Reactive Intermediates: Carbene and Nitrene
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Lecture – 19
Reaction of Nitrene (Contd.)

Hello, everybody. Welcome to my course Reactive Intermediates Carbenes and Nitrenes. So, far we have discussed various aspects of nitrenes; as per example how you can generate them, what is their electronic structure and what will be their different type of reactions. Among that we have already studied that addition reactions from nitrenes. So, today we will learn about the insertion reactions of nitrenes, ok.

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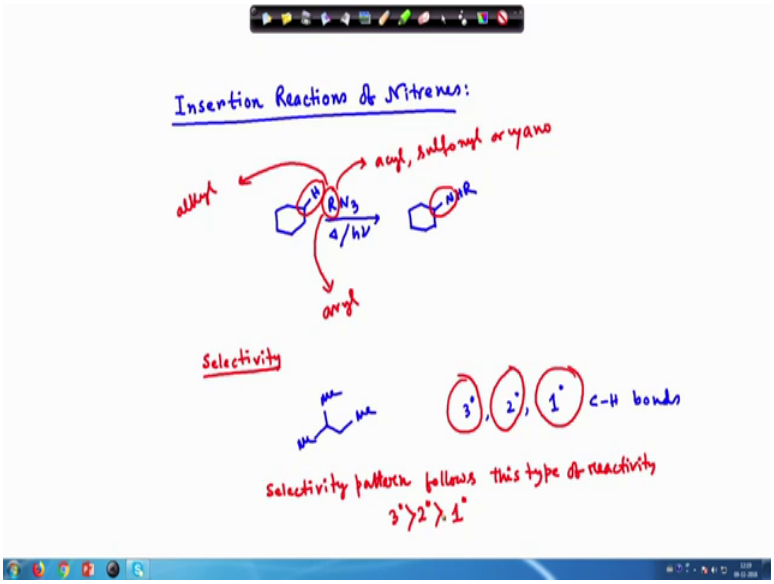

Insertion Reactions of Nitrenes:

Selectivity pattern follows this type of reactivity $3^\circ > 2^\circ > 1^\circ$

So, what we will learn today that is called of nitrenes. As you already know that the nitrenes are also similar like carbines, they are also elected deficient species and they are also wants to have various type of electrons to fill up their octates. So, that is why these insertion reactions are very much common with this nitrenes, ok. And, why it is important this insertion reactions because the generation of carbon nitrogen bond via carbon-hydrogen bond functionalization is very very important topic because, in these way we can actually make various type of pharmaceutically active or bioactive compounds, ok.

So, for that reasons in a to make these type of carbon nitrogen bonds in a step economic way this reactions are very important because, in these case you can take some unactivated carbon-hydrogen bonds and there you can insert this electron deficient nitrene species, ok.

So, these way what we can see that let as for example, if you take this cyclohexane these are having carbon-hydrogen bonds and now if you use these azide then under thermal or photo chemical condition this can generate this carbon-nitrogen bond. If you see here this carbon-hydrogen bond in between this one, in between this one this carbon-nitrogen bond as formed, ok. So, basically it got inserted into that.

Now, what kind of nitrenes that will give acyl reactions for animation or rather carbon nitrogen bond formation reactions. As per example if R equals to acyl sulfonyl or cyano they give very facile reactions rather the insertions of this nitrenes are very facile to generate the desired product.

However, when this is alkyl group alkyl group there is lot of side products formations due to the one hydrogen one to hydrogen shift, ok. So, the overall yield of the desired product will be very poor, and what happen when this is aryl ring that time most of the cases the n product forms that aniline type of derivates. Why? Because once this aryl nitrene will generate that will abstract hydrogen and that will give you the aniline derivatives, ok.

So, these are the different types of aspects for various type of nitrenes and in terms of selectivity in terms of selectivity of insertion by this nitrene intermediate reactive intermediates that always guided by the different type of carbon-hydrogen bonds. As per example if some compound like 2 methyl butane. So, they will have 3 degree, 2 degree, or 1 degree; that means, tertiary, secondary or primary carbon-hydrogen bonds, ok.

