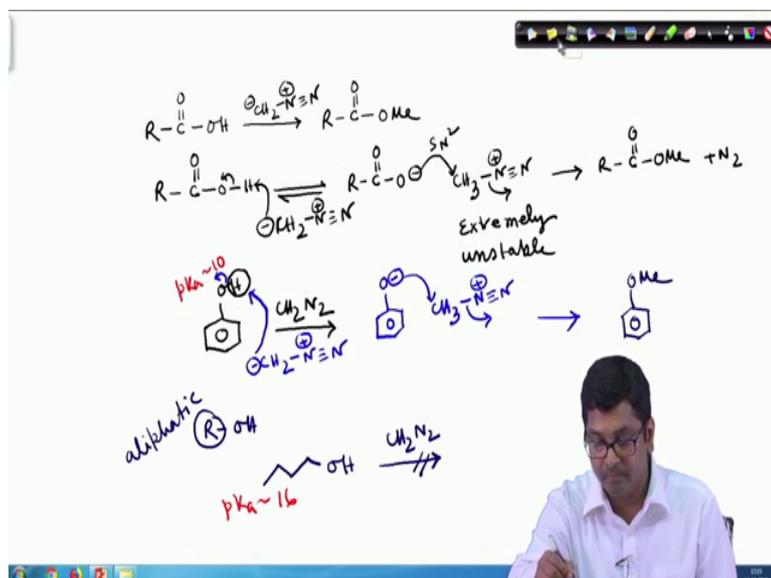


Reactive Intermediates: Carbene and Nitrene
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Lecture - 05
Generation of Carbene (Contd.)

Welcome everybody to my topic that Reactive Intermediates Carbene and Nitrene, we are discussing about the Generation of the Carbene. Among that generation of carbene, we have started to discuss about the diazomethane because on decomposition of diazomethane; it can generate the electronically neutral species that is the carbene.

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So, last class we were discussing about the preparation of methyl ester from carboxylic acid to it is corresponding methyl ester using the diazomethane ok. So, we have seen that once these carboxylic acid is there first; this diazomethane will pick up the acidic proton and that will actually generate this carboxylate anion. And once that will generate it will actually react with the extremely unstable diazonium cation; that is the CH_3N_2^+ plus and this carboxylate anion actually can work in $\text{S}_{\text{N}}2$ mode and give this substitution reactions to give this methyl ester ok.

And here this nitrogen will eliminate and this compound is extremely unstable compound. So, now in these reactions this carboxylic acid in presence of diazomethane; it can generate the methyl ester of that corresponding carboxylic acid. Now, if we see let

us say phenol will it be possible to make it is corresponding methyl ether using this diazomethane. So, if we use diazomethane over here; then actually this proton is acidic enough it is pKa; is around pKa of this particular proton that is the around this hydrogen is around 10.

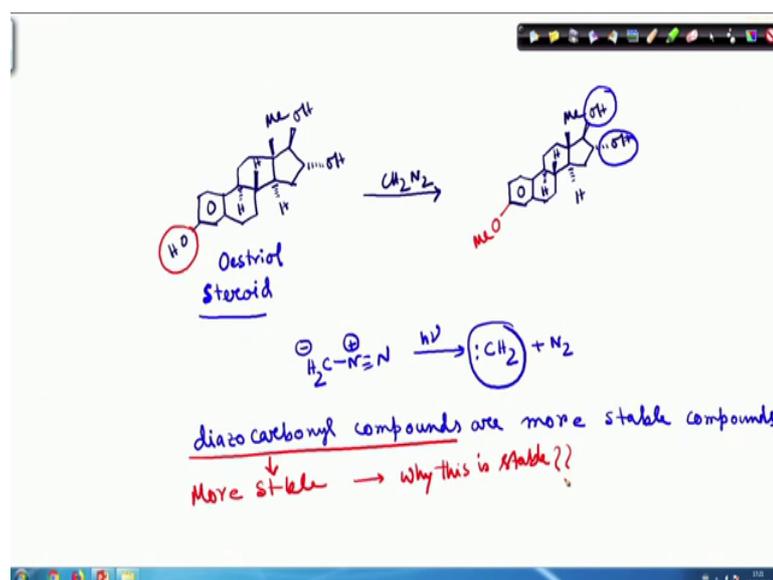
So, now this is sufficiently acidic so that these diazomethane that can react with that in similar mode of fashion. That means, here also you can write like this; it can pick up this because this phenolate anion that is stable and this one is pretty acidic this hydrogen. So, it can pick up this one and generate corresponding ok. So, rather I should draw like this way like previous way and this can attack over there and give you the corresponding this is called anisole.

So, from phenol to anisole you can easily prepare in presence of diazomethane. But, will it work if we use in spite of this phenolic compound if it is aliphatic alcohol. That means, I am talking about R OH; when R is aliphatic. As per example let us say we have this alcohol and we treated with diazomethane will it work but actually it does not work; why?

