Heterocyclic Chemistry
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Lecture - 25
[3+2] Cycloaddition in heterocyclic chemistry

Good morning, so this is ((Refer Time: 00:24)) in the last class in this semester. And very quickly let us review what we discussed in the last class. In the last class we talked about the cycloaddition reactions right, that was exclusively 4 plus 2 cycloaddition reactions, in heterocyclic chemistry there are all kinds of cycloadditon reactions, but the most popular once are 4 plus 2, 3 plus 2, 2 plus 2, 4 plus 3 and 5 plus 3 these are few, but there are many other higher order cycloaddition reactions.

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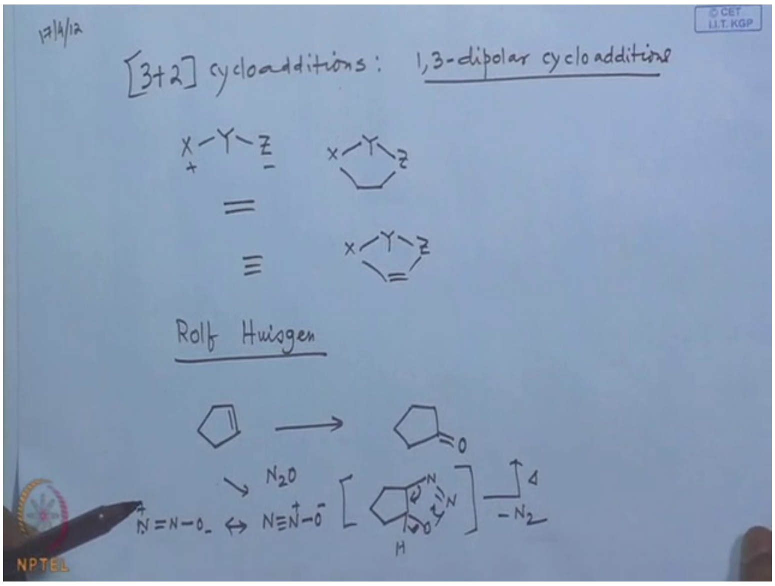

And we began with 4 plus 2 cycloaddition reactions, today we will begin with 3 plus 2 cycloaddition reactions. And quite often, you will be hearing also a terminal logic call 1, 3 dipolar cycloadditon reactions, that both are pretty very similar, I think you all understand the meaning of 1, 3 dipolar cycloaddition reactions. 1, 3 dipolar cycloaddition reactions means, you have three different atoms x let us say x y and z, and; that means, three items atom Simpson or reagent, in which the terminal atoms will have chart separations; that means one end should be negative other end should be positive.

And it could be and they are intervening bonds could be double bond, triple bond and all kinds, a double bond and triple bond at least one double bond must be present in one of those. So, the dipole means, once the dipole means the chart separation takes place between the two 1 and 3 atoms and one and third atom. And they are also of different charges like, plus and minus not plus plus or minus minus.

And common reactions all of you understand, that this sort of molecules or this sort of things can react with ((Refer Time: 02:50)) this and so; obviously, what will find after the reaction. So, we will have kind of a 5 member ring system, so the mean product 3 plus 2 cycloaddition reactions exclusively the 25 member reactions and there are other reacting partners I means, if they react with triple bond. So, this x and y and then z then you will have a double bonded compounds.

So, this methodology is a very powerful methodology and this lecture would be, sort of a devoted two one of the very pioneer in this field rolf huisgen which is a German chemist. Is now, more than 90 years old and very pioneer when I he actually, throughout his life may be 30, 40 years he works exclusively on 3 plus 2 cycloadditon reactions or the 1’th dipolar cycloaddition reactions. And many of you probably know some of the reactions will talk about, but the one of the earliest reactions in German industry, was the conversion of cyclopentane to cyclopentan one in one step, how can it be done.

And again this was due to Rolf which can an a German company, what they did they reacted with nitrous oxide. If the nitrous oxide what happens, if you write the structure of nitrous oxide, it would be it is again extra cell like this and all of us know the structure would look like. So; that means, first and third atoms are chart separated and one is plus and other is minus, so it is 1, 3 dipole and that under goes cycloaddition reactions, this is what we called this 3 plus 2 cycloaddition reaction.

And, so what will find, we will find a pyrazole derivative pyrazole derivative. Now, what next, the next is simply heating, heating is good enough that would rearrange or that we shift the hydrogen. Eventually what we will get this with loss of nitrogen you can get the cyclohexanone a cyclopentanone that, was one of the earliest reactions. And I do not know whether this is now being used in industry or not, but this just example, tell you the cycloadditon reactions could be very powerful. Otherwise and in heterocyclic chemistry also, there are many kinds of actually 1, 3 dipoles.

