Heterocyclic Chemistry
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Lecture - 31
Pyrrole Synthesis II

Good afternoon. So, last time we talked about pyrrole synthesis; pyrrole synthesis 1. This time pyrrole synthesis 2; that means what it means actually there are so many methods for assembling the pyrrole units structures. And it can be subdivided into several classes and there could be I mean if you go to the website go to the Google; and find atleast there are 60 different methods listed in the Googles. And there is site call organic portal we will find.

So, it is not possible to obviously to talk about all those methods. But I have picked up some of the methods in the last class we talked about largely Barton Zard then van Leusen; then piloty and Robinson, piloty Robinson and Jana also one. Today what I will do I will just go through very quickly the conventional once; the 3 conventional once. And then I will talk about there is method developed by Chiba and then methods based on alkynes; and then method based on ring construction and ring expansions. So, these are few things would be talking about today. And then if you see if you try to master the methods on pyrrole synthesis is to be very useful nucleus.

We will find in by bispyrrole, tripyrrole then so many natural products then obviously many of you know 4, 5 in itself is a Bizial big class. So, if want to make a profile in modified compounds or profile based compounds; then you have to know about the pyrrole chemistry ok. So, what we do today just a basically we classify them into terms of like the components; if you recall in the last time we talked about the most of the pyrrole synthesis are based on 2 categories; 4 plus 1 and 3 plus 2. So, when you talk about the 4 plus 1; then among them the most popular once are Paul Knorr synthesis; that is the first one.

Then, this Paul the what is that next one is Hantzch synthesis; that is a most and then Not synthesis; these are the 3 conventional once. But among the three then Paul Knorr very powerful; even today if you come across a pyrrole nucleus is a very first thing what you should think about is to think about the Paul Knorr; because thus more at most reliable.

And primary this is most popular because of what? Because of ready formation of a very fissile formation of five member ring system; see all of us know that cyclizations you know among cyclization five member formation is very fast; I mean officially 3, 4 all these people arguable. But in practicability the five member ring formation is much faster than many other ring systems. So, that fissile formation of five membered actually makes this Paul knorr more popular than other. And I will just give you one example that just tell you that how powerful it is.

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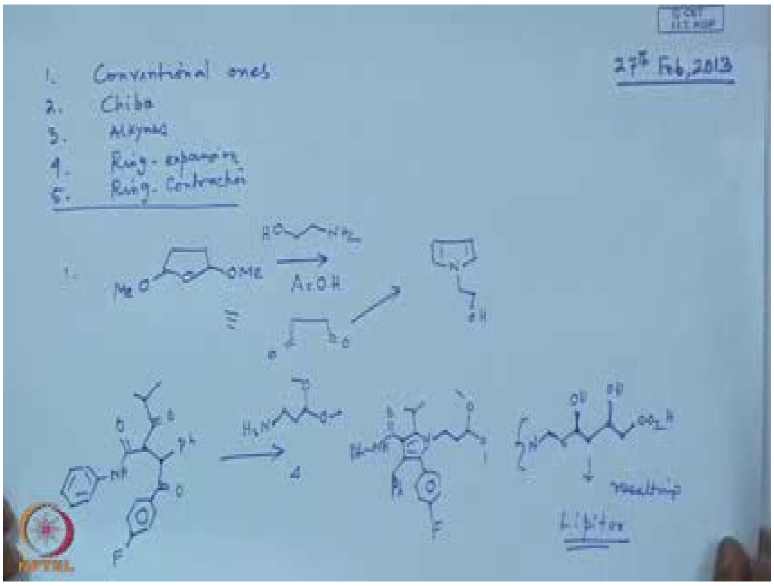

So, that means today we talk about the 3 categories; the first category we talk about the conventional once and then second category we talk about this is basically this equal is Chiba method. And third one starting with alkyne precursors; then forth category could be ring expansion. And then obviously this other one could be the ring contraction, construction strategies ok.

Now, as we talk about the Paul Knorr I think many of you know you it requires basically one Paul Knorr requires 1, 4 diketo compounds. But there are examples where you will find we do not need to have this 1, 4 diketo compound; but the corresponding precursor is good enough. If you look at the one I have written here it is basically a tetra furan derivative right. And then you react with ethanol amine and using solvent acetic acid. So, what do you expect here? Just a pyrrole.

So, that means the product here is just a pyrrole ethanol side chains on nitrogen. Mechanistically this is equivalent to what is this is equivalent to so again is a just a succinaldehyde is not it; just if you hydrolyse this as a it will give rise to a succinaldehyde. And then now the questions what we have been talking about that between amine and alcohol all of us know I mean which more nucleophilic. So, it will go condensation and then ((Refer Time: 06:19)) formation is also very fast. So, once this condensation takes place then there are all possibilities of course the five member ring system would be come first and this is the one that is.

Now, just will have a little more complex example to illustrate this particular one; how so powerful it is. Let us say if you begin with a multi substituted; let us say multi substituted ketone and in this case the substituents could be benzene ring. Then, one more ketone here then N H and then see I mean you have all kind this reaction particular this reaction. So, what you see here you have an isopropyl side chain; then phenyl side chain here, fluorophenyl side chain here then this aniline side chain. And you do not have to do much just take an amine take an amine and then of course; in this case this is a protected amine here with a acetal protection this one.

