# Heterocyclic Chemistry
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## Lecture - 21
## Dehydrogenative (Oxidative) Cross-Coupling

Good morning, and so what we see now or what will see, today something little different from Cross-Coupling, but yet the name is Cross-Coupling and if you see the name.

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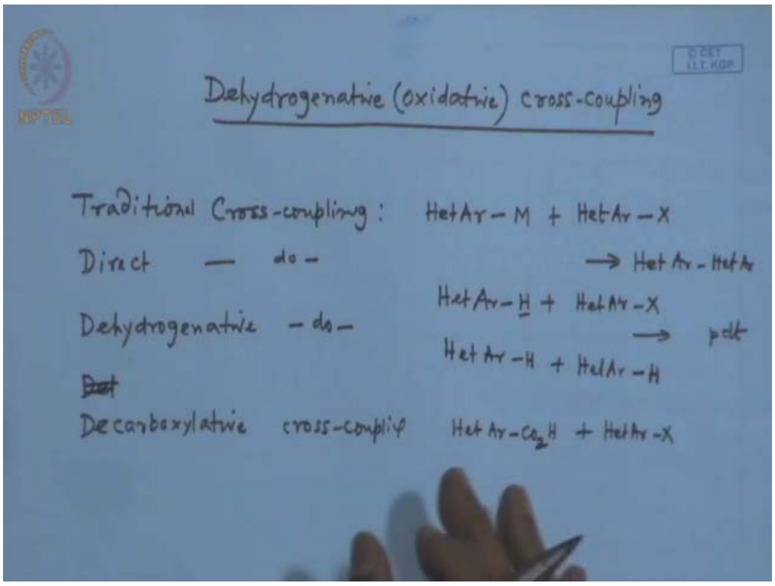

Dehydrogenative (oxidative) cross-coupling

Traditional Cross-coupling : HetAr – M + HetAr – X
Direct — do – → HetAr – HetAr
HetAr – H + HetAr – X
Dehydrogenative – do – → pdt
HetAr – H + HetAr – H
~~Deat~~
Decarboxylative cross-couplig HetAr – $CO_2H$ + HetAr – X

The name implies dehydrogenation oxidation reaction, so it is a dehydrogenation all of us know oxidation. So, dehydrogenative and in bracket, I call oxidative and cross-coupling, so by now all of you have known what is the meaning of cross-coupling right. Cross-coupling what is the meaning.

Students: ((Refer Time: 01:08))

No even it is broader, it could be carbon nitrogen also involves carbon nitrogen. So, and typically, most of metals are of course, paradigm and some cases nickel and some cases rhodium and some cases many other metals also, but mostly. And so first if you summarize traditional I say cross-coupling, so and it could be abbreviated as traditional cross-coupling, it should be abbreviated as what you need necessary group is in heterocyclic chemistry, so I will say het A r means, heteroaryl and then what then a metal or metalloid metal or metalloid right.

And then you take one may be, hetero aryl may be and then x, so the product is so het aryl and het aryl combination product, so by aryl product, so that is the traditional 1. So, you have to recall that these sort of cross-couplings moved require a metalloid or metal metalloid or organometallics, you can say organometalloids and then the corresponding the halogenated compounds deflects and ammonium salt or the diazonium salt all these things.

Then we have also seen something like called direct cross-coupling is something like you have a hetero atom heteroaryl group and hydrogen, we have seen only one example hetero again aryl and x, we have seen only one case in the last example, if you have aryl C H with intermolecular, this can go to the product is again, this is diaryl and biaryl. In this case what you that means, hydrogen is somewhat, analogues to a metal like silicon, we call some super hydrogen means, this is metal, but metalloid, we can say.

And so let me say it has some hydrogen reactivity and so that means, that the direct cross-coupling where, we do not have a metal rate or metal derivatives and then the today's one dehydrogenative cross-coupling. So, and what it is now, we can say hydrogen and one more heteroaryl and there is no x just basically, hydrogenation dimerization, so dimerization right.

And what is what are the other possibility, there is a possibility all of us know, but that sort of combinations are not very useful, what is the other possibility, in early in one of level, we have learnt that, if we have a carbon metal and a carbon metal, you can oxidatively dimerize like sodium salt ethyl acetoacetate treated with iodine, it gives a corresponding dimerized product. So, you can say two metalloids, that means, hetero another hetero metal can be oxidatively couple to the corresponding biaryl compounds.

And there is one more very interesting and quite I mean, very useful are the very useful coupling is coming up, that is not well studied, but there is a possibility that, in future this reaction could be a popular reaction again decarboxylative cross-coupling. What it mean by that that is an heteroaryl instead of the hydrogen, we can take a carboxylic acid and then other reacting partner should be heteroaryl like any other reactions like halogenations are next.

So, any other that means, in other words by giving, if the this chart, I am try to say that the sort of cross-couplings are very, very broad, I mean almost any kind of combinations can be used to make a carbon-carbon bond formation between the 2 aryl unit or alkyl unit or heteroaryl units. Since all class is on heterocyclic chemistry, we will have example from heterocyclic.

And today especially, we will concentrate on basically dehydrogenative means, at some point somewhere, you need an oxidizing agent, oxidant and the catalyst obviously, the metal are normally paradigm, it should be in a lesser point, it means less than may be 20 more percent.