Now, nitrenes are having specific target; that means, nitrenes will first prefer to insert into tertiary group, this one, then this will insert into this then this will insert into primary; that means, their affinity towards this tertiary carbon-hydrogen bonds. It will selectively first go to tertiary carbon-hydrogen bond, then secondary carbon-hydrogen bond, then primary carbon-hydrogen bond, ok.

So, the selectivity patterns in general follows so, selectivity patterns, follows follows this type of reactivity that is the tertiary, then secondary, then primary, ok. So, in that way if you take any molecules which are having different type of carbon-hydrogen bonds and their bond dissociation energies are different for those type of carbon-hydrogen bonds in that cases the nitrenes that will be inserted into those carbon-hydrogen bonds in a different selectivity; first it will go to the tertiary one, then secondary one, then primary one.

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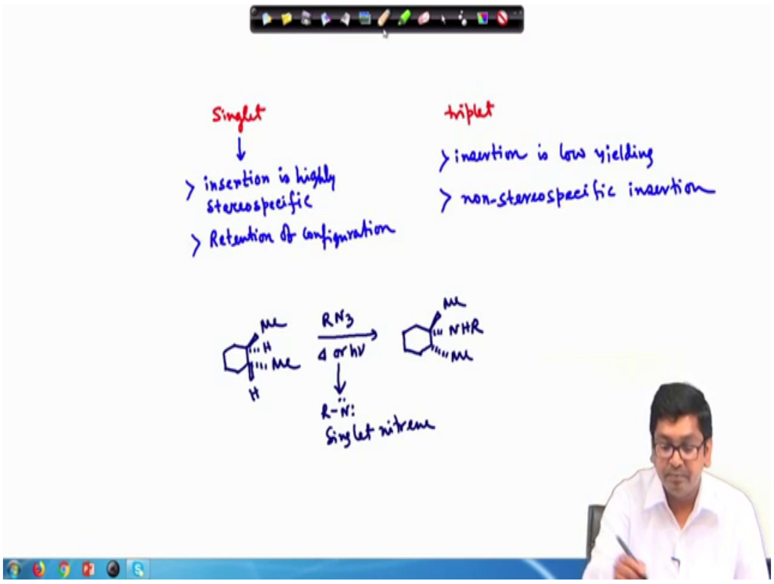

Singlet

- insertion is highly stereospecific
- Retention of configuration

triplet

- insertion is low yielding
- non-stereospecific insertion

And, when we will see the nature of this nitrenes; that means, we found that there are two types of nitrenes can be possible one is called singlet, another is called triplet, right. So, in case of singlet nitrene they are in general they are inserting they are inserted into this carbon-hydrogen bonds, ok. So, what happen mostly these singlet nitrenes they insert into the unactivated carbon-hydrogen bonds, ok.

Once they will get inserted then only this carbon nitrogen bond will form and as this is a singlet nitrene most of the cases these reactions are highly stereo specific rather all these singlet nitrenes they are inserting into the carbon-hydrogen bonds in a concerted manner ok; that means, definitely they will be the reactions will be highly stereo specific and obviously, the retention of configurations, ok.

So, what we can say that insertion is highly stereo specific and number 2 is that this reactions they will be giving the retention of configuration, ok, or; that means, that this retention of we can write in this way retention of configuration, ok. And, in case of triplet what it is found that in case of triplet us generally this insertion is low yielding, and they are non-stereo specific addition sorry, non-stereo specific insertion, ok. So, these are the different type of reactivity for different nitrenes, fine.

Now, if we see what I said here as per the example if we take trans 1, 2 dimethyl cyclohexane ok, then if we treat it with nitrene, what it will generate? It will generate the this if it is a singlet nitrene, if it generates singlet nitrene ok, then obviously, the insertion of this nitrene will be stereo specific manner and it will be in a concerted way, ok. Now, we have seen that in case of singlet nitrene the insertion is in concerted manner and definitely in case of triplet nitrenes we have seen that triplet nitrenes are behaving like a diradical way. So, in that case we have we can say that reactions will go in a step wise manner.