And, just simply take acetylic acid and heat it. So, what do you expect? Let us say if you did not know Paul Knorr synthesis; now we know Paul Knorr synthesis so it will give so it will give or it will provide pyrrole nucleus. But if you did not know why do you start from? Basically you have to look at the different functional groups you have 2 ketones; you have 1, 4 diketones then you have 1, 3 diketones also.

But when you heat it actually what you get is again a pyrrole; so you should know tetra substituted pyrrole. Now, what you get is a tetra substituted pyrrole and I think something is wrong somewhere 1, 2, 3, 4. So, this should be fluorine up here right and then this should be phenyl; and this is a C O N H and this is again phenyl. And then what then you have this nitrogen this one ME, OME and OME.

So, what you see is the means out of the 3 carbonyl groups of one can very quickly guess that amide carbonyl is less reactive, less electrophillic in nature. So, that means 1, 2, 3, 4; these 4 I mean this 4 carbon unit would condense with this ammonia to give this pyrrole unit right. And what is specialty about this reaction? Because it can assemble all the 4 different substituents in nice manner; and that actually tetra substituted pyrrole formation is difficult. If you try to carry out in step wise manner first one R 2; first and second can be introduce very easily; third one you try to introduce that would involve steric effects. So, then fourth one even most steric effects.

That means, step wise processes are not that welcome in this sort of reactions; but what next? Actually if you just change this side chain with a 7 carbon unit 1, 2, 3, 4, 5, 6, 7 I think 1, 2, 3, 4, 5, 6, 7 carbon unit here. And then if you have O H groups here 2 O H groups that basically this is nothing but it is the substitute for the amine. Then, the resulting product that the resulting product could be if you take this amine and resulting product would be the something is one of the highest selling drug in the world; this is called Lipitor is marketed by Pfizer.

And, it actually is use for the treatment of audio muscular diseases; and actually lowest of the cholesterol level in the blood. So, very high cylinder when so you can see here this is a carboxylic acid; that means very useful one ok. And, so likewise many of the addition pyrrole synthesis would depend on this sort of Paul Knorr synthesis; the second one of course Hantzch synthesis I think many of you I guess you know right. What are the; how do I remember how do you remember?

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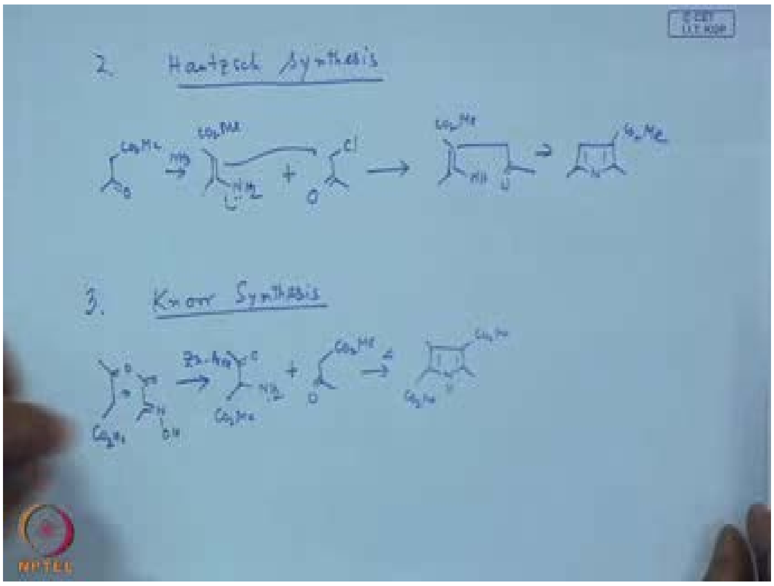

Hantzch synthesis basically in heterocyclic chemistry try to remember on the basis of this starting material; that is actually makes you learn heterocyclic chemistry little easy. Because likes in the previous example 1, 4; so the 1, 4 plus 1 unit in this case 3 plus 2.

Now, it depending on the situation you can remember which one is 3, which one is 4; so here 3 means normally what we talk about we talk about this inamine right. So, we talk about the say inamine right then other thing is other thing what else; you need 2 carbonyl unit. So, it has that means this nitrogen side will have to have a

Student: ((Refer Time: 12:28))

Right. So, you have to have fluorine in one case; and the alpha flora acetone kind of thing ok.

And, mechanistically I think all of us know; how do you carry out this reaction? Just simply mix them and heat it nothing else. So, all of us know there are could be 2 different mechanisms; one can involve this disbasement of the fluorine through the inamine here; and then condensation and the vice versa you can do also without any problem. But impact this is more likely that inamine has will undergoing; see one formation to give the corresponding. And then as usual ketone I mean ketone amine condensation would give rise to the product; which is now what you will see 2, 3 disubstituted. So, this is standard protocol of the Hantzch.

And, then how do make this inamine? Inamine ester also I told you before it is pretty easy to make; simply take this corresponding ketone compound out of ketone compound; and just treat with ammonia that is it. And in this case you can so just aqueous ammonia is sufficiently good enough; aqueous ammonia that would forms imine first and then isomerization inamine ok.

And, it hard third category I think all of you know this is this is call knorr synthesis; this is not that very popular though only in certain special cases they are used it is used. This is again so you have to as I said before you have to best your memory another; you have to memorize this thing on the basis of the starting metal. What is the starting metal, how do you remember? Knorr synthesis.