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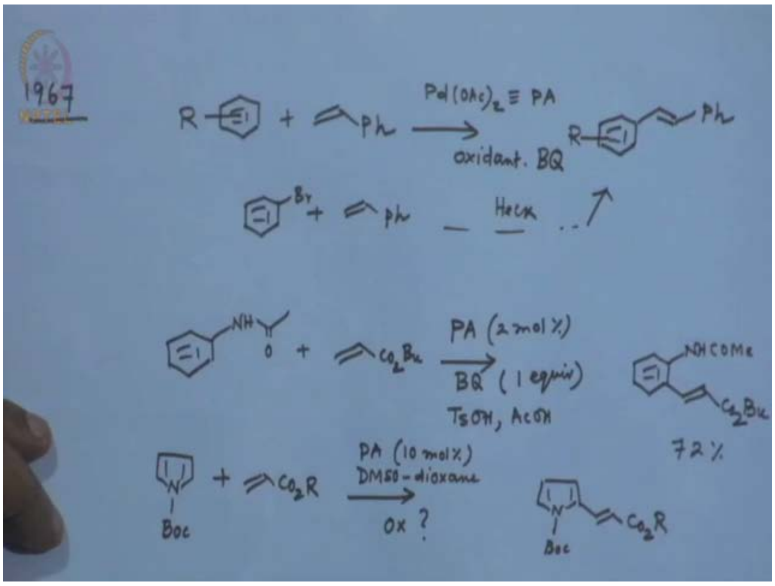

One of the very first examples in this idea was published in 1957, historically this was again by a japanese person call murithani, what was the reaction, the reaction was a simple benzene and styrene. The of course, paradigm acetate, so from now onward, I will write paradigm acetate name it P A, how is that abbreviate, because where the paradigm acetate, in this lecture will come in a many times.

So, I will write P A, so and an oxidizing agents say oxidizing agents is an oxidant is some many times is B Q is benzo quinone and what you get actually, he they were getting a product which is called is stubble right, and previously, how we made, this compound starting with corresponding bromo compound and this styrene. And then again this is the typical heck reaction, but then we can go on writing things like, this suppose if you have R here substituent’s, so you will have R here, obviously, then you can have broader utilities of this reactions.

But, these monotonic reaction the first one that means, without any halogen without any metal, you can do the cross-coupling type of reactions, but the yield was poor, religious selective to us poor mean, if you have an R here, you can get all kinds of products. Now, thirdly, they have to use a lot of excess amount of the arines I mean, so that is basically wastage like in filter of reactions, you get you put lot of arines actually, equivalent of arines is more then, we correspondingly alkali halides.

So, but it was in indication that it is possible the without a metal, that sort of reactions has been tested in an non-heterocyclic compound, suppose you take acetanilide and then as usual an acrylate. In this case butyl, because it is little higher boiling and again P A, I use a paradigm acetate percentage is very little mole percent and then B Q.

So, mind it now, is an oxidizing agent say 2 hydrogen’s are getting eliminated from this let me see, what should be the equivalent, it should be at least one equivalent, because you have to remove 1 equivalent of this hydrogen and the other catalyst is other equivalent is toxic acid and acetic acid.

So, throughout these you know basically, we will study the reactions, we will see the electronic, we will see the acidity, we will have a set of reaction conditions and products all of us known by now know product should be some sort of a byaryl all these kind of things and one of the components could be heterocyclic that is it. But, while I write you have to just note take care of the types of the religions, types of the oxidizing agent, you need to do, we do not have many options the very few options very few, that is what you have to note.

And also you have to note this homocoupling etcetera, why the homocoupling is not taking place and particularly one, then regioselectivity all these things, in this case what do you expect you say i mean normally we do not expect reaction right. Because, it is not satisfying the prerequisites of hake reaction ((Refer Time: 11:07)) reactions etcetera, but you say again a new kind of reaction. So, if you see the product you will find, it is a nice way of so it is I should say it is known as alkynylation, it should the means a benzene leak is being alkaline metal.

And other portion is as it is this is a single product, the percentage yield is 72 percent, so what do you see here, that is what you have to see, you have to see the striking features of this reaction striking feature. What do you see this striking feature is very ortho selective, whenever you do a reactions like anilines etcetera, all these things, they will definitely give you the a larger quantity, but in this case you have very ortho selective.

And then what else, you do not require metalloid like boron suzuki and then zinc magnesium lithium, you do not need anything just and that to paradigm, you see all those very expensive, we can only 2 mole percent. Only this advantage, we can see benzoquinone, benzoquinone is quite expensive also in large scale it is not a vulkem reagent right. So, you will see some more reactions, where the oxidant a oxygen is the terminal oxidant, so in that case we are very good, you should be classified as the grain reactions.

Any case that was an indication and now if that is, so because if we recall aniline has resembles with an heterocycle, what is what is the heterocycle, which resembles very good pyrrole or pyrrole. So, that means, that means if this works here, then the next reaction that should work, it should be pyrrole and in these case, it is the boc, let us say the nitrogen has to be protected. Otherwise all of us know the pyrroles are successable to undergo oxidation gives you what right.

What is a polymer poly polymer no there is a popular polymer call panni, what is it right polyaniline, this called why few years ago by 1 american and 1 japanese alan megabit, he write few years ago and after ((Refer Time: 13:59)). So, that means, what I mean to say these heterocycles like anilines where successable to undergo oxidation, few also this undergo acetic, so you have to think about that and so you need a protection here of a nitrogen.