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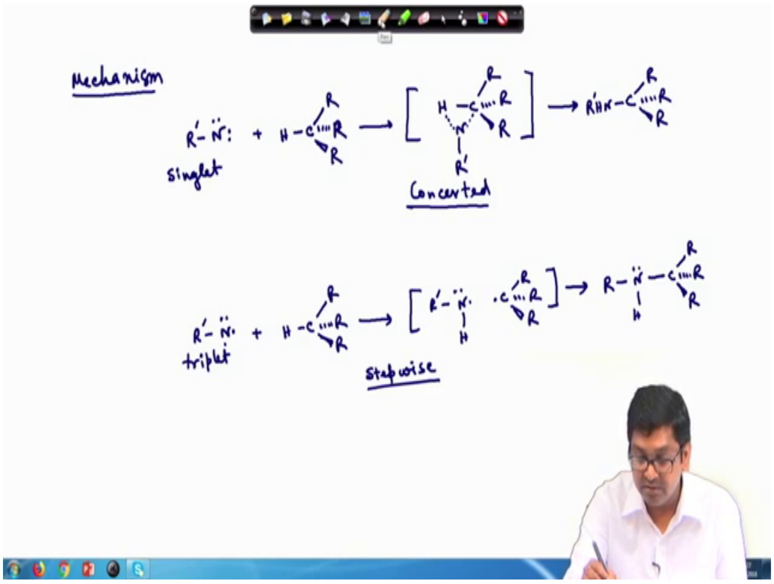

As per example if we take this singlet nitrene ok, then the mechanism we can think in this way that sorry, we can put here R, ok. The insertion mechanism will follow through this transition state, and ok, to this concerted manner finally, the insertion will happen and it will give the inserted product or we can give their R prime here R prime, ok. So, here R prime, ok. So, these way actually singlet nitrene got inserted into the carbon-hydrogen bond.

What will happen if it is a triplet carbine? This is triplet nitrene, ok. Now, in similar fashion this can react with carbon-hydrogen bond, but the mechanism will be different. They can also got inserted even though lot of cases the yield is pour, but what it will give in a finally, this will form this carbon-nitrogen bond, ok. So, this is some kind of stepwise. So, these are the two overall mechanism for this nitrene insertions, ok.

So, one case definitely the retention of configuration or it will be highly stereo specific reactions whereas, in another case as for example, for triplet case definitely the non-stereo specific reactions or non-stereo specific insertions of this nitrogen species will occur, ok. Next what we will see? Next, we will see that some examples.

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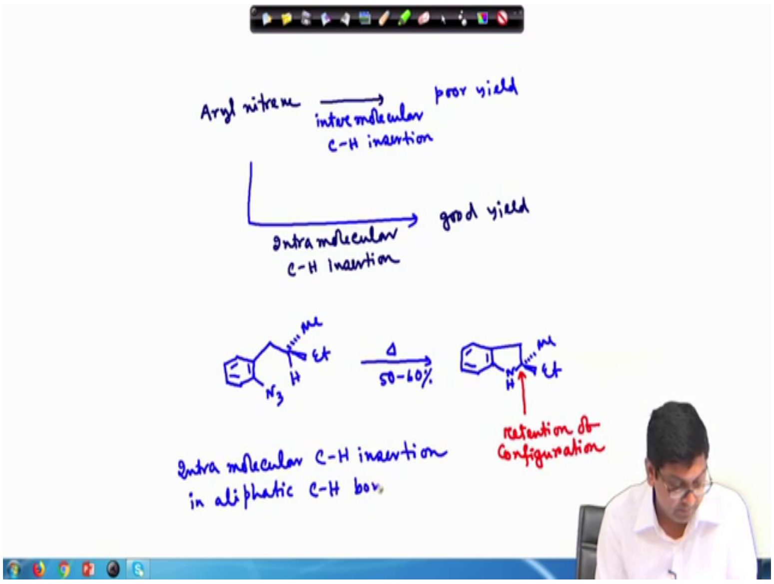

We have seen that if we take aryl nitrene as per examples, for intermolecular as we I have told that for these intermolecular C-H insertions we have seen that aryl nitrene for intermolecular C-H insertion generally gives poor yield, ok. What we have seen when this in spite of aryl nitrene if you take sulfonyl, acyl or cyano group then this type of insertions will give better yield, ok.