The reason is very simple that is if you see it is this hydrogen pKa; that is around here pKa is around 16; all this aliphatic alcohols this type of alcohols is around this particular 16 approximately and this is not acidic enough. So, that this diazomethane can pick up that particular proton to give these corresponding anion. So, in this case when it is aliphatic alcohol these reactions will not work ok. So, what is the basic fundamental criteria here? That these corresponding hydrogen has to be acidic so, that it can be picked up by this diazomethane and give this extremely unstable diazonium compound or diazonium cation.

So, that these corresponding anion in case of in carboxylic acid it is the carboxylate anion, in case of phenol it is the phenolate anion they can react with this extremely unstable diazonium species to give it is corresponding methyl ester or methyl ether sorry.

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Now, we will see one example; where both these aliphatic as well as aromatic alcohols are present ok. So, this is the corresponding steroid molecule the name of this molecule is called oestriol oes; oestriol and this is a steroid moiety. So, now, if this molecule react in presence of diazomethane; what will happen? As we explain previously that this particular molecule contains two different type of OH group; one is aromatic that is phenolic type another one is aliphatic type.

So, definitely this particular in this OH group here this is more acidic this phenolic OH. So, it will definitely it will react and give you the product like this ok. So, what we will get? We will get the corresponding methyl ether and here the interesting thing is that here both of these hydroxyl groups they does not work; they remain intact ok.

So, in this case only this particular hydroxyl group that will react and give the methyl ether ok. Now, why we are actually doing so many reactions with the diazomethane or we are trying to learn the chemistry of diazomethane reactivity? Because, the photolysis of this diazomethane actually produces carbene ok; one of these precursor for generating this carbene is the diazomethane.

So, in principle we have diazomethane and this photochemical decomposition actually give it is the corresponding carbene with the elimination of this nitrogen; it is a very stable molecule nitrogen so, that will generate this carbene species. But, as we have

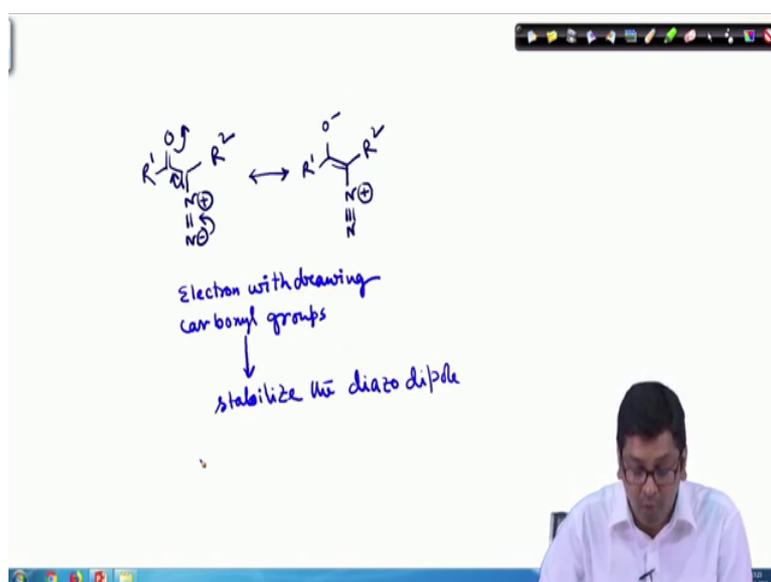
discussed in my previous class that diazomethanes as a carbene precursor even though it is very much useful.

But, in lots of cases we found the generation of this type of diazomethane is very tricky. Why? Because, these are having lot of limitations. As per example this type of this compound is extremely toxic and can be a potential explosive and as well as in that reactions that has to be taken care with very carefully with extreme caution; so, there are many limitations ok.

So, another one is that always you have to keep it like in a solution; its boiling point is pretty less. So, this kind of limitations made these; diazomethane use of rather use of diazomethane as a carbene precursor quite limited. So, having this having such limitations people have started to thinking about diazo carbonyl compounds for the carbene precursor ok. Because, the diazo carbonyl compounds are more stable compounds. So, handling of these compounds will be much more easier ok. So, once this is more stable compound; so what I am talking about? More stable so, diazo carbonyl this compounds will be more stable.

So, now, if something is more stable; that means, what we can do that we can easily handle them or the use of this diazo carbonyl compounds in the reactions will be easier ok.