So, again say category it belongs to 3 plus 2. So, that means you have to know the 3 plus component; 3 component and 3 atom component and the 2 atom component. So, this how one can remember; this is basically amino ketone alpha amino ketone; that is what you have to remember 1, 4 diketone. Then, the next one was inamine and the third one knorr synthesis would require alpha amino ketone. So, that is it once you have this then this amine would require a carbonyl; and then the other part would require an active methylene compound. So, somewhat like a butyl keto ester kind of thing; and then you have I mean for different you have different substituent. And if you just again just simply heat it reflux; so what we will find? We will find through this a amine ketone condensation. So, you will get this formation of is a would much problem but without much problem here; but then it is not very popular who can tell me, why? This is not very popular is not widely use like for Paul knorr synthesis; what could be the reason?

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So, basically that mean first of all this amino ketone formation is little difficult. So, actually the number of methods available for formation of this alpha amino ketone, and all of many of you know this all amine and ketone mixed together the automatically forms you mean to some extent; once the amine is found it can undergo isomerization, ((Refer Time: 16:27)); so all different kinds of things.

So, any case but all of you know I guess how to make this amine in the standard way? Standard way is to basically you take the corresponding beta keto ester right; and then you treat with nitrous acid. So, if you treat with nitrous acid so what you will be the getting? You will be getting ketone here; and is then oxime this oxime. So, you just like the your nitration in up phenyl is a nitroso compound but nitroso compound in this case isomerization to oxime. And then this oxime is reduce with zinc acetic acid; so this is the standard of protocol ok. So, what next? So, that means you see here in Hantzch synthesis you have basically a component with nitrogen with 2 carbon C C N. And in knorr synthesis also C C N system; that is a very recent method which has been develop to but a scientist name Chiba.

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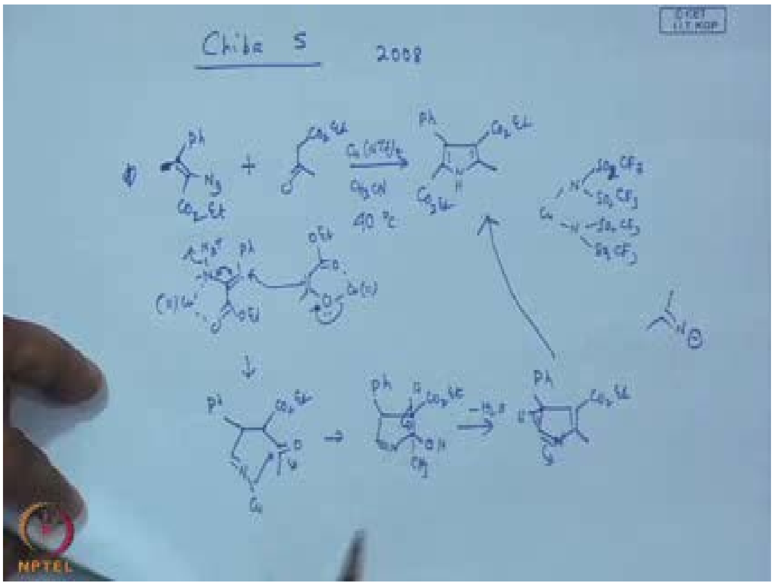

And, he developed a new synthesis in 2008; what he did he starting with very simple a study materials are very simple he used this something like this; sorry so this is what is that two azido acrylate; so this is a starting method. Then, he what he used and other thing that what he used is again a 2 carbon unit; so is in ethyl ester and ethyl ester carbonyl and C H 3. So, here see that means basically again 1, 2, 3 carbon-carbon-nitrogen. So, azide group actually provides only one nitrogen and at the end of the reaction what you get is now is a tetra substituted pyrrole. And this is phenyl then ester here and this is then in this case it is ester. So, I mean very similar to what?

If you can just basically compare this is when you proceed forward and forward you have to have something in backup your mind; it resemble something. That means, you have to a foundation based on the foundation you glow your knowledge right. So, in previous example; so we have seen 3 units 3 inamine; so it is very similar to inamine what it is have carbon-carbon and a nitrogen. So, carbon-carbon and a nitrogen and the azide actually provide a single nitrogen; and the other 2 nitrogen lost as a nitrogen molecule ok.

And, of course it is not that easy to discover a reaction I mean it took long time. And it was pretty well with a catalyst with the catalyst in this case catalyst is copper 2 Bistriflimide; copper 2 Bistriflimide I guess, I do not have to explain the structure copper 2 Bistriflimide means N here and tri fluoro sulphonyl. So, in this case so that means would copper here one more right; so basically structure would be tri flouro this Bistri flouro Bistriflimide ok.

So, this the but the amount of catalyst is very little; so normally it is 10 to 12 percent; and what else? And what is unique about this it is the structure sorry it is a reaction condition only 40 degree centigrade. So, we get very height in most cases are very good there are about I mean dozens of examples done. So, what is the mechanism?

Mechanism actually I can write the mechanism but you can also workout this mechanism. First of all see many of you know most of the transition metal like copper iron all these things they forms on the complex with diketone compounds 1, 3 diketone compounds. So, in this case what has been done here? So, it in all form I should write here in all form here let us and then in all and this is let us say ester. So, this then a it forms again a sort of copper complex here and in the other case so what will have this is a phenyl then you have ester here. So, some sort of activation must be there and this copper the actually assist actually copper serves dual role in this case.

