Organic Photochemistry and Pericyclic Reactions

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Lecture No. # 22

Remote Functionalisation

So, in our previous class we were discussing something about organic reactive inter mediates, right. We tried to understand what are carbines and nitrenes; different type of your carbines and nitrenes and their reactivity, how to generate this organic reactive inter medias? So, one more part which I have to cover in photo chemistry is remote functionalisation; you can in that we can discuss about Barton reactions, we can discuss about Huffman and some photo chemistry of (( )).

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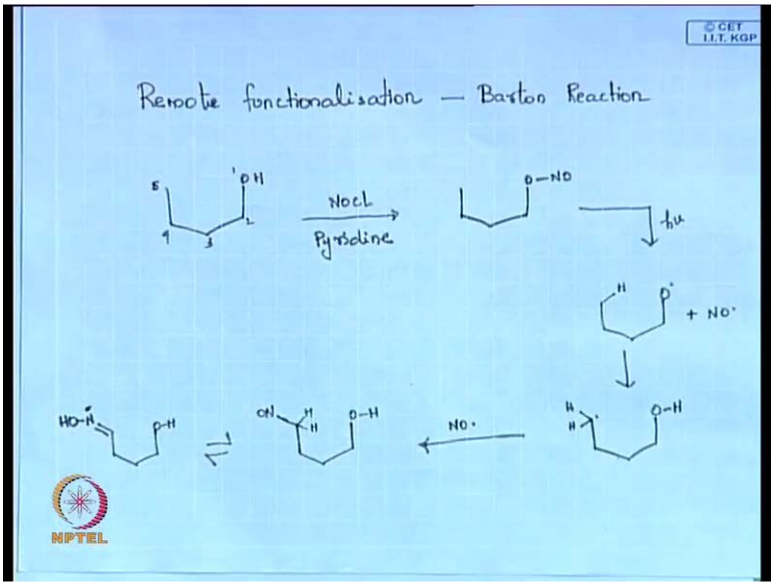

So, today's class we will be talking on remote functionalisation. What I exactly mean here is that, have a system like this; so, 1 2 3 4 5. I want to do some functionalisation on this carbon, which is no where connected to your… It has no connection with any other function group. It is just a methyl; I want to functionalize this methyl . It is very hard, because like if it is an allylic then you can think about, if for example, if you just an allylic like system, I want to functionalize it; what you do?

Normally, you do an n b s reaction, right? You take allylic system and you do endomous accinamite, then you get an allylic bromide and from there you can do whatever conversion you want function group conversion. But if you have a system like this which is very remote this methyl, and if you want to functionalize this methyl, then these types of reactions are very important. One of the famous reaction for that is here Barton - Barton reaction is very famous in remote functionalisation.

How you do this is that, you take any alcohol like your cyclopentanol or cyclobutanol - not cyclobutanol – then, you treat it with an N O C L in pyridine. So, you end up with, you can end up with your O N O. Fine, now you fertilize this part; so what happens? Once you fertilize this you know this is your weakest bond - the O N bond. So, it can undergo a proper homiletics cleavage. So, if it undergoes a homiletic cleavage this, then you can end up with an O dot plus N O dot; then what happens? It can abstract a proton, correct? So, I write like this; you can think about your six membered transition, its right; so can nicely abstract a proton treating me a C dot. Now, this can react with your NO dot, because that is in the solution.

To get you what? Can I put like, because it is right is an NO there and this can easily (( )). So, you get your N OH right? So, basically what I am doing? I am just functionalizing your remote carbon. Once you get your oxygen then, you know how to do sorry, there is no dot there; once you get your oxygen then you know you can do many things with your oxygen then and you can convert into different function group; there are many reactions. So, basically I can functionalize my remote carbon without doing anything and these type of reactions are like, goes like most of the times 70 to 80 percent is conversion. So, no need to worry about much there, clear? This is your Barton reaction.