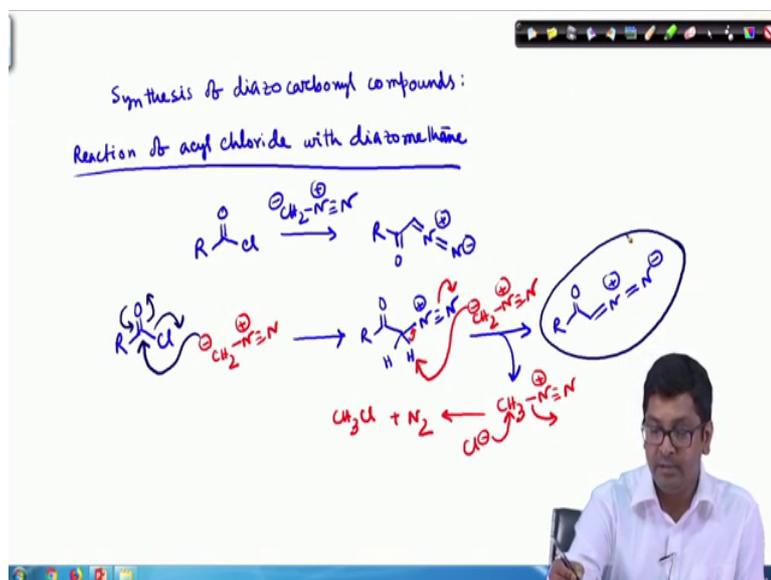
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So, now why this is stable; why this is stable; why this is stable? If you see the structure of this diazo carbonyl compounds something like this ok. Now, this could be in resonance like this; so here electron withdrawing carbonyl groups that stabilizes the diazo dipole. So, what stabilizes this diazo dipole? Electron withdrawing carbonyl groups ok; so, electron withdrawing carbonyl groups that stabilizes the diazo dipole ok. So, these actually triggers the stability this will stabilize; stabilize the diazo dipole fine.

So, overall these diazo carbonyl compounds are more stable than the diazomethane; so obviously, we can use these diazo carbonyl compounds as a very good precursor for the carbenes. Now, we will learn the synthesis of these diazo carbonyl compounds because these diazo carbonyl compounds on decompositions will give you the stab[le]- more stable carbenes fine. So, we need to know the synthesis of these diazo carbonyl compounds and their; possibility to form the carbenes ok. So, let us see that the synthesis of diazo carbonyl compounds.

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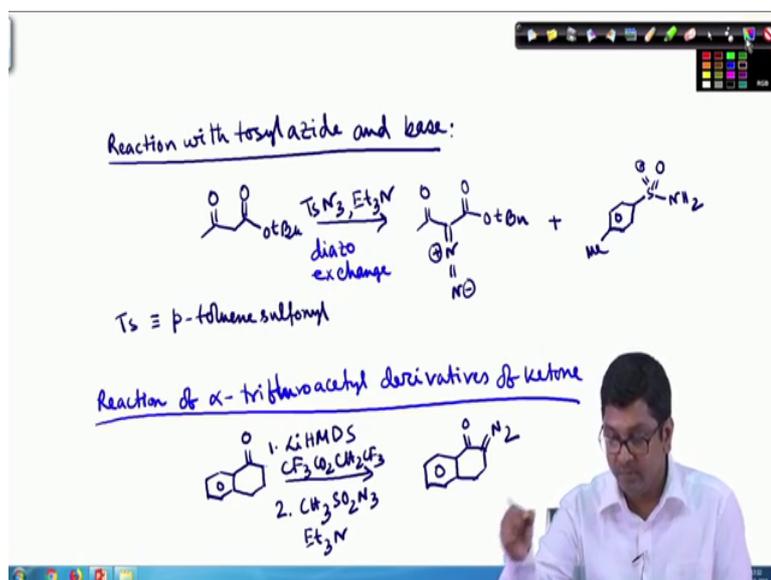
So, what we will start with that first the reactions of acyl chloride with diazomethane; so reaction of acyl chloride with diazomethane ok. So, what is acyl chloride? So, if you take the carboxylic acids and you treat with thionyl chloride or auxonyl chloride. So, that will give the acyl chloride; now you treat it with the diazomethane ok. So, now, it will react to give you the corresponding diazo carbonyl compounds what is it is mechanism?

Now, if you will have these acyl chloride; now you have diazomethane. So, this can easily react over here and once this will go so will come back and this will go out. So, what it will form? This will form as; so, R C O this putting 2 hydrogen's like this this CH₂ and then the corresponding N₂ plus. And once you have this then again one more molecule of this diazomethane that will picked up this acidic proton ok.

So, once it will picked up; so now this will have the corresponding diazocarbonyl compounds fine. Now, what it will generate from here? It will give actually this extremely unstable CH₃N₂ plus this one and we have from here this chloride minus; that will react over here and give the corresponding nitrogen eliminations and methyl chloride, there gaseous ok.

So, overall we can generate our desired diazo carbonyl compounds in efficient way ok. So, what is the starting materials here? The acyl chlorides and diazomethane and that will react to give you these diazo carbonyl compound ok. Now, in another method where the parent carbonyl compound will react with tosylazide in presence of base that will also give you the corresponding diazo carbonyl compound ok.