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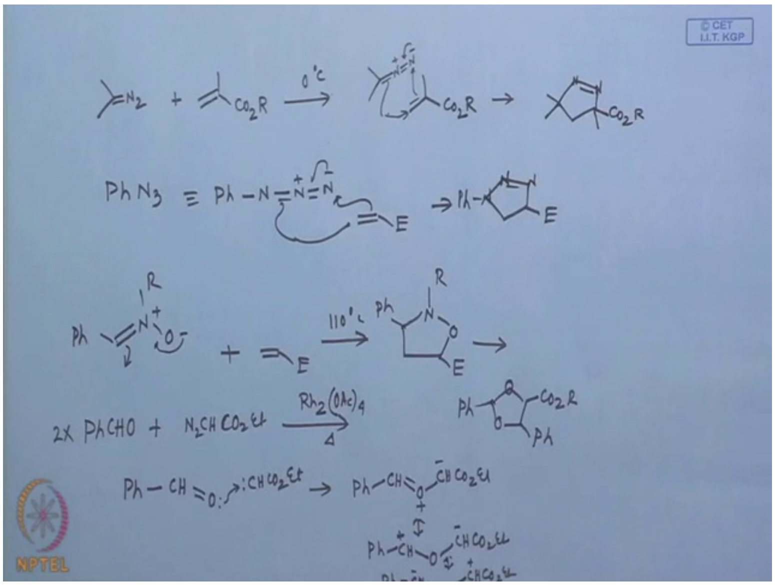

So, some of the reaction call you would know. Let us say, if you have an ester group here dimethyl diazomethyl or you can said dileo propane and if you allow it to react at let us say 0 degree centigrade. So, what is the reaction, diazomethyl normally is say again a cycloadditon reaction takes place, but so one can quickly write, let this is the structure and the double bond participates in the reactions. And there is an ambiguity that nitrogen can react on this side and carbon ends can reaction this side.

Normally the carbon ends, becomes this negative charge. So, you can say, this is a negative charge and if you write this is what plus, this is minus and so electron flow as if comes through carbons and so adopts this beta carbon here, and then this one go through this. So, what will find a 5 member ring, this is an ester here and this is methyl group, nitrogen and nitrogen and sorry nitrogen, then you have this methyl group here right.

Any something wrong, this should be double bond. So, this sort of this is pretty well known right for example, now a days one of the very popular reaction is already say, if you begin with phenyl azide and which is equivalent to phenyl this is nitrogen again nitrogen and so one can write this, is best way to write as I write here. And if it is reacted with an alkyl, so you have to efficient alkyl. So, the electron flow again through what sort of phenyl and it takes place then so what will find again a 5 member ring.

So, it is a nice reaction; that means, you do not lose anything, like addition means you do not lose anything, so will have. So, triazole derivative and by now all of you know, this sort of the reactions known as click reaction. So, click reaction then few days ago and it is petty popular you know, but and almost everybody knows, but you have to know what are the qualifications, to be met to for a reaction to be called as click reaction. What is the first criteria, this is cycloadditon reaction there are several criteria that to be fulfilled by a reactions to the known as click reactions.

But, now only click reaction is a result for the azide alkyl or alkyl cycloaddition reactions. There are other 1, 3 dipole, so example impact in there compounds of this kind all of us know, if you have compound of this time, then again and electro efficient system. So, sometimes the room temperature, sometime heat in this particular example just heat is required. So, what will get, we will get isoxazole, once again vaporization is an attack to takes place to the carbon here and so E, but normally now this is R and this is phenyl.

And then of course, will have this isomeric problem, the isomers are often obtained. And what is the net result, this is a basically again a reaction and the substitute here known as, nitrone. So, nitrone cycloaddition, sometimes you call nitrone cycloaddition, but these reactions and what does it do, essentially if you normally the nitrone cycloaddition products are broken or other all Clint wood at the nitrogen oxygen bond. So, this is clip then eventually, it will give you an open chain compound.

But, net result, if you look at this is a formation of a new carbon coupling bond between the carbon adjacent to this, adjacent to the nitrogen and the beta carbon of the acrylate. So, you say again simplified version of CC bond formation, but we mechanistically we give the such a 1, 3 side dipolar cycloaddition reactions. Quiet interestingly I will give you one more reaction, if you begin with benzaldehyde then ethyl diazoacetate and of course, this is 2 times twice.

Then the reagent that would decompose diazo compounds, what is the reagent normally use for decomposition of the diazo compounds, copper, silver perfectly all right even copper slats also useful ethyl acetate ((Refer Time: 11:55)) all these things. But, one of the finest one is, dilodium tetraacetate is one of the finest dilodium tetraacetate or you can substitute the acetate with longer chain acids, just heat nobody toluene bulb benzene temperature the sufficient. What will see, the products here this is very interesting product, say ketal, see ketal with phenyl here and the phenyl here. Suppose, you did not know this method, then for the preparation of this sort of ketal, what you would have done, you have taken a diol and they benzaldehyde and they assist a conventional one.

But; that means, that requires acid part, in this case the somewhat like a neutral to reaction medium the reaction neutral. And what is this mechanism, the mechanism goes like this, so once it forms a new kind of a dipole, you have if you rewrite this structure would look like this, and if you decomposes it forms carbine right. So, this will a carbine and their lone pair oxygen goes to the carbon here, so what will find, you will find. So, is CH right double bond and then electron of oxygen is donated to the carbon. So, this should be plus and this should be minus and this.