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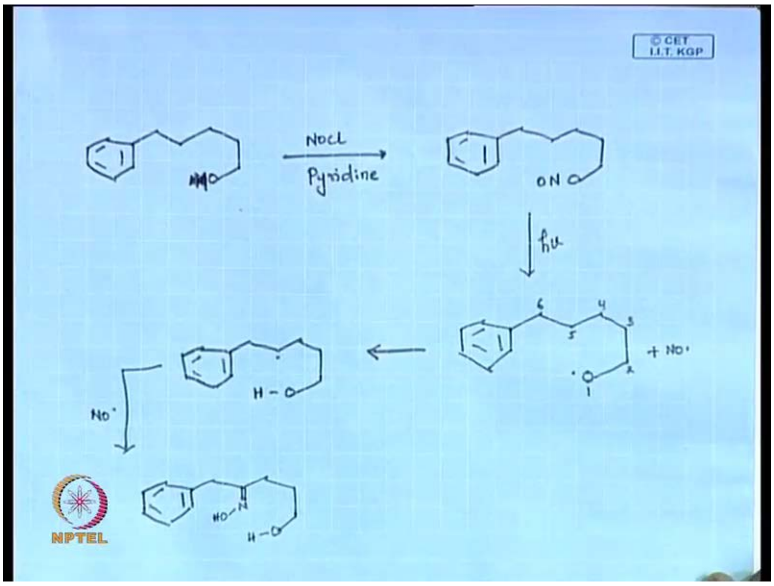

We will take another example sorry, this O H, then you end up with when right you did. Now, I fertilize this get O dot plus NO dot; where we can abstract hydrogen? Now, it has several possibilities to abstract an hydrogen; so 1 2 3 4 5 6; 6 if it is abstract from 6 then what membered ring you are getting? Type of 7 number, right… Yes not (( )) 7 number cyclic transmission state, correct? If you abstract from 5 then you can think about some 6 membered cyclic transmission state; more like that so it abstracts from 5. The radical here then you know what happens. Then, your N O dot followed by your (( )) to give you or you can. So you can take this Barton reactions are same, has got famous because you can do this remote functionalisation in basically natural products.

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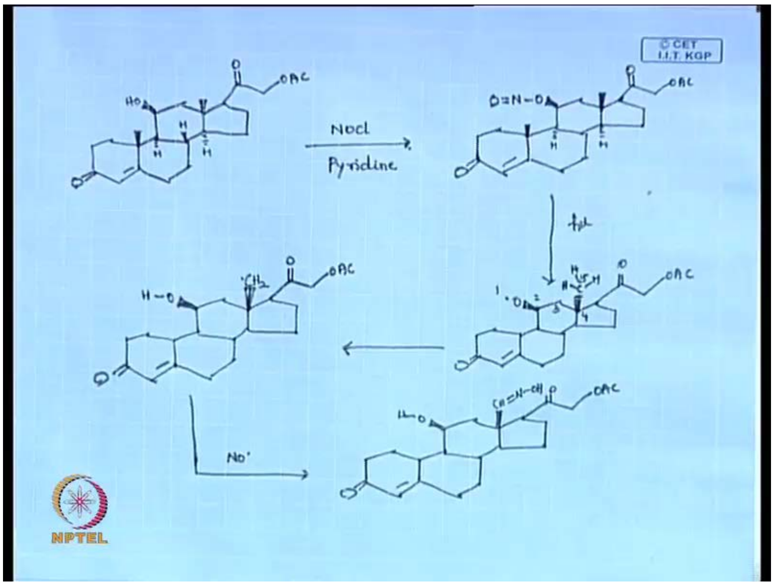

You can see many reactions have been done in you can see Barton reaction, because one of the best example I will take is this methyl. Most of the term is that is what the once you started, you know natural products drawing, it is always nice to this methyl also should be in this question and you all have OH.

This hydrogen will be the down (( )) and another hydrogen to check and draw, if I want to draw a isomatrigen is should be here like this, right? So, these are if you keep practicing natural product structure is always nice you know, how to draw the methyl's mostly angular methyl's? We call it, see now, whenever you take natural products for example, like you look for most of the attainment activity, right? You take natural products for example, like many of natural products are fungicidal and you have insecticidal activities like your neem tree; most of you are terpenoids from neem tree are insecticidal.