But, if you take it is intramolecular version; intramolecular C-H insertion then it gives good in with retention of configurations, ok. So, what it will get? We will get good yield of product with retention of configurations. If we see some examples as like this way, so, as per example if you take this substrate where we have some stereogenic center and we have aryl azide as a aryl nitrene precursor.

Now, if we heat it, it will give the desired product with retention of configuration, ok; this is important in a 50 to 60 percent yield, ok. So, if we see here this is important here retention of configuration, ok. So, we have seen that when these intramolecular fashion of this C-H insertion is having happening for aryl nitrene, we are getting good yield of product with retention of configurations, ok.

And, this is actually the one of the examples where intramolecular insertion is happening to the aliphatic carbon-hydrogen bond, ok. So, what is happening here; so, the intramolecular C-H insertion in aliphatic carbon-hydrogen bond, ok. Now, we will see some intramolecular insertions of nitrene into aromatic carbon-hydrogen bond.

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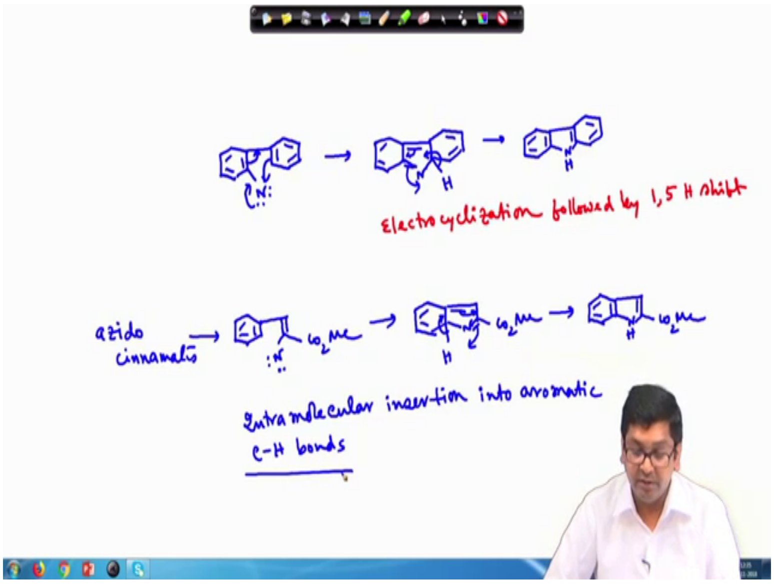

As per example if we take this substrates. This bi aryl nitrene, ok; in that case now, this can react in this way and will give this intermediate sorry, not though this stepwise way this is actually happening ok. Now so, finally, it will give you very important heza heterocycles that is called carbazole, ok.

So, here what is happening, first is this electro cyclization, and followed by the 1, 5 hydrogen shift, 1, 2, 3, 4, 5. So, electro cyclizations followed by 1, 5 hydrogen shift ok. In similar fashion if we take another example this one, this vinyl nitrene, and this can come from some azido cinnamates. Similarly here also it can come from this biaryl azide, ok, here it is azido cinnamates ok.

So, in these case what it will give it will also go in a similar mode of this electro cyclizations followed by 1, 5 hydrogen shift and in that case first it will again it will give and then 1, 5 hydrogen shift to provide, ok. So, these reactions also following the similar mode of path way, ok. Similar way it is also as per previous way this is also working in similar way, ok.

Now, so, however, this we can give one example this is intramolecular insertion into ok, into aromatic carbon-hydrogen bonds, ok. So, we have seen initially the intramolecular insertions into aliphatic carbon-hydrogen bond here it is going through intramolecular insertions into aromatic carbon-hydrogen bond.