So, essentially you can write resituating structure, if you resituating structure we will find this is plus oxygen and CH and then C O 2 e t and this minus right or I mean there are all kinds, this is all kinds of problem this could be CH minus oxygen and c plus. So, what next and all of us can guess between all the among the all the three, the one that would be or other.

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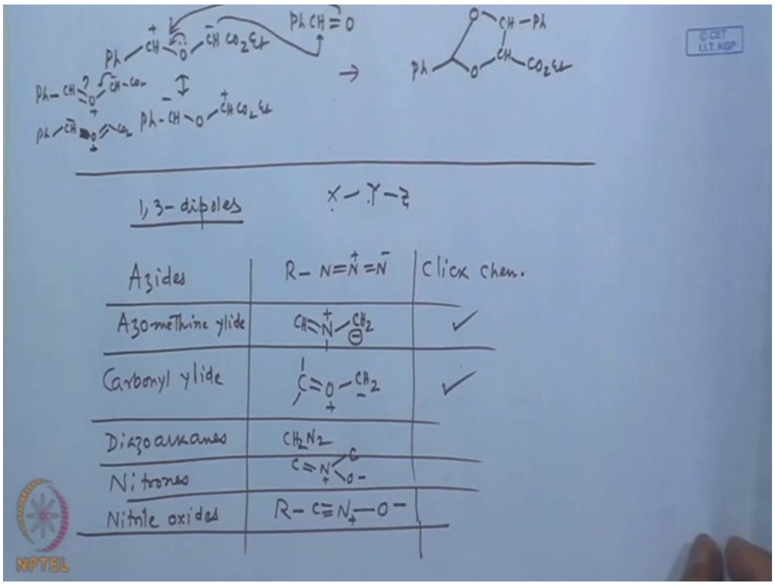

1,3- dipoles $X-Y-Z$

Azides	$R-N=\overset{+}{N}=\overset{-}{N}$	Click chem.
Azomethine ylide	$CH=\overset{+}{N}-\overset{\ominus}{CH_2}$	✓
Carbonyl ylide	$C=\underset{+}{O}-\underset{-}{CH_2}$	✓
Diazoalkanes	CH_2N_2	
Nitrones	$C=\underset{+}{N}(-C)-O^-$	
Nitrile oxides	$R-C\equiv\underset{+}{N}-O^-$	

Let me quickly write the dipole here, this say carbon, oxygen and CH this is plus, this is minus and this is problem here, ester here. So, I mean you can write, the you can rewrite also this is c minus oxygen and this is plus and this is ester what next, then we have additional molecular of benzaldehyde. So, benzaldehyde the means it would react with this end and this oxygen would attach this. So, what will find, the entire product would be this is CH this is water is CH P then oxygen and this, case you have this ester.

So, this is just example of basically, they 1, 3 dipole then just very quickly. So, what are the I mean in principle, what you need is an hydra atom; that means, like oxygen, nitrogen etcetera, you need nitro atom and in all cases the products you gets in a heterocyclic product. So, what are the possible 1, 3 dipoles, there are, so many possibilities right. So, what are the possible dipoles; that means, x y and z, so you can have all kinds of the combinations nitrogen- nitrogen -nitrogen and carbon-nitrogen-nitrogen, nitrogen-carbon-nitrogen all permutation combination.

But, in heterocyclic chemistry only few of them are, regularly used or I should say more popular, one of them is I think one I will today will basically talk about yes, how these structure obtained, may be this is it any questions or tough question. Then I will take it up, otherwise I will not take it up, you can just do this little bit. So, that then it becomes CH right, so this find, so it becomes CH minus, this is right you see good question for ((Refer Time: 17:45)) any case.

So, 1, 3 dipole is this, so you can have all kinds of combinations and just very quickly I will just summarize. And only I will take up today only two of them, I think some two means, one as is known as I think already talked about, azides right. Azides means you have this nitrogen again; that means, all the atoms are nitrogen and this is plus and this is minus. So, what are the comments I think you have already known that, this should be known as the we will we are not going to talk about today, what will be talking about today is azomethine ylide is a very popular dipole, it is very popular dipole.

And how does it look azomethien ylide, the name tells in this case somewhat like a miss number right, when you of it. Diazonium salt it has two nitrogen, as a compounds as how many nitrogen as compound, you see diago is one, diago is two, again and the diago also two. So, there are there is a little difference nomenclature when you say this is classical name. So, ago means actually it has a nitrogen here, double bond at nitrogen a methane means CH.

So; that means, it will have a CH and ylide, ylide means will have one or more sort of a carbon, so; that means, is a negative charge and this one is positively charged. So, this is called agomethine ylide. And then there are carbonyl ylide, again instead of the nitrogen, what we will have, we will have something like this minus and oxygen plus. So, these are all these carbonyl ylide and you have already known, say diago alkanes this is constitute another category of this thing I will not write that I think all of us know, how is that fine.

Then, there is a we have already talked about nitrones, nitrones means how do I write nitrones, nitrogen, oxygen this plus double bond C here and mind it. This nitrogen must contains another carbon or which sometimes carbons can substituted by nitrogen like alison ketone, the name is deduct from ketones, nitrones and all these things. Then this is another very popular one, nitrile oxides, nitrile oxides means all of us know, nitrile is essentially the cyanides and if you just oxidize at nitrogen. So, it becomes nitrogen plus and oxygen minus.