And we will see some of the cases probably, we will see, we do not have to do the protection, if it is inter molecular reaction, so in this case, let us say just, we do not worry about the alkyl part, I write let us say R here or butyl whatever. And this again P A means paradigm percentage, in this in this example, that is 10 mole percent and D M S O as a solvent, D M S O is a solvent with a mixture of and in combination with dioxane.

So, what is the expected product, see here, you see you do not require any metalloid and the reaction is, so good you get this product, what is the oxidant oxygen, So that means, you will find some many many examples about, I think we have already seen, such a thing means same reagent sorry.

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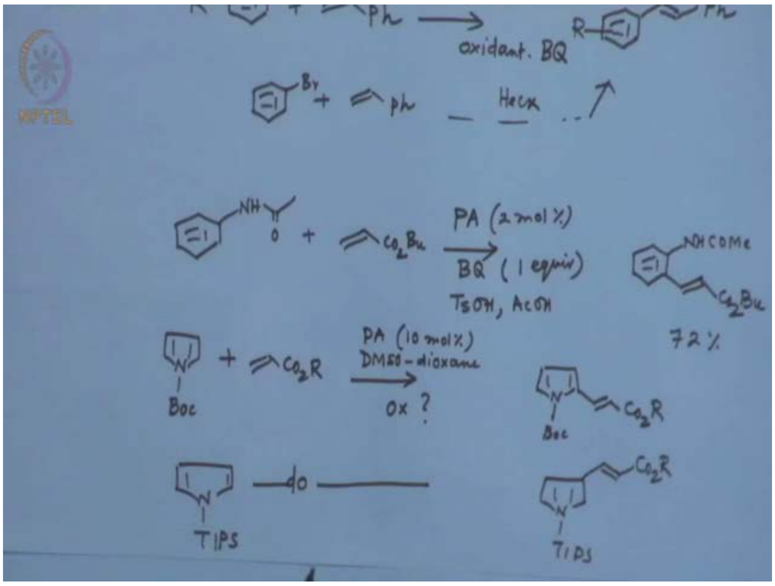

So, what do you expect, same condition only one thing, we have put a silicon here, tri isopropylsilane positions actually, is the yield is not mentioned, but it suppose to be very good yield and tips and this. So, what works down to is that, it is not require to study suzuki hake and all these things that, you can do without metals, there are many other examples for, let us say in case of now, I mean you can just pick up any example.

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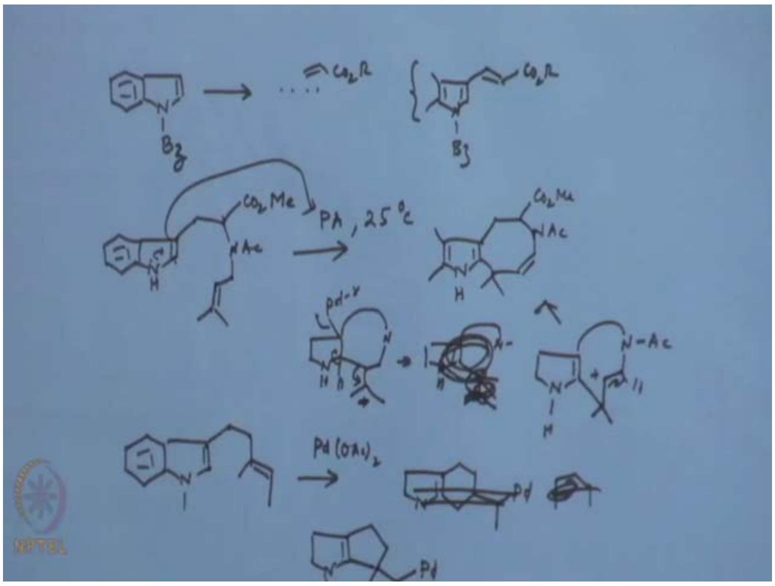

For example, in this you say the indole derivative and it is benzoid and do this again the same kind of reaction with acrylate and obviously, the product would be I do not have to write, I just you can abbreviate again the product would be this type reaction, what is the advantage. So, I mean you can do that means, it is quite is what is the advantage, advantage is that you know see although, you are being an homologation by 1 2 3 carbon atoms.

You can actually, you do all kinds of manipulation, I do the hydrolysis convergent to carbolic acid do the de carboxilation, you get 2 carbon homologations, you do the homologizes n, you get 1 carbon homologation that means, once we have a 3 carbon functionalize, 3 carbons, you can have all kinds of possible homologations. And next reaction would be again from indole series and now you see, this little interesting, this is a tryptophan derivative and then say a phenylated compound.

And it was very recently discovered and mind it the temperature is protein low just room temperature, so what do you expect.

Students: Cyclization.

So, cyclization taking place. And but in these case, I mean this cyclization is little again a trig cyclization with little bit of the rearrangements and so what do you get here, you get 1 2 3 4 5 6 7 8, so you get a 8 member ring system and nitrogen up here ester up here. And then an A C and double bond and which is later unusual though, which will little unusual this one and you can sit down and you know workout the reaction mechanism.