What is that famous compound which you get it from neem tree, which is aza directant aza directant, I think. It is 1 milligram; it costs about like 7 rupees something closer about 100 dollars. It is really expensive one but you can use, extract it from your neem, so aza directants are different like a, b, c, d, e, f; like that and they are very good in very good in insecticidal activity, because what happens is aza directants is more like entropion. They mimic 20 beta hydroxyzine; have you heard about that? 20 beta hydroxyzine is type of a juvenile hormone which insect has which makes the insect to move from its childhood to youth age.

Then it goes to older age; so what happens? This aza directing indica goes into the insect, just overlaps with the 20 beta hydroxyzine, and because of that the insect becomes, they bypass their youth age and become directly old. So, in the youth age most of the times insect eat lot. Now, you can over, you can bypass them and if you go in excess they even kill them. So, why that is more important is that this type of positions right, if you take aza directants this there is a position at OH where is a 20 beta beta hydroxyl OH. If it is not there then, the activity is completely lost. So, that is why the particular O H s, and the exterior chemistry natural products play a very important role 1 O H, if you change one methyl, if you change you can tremendous increase in the activity or activity goes completely down.

For example, I have a methyl here and thinking like that I want to functionalize, it is basically a structure activity relationship study. So, I want to functionalize this methyl to see whether the activity of particular compound increases or not. So, how to functionalize, because it is a very remote angular methyl you cannot functionalize by any very good synthetic methyl's where you have to functionalize this in that case you can use your Barton reactions, so what happens? If I put NOCL in pyridine?

I am going to make this right; I will get this if I put in a NOCL. Yes, other exterior chemistry is much preserved like I can have my hydrogen here. Yes, these are like icons; now you can fertilize; what will happen? You know this step; you get this right? So, what this O dot does if I go 1 2 3 4 and 5. It can pick this hydrogen type of C is to dot here like it will be like O H. fine, then you can know that NO dot can come in further you can undergo it as (( )) session to give me. This can be anywhere; this oxygen can meet this direction or that direction. Now, you should take this particular molecule and put because these are the photo products, you take this compound make the N O C L pyridine then you fertilize, you get this as your photo product. If you put nitrous acid you take this compound and stir it in nitrous acid; what will happen? Organ chemistry.

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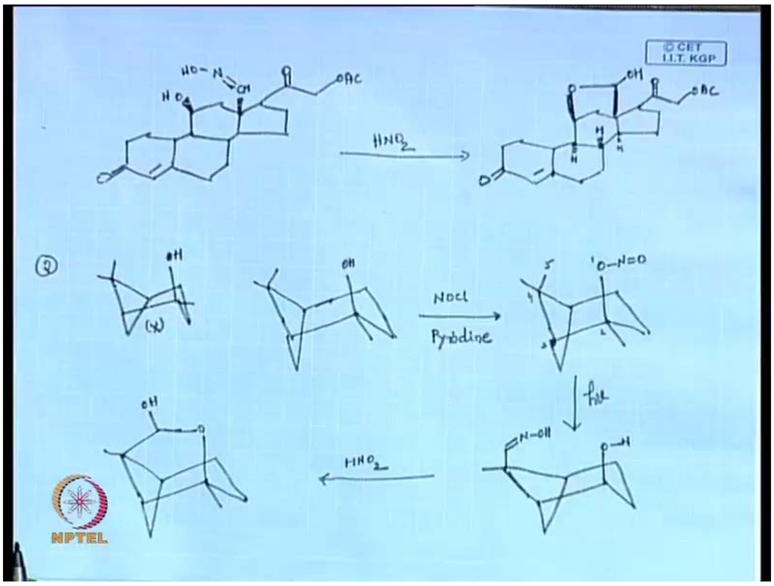

For example, I am writing like this for you like make (( )) in the same structure, no you do not write. So, if I put this nitrous acid, what you expect? See, I can see the structure activity of this compound also, I know then methyl as some activity, so you end up with an (( )), so end up with a nice product.