So, basically active it activates this azide; and so it weakness this nitrogen –nitrogen bond here. And in this case on the other side actually it makes this 1, 3 diketone more nucleophilic. So, as you are used to the electron ((Refer Time: 22:42)) keeping what we can see here this is the oxygen minus you can if you consider oxygen minus. So, it goes by a this electron movement as if it is undergoing kind of a michael addition kind of a michael addition; see here alpha butyl unsaturated ester right. And beta keto esters actually forms a nucleophilic center at the middle carbon right it under goes michael addition. So, this then it forms this anine here; then anine now anine goes to a expel this nitrogen; so expel the nitrogen.

So, what we eventually get? So, what will have this is ester part and then this should be converted to the ketone and then you have this phenyl group. And now you see here the carbon and nitrogen will be now carbon double bonded nitrogen; and then copper to is attach to the nitrogen now. So, I mean you can have all kinds of mechanism but to my mind nitrogen is now a sort of a nucleophile again a carbon nitrogen minus; so this to this minus would now condense with the ketone here and right.

So, nitrogen, ketone and this is O H and the C H 3 and then ester eventually you work it up and then ester. And I think from now onward all of us should be able to write this structure right. So, this loses water and so what will be getting? You will be getting this part unsaturated then I know then what? Then, obviously this imines do not stay in the form here; so in the presence of acid it will protamarise to the corresponding this one.

So, what is the conclusion, how do it how do describe this? How do the whole see I have full slide. Now, we have to describe; how to describe? That this is was procedure depends on the utilization of vinyl azides this is important number one. And other component is beta keto ester is a standard protocol in pyrrole chemistry fine. Second important is that you need a copper triplet sorry triflimide copper triflimide is the catalyst; and what else? And you require a ester group here; so that initial michael addition is feasible fine.

Then, it will and what is the very important here actually this is unique mechanistically; reason being you will not see many examples where you will have an imine nitrogen minus. Then, what I am talking about system like this you will you will rarely see something like this; we see imine we see ((Refer Time: 26:21)) everything but here you do not see something like this one. So, this is being formed and very easily with 10 to 20 percent of this catalyst.

And, then but it has some limitation though it has some limitation; what is the limitation? It requires electron withdrawn substituents like ester; but same person in same year a letter paper what he has done he had just modified this clues.

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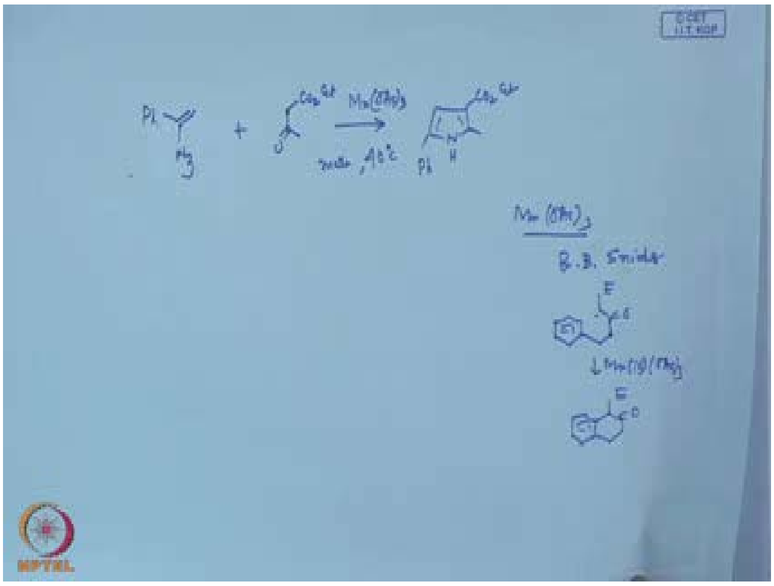

He has modified this and what he did again phenyl azide in this case there is no electron withdrawing group, and this then again a beta keto ester here ok. Now, what; how to so you have just basically again at around 40 degree centigrade in methanol; in presence of a catalyst he could produced the compound of this kind is a phenyl here. So, what is the again this is a 3 component 1, 2, 3 carbon-carbon-nitrogen; in this case 2 atom component. So, principle is same; instead of the ester here you have a phenyl but that did not work under the influence of the copper catalyst. So, you have to choose a right catalyst; so what is the catalyst could be?

Let us say when the many of you this research scholars right; when the reactions fails what do you do? When a most obvious reaction fells what do you do? You repeat first whether you are your hands are doing any mistakes or not; you fails second time then what do you do? Check the reagents. So, there are so many steps actually; if it genially fails then of course then you have to think about the reaction mechanism revise your the project or the scheme ok.

So, let us say in the I mean paper say it does not work with the phenyl azides without electron growing group. So, what can I do then? He could solve this problem in the same year; he just change the mechanism. Because we are organic chemistry right; we know good we have good knowledge of mechanism he change the mechanism. And mechanism and we have in wide area of mechanism add one and you have carbonium ion and the other end you have carbon ion; in the middle you have anion radical, anion cation, anion radical all this is radical carbine, nitrene all these intermediates right.

And, there are other possible is the pericyclic reaction. So, this we have a wide range of the reaction mechanism; in fact when I mean all of us know the michael addition requires electron withdrawing group. But also at the same time we know radical does not require.

Student: ((Refer Time: 29:34))

Does not.