So, what is the what could be the mechanism paradigm acetate is an electrolyte, so if you have paradigm acetate means, if you have this spring, it will go to the paradigm. So, we will have a carbocation here, at the second potion that becomes C 2, then we have a lipophilic here that means, you come to this and this lipophil, then you get a carbocation here. The paradigm then up to oxidative, if you have paradigm something, so it will again reductive elimination will go on this thing.

And eventually, what next you see here, if say 1 2 3 4 5 6 7, so you have to make it 8, you have to make them 8, that means, use a carbocation here, which is less lightly though, it will undergo migration here. So, you get a positive charge here, so nitrogen and this and so nitrogen here and sorry, forget about it, hydrogen and this thing and then let us say as nitrogen here and now this should be plus right. And then you have something like this and obviously, what next I mean all of us know is the basically, the eliminations, so elimination to get to the this compound.

Students: Sir actually, paradigm formation is to double bond as well abstract the hydrogen forming a hetero 4 time system and the electron density on the tertian carbon is more. So, that is why that arise analytic forming a then that attaches to the pyrrole ring.

Then attaches with the pyrrole ring, that means, carbon is directly attaching this.

Students: ((Refer Time: 22:22))

Actually there are many examples, the paradigm indole chemistry has been, so well established. So, apparently indole should be more nucleophilic in nature not the reverse.

Students: Sir, how that is true 2 carbons.

Which 2 carbon.

Students: Sir, because the addition happens 2 carbon and the external.

Right

Students: Carbon chain

Yes 2 carbon yes in indole, if you let us say 3 carbon is blocked, all the substitution as take place at 3 position, that is well establish as well establish and so many example that is why the mechanism has been suggested this way, yes you can all go all let us look at like this, one more example from the indole series. In this case again paradigm acetate, so and what do you expect here, paradigm acetate, so 3 position is blocked, 3 position I mean 1 can do, I mean all kinds of thing, I mean you can do this activation here and then reactions from this side.

And this thing eventually, so that means, one can expect a reaction, and right sorry sorry sorry sorry.

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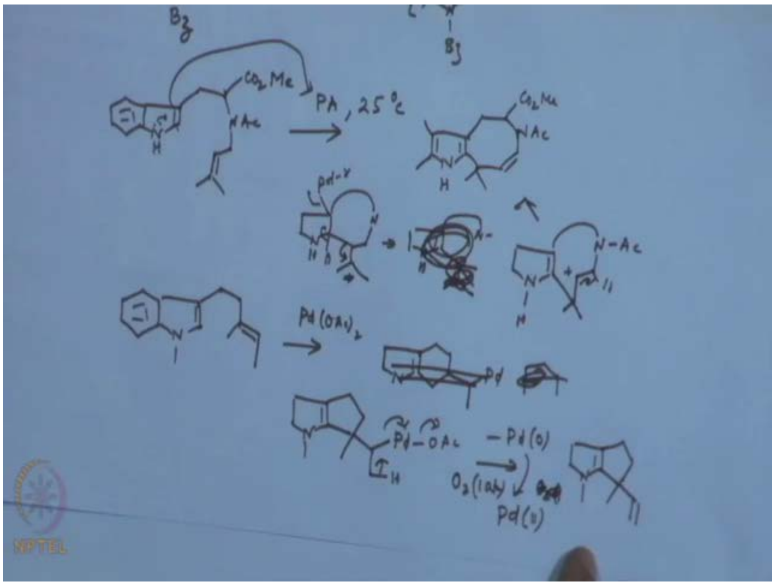

It should be 5 member then, again it should 1 2 3 4 5, so say 5 and one can expect a paradigm of here right. This methanol and what is the fine. Now what so now, I will mention that is it that means, you are losing paradigm 0 and the product is what do you get is the so what is eventually, if you look at eventually and then paradigm 0 must be converted into again paradigm 2 and this sort of paradigm 2 a 0 can be converted by simple oxygen, just one atmospheric oxygen is enough, oxygen one atmosphere is enough.

And this if you just look at the oxidation state of the starting material the product, you'll see is nothing but is an oxidation and also if you compare the molecular formula, they differ only by 2 hydrogen's. So, and that is why these are this sort of reactions are known as the oxidative coupling and while interestingly, if you do such things, I mean like if you try to extend this sort of reaction to paradigm this reaction would not takes place, so what is the requirement. So, that means, most of the 5 excesses molecules would be reactive indole pyrrole thiophene benzothiophene all these things. So, this sort of oxidation reactions or dimension reactions are less important in pyridine chemistry.

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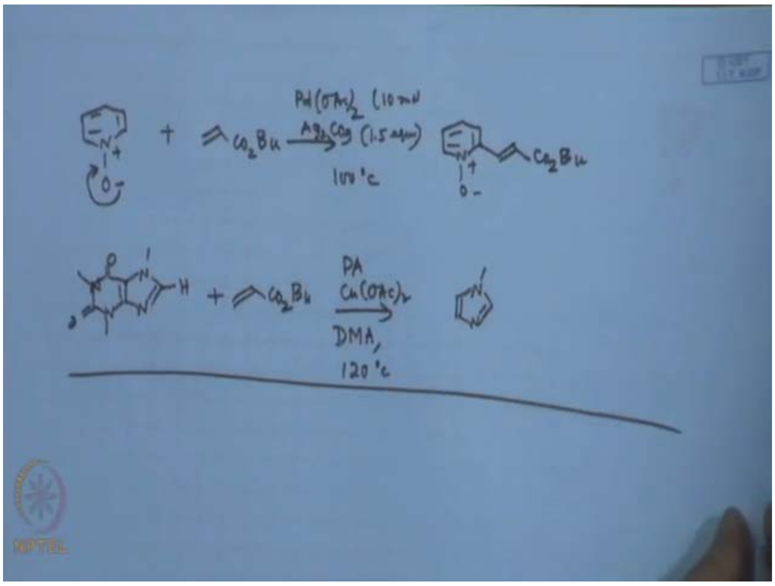

But, then someone has to try and since, we all know that, this pyridine oxide apparently it should be, where to do [FL].