Just try this mechanism and let me know, because is an oxygen mechanism which you know what happens in nitrous acid. If you have A O H and as well as oxygen see type of systems, can you know it as A O H? You can think about see, always see I mean O H which can have like sort of hydrogen bonding interactions with your, have you design a drug molecule. If you, someone wants to design a drug molecule or someone design you a molecule which can be a fungi cider how you go through? What will be your, how you look forward? What will be your (( )), if someone wants to you to design some molecule, some particular disease? Yes, first you have to find out your receptor you know how the receptor should be, right?

Nowadays, you have very good method where you people precellys protein also, you know your receptor side. So, once you know your receptor side, if it is like this with A O H and amine like pyridine. Then you design your molecule, so that which has carbon alloys and which has attached with your receptor side that is how you build up your molecules right. So, in that case having an OH carbon alloys amines, they have also important role to play, because they might have secondary interactions like hydrogen bonding hmm all this things happening with you receptor side, fine.

So, that is how these are very important functionalisation remote type of functionalisations end out. Now, we will take another good application this is a methyl here. This is O H and a methyl should be if it want to be drawn properly. Write a structure like this you can write it properly like this so I have N O C L pyridine. So, I will just write the so called Barton reaction; so what happens if I do Barton? I fertilize this; what product you expect? After (( )) session and all these things, what product do you expect? So, if count 1 2 3 4 5 right, I will end up with right… So then, you know if I put nitrous acid what will happen. Then you can have a type of cyclization you want to write the structure; what happens? If I put, try by yourself.

So, end of with the molecule like this, these are good examples which you should… You will start to understand, because how this type of Hoffmann reactions very sorry, Barton reactions are very important. People use lot because of their remote functionalisation idea which you cannot try to do with other compounds, other synthetic procedures are very hard; is very simple to be one or important, one more applications.

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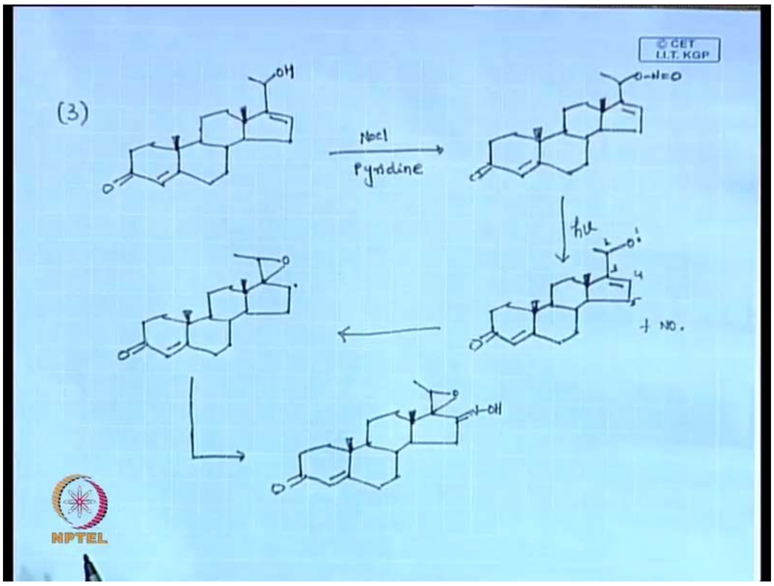

I will try with half with Barton type of natural product; even sometime you can think like how this radical react, all this things which is very important as now. If you this part you know N O C L in pyridine, which you are happy to draw.

Now, I fertilize; so if I fertilize this one, this is little bit different from exact Barton plus an onus is that see, I since you are looking into Barton if you an N O dot radical with your, so called terpenoid with an alkoxy radical and you know alkoxy radicals are highly reactive. Not like that much stable to be in the solution, what happens immediately? It tries to cycalise with here to form a epoxide, so that you can generate a radical in C 4 fine.