Student: ((Refer Time: 29: 37))

Does not require even take polystyrene could would you know just empty bottle it would gets polymerize. So, if ((Refer Time: 29:44)) even polymerizations can be done under cationic condition, anionic condition, radical condition all so one is the this. So, actually what he used in this case he used a manganese triacetate; why suddenly manganese triacetate that also important I mean fall so many acetates, so many things; why suddenly manganese triacetate? Because in the literature in the if you go to the carbocyclic chemistry we will find manganese triacetate is known to produce radical on the carbon between the ester and carbonyl fall beta keto ester that is a another standard protocol. I mean so manganese triacetate is a has been a very useful reagent, and one of the pioneer scientist is Barry b snider; he has made of lot of carbocyclic I mean at the movement I cannot give you exact example. But I can roughly give you what he has done; let us say if you have something like this. And then you have ester group here I may not be exactly correct but almost correct; something like this then you treat with manganese triacetate. So, you are likely to is unlike simple aromatic chemistry; you can get this sort of compound.

What is the mechanism? It looks like a ((Refer Time: 31:25)) reaction right; but it is not actually it produces the radical here. Then, of course the benzene can trap this radical etcetera then rest of the things as usual. So, this is what this is what he has modified though; I mean you can sit down and to this mechanism no problem. Just again let us say how he did I have not picked up. But just basically he had used manganese to produce radical here, radical under goes coordinations. Then, keeps on adding electron transform here and there eventually you get this loss of nitrogen like the previous one; only thing that he has involve to reagent which can produces a carbon radical. What next? Again, the same similar very similar compound you just look at the compound; and just give you one more compound.

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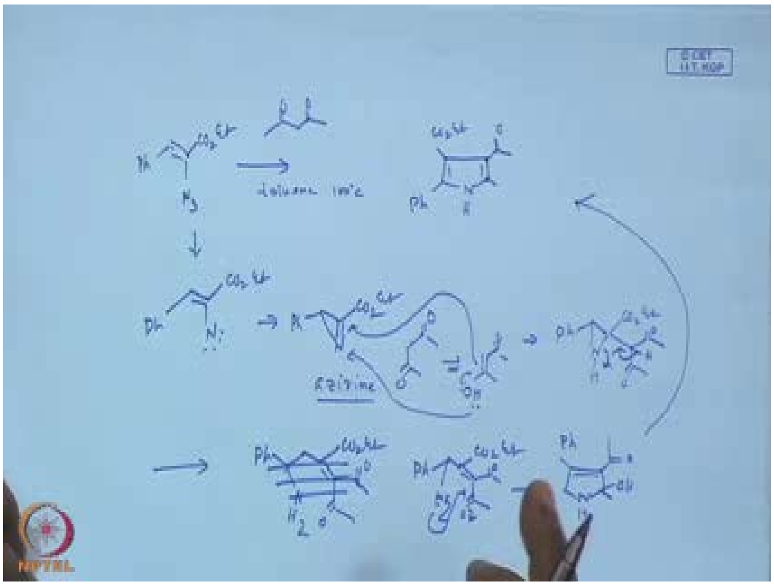

And, the same compound let us say the one we did previously. Let us a take ethyl and the phenyl and take acetyl acetone. Then, just heat it in toluene at 100 degree centigrade; you get 100 percent yield of a react of a your product; there is pyrrole. What is it? No, catalyst now; if product is this and phenyl; and in this case we have here is in a ester group here. So, what do you see carbon-carbon-nitrogen that means azide phenyl azide gives the carbon-carbon-nitrogen? Then, beta keto diketone gives this again this only 2 carbons for the pyrrole; and it is strikingly different from the other 2.

What is the different? Other two is also very similar but if you go back and see in if with copper Bistriflimide the phenyl was at the 3 position right. But here you get the 2 positions; that means the reaction is somewhat complementary. And then reaction condition is very result simply mixing them and heating them in the toluene ok. So, what do you guess? So, what is the mechanism then? That means, we have change the mechanism now form copper which is a michael addition with manganese with radical. And what else typically think of here any mechanism; what is the mechanism you can think of?

Student: ((Refer Time: 34:34))

Carbanion in case of copper.

Student: ((Refer Time: 34:39))

What will be generated?

Student: Carbanion will be generated.

Carbanion see I think in the fourth year also we talked about this thing; how to see in the very first class we talked about the classification etcetera. So, see you are starting any for any organic purpose when we even listen to the seminar you know you try to concentrate on the reagent thing, try to recognize the reagent ok.

What is the reason in this case? A heat only heat and when we when you come across heat then you go to the straightway go to the pericyclic chapter right. So, thermal reaction most of all the cases all these thermal reaction are the pericyclic reactions. And other cases and you get this neutral intermediates nitrenes and carbines. So, the all that means under thermal and photolytic conditions what you come a across only pericyclic reaction and nitrene, carbine all these reaction benzynes; those sort of reactions thermal conditions also you can produce the benzynes; say reacting intermediates or neutral reacting intermediates not carbanion, not carbonium ions ok.

So, I mean I think answer is now given write; what is the answer? It ester here it produces nitrene; so what next? If nitrene is produce then it forms the nitrene is produced it forms this is p H. So, it will be forming nitrogen double bond this thing p H and this. So, what is it? Azirine right; so you get this is p H sorry so not aziridine so azirine nucleus you get; then what?