So, pyridine an oxide all of us know it is more, electrophilic or nucleophilic although, we put an oxygen of here and nitrogen here. And in terms of nucleophilicity or electrophilicity around the nuclear position means, the ring carbons then it is more nucleophilic and if it is reacted with this acrylates, now is a butyl acrylate and once again the condition here is paradigm acetate.

And the mole percent is 10 mole percent and what you are likely to get and this and I want to able to explain to you why the region chemistry is C 2, but it gives you this C 2 alkinilated product. So, special case probably increase electron density in the ring all of due to the electron delocalization of the oxygen minus all of us know and this. Then what else you require an oxidizing agent, in this case this oxidizing agent is silver carbonate and 1.5 equivalent and then 100 degree centigrade.

So, long we have come across from how many oxidant, first was benzoquinone, second was oxygen, third one is I mean silver carbonate and only recently gain, I mean they are all different only recently very recently, this sort of reactions has been extended to other heterocycles. But, in this case of course, it is apparent nucleus, purine nucleus and all nitrogen’s are protected here, so all of us know this purine, this kind and if you have only one hydrogen functionalizable, so imidazoles typically, nucleophilic in nature.

And then the other gain acrylates butyl acrylates and P A I write, then what else this now the new oxidant here is a cupric acetate and the solvent is little different D M A dimethyl n n-dimethylacetamide acetamide little higher boiling higher boiling. So, you can temperature can be rise to 120 and then, so we can all of us can now write the product right. Without any, so product, so once, we have that means, in this case now oxidant is cupric acid, that is all I mean those sort of oxidations are chosen by doing lot of trial and error experiment optimization experiments most cases most cases.

And So, I mean this paper has given so many examples, so that means, this sort of dehydrogenations with 5 member systems general useful and now what will show you something quite interesting by different reaction conditions, you can direct the alkinilations in different positions. This has been again published quite some time ago and what we will find, that with cupric acetate the reaction goes to the a 3 position in case of indole.

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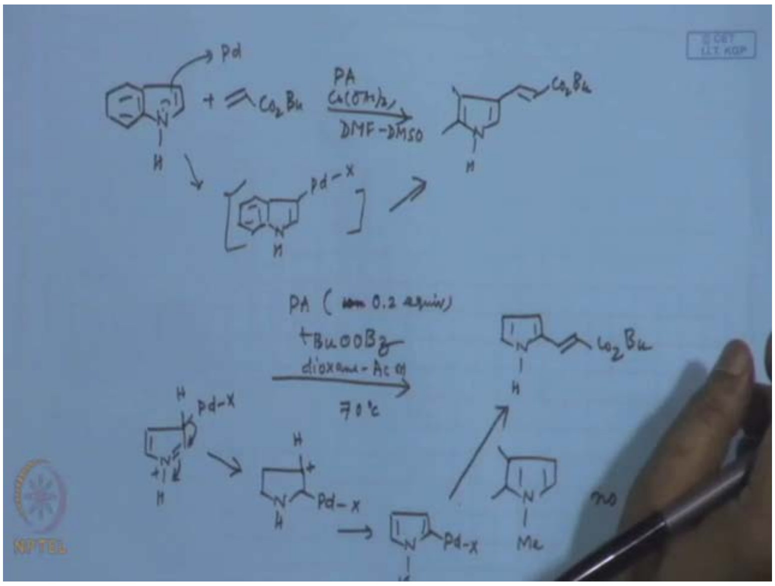

So, if you take indole here and without any protection of nitrogen, you see that means, these things are slowly changing improving that means, no requirement of nitrogen protection and same old thing this acrylate and the reaction conditions. Reaction conditions like this again P A paradigm acetate percentage is not given and then cupric acetate solvent is D M F and D M F, so combination.

And the product is so that is an advantage here, that you do not require the protection of this thing and the reaction takes place at C 3 plus I think all of us can write the mechanism right, what is the mechanism. Just like see, what should be first step should be that paradigm goes here, so and then admiration takes place, so just as if indole is undergoing substitution reactions with paradigm.

So, what will find this the reaction mechanism would involve something like this that means, it is organo paradigm complex will be form. And then once this is formed, what equivalent to essentially the sort of this hake reactions, so eventually what would this one, now what is most striking, if you chase the reaction conditions, this is very reaction actually there are, so many examples, I will not just bother, you with many examples here now you just see the contrasting reaction conditions again the same combination the reagents.