So, yes I will just write the structure you know already so what happens here is that see you are O O radical can easily form an epoxy like this, then you can generate a radical here yes till it waits for your N O dot to come and pick up the proton alkoxy radical are highly reactive, so immediately it forms, because it can see an polyphoni there, so it forms A C centre radical this C centre radical then can react with your N O dot.

So nice to do this type of reactions, because know you are ending up with epoxide and as well as your oxine. Fine, so that is how you can do remote functionalisation using your functional group O H. If you have a b O H functional group you want to functionalize your C 5 then you can convert your O H to your nitride using your… and then do your Barton reaction fine.

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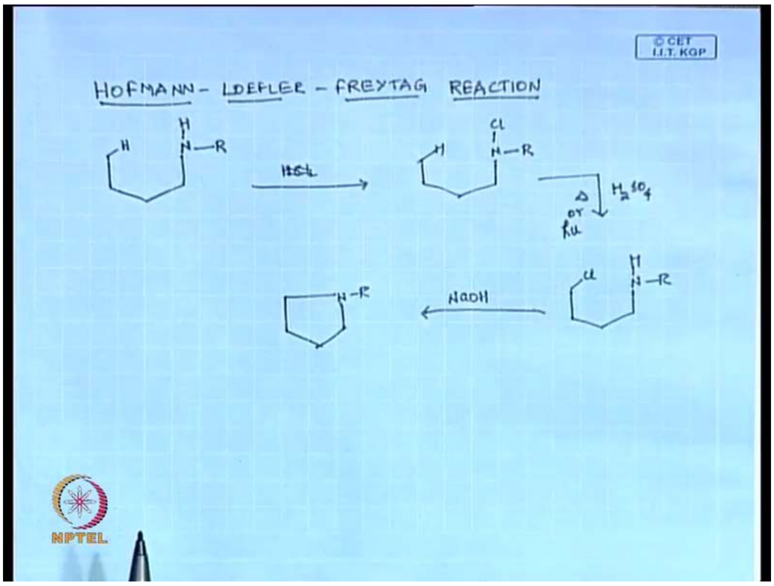

Now, there is another reactions where if you have an amine type of system and (( )) you can do the same thing previously we are talking about O H, right. For example, I have type of an amine system, and I want to functionalize this hydrogen just instead of O H I have an amine, what this reaction you call it you studied this reaction in the bachelors.

You want to functionalize this hydrogen if you have any way it is called as Huffman Loufer Freytag reaction. This does not you does not need to do in Freytag lyses Freytag of one. Normally, people call it as Huffman reaction, because you have not seen this part, but just I want to know that all the authors should be there.

At this reaction normally, people do a synthetic lab also it goes very nice. So, if I put H C L for example, all H C L are basically even not H C L; do not write H C L if I can. How you can chlorinate this? I want to have this part. I want this product N O N X N O Na O L C L 2 any other that is good any other a many good methods lot ha p C L does not work, if you have N H Na any synthetic idea come on man very simple that you have N H R you want to take your second termini, and second termini and make it a echoer that is all chlorine. If you put some little bit base, yes it happens any other good synthetic approach look should be simple reaction. Yes, we will come back that you just give a try on that. If you make this compound it is called N chloro derivatives; you can call N bromo derivatives; you can call N bromo derivatives. Now, if you put sulfuric acid or in just heat or you can use light whatever you want when heat or you can light.

Then, when you work up with this O H minus this, normally people do; that is why I am saying you get a hector cyclic nitrogen; hector cyclic compounds simple fashions which does not need to even heat this light. You can just heat the solution in the pre in the acid and once you head than… And then you work it up with your base and everything it gets cycalise. Hence, it to give you this ha nitrogen hector cyclic compound many reactions have been done based on this receive first the mechanism and then some application of this, what molecules you can make out of it, I have this compound.