Then, you have beta diketone right; all of us know that in the equilibrium and it is a phenol. And you have now this vinyl hydrogen can be transfer to nitrogen here and then this goes to carbon double bond nitrogen; what is this reaction? Thermal condition; pericyclic reaction.

Student: ((Refer Time: 37:46))

Very good.

Student: ((Refer Time: 37:48))

Very good in reaction. So, in reaction so once you have this reaction that means p H now; and nitrogen you have this ester here and then this one; and what next? What is the expected next here see many of you people already know aziridines unlike epoxide it has specialty? What is this specialty unlike epoxide it has a special kind of a reaction or other between epoxide and aziridine; if you have proper activation you will find azirine opens up very quickly, ring opening takes place; that is what right be take in your lab what you do aziridine ring opening right you do not do that ok.

You will see there is lot of papers comes ((Refer Time: 38:55)) lab you will find aziridine ring opening and then recyclization aromatic compounds. So, that is but in this case there is a not much activation though but under the thermal normally this nitrogen is substituted by sulphonyl group or electro withdrawing group. So, that you can make it open; and so once this is done then one can see that there is a thermal ring opening. And then of course you can impact simultaneously do but formally one can write this; so a though double bond here, carbonyl and this is a carbonyl here.

And, you can write nitrogen N H 2, N H 2 right then of course 1, 2, 3, 4; I think 5 any mistakes somewhere may be I think you had made a mistake. Yes, number of carbon is increased. So, is the write please; so that means this ester here double bond acetyl group then you have acetyl group here and you have N H 2; 1, 2, 3, 4, 5. Now, a just a regular condensation of amine and etcetera; so we will be with O H, methyl here and then double bond ketones; and this is a phenyl here and all these things. So, eventually you go to the product.

So, you see here that means so what is the conclusion? The vinyl azide is a very versatile substrate; you can use it in different fashion but one of the other reacting component has to be one three diketo compounds. And vinyl azide does not have to have necessarily the electro withdrawing group. So, you can have all different kinds under cationic condition; a sorry anionic conditions sorry under radical conditions, anionic conditions and thermal conditions ok.

And, same so that means what do you see in all the 3 examples we see if you see that 1, 3 diketo compound and it incorporates at least one electron withdrawing group. Because you one of the components is 1, 3 diketo compounds but again in 2011 very recently what has done just a small modifications here.

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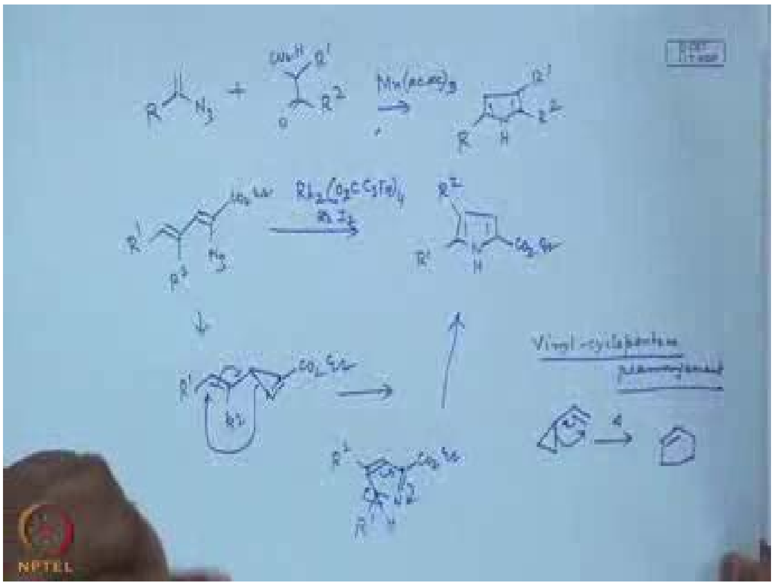

So, that you do not have to have let us say if you taken R again vinyl azide. Now, in principle it is a diketo compound now let us say R 1 and R 2 here; it is see very similar to the previous example; this is also beta ketone acid now. But without the carboxylic acid it is looks like a just a simple ketone. So, result would be then this is a pyrrole with now plane alkyl groups now without a ester group and this ester group and this. So, that means from the corresponding beta keto carboxylic acid very similar. But in this case because it is a carboxylic acid eventually it is lost from the reaction. And in this case the mechanism is very similar to again a radical mechanism but a catalyst here is manganese acetyl acetone. And the percentage of course is a normally 10 percent ok fine.

What next? I think when I talked about the this let us say there are other methods may be very similar fashion actually; let us say now if you have an azide and again ester then double bond, and something like this. Now, do the same thing very phenomenon in the so now we have azide now we do not have second component now; it is just phenyl azide now in this case 1, 2, 3, 4, 5. So, you have all the carbons and nitrogen what will find if you use dirhodium carboxylate in this case the carboxylic acid is a heptafluoro propulate right.

And, now on it is I think a dirhodium it is it has to be 4; and the catalytic amount of zinc iodide; what do you expect? You expect here and once again a pyrrole and many of you can guess what is the mechanism right? And let us say we could R 2 here so it is R 1 on this side, R 2 here this side. So, what is the mechanism? Again, nitrene. So, many of you probably know that rhodium is a has a I mean let us say if you want to do a produce carbene from a diazo compound; what is the catalyst you use often?

Student: Copper.