And the reaction condition involves again paradigm acetate paradigm acetate only 10 percent ten mole percent sorry, it is something like, it is about like 0.2 equivalent is better how you will find out the percentage and the oxidant here is different, tertiary butyl B Z means benzoid that means, benzoid ester of tertiary butyl hydro peroxide tertiary butyl. So, that is it I mean, we are I mean paradigm acetate is common only, we are changing the oxidizing agents from time to time and the solvent is dioxane acidic acid, we are all typical polar solvent.

So, dioxane acidic acid and temperature is not very high is seventy degree centigrade, so what do you expect, expectation is and just by changing and this actually, in this case nitrogen is protected in this case. And they do not say anything R 1 all know without protection is yield is little poor that means, this nitrogen is without nitrogen protection yield is poor around 50 percent.

But, if you protect this nitrogen less kind of strange nitrogen is not protected and the reaction gives you this. So, what is the explanation, no there is radical actually, I will give you a hint let us say, if you can come up with any particular any kind of rather explanation. If you have a methane lab here, there is no reaction, you know in oxide, why in oxide would form pyrrole is not known to form in oxides indole no reaction.

Let us say look at, if you have a paradigm, so all of us know that, this would form a paradigm kind of this acetate or something like this right. And you have hydrogen appear, hydrogen appear and by tuning the oxidations or oxidants oxidant, you can actually delay the oxidation, then in that case you know there are 2 case in the first case, the hydrogen was eliminated.

So, it depending on the nature of the oxidant cupric acetated, so if for the cupric acetate then the oxidation probably was first, if you delay the oxidation, when there is a likely hood that the paradigm would migrate in this way, paradigm would migrate to this. So, that means, hydrogen here and you see and that is also require the umimium kind of a sort here. And so what will see here, then paradigm and x and this hydrogen and so you will have this and what next and this would then after paradigm migration then it aramotizes and that could be the then the typical hake kind of reaction.

So, that means, you have to have a right oxidizing agent to promote this paradigm migrations, you can delay the oxidation and then once this paradigm excluded as paradigm 0 then, you do this low oxidation to this. I think, that is that could be and the reaction also takes longer time like 18 hours the previous one, I have that also 18 hours. So, but it does not tell, you anything more, then the so that means, that you can add your will you can just direct the positions of the substitutions of the alkalizations in this dehydrogenation reactions. And then there is there are other kinds, so far, we have talked about this then there other reactions, let us say there is a possibility also call.

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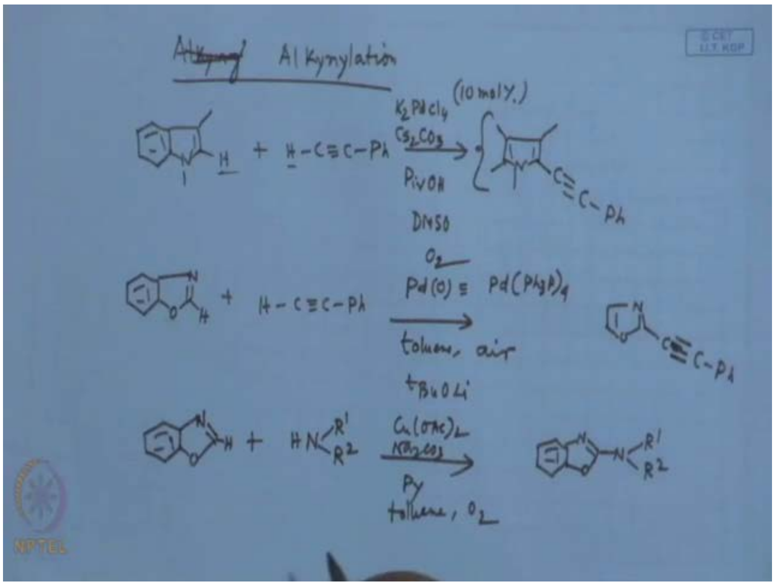

Alkynylation and what is that means, replace of acrylate also, you can use the corresponding alkene sorry, alkyne and you can get to this product, so you can get to this product, what as I tell you. So, it is a substitute of is a substitute of reactions, you do not have to have an halogen, you do not have to have this that means, if you have and the conditions here, but you have to look for the right kind of the combinations of the reagent.

In these case it is tetrachloro potassium tetrachloro palladate, these combinations of it comes with little bit of experience then other base here is cesium carbonate and very interestingly, this acid in acidic required to protonate the nitrogen.

So, pivalic acid is 5 carbon right 5 carbon tertial butyl carboxylic acid pivalic acid and of course, a solvent is required and now do you need any oxidizing agent, that is it. I mean the basically, you have to compare the starting metal and the product, if you see just you do not have to even count for the count these oxidation levels of this starting metals on the product. In this case is, so simple the title says dehydrogenative reactions, so you have to hydrogen’s where getting eliminated that means, you need an oxidizing agent and oxidizing agent is just oxygen plane oxygen.

And the catalyst is 10 mole percent, so I mean once again that means, we have to little concentrate on the reaction conditions and you see the outcome of the reaction, but mind then you do not have to use any kind of metals or metalloids. But, there are say this sort of reactions can be extended to oxazole or thiazole, but then there is a little differential here, take this again alkyne. And here first they use this is I mean is quite, I mean there are so many this basically, that fine tuning of the reactions conditions have to be done and the paradigm 0 is used.