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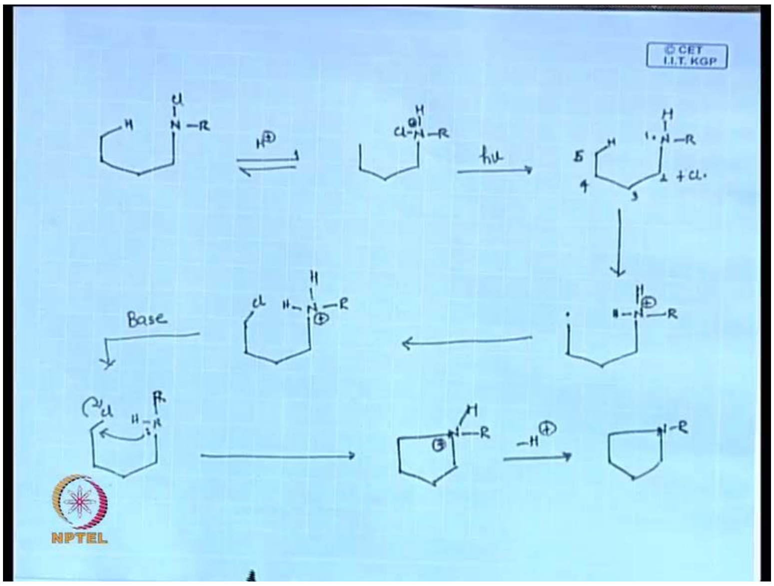

I put it in sulfuric acid H plus what will happen sort of it a salt threat you get a salt encore salt, if you want you can write and then if you heat, and then if you fertilize again you end up with a nice homiletic clued then you know that it can abstract, because its 1 2 3 4 and 5 so it forms an I 6 membered.

Yes; so, what is your solution? Solution is with your core system is there that can give you a chlorine item or a chlorine dot is there. So, like, just like Barton you get this then, in the base because you are going to work it up, you are going to neutralize the system and then you have to take your compound out. So, your base can, so N R with a chlorine you all C dot minus comes out; way close on that its mechanism to give me a cyclic - recyclic compounds so you can look to be mechanistic part looks to be step wise but once you do the reaction it is simple. Once you fertilize, this part is very high to isolate this part. It is instead to this one before fertilize this part yes yes this is no, you can carry out to the same reaction you show the whole process nothing wrong, anything? Yes, because you, yes it is H plus you can do this because your C L dot can come out. Even you can do this reaction; goes nice if you are doing with your iodine.

Iodine does very nice reaction like this iodine bromine chlorine but bromine iodine are much more favored and you can see interesting applications done on this that will be lot of lot of done on this particular reaction, you see one good application.

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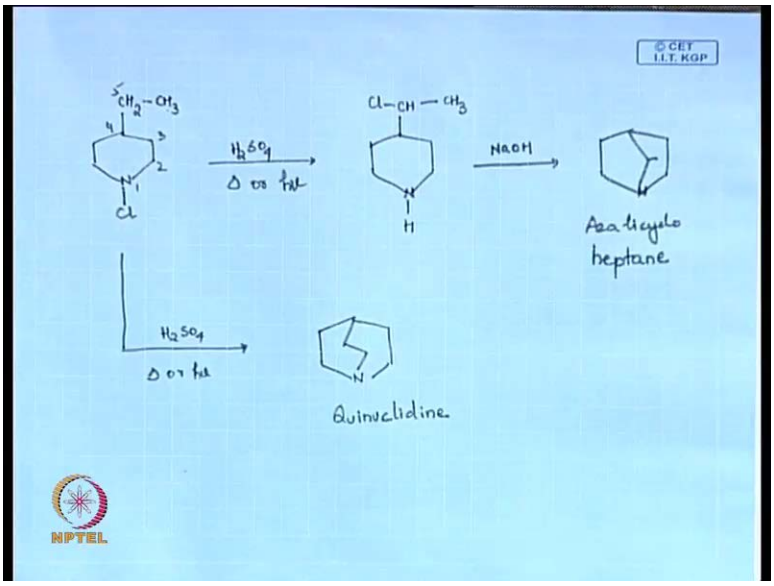

You take this compound sulfuric acid; you can heat or you can shine light. So, what product you expect? You get a very nice product in this reaction one will be the major 1 1, you get a side one both are interesting products.