Copper right; copper, zinc copper, copper sulfide is also sometime work so produce it. So, to produce nitrene or nitrene with similarly also the dirhodium as tetra acetate is a very useful catalyst to produce carbine from diazo compounds. And in this case it is basically producing the nitrene. So, once you have this nitrene then I can I think all of us can all of us can write I have now work it out but I think if you have nitrene. So, what will find here nitrogen double bond and right and the ester.

So, you say again azirine right; and what next? I think those who will be specializing in organic chemistry; I think they must doing it one reaction this is a very facilitating reaction though very facilitating reaction. This is known as vinyl-cyclopentene rearrangement again a thermal reaction; this is thermal reaction phenyl cyclo pentene rearrangement.

What is it? It is nothing but you see here the starting metal is vinyl cyclopropane if you heat it I mean again just like in temperature that means 200, 300 degree centigrade just heat it. What we will find? We will find a cyclopentene is a very good reaction I do not know why most many people were interested one point but now I do not see many examples literature. But very general reaction you can accommodate all kinds of the substituents in both the substituents I mean in the starting metal on the product. And if you look at what is the transformation basically? It is basically although many of you know in the pericyclic reaction 1, 3 sigma tropic arrangement is not allowed right; not I should not say not allowed is not favored. That is the but what do you see here this is a thermal is a thermal 1, 3 safety; normally 1, 3 safety which is often seen in photo chemistry ok.

So, if you just basically shift this sigma bond to here 1, 3 is a shift sigma bond. So, that is what I mean so all these reactions now here. Now, you see there are plenty of examples in heterocyclic chemistry although carbocyclic it is only limited to the vinyl cyclo propants, cyclo cyclopentene rearrangement; in heterocyclic chemistry we will find plenty examples where you will find one three sigma tropic set. And in this case I mean see here this bond comes here migrates right. So, the that means this end breaks migrates here and 2 components discharge and this double bond moves that is it.

So, what you will find? That means, this is ester here nitrogen now if you bend this so this should be R 2 and now this is R 1. Now, you know once it is forms this way; then of course there are ways to isomerisation to corresponding the product. So, we are running out of time. Let us look at one more very quickly; so you can say this is considered this is considered to be ring expansion now right. So, vinyl cyclo ring expansion next example I will show you something quite interesting.

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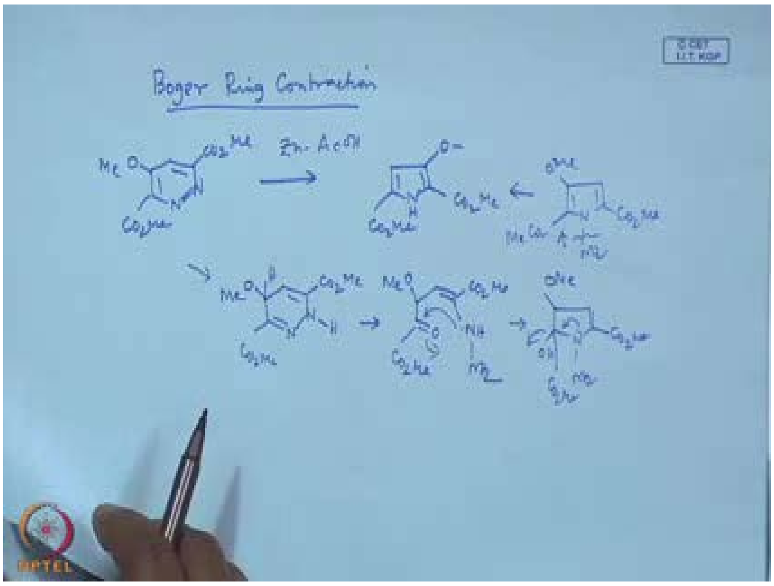

This is I would name although it was just called by somebody else; it should be named as ring Boger ring contraction; what is it?

See, if you have pyridazine like means 1, 2 nitrogen and then ester group here; ester group on the other side, and then methoxy in one step it is a very beautiful reaction; we have been try to do it so for we have not list the point; what you will see? So, we will get in one step is it not very interesting; how do you get it? See, one nitrogen is coming out; so that means you have to choose a reagent and one nitrogen means it has to be ammonia. So, it has to be ammonia then you have to supply hydrogen; so how do you get the hydrogen? In this case the reagent is almost always in almost always zinc acetate, zinc acetic acid sorry zinc acetic acid.

So, mechanistically there are many possible mechanism but it is now agreed by most organic chemist; that it gives first a dihydro compound where dihydro compound where hydrogen are added across this pyridazine nucleus in 1, 4 fashion. Then, rest up to this first everybody agreed there by rest there are so many different possibilities ok, nitrogen-nitrogen can break can this thing, that thing.

But what Boger suggested this bottom portion this one this is imine. So, it will undergo hydrolysis and then you have the rest of the thing here N H; then you have N H 2 and this is O ME right O ME. So, basically you get the hydrazine kind of thing hydrogen kind of thing. What next? I think all of you guess now; once it is opens it was a six member ring in the beginning of the class I said the formation of a five member ring is very special. So, obviously then it undergo condensation with carbonyl group and rest; so you will get amino pyrrole now. So, amino pyrrole O H and this is the ester part here; this is again ester part and then you have a methoxy here right.