So, this is basically, tetrakis triphenylphosphine paradigm complex as paradigm, which is basically paradigm 0 and toluene is the solvent then the product, because you are coming to the product of this dehydrogenative product. So, the that means, what do you require is an oxidizing agent in this case again not a even oxygen, it is just air is sufficient, but what do you knew that, this sort of compounds undergo is lithiation, So, if you then, if you use a base lithium tertiary butoxide, so the reactions that means, that was you see.

You have to just compare the pyrrole can be protonated with pivalic acid and you can activate this C 2 hydrogen and then subsequently the reaction taking place. In this case, what you are doing where actually, promote in the lithiation said this 2 position and then eventually, the substitution and the paradision all these all these, we hake reactions or reactions are taking place.

So, at some point that means, you do not have to do a separate preparation of the organo metallic's just, we can do it and then do the subsequently reactions in presence oxygen. And similar reactions, so if we recall begin in the class, what I ask that, what are the coupling reactions and on in the set, this C C bond formation reactions, but this is an example, where you do not have carbon nitrogen bond formation for example, if you take oxazole benzoxazole and nitrogen secondary amine.

And of course, let me the 2 hydrogen's, so that means, in heterocyclic can be emulated that means, functionalized with a nitrogen that is it, that means, if you did not know. So, how do you do, let us say, if you are given like an oxazole and try to incorporate in dialkyl amino group at 2 positions how do you do, if you did not know this answer how do you done lithiation followed by chloramines, chloramine is not, chloramine is very rarely used as emulating agent.

So, in on of the earlier classes, I said that amino triazole that can be used in the this aminating agents rather victoria substitution reactions, no mechanistically what he said is mechanistically possible, it do the lithiation. And then do this amination fine, N H 2 you get then how do you do this selecting alkylation's R 1 R 2, the set of that is what you studied in B S C right, something like that Gabriel lamination you right.

So, you first protect where and side by side, the direct calculation is a serious problem, problem that is why this reaction is called very useful, I mean most of the reactions actually, have been published very good journals. I mean, so far whatever I have either from ((refer time: 47:40)) that means, we are very important of it, we can just directly functionalize and the catalysts normally you have seen this oxygen in this case also this cupric acetate, I mean sodium carbonate, then other combination is pyridine toluene all kinds of thing.

So, toluene and of course, oxygen is there mind it, so sometimes you will see the reaction condition is use pyridine that means pyridine is not getting affected, in this hydrogenation dehydrogenation process. So, far we have done this alkynylation and I mean cupric alkynylation and now let us look at this whether, this alkene can be substituted by an aryl just state way aryl. And I have one more example of ammunition, I think I will, I mean, let us say I think I should take this example also at example this is again.

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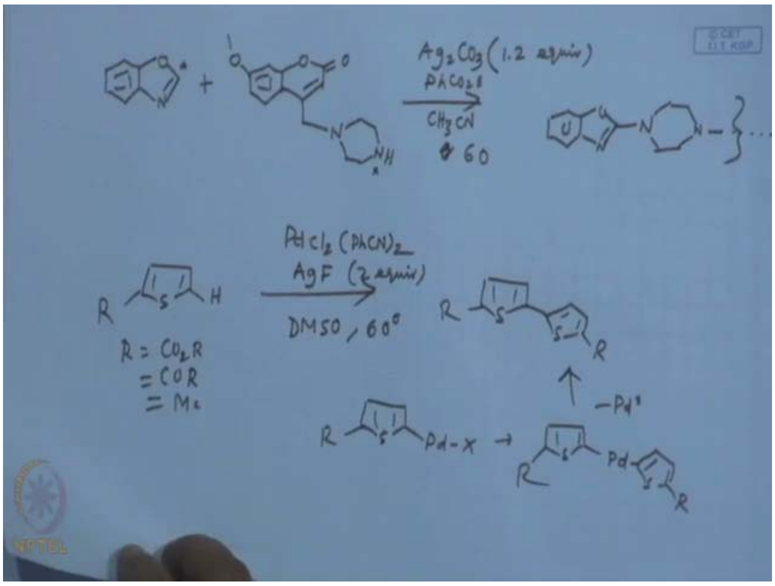

A reactions of a benzoxazole and then other reactance is a coumarin is a functionalize coumarin, you see here, you have a methoxy, the other portion is a piperi gin system with nitrogen fine. So, now, we have to basically, join these 2 opposition selectively how do you do say if you think all the lithiation etcetera. It is actually in the this nitrogen, should be connected to this start carbon given this to substance in a it will be tuff for example, lithiation etcetera, would not do would not walk, if you do a lithiation here.

And try to react with this preferential in the lithium would undergo the reactions with the lactone ring system, think about and here, let us say if you say lithiation. And then forward by transmetallation like all then equipment for example, that is a likely would that, the reaction would undergo conjugate addition organic pressure well known for conjugate additions. So, conjugate additions anything else you can think off any other or metals.

Let us say you can do a lithiation followed by borylation, you can do all kinds of thing, but in general that lithiation is tougher than the lithiation in simple aromatic chemistry.

So, lithiation in hectrocyclic chemistry is tougher than this than lows in this aromatic chemistry, so that means, lithiation magnetization all these things are not very well come in hetrocyclic chemistry, if you can avoid those reactions that it much preferred. And so in these case and the what do you have, they have done.