What will happen so you have then its best way is to numbering rather than thinking lot so 1 2 3 4 5 right you know it takes from your so it should be just a type of sort of right you get sort of this because here a this goes a b abstracts and hydrogen then your C L dot comes back. This is there so I am not writing the full mechanism just I am writing because you know it. Now, interestingly if you put it in this is your working up, what you can expect?

What you see here in this earlier case? What you see? You see a line here; so you form a bond between a carbon which is connected to your chlorine. Can you try the same step so what is that? That is all aza bicyclo heptanes. Fine, if you think like there is another possibility which you can, which is not major, but it happens also what another possibility will be thinking of. Just from theoretical point of view, it can even take from this little bit because it has it.

Then, what you get if it takes from C H 3; here can you write the product after sodium hydroxide; what that compound is called? It is a very nice compound namely, get this, what is this? Very good connect will be this is a, that is why I say set of reactions are very important and they have been used in lot because you end up with nice aza bicyclo heptanes. You can make a quinuclidine, any other due to any good base like this (( )) other word dap co right diaza bicyclo octal design, these are all very good basis sometime, if your reaction does not want a nuclear file your base should have a proper base. (( )) d b u cannot act as nuclear file most of the time, because of their very big static nature; so they act as a very good base.

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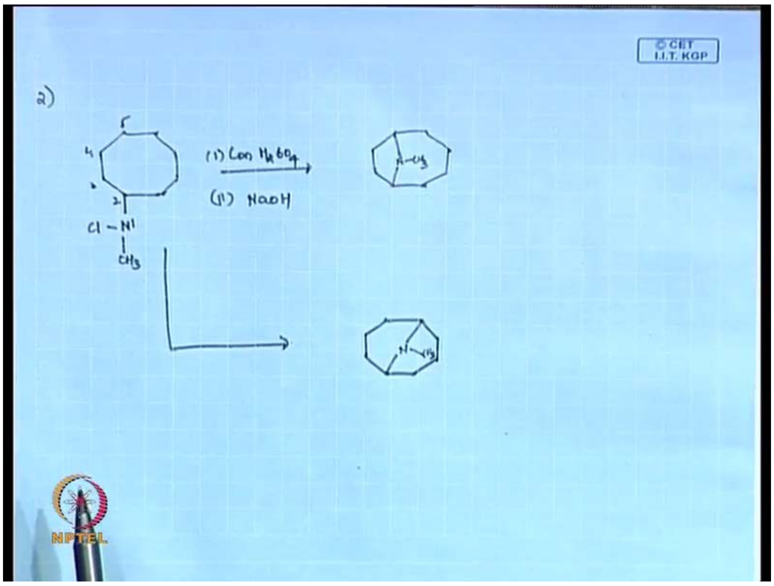

We will take this particular example. Another example see you start appreciating the name reactions or this type of reactions. One you once you start knowing the applications like knowing like what is Huffman, that is all what is Barton? It is not like its more about knowing their applications where they are really loose, then you can start enjoying the name reaction and then you know how these reactions are becoming popular. You can do many things right now also; so that is all your 5th carbon. So, what is the product even this step like first step like concentrating sulfuric acid and your second step is sodium hydroxide, what will be your product? Nothing, it should be straight forward. So, C L will go there then you have to connect a nitrogen to this; that is all for example, if I want to like this right. Yes or no? Sometime, you can even get your 6 that is also possible the 6 hydrogen; then you will end up with this compound you have studied.

You get both of this, but this dominates across this one but this to be most famous. So, that is why this remote functionalisation is very important. This have been people are doing this does not need. That is what I am saying this reaction does not need light also just you take the compound heat it in the acid biennium; then work it up you end up with the good products.