And, I think some mistake somewhere so far O H right. So, let us say then probably I think; eventually it has to reduce this I think this suggested that it has to be methoxy here then ester methyl ester and this methyl, there are methoxy. And then obviously then it has to a undergo nitrogen-nitrogen cleavage; one more nitrogen-nitrogen cleavage to corresponding this pyrrole ring system; obviously all of us know nitrogen-nitrogen bonds are pretty big bond compare to carbon-carbon bond. So, this is a possibility ok.

And, what else? So, I think we have talked about ring expansion, ring contraction and we missed one important point today that is basically initially we talked about that alkyl precursor. If you go to the literature now days you will find in many cases the alkynes are being used. Because they are relatively optimable and it can display variety alkynes can display varieties of reaction; one of these reactions I will just this is last example today.

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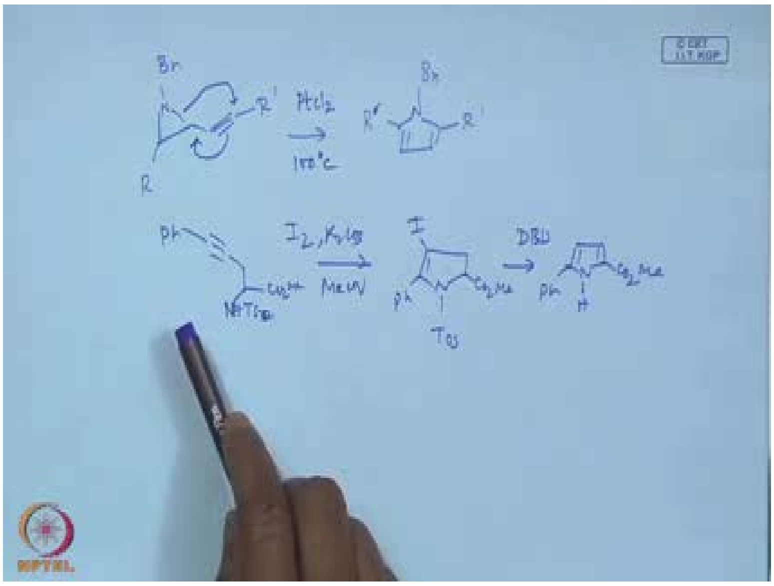

If you take this aziridine here and then you taken a alkynl bond nitrogen and this is benzyne R. So, what will find in one step; one can produce this is benzyl here and this is R in to produces sorry R; You can produce this pyrrole ring system. What is the mechanism? In this case how do you do one can think about thermally because if you look at it is formally a 1, 3 sigma tropic shift. But in this particular example platinum chloride has been used platinum chloride; and around temperature 100 degree centigrade many of you know I mean this is O N O; this noble metal can activates the triple bonds.

So, either gold solubilize gold catalyst, platinum compounds, and this is because platinum. So, you have to use water and dioxin is a highly polar solvent to make this reaction gold. But once again mechanistically it is basically the platinum closest to triple bond. So, it is gives the double bond character and then all these migrations takes place migration takes place. But formally this one can think about just as if it is a 1, 3 sigma tropic shift.

So, likewise there are many likewise there are many examples actually likewise there are many examples. There are other kinds also there are I mean one can think about let us say alkyne; and then let us say N H tosylate and then ester here let us say phenyl. Now, how can you make a pyrrole unit let us say? Again, you see here from slowly to slowly I mean ketone compounds should vinyl azides. Now, we are talking about the alkynes ok; alkynes could be group successor pyrrole precursor, pyrrole products. And how do you do this is tosylate sorry this is tosylate. How can you cyclise? One of this way is activate noble metal like platinum, gold, mercury, silver all these things actually all of us know activates triple bond. But there are also in non-metal which can activate the triple bond; what is it?

Iodine; you must of heard the term iodolactonization. If you have olefin and the remote carboxylic acid right you have not; I how come you do not talk to your lab mates. He should actively you also on hydro cyclic reactions, hydrolactonization I think some works is based on that. So, if you if you do in this example let us say just iodine, potassium carbonate and potassium carbonate and acetonitrile you just in one shot you will get this done corresponding iodine activates this tosylate.

And, this then obviously I mean you have an leaving group and if you just add D B U and that at room temperature it does 2 things. It creates a double bond isomerization is a double bond and tosyl is also removed. So, I mean such 3 purposes but main thing about this example is to see that cyclizations. And you are starting material; so today basically we concentrated on this nature of the starting materials.

So, 4 units study metals, 3 unit study metal and in most of the other reactions are obviously 2 or 1. And so substrates varies from these substrates varies from this amino ketones, diketones all these things; vinyl azides is a very good source of pyrrole unit. And now we are seeing this aziridine also could be pyridazine. Pyridazines means that the substrate use for the then there are so many actually, there are so many methods on alkynes; I mean if you are interested I can show you the printout I have there is a let say more than I think I counted here.

And, this is printout taken from organic portal it is keeps only giving only pyrrole there are more than 60 different methods. So, but mechanistically an ideally they enterer only few things either poly knorr or ((Refer Time: 59:15)). For example, you can say Paul knorr the one that we talk about the nothing but this is Paul knorr extension; why? Because all of us know acetylene can be converted to corresponding keto compound; how?

Student: ((Refer Time: 59:29))

No, that mercury mercuric sulfate or this thing that thing. So, that means when you are using a alkyne essentially is a carbonium precursor; so like that you can go on mixing that things.