Next, we will see some animations carbon-hydrogen bond animations through intra versus in sorry this will work in intramolecular way, but in different regioselective manner; that means, as per example in a molecules if there is two possible centres are there where this carbon-nitrogen bond can form; that means, insertions can happen in that case how that will react.

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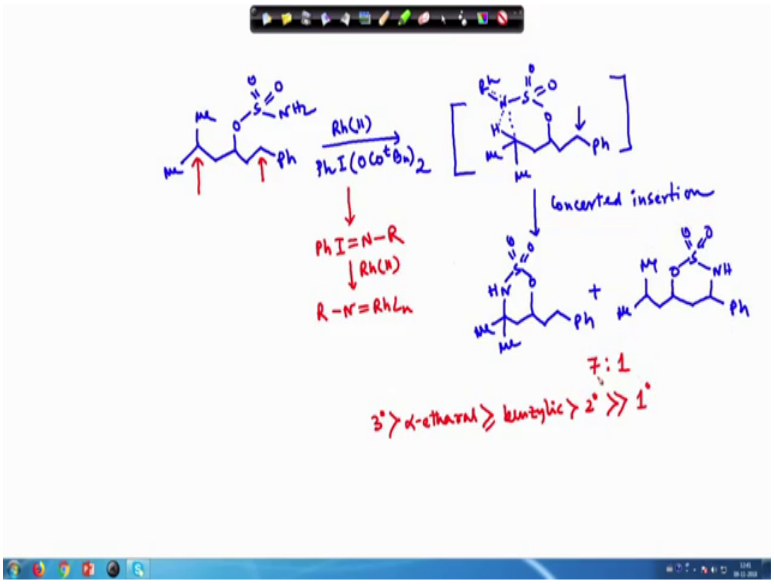

So, if we see this compound this sulfonamide as precursor for this electron deficient species, it will generate the metalo nitrenes. As per example here it take some rhodium two catalyst and some oxidant hypervalent iodine based oxidant, ok. So, this is the (Refer Time: 24:11) group (Refer Time: 24:12) whole to that will give first what it will generate this things actually will generate some amino iodine amino iodine in like this, ok.

So, I am not writing whole things, and then in presence of rhodium 2 catalyst this will give you the metal of nitrenes or nitrenoides, ok. So, once it will generate then, now this electron deficient species can be inserted into two possible way here; as per example here this place it can be inserted if you see here that total ring member it will be like a 6-member ring and it can be inserted here also ok.

This is in this case this is 3 degree tertiary carbon and in these case this is the benzyl liquid deposition. So, now, we have to see that in which one or in which carbon-hydrogen bond it will inserted more and in which carbon-hydrogen bond it will be inserted less. So, if you see the mechanistic way to get inserted into a carbon-hydrogen bond for this nitrenoid species then we can tell. So, this is the this nitrenoid species, ok.

Now, have this carbon-hydrogen bond that can be get inserted through this, and ok. Then similar way it can be inserted into this place also this benzyl equation also I am not showing the both, but now this is the concerted carbon-hydrogen insertion of metallo nitrene or nitrenoides concerted. We can write it concerted insertion, ok. Once this will happens it can happens in similar fashion to here also ok, I am not showing that, but overall the product will be we can write in this way that there are two products will form; first this will give the insertion into the tertiary carbon and fine.

So, this will be this product plus what will happen the insertions can happen in different benzylic place, and the ratio between these two products will be 7 is to 1, ok. Why? Because it has been found that carbon-hydrogen bond reactivity for this intramolecular oxidations, the qualitativity rate as for examples it has been found that it is like 3 degree then the alpha etharal, then the benzylic then secondary and then for primary, ok.

So, here we have seen as for the reactivity rate for this oxidation they are what it has been found for this tertiary carbon that is getting faster reactivity than the benzylic. So, that is why here the reduce selectivity happens in these way that carbon-nitrogen bond formations occurs mostly in major product this one and then the minor product is this one, ok.

Thank you.