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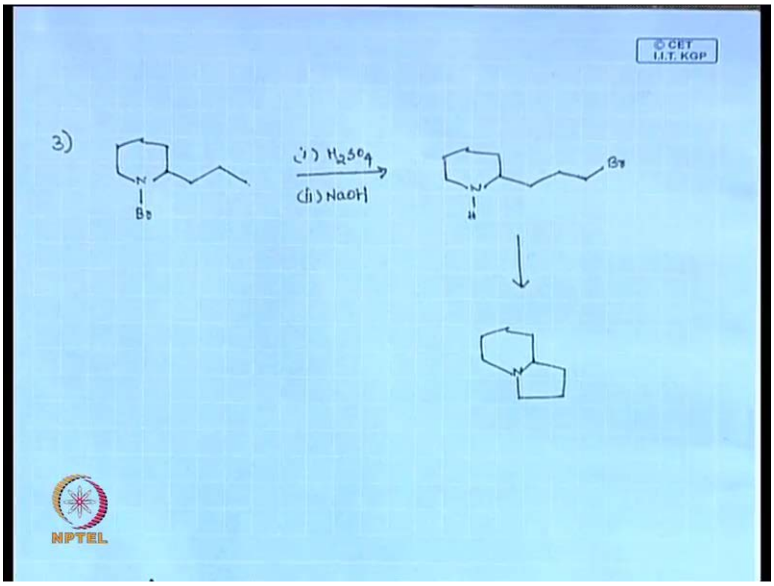

Another natural product which people are making in large scale using this reaction, which you even you can try in your lab know some reactions have been dry dried in micro wave. I do not know what product you can think about. So, if I say first step is sulfuric acid; second you want to use little bit of base. You can heat or you fertilize can you write the product, any product. So, what happens? First step you end up with N H you get a nice cycalization right. I can start doing my bicyclo rings as I aza type even you can take lactams also by using this you can make lactam chemistry. These are very popular chemistry of this charka; so this is one type and these are the two main reactions one O H, and another is your using your N O and one important.

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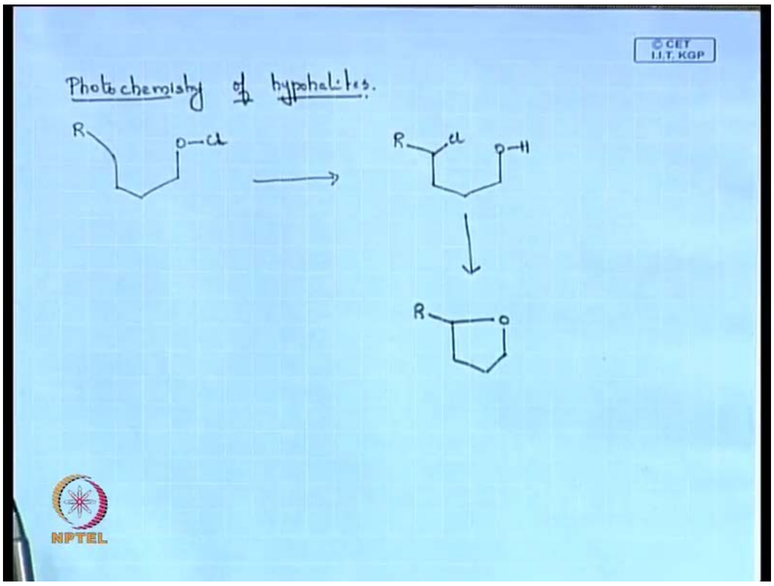

Another way you can make a reaction remote functionalisation is using your O C L, what you call this hyper highlights effect. You can hypo chlorides, you can generally hyper highlights photo chemistry of hyper highlights are known if you fertilize again you do your same Barton reaction same like Barton reaction. So, take your O H then you get your C L same your Barton and this interestingly cycalises to give you a oxygen 5 membered ring see in Huffman. You saw nitrogen 5 membered ring; you can make nitrogen type of 5 membered rings. Here, you can make oxygen type of 5 membered rings; this you called as photo chemistry of hyper highlights.

So, these are the three main reactions which you can functionalize your remote carbons. Fine, one is your Barton, another is your Huffman, and your hyper highlights, so that sense are mostly of your photo chemistry; thanks.