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As per example; so reaction with tosylazide and base ok; so what will be the this is the parent carbonyl compound ok. So, the corresponding diazo transfer reagent is tosylazide here in presence of base like triethylamine. So, the diazo exchange will happen ok; so diazo exchange and the product is our desired diazo carbonyl compound; this one ok.

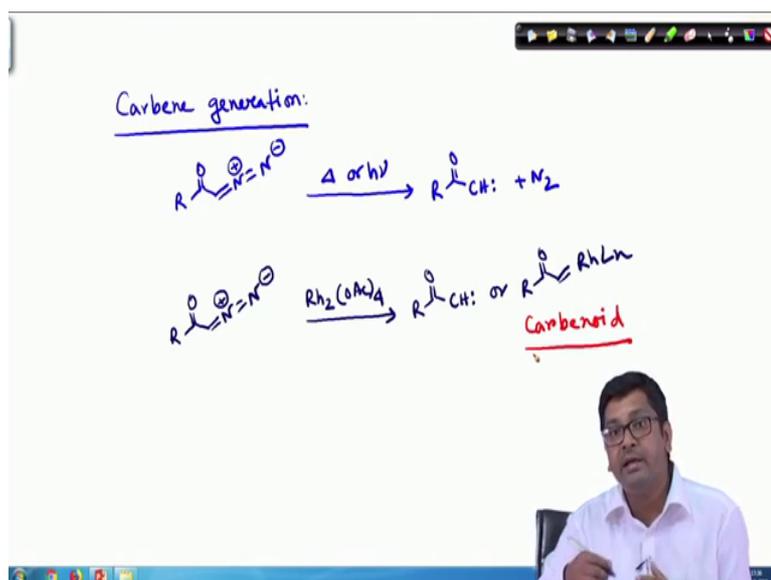
And the by product is the corresponding sulfonamide here and I think you know already that structure of tosylazide. How does it look like? Para toluene tosyl is para toluene sulfonyl ok; so para toluenesulfonyl azide fine.

Now, in another method for the preparation of these diazo carbonyl compounds; people have used that alpha trifluoroacetyl derivatives of the ketone to prepare corresponding diazo derivative. As per example, so here we can write reaction of alpha trifluoro acetyl derivatives of ketone.

So, for example we can take the corresponding ketones ok. So, if we take this ketone and then in presence of some base; strong base. As per example lithium HMDS and these ester $\text{CF}_3\text{CO}_2\text{CH}_2\text{CF}_3$ and number 2 is that the for the diazo exchange that is the methane sulphonyl azide in presence of base that will give this corresponding diazo compound in a very efficient way ok.

So, this type of substrates that can also first in presence of base; the anion will generate and that will pick up this corresponding from the ester that will react with this and finally, the diazo transfer will give you out the desires diazo carbonyl compound. Next what we will see? Now, we have all these diazo carbonyl compounds; now how we can generate the carbenes from this.

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So, our main target was to generate the carbene or our topic of the discussion here was the carbene generation. So, to know that we have first learned these kind of diazo carbonyl compound synthesis. Now, we will try to find out how these diazo carbonyl compounds actually convert into carbene ok; so let us see the carbene generation ok.

So, these are the carbenes that we have generated fine. Now, under thermal or photochemical decomposition; this will give the corresponding carbene plus nitrogen. Now, what drives this kind of carbene generations? What is motivating for such kind of decompositions of these diazo carbonyl compounds to generate the carbene?

We see that generation of nitrogen that is the most one of the most stable compound that drives or forces for the decomposition for such kind of decomposition to generate this kind of carbenes ok. So, this generation of the stable small molecule is very important for preparation of these carbenes. In another example, it is a very important one because in this case we will use in place of heat or photochemical decomposition; we will use the corresponding transition metal to generate the carbenes.

So, let us see how it works; as per example we have these diazo carbonyl compound and in presence of this rhodium 2 complex; it generate these carbenes or rather I should say that it stays like here L equals to legit ok. This is actually called not rather carbenes, but these are called in another term; this is called carbenoid.

So, what is carbenoid? Carbenoid also similar type of species like carbenes, but in that case it is actually partially bound to other atoms ok. So, carbenoids are the species that also reacts in a similar mode of a fashion like carbenes, but in general that partially bound to some other atoms; that is called carbenoids. Like in this case it is bound to this transition metal rhodium and this is called that carbenoid species, but they react in similar mode of similar mode or similar fashion like carbenes.

We will in many occasion we will show that this type of carbenoids are generating during the reactions and that actually reacts in similar way like carbene works. Our next carbene generation will be the carbenes from tosyl hydrogen's ok; that is all for today.

Thank you.