Then, there are many other thing nitronates and all kinds of things nitronates, I mean we have many, many. So, today we will just take it out, take up only this one, agomethine ylide is a very popular and the carbonate ylides and rest will not covered, may be it times for do little bit exercise this sort of things. So, in discussing about the agomethine ylide, what is the first thing we should know about little bit of the history may be I mean how the this sort of concept was derived or and how it is used. And then how it was developed in to the synthetic chemistry, say synthetic chemistry.

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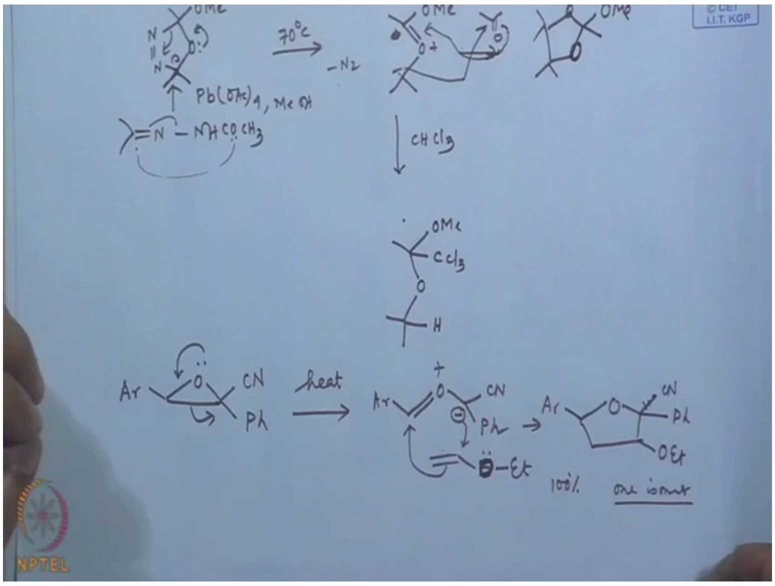

One of the earliest reactions and the chemical literature was, this hydrogen derivative transforming to a cyclic compound, with a in presence of let tetra acetyl you see a let tetra acetyl. If you take the let tetra acetyl and methanol what you will get, you will get a 5 member diago compound or say pyrazole 5 member of pyrazole and like this. So, you have ethyl group and then on side you have the, so this was known and you can guess I think the mechanistically. If you look at this lone pear goes to the nitrogen the double bond see, if hydrogen goes to the late eventually the cycle nation takes place.

This is one of the very earliest example and if you heat this molecule here 70 degree centigrade. And one can guess and what is the product, I mean someone probably ((Refer Time: 23:24)) this compound, will have a diradical structure, with loss of nitrogen. But, the mechanistic organic chemist this suggested that this compound, as a dipolar structure like this. So, dipolar structure and sorry all you can write like this, as if this lone pair goes here, nitrogen and this.

So, you have a, so again this is known as, what this is known as carbonyl ylide. So, it looks a you have a carbonyl plus and then corresponding carbonyl is negative charge, these are the things and this have been oval proovan. Oval proovan means, if you carry out the reaction in presence of acetone, what will find the product that would forming, again a 5 member ring with 2 oxygen here and this O M e and this methyl and so I will got this carbon, this negative charge goes to the carbon and then oxygen, oxygen attaches attach this carbon here. So, eventually we get then 1, 3 dioxilene.

Now, one could have ((Refer Time: 25:11)) intermediate these now radical etcetera, etcetera, but this sort of intermediate has been also a trapped by chloroform. So, one can guess we know what will be the product here, all of us know the chloroform does not go the radical kind of reaction very easily. So, the where it has been, what has been found that this negative charge pix of this hydrogen, then see self 3 minus goes to the other carbon; that means, the product that would be found here, this is c shell 3 and then oxygen of here and then you have two methyl group and the chloroform hydrogen is picked up this is one of the earliest example.

What does it I mean by giving this example, what I meant to say that this sort of elides structure, which originally proposed and very old literature could be, sort living or existing or is it could be a reality. With this then I mean people have tried many other examples for example, very nice let us say I think whether, you can predict any reactions from a compound of this kind where you have, few substitute around epoxy ring system and this will arrive here.

Suppose we did not know anything about this chemistry of the epoxide, special chemistry of the epoxide. And if we heat, such a compound what do we expect, c normally c bond breaking, why shall be epoxides are not known to undergoes CC bond permissions breakage, but because of the substitutes I think the epoxide undergo electro cyclic ring opening, polar electronic electro cyclic ring opening. And if you look at the intermediate, what will find this is oxygen now, positive charge here and this is very uncommon among the epoxides, but when you have heavily substitute dipoxide will find. This epoxide undergoes ring opening.

But, how do you know. Suppose, should be if we heat it and then cool it, go back to the starting material. So, but we cannot prove right, but only prove which is somewhat indirect is this, if you can carry out the reaction in presence of let us say presence olupine, electron reach olupine of this kind and you see ethyl vinyl ether. And the way have written one can quickly understand, what should be the product because this oxygen lone pear and drives the lone pear to this end and the negative charge go through this one, so eventually what will find.