Aand they use silver carbonate and benzoic acid then acetonitrile and 60 degree and the product is as obvious, now it is this ammunition direct and then you can write rest of the things, so rest of the thing. So, you can do direct ammunition without affecting the O l methoxy group without affecting the other nitrogen, we are without affecting the this lactone ring, you can do it.

But what is the role of silver carbonate is in these case is the oxidant 2 hydrogens are getting eliminated, so is oxidant and this equivalence in the required is this. So, we have seen alkalization and this example now amination now. So, now, let us look at if we can let us say substitute and alkanol or alkyne or amine by aryine and that whether this is possible or not, the one of the simplest example, which Phosphine

Phosphine normally is a popular molecule in polymer chemistry, because polythiophenes are conducting polymers and in this here is an ester it could be acyl group or even it could be methyl group. And if you react these with palladium chloride acetonide sorry, benzonitrile complex and D M S O then 60 degree again, so that the I write all this details of this reaction condition, just give you a fill about the ok.

So, what do you except quick that means, you say dimerizations isone that is it. So, what is the intermediate, intermediate is you can say the first thing, first intermediate could be that electrophilic, sub electrophilic substitution reaction of pioppin with palladium x and then once, you have polladial x, second molecular come right. Second molecule come this x can undergo, again illustration substitution reactions with another molecule another molecule.

So, eventually, we will get a parallel detrate, this thiophene parallel detrate, this thiophene and this thiophene then what then the reductive elimination reductive eliminations minus paradigm 0.

And So, to speed up the second step, first step is quite easy, because paradigm 2 is pretty electrophilic in nature, but this one is not very electrophilic in nature. So, what you have to do, you have to make this little more electrophilic, how do you do put you have to make this electrophilic put add silver fluorite in this case obviously, you have to use because halogen is there, so you have to use 2 equivalent of the silver fluorite.

And diclouro phenyl cyanide yes paradigm chloride it is a complex, this is complex and very recently something else is coming up, there is a I think just stop here, there are somany other examples on this kinds very similar that means, in principle that dehydrogenative reactions can be feasible. And like even, if you already say these are the reactions possible.

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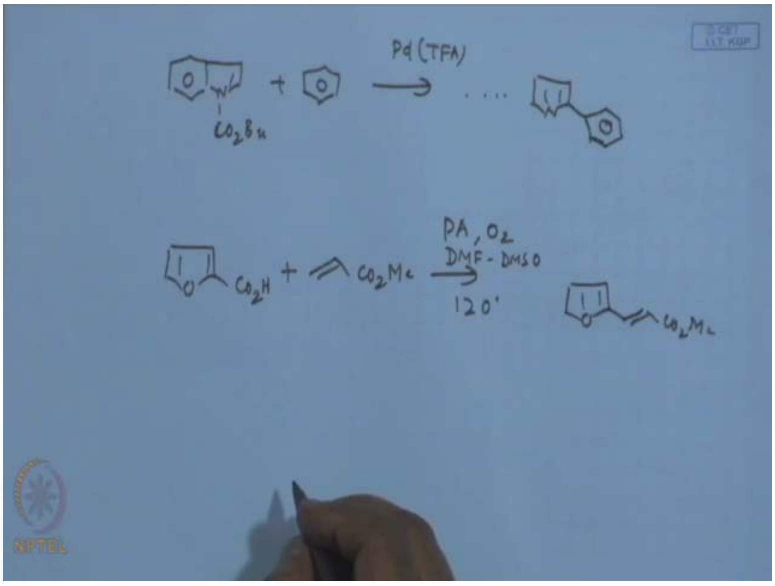

So, if you take an indole and the substituted indole is a plus benzene of course, paradigm trifluoroacetate you can go to these eventually, what will find under certain conditions, you can directly do the arylessence. You do not have to do any standard traditional cross coupling reactions, I think I will give you the last example. Last we have, so many examples, but this is a topic, which coming up quite fast and if you take let us say fluoric acid then acquitted.

And again P A, which I called paradigm acetate oxygen and D M S O D M F whatever and just heat it right. What would you expect you would expect again a dihydrogenative kind of thing, because paradigm is there etcetera, but when you have a carboxylic acid, there is the reaction was called as decarboxylative. So, this is coming out this reaction is coming out and you can, so advantage, you say religious specific means, it will only alkylate alkynylate at the place of the carboxylic acid group.

The previous cases, you know that it sometimes there reactions are not very religious selective. So, what is the summary, summary is that you can do with metals and metaloides, I mean if you know the how to tune the reaction conditions, I mean little bit of reaction mechanism normally involves auxiliary additions or the electrophilic substitution, they are some electrophilic addition of the paradigm 2. So, these are the 2 important possibilities, if you keep them in mind then it is easy to tune the reaction.

And what else and vocationally, you can activate paradigm by silver addition of silver, third point that you need to remember, what is third points kinds of oxidizing agents, which are comfortable with heterocyclic compounds, because that not many heterocyclic oxygen would permeate this sort of the reactions.

For how many types of oxygen’s, we have come across today, benzoquinone sometimes ridicule also use, benzoquinone is very similar to ridicule oxygen of course, A r silver carbonate cupric acetate. Cupric acetate also is a very useful one especially, in case of decarboxyl deep reactions, why you know why right. Why any guess cupric salt are very useful in decarboxylate coupling reactions [FL], because let us say how do you decarboxylate benzoic acid in lab.