphthalene; that means, it is another isomer that is nothing, but these alpha methoxy naphthalene, now we treat this with dichlorocarbene it will form the corresponding cyclopropane ring and once it will form again in similar way the this will

ok, so the ring will open and what it will form that the corresponding ring opening product that will give ok, so what it will form overall this product will be this benzo tropane type of moiety ok.

So, in this both these cases we got the expansion of the ring by the simple reactions with the carbene with some aromatic ring ok. Next we will see that same carbene reaction with enamine the epoxy systems, what will happen if the dichlorocarbene will react with the enamine system. Let us take that, let us say with the enamine system I hope that you know how to prepare different type of enamines. So, we will directly take this enamine as per example here, we have taken this enamine and treated this with dichlorocarbene.

So, what we know that these double bond now will react nicely with the dichlorocarbene to provide the cyclopropane containing derivative first or the intermediate first ok. So, that will give you this cyclopropane ring ok. So, now this nitrogen containing its lone pair, so now, that will come and the ring will expand by this liberation of cl minus so that what you will get you will get you will get the ring expansion ok.

Now, after this the hydrolysis will give you the cyclohexenone type of derivative ok. So, you have started with the 5 membered ring now you obtained these 6 membered cyclohexanone derivative just by using dichlorocarbene. So, that also again this dichlorocarbene is making first cyclopropane ring, after that ring expansion that gives the enamine system to the corresponding cyclohexanone system ok.

So,. So, far what we have learned in that case these dichlorocarbenes are actually first forming the cyclopropane and then it is converting to its higher higher higher ring number containing the derivative. now what we will see that if any substrates that is already in a bigger ring than 6 member, in these case if we take the cycloheptatriene as the starting material what will happen, we will see that.

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Let us see first we will take the cycloheptatriene as the starting material ok. So, let us see how many rings sorry, so this is the cycloheptatriene ok. Now if we treat this with the diazomethane and copper chloride, then what will happen? Then definitely it will generate the carbene and that carbene will make the addition reactions to the available double bond of this cycloheptatriene. So, what are the possible? Now actually there is possibility is that there it can react with 2 different type of double bonds are present here, like this way these 2 double bonds can react, so what will be the product in this case? The product will be first this will make cyclopropane over here and another one that will give you the product over here; that means, the cyclopropane ring will form in this side ok.

Now let say this is the 2 different cyclopropane containing 7 membered ring has formed as a product, Now if you see these particular substrates, this is a very good substrates for further forwarding to another sigmatropic rearrangement and give another product this is called 3 3 sigmatropic rearrangement that will happen.

So, if you see the numbering 1, 2, 3 and here 1, 2, 3. Now if there is sigmatropic rearrangement happens then actually this will form another product and which is actually the degenerate with these particular product. So, the product will be ok, so in these case if we counting it 1, 2, 3, 4, 5, 6, 7 so the number of number of I mean the ring number is remain same, but we got the 3 3 sigmatropic rearranged product this is called 3 3

sigmatropic rearrangement ok, why because here if we see these at 3 position here also at 3 positions that new sigma bond is forming by the relocations of this pi and sigma bonds that is over all these 3 3 sigmatropic rearrangement is happening here; that means, at the 3 3 place the new sigma bond is coming and here at 1 1 place that another older sigma bond that is getting break.

So, overall what we are getting? We are getting the 3 3 sigmatropic rearranged product by this method and this is very rapid reversible and because energetically both will be same. So, this is a very rapid, reversible, degenerate, 3 3 sigmatropic rearrangement and these 3 3 sigmatropic rearrangement this is called this is a very well known name reactions this is called cope rearrangement ok.

So, this is another type of pericyclic reactions rather or concerted reactions that is giving the cope rearrangement by 3 3 sigmatropic rearrangement ok. Next part we will see another similar type of substrates that is the octatriene cyclooctatriene if we take ok. So, this is the substrate, now again in similar conditions if we generate the carbine. Then in these case also there are 2 possibility; that means, here there are 2 different type of double bonds are present. So, what we will do under these conditions if we now expose it under the this carbene then what will happen again this will also form 2 type of cyclopropane containing ring ok, first case we will give this one plus in another case this will give this product ok.

Now, you see these substrate these 2 among these 2 substrate this is also now ready for another 3 3 sigmatropic rearrangement, let us if we see the numbering ok. Now, this can nicely proceed through 3 3 sigmatropic rearrangement to give the product ok. So, in this case the number of if we see that total number of carbons that is over here here total 8, 1, 9.

So, if we start from your 1, 2, 3, 4, 5, 6, 7, 1, 1, 1, 2, 3, 4, 5, 6, 7, 8, 9. So, overall number of carbons are same, but here what happened? Here the ring has been converted from 3 membered cycle propane ring to another 4 membered ring and this gives the another 3 3 sigmatropic rearrangement. So, this is 3 3 sigmatropic rearrangement or you can call it cope rearrangement. Through this pericyclic reactions of the concerted reactions these particular cyclopropane containing 8 membered ring converted to its another 4 membered 4 membered ring containing substrate or product that is this one ok.

So, in these case there are 2 possibilities that 2 cyclopropane containing product will form, but after that one product which is easy to proceed through 3 3 sigmatropic rearrangement that will give another product and that is nothing, but these 4 membered fused product ok. Next we will see another type of derivative that is called valve in derivative ok. If the carbine will react with valve in type of derivative what will happen.

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So, these type of substrate that is called valve in type of derivative. Now if we treat this one with dichlorocarbene that will give the cyclopropane containing substrate and if it will stay longer at minus 10 degree centigrade and with the presence of excess dichlorocarbene then what will happen? Then actually these olefin that will also react ok, but at room temperature what will happen? At room temperature there these ring expansion will happen and overall this migration of this chlorine to these carbon then followed by ring expansion will give this 6 membered benzene derivative and here this one is the chlorine.

Now, if it contains R equals to alkyl then the liberation of this HCl will give the corresponding olefin derivative ok. Similarly if R equals to phenyl there is no possibility of this eliminations. So, in presence of sodium methoxide or other alkoxide this will simply give the substituted product can give a double prime ok. Now what will happen if these reactions will work with the alkyne.

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So, let us take the alkyne and if we treat this with the carbene then; obviously this triple bond that will react and generate the cyclopropane type of system like this ok.

So, these are the cyclopropane ok. Now if there is anine type of system; that means, if the substrates contains double bond as well as triple bond, what will happen, which one will faster react? Most of the cases in general it has been seen that if we take diazoester as the carbene precursor then if there is a enediyne substrate then first the double bond will react; that means, the alkene that is going to react first to give these product as major product and the further it will react to give this product as the trace amount ok.

So, mostly this olefin that will react faster in another example if we take the cyclohexane containing enediyne type of derivative then, in presence of dichlorocarbene these will give that olefin will react with this dichlorocarbene to this cyclo to give this cyclopropane containing bicyclic compound Here interesting to say that this derivative will further can lead to cyclopropenone type of derivative, but at this present these under this dichlorocarbene conditions, this enediyne type a moiety can react with the specially with the olefin moiety. So, these are the all type of reactions addition type of reactions that we have discussed with the carbene.

Thank you very much.