We will find a furan derivative, furan derivative with ethoxy here, then c and this phenyl on this side, will have aryl group. And the yield of the reaction, in this particular case is 100 percent and one isomer of course, this is somewhat I mean unpredictable, but you got one isomer. So; that means, the earlier example, was an historical example or for a long times this chemistry was not explode because of the non available of the methods by which one can produce, if the carbonyl ylide. Now, this is one of the finest way of getting with the carbon, epoxide can be ring open to the carbonyl ylide and then subsequently, this ylide can be trapped by various oleophilic substitutes and this has been generalized by a many other cases.

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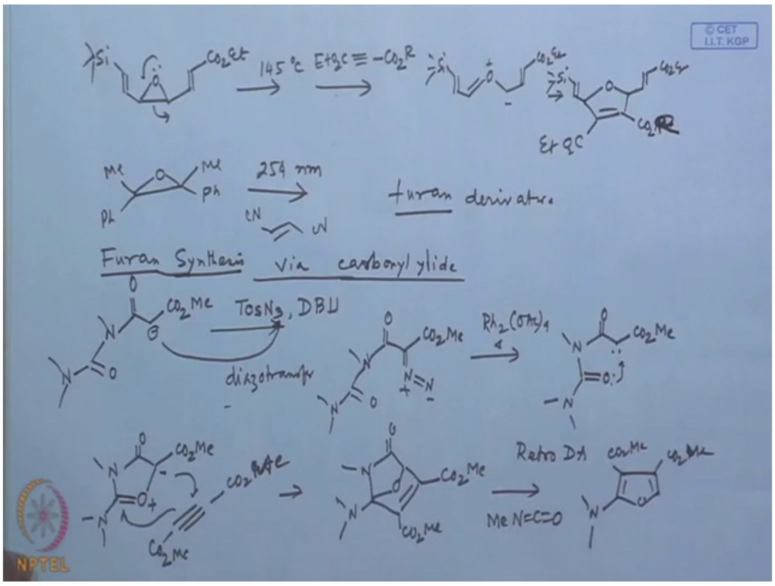

Like, one of the cases could be here, is heavily substituted again in epoxide, internal double bond that substituent like acrylate part. Then you have this vinyl, silent and it because little high temperature 145 degree centigrade and if you, then if you mix up with there are if you mix with acetylene dicarboxylate. So, when as usual, what you would expect again a ring of the epoxide, takes place in this direction probably because. of this electron is going grow.

So, I think I will just write the part of it, so what will see, this becomes positive end and this become negative end and then you have this ester part, this show this silicon here and this. Then one can I mean all of you can write, the structure would be ((Refer Time: 30:58)) structure would be, again if you run derivative, if done derivative here and all these substituent's are as it is, ignore the start the movement because there is no specificity here, and so this is R I am sorry one and R it has to be just take the, this is say e and then you have this vinyl, silyl groups.

So, these two examples tells you that, this sort of reactions are quite general. And more interestingly, there is one more example where you will have heavily substituted epoxide methyl and phenyl and the substituent's, this then if you photolyze at 245 sorry 254 nanometer, you can get also this carbonyl ylides. And then it can be trapped with this, syniol compound with the syniol compounds and the corresponding furan derivative is often.

So, it is a very general reaction, what else can we do, the general interesting way of producing this carbonyl ylides, this example could be again from the decomposition of the diago compounds, like you have seen decomposition between one of this previous examples, we have seen that decomposition of the diago compounds. So, that is a very general reaction, I will just give you one simple synthesis of substituted furan, which starts from a meronate derivative.

Where, will you have the one end is this amide, other end is the ester then do a typical reaction of this is, so I shown new kind of a furan synthesis let us say. So, we will begin with I say furan synthesis, via carbonyl ylide. So, let us see whether you can predict the product one of the reactant, reactants is tosyl azide and the basic used this is DBU, anybody can guess, what is the product.

Azide transfer.

Azide transfer, you say azide transfer reaction. So, it should double bond C O Me and then nitrogen up here and negative charge goes to the nitrogen and tosyl amide is produced. So, what will find, this is basically, the corresponding diago compound, so it is not it is not azide transfer it is diago transfer, this should be known as azide means 3 carbon nitrogen. So, it should be known as, diago transfer this is very useful method, one of the Indian scientist from Hyderabad actually described this one, but now we have all kinds of variations.

But, interestingly now, this popular reagent say disodium, tetra acetate and normally is told in a benzene and heat. So, what do you expect sorry I think I made mistake here, I made mistake actually this is not the meronate, it should be N sort of E R derivative. So, you have one more carbonyl up here. So, if you heat it; obviously, think by now we know, that it forms a Calvin, so say Calvin here, then double bond and you have a nitrogen up here.

So, what next, I think lone pair goes to from the carbonyl amide. So, nitrogen and then the ester here, carbonyl ylide means oxygen plus and this carbon minus and the substituent here is methyl group, and this sort of compound once again, if you react with the alkynes electron deficient alkyne or electro deficient alkyne methyl here and C O 2 Me. So, all of you can write, the product would be a by cyclic compound, so carbonyl then you have this two ester groups and ester groups here, and then you have this nitrogen and this nitrogen and you have this.

So, it is a by cyclic compound right understood. So, what next, if you recall the title was furan synthesis by cyclic carbonyl ylide foremost you have carbonyl ylide. So, and actually retro ((Refer Time: 37:44)) takes place there after. So, what is the product, product would be this is a furan derivative, if the two ester groups here at 2, 3 and 4 position. And the two position is occupied by dimethyl amino group and what is the loss, the loss is the molecule that is the being loss, methyl isocyanate, is a very # methyl isocyanate. So, this reactional say one more example probably I will give you, see whether you can write the structure of the product.

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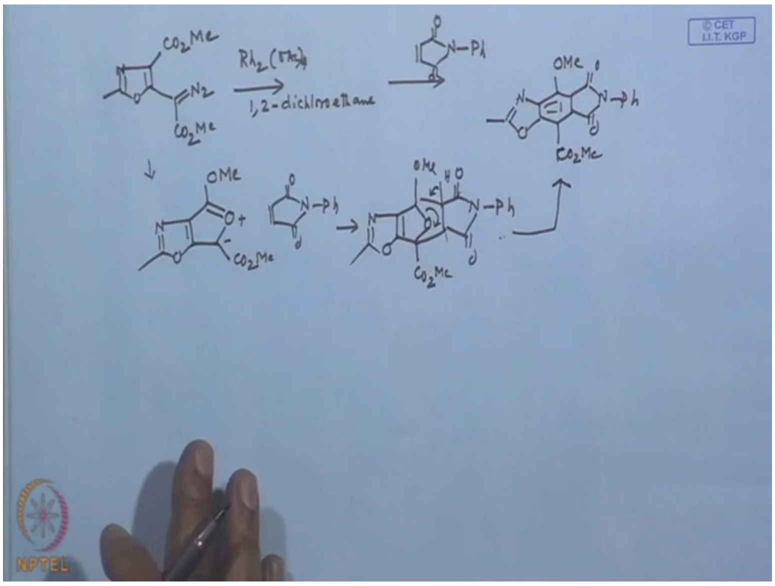

This is from an oxazoline derivative. So, and the substituent’s are the ester and here I think I will straight way write it is a again a diago compound it is a diago compound. Now, as usual this dilodium tetraacetate by this equals at low temperature 1, 2 dichloroethane which has boiling point around 80 degree centigrade. So, I think all of you can guess, what could be if this reaction is trapped with phenyl maleimide. So, what should be the product in fact, the product that is found here, as a straight way write the product is a benzenide.

Now; that means, this carbonyl ylide is being used for the formation of benzenide, not the heterocycle. But, the diago compound the carbonyl ylide actually forms from a heterocycle and so this is ester group here, this is O Me and the other portion is the corresponding dienophile. So, mechanistically once again say, so sort of a like a repetition, so we will have nitrogen, then oxygen here on this side. Now, after this formation of the carbine, it will form the carbonyl ylide of this kind and here, will have the methoxy.

So, this methoxy is retained, this ester is retained and if you have then ((Refer Time: 40:58)). So, under goes thermal reaction, what will find see if this is a typical cycloaddition reaction and this is O Me, then there is your oxazole part and then you have this ester here. And what next, I think again thermal loss of water, so you will have this then eventually we will have one more hydrogen, that undergo thermal isolations to this product. So, giving all these examples basically, we are trying to tell you this sort of carbonyl ylide reactions pretty useful reactions. Now, what is the other way of having the cycloaddition done.

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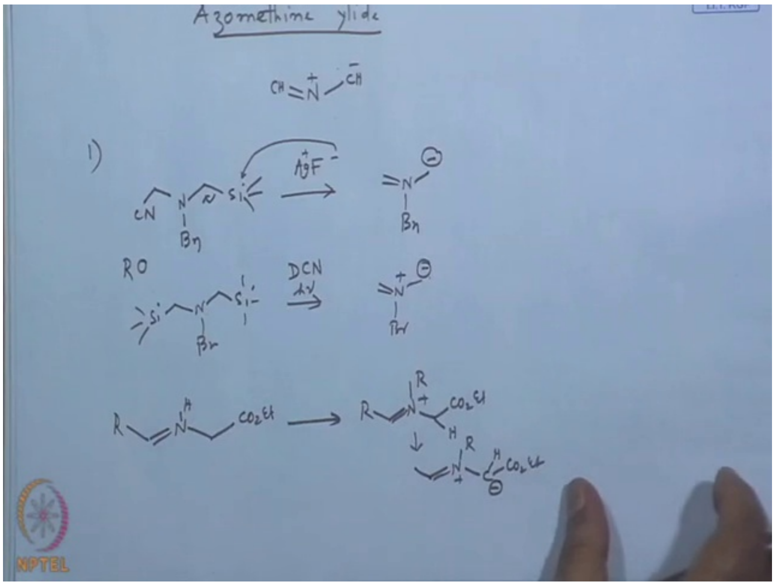

The next most important that will be talking about, this azomethine ylide we have already told you, how to write agomethine ylide ago in this case it is basically unsaturated nitrogen, a methane means this. And then you have the ylide means you have to have negative charge and this is positive charge. Once again this sort of chemistry was not I mean known for long time, but when people came up with the methods by which they can be easily be produced, then this reactions become a very popular in our country correspond as mean very pioneer in this area.

The one of this way is produce the sort of in tabulate, how to produce was to have and this halide compounds. So, with a sylal group, adjacent to nitrogen this why the minimum requirement and then you have if you look at this structures here, you have to produce a double bond, so the means you have to have a good living room. But, many of you know, many of the living rooms adjacent to nitrogen or not viable, having living room close to nitrogen is a viable foe example, if you have an OH here, is not very stable because of the lone pair of the nitrogen.

So, you have to have a living room which should be poor of them OH and amines and etcetera. And but then it should be livable or, so it should be I mean departing this group I mean substrate. So, in this case, let us say the one that was suggested synonym, so and the other portion is of course, this say productive group here. Now, if you treat this is a fluoride all of us know fluoride two attack at the silicon. So, it forms a carbonyl when, but at the same time, you have to have a I mean driving force for releasing this synonym group.

So, how do you do, so you have to have an electrophilic kind of a thing that would abstract the syano, a some special affinity to which one silver right. So, in fact this was done with silver product, see silver product if you do, so; that means, one can quickly make this one is that, so this is agomethine derivative, there are other methods I think I will not may be I will give you one more example, let us say there are other way also. In fact, instead of the syano, we can also have OR alkoxy. That means, the group poorer than the OH groups etcetera.

So, alkoxy is all of you know this under; that means, syano can be replaced by alkoxide and there is a another way of making it, you can have two silicons, around this nitrogen. And that requires; however, say photo lighting reactions DCN dicynone, if you got or naphthalene right. Dicynone naphthalene 1, 4 dicynoen naphthalene and then light, so you can generate again, this sort of dipoles 1, 3 dipoles in N negative and N positive, see this is one of; that means, silyl derivatives of the corresponding, I mean compounds can be de silented to produce this agomehtien ylide.

And then there is another sort of way of doing it. I think the best think would be, I means just, imine sorry iminium salts for example, if you have a substrate of this kind right. Then if you put a electron with growing group here, let us say ester group and then of course, ester group, then one can found from here the ammonium salt, let us say ammonium kind of salts here. Then automatically the alpha position becomes little more susceptible to hydrogen abstraction and so hydrogen.

Now, in presence of a ways you can produce this is one of the finest and quickest way of doing it, this is hydrogen and R plus and this. So, you have a nice agomethine ylide, this is one of the I mean, that mean formation all of you know is very simple, imine formation is very simple from carbonyl compound say I mean. So, this part looks like a amino acid and other part RD height. And I will just illustrate this agomethine ylide formation by synthesis of a natural products call.

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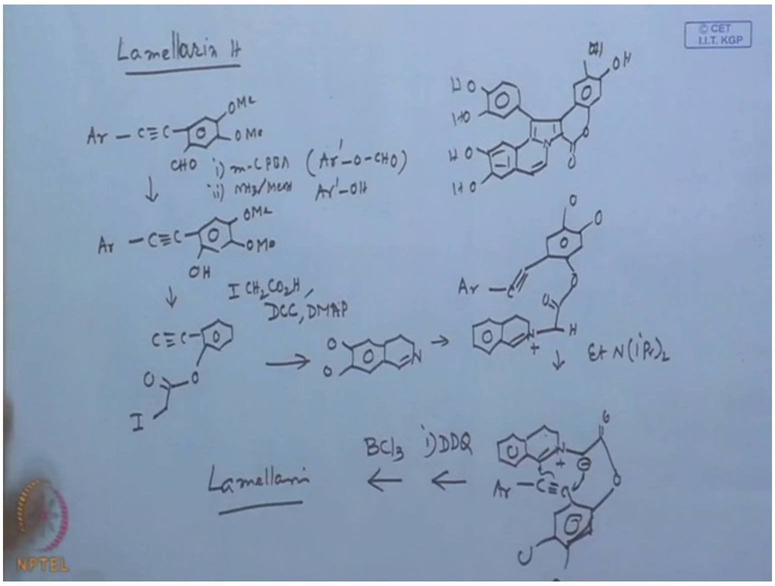


Lamellarin H the molecule looks, I think you have seen it before you say pyrrole derivative is said pyrrole derivative this a tetra substituted and pyrrole derivative. And the molecule would look like, real big molecule it is a biological active molecule and this then you have OH of here, OH this is basically here and there OH and then you have, so many OH groups here, this is the target. If you recall, in one of these previous classes we talked about the synthesis of this see this kind of molecule, by application of Suzuki coupling, you start with a pyrrole derivative and go on putting this aryle groups here.

What if you see look at this synthesis will be describing now, this much more convenient. And looks little interesting, in the sense that the formation of, this pyrrole ring by cycloaddition is pretty use very easy, very easy you do not any sophisticated methods. The first thing what is done, let us say I think in brief I will write A r means one of those phenyl groups, begin with a acetylene compound and then within aldehyde and here and the methoxy here and this let us say again methoxy for example.

First this one, is converted to a phenol, protect other side have O R Me and this is O Me. And how do you do it, I think this is a under the heat chemistry right, sometime let us hear from you dakin reaction, requires an OH group right, adjacent OH group, is an under agent problem though, very interesting problem ((Refer Time: 51:19)) or else can we do. Let us say, in this case first one was m CPBA, what does it do, m CPBA actually converts this formal group in to format; that means, aryl group migrating to the oxygen.

So, what will see here, no it is not in the dakin reaction, dakin reaction possible, but yes but dakin reaction normally in some not that great, see if you have an aldehyde, yes that is telling, if you have an OH group that is very easy, dakin reaction itself ((Refer Time: 52:29)) aryl group migrating to the oxygen. So, what we will find here, let us say a prime, so what that is it, I mean see insertion of an oxygen between the aryl group and the formal group.

Then, what you do, you have to just release this two OH group, how do you do that hydrolysis C S hydrolysis that is; obviously, it is format you convert it, but the preferred method, that at this movement you have to think about other methods also not classical OH etcetera, etcetera. The preferred method is simply ammonia and what else, methanol that is the basically see transistors function, so then this is converted in to OH and once again, an ester here and so you take iodoacetic acid.

So, from iodoacetic acid you correspond the ester. And how do you do, it is not very trivial though, you have to use DCC here, DCC and DMAP. Next, you do take a dihydro isoquinoline and this oxygen and all these things, then this solvent, so that would relate to the quantization and so and nitrogen here and this is this acetic acid part, let us say this one and then this. So, you get the quartenization here. So, what then if you see, that is a triple bond here and that is the aryl part here.

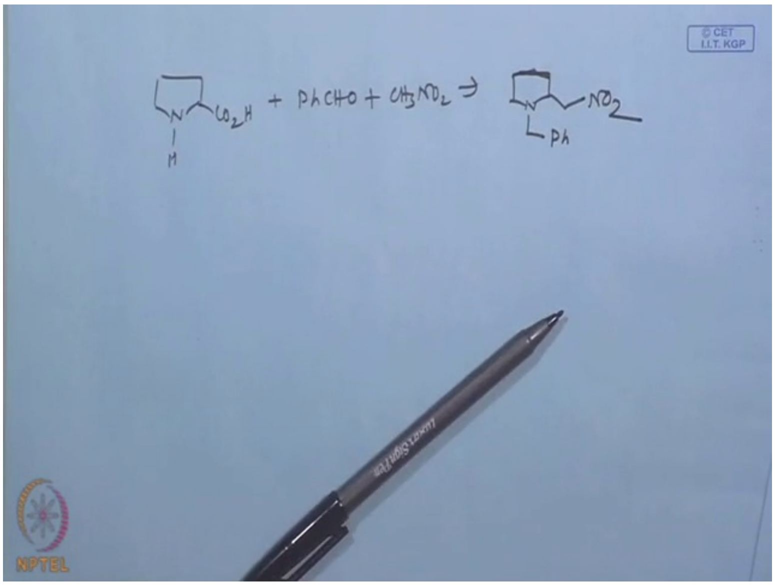
And there are rest as it is you know, here and there you have this oxygen here, oxygen here, this oxygen here all these things. So, what you will see that now, this is an iminium salt and we have a hydrogen here, which should be abstract able, in a presence of a base which is known as unique base, isopropyl basically say tri this is trialkylamine base. This gets converted in to the dipole 1, 3 dipole. So, what will have now, this is negative charge and this is positive charge here, I think I will write this way.

Otherwise this is then carbonyl, may be now we will have this sorry this one and then you have this triple bond right and this is A r and then you have all kinds of this oxygen here and here. So, this will undergo now, this C here, the triple bond is not a very activated one, neither does it have any electron growing group nor it is no, otherwise activated. So, this under the condition, this reaction takes place it forms the pyrrole ring this pyrrole ring.

So, the pyrrole ring then of course, if you write the pyrrole ring, then you will have a product without the double bond up here. So, you treat this with DDQ like dihydroisoquinoline, benzoquinone and that would aromatize this quinine ring and then subsequently, you treat this with boron trichloride is a reagent known for demethylations, O demethylation. So, O D demethylation, so you get to the compound part lamellarine, so this I mean very quickly I have said about this one, but essentially you say agomethine ylide.

And there are two kinds, one is that silicon substrate silicon substituted substrate for the synthesis, the other one this one is an iminium salt, which can be converted in to the agomethine ylide. And my need, this does not require any activated alkyne, so similarly this sort of reactions also very useful for un activated alkyl provided, it is with in present within the molecule; that means, the reaction is an inter molecule one, this 1, 3 dipole is nicely react with an un activated ((Refer Time: 57:58)) otherwise un activated. And may be I think you have ((Refer Time: 58:07)) time and you can try to work out, one of these problems at home, the problem is like this.

(Refer Slide Time: 58:17)



This is again from ((Refer Time: 58:26)) literature. So, mix up with proline heated with benzaldehyde in the presence of nitro methane, you get nice CC bond formation and see further you can work out the mechanism.