Heterocyclic Chemistry
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Lecture - 27
[4+3] Cycloaddition

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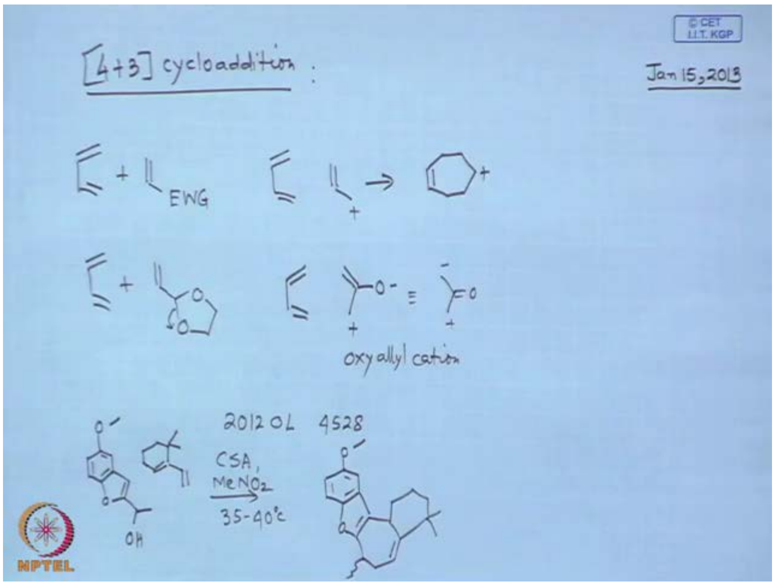

[4+3] cycloaddition :

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Good morning, today’s lecture is on another Cycloaddition reaction, that is 4 plus 3 cycloaddition reaction, it is very similar to one we talked about in the last class. If you recall last we talked about 4 plus 2 cycloaddition reaction, and we had given examples, on the 4 plus 2 cycloaddition reactions were the furan molecules undergo 4 plus 2 cycloaddition reaction. In addition we have seen some of the Bogar kind of the chemistry, where you have these dia jeans, tetra jeans, those molecules also participate as dyne components. And then we have also talked about this Diels Alder reaction, one of these reaction is popularly known as povarov reaction, which is basically involves amines or sometimes we call has amineno Diels Alder reactions.

Today, we talked about a very similar reactions although it is 4 plus 3, if you recall these 4 and plus 3 all these numbers refers to the number of the atoms forming the rings. So, it is basically they are numbers of the each reacting component and to compare with what do have been will talking about today, let us say this is the standard protocol for a diels alder reaction or 4 plus 2 cycloaddition reaction.

And then normally what we require is electron withdrawing group atom one component that was a standard one, now today's one is very similar one, but only thing what will you find that the dynofel does not have a electron withdrawing group instead will have a carbo cat ion that it. So, I mean what do you think about, actually many of the people all know that the diels alder reaction can be carried out like say in presence of a double bond here, with like say kittle for example, if you take kittle here.

Although, it is not a electron withdrawing group, but many of you know mechanistically, this carbon can form a likes carbon cat ion in the presence of louise acid. So, essentially it is a double bond and carbon cat ion, very similar to that if you think about reacting component were you have alkathene, than you have a double bond; that means, carbon cat ion as if serving these purpose of electron withdrawing group.

So, the reaction undergo should have undergo Diels Alder kind of reaction, but instead what do you see the result is little different 7 modeling; that means, all the three atoms of the alloy carbon cat ion. This is the basically alloy carbon cat ion would undergo reactions, so that is the reason why it is known as the 4 plus 3 cycloaddition reaction.

And obviously, on your left hand side that means dyne side you do not have much choice, so dyne has to be or dynes has to be electron rich and dynofiled is now alloy cat ion, but I again the simple version is not really known. If you look at the reaction here it is not these cyclo haptene, it has to be a carbon cat ion it has to balance the charge, this is basically formal 4 plus 3 cycloaddition reaction.

And what are the and then there are, but this simple version is not really known, but what is known is equivalent to that kind of things, and you want more kind of reactions probably as which is more popular. And suppose you have taken, you have something like this than a carbon cat ion here this alloy carbon cat ion, actually has to be stabilized by choice of different substituent.

This is very important on the left hand side dyne part we do not have much option, but what will see as go proceed along class, will see that most often these reactions are tuned by placing different substituent here and there, most often hetero atoms. And commonest one is oxygen here, and that is called oxygen minus here and this is very widely in literature is known as oxyallyl cat ion.

So, one can invents invent call 4 plus 3 cycloaddition reaction of oxyallyl cat ion so; that means, and if you look at these this is nothing this equivalent to something like this, than as you have carbon compound and one side you have carbon cat ion and another side you have negative ion. So, this is primarily the basic reacting unit for all these 4 plus 3 cycloaddition reaction, then we have different example different methods of making how they are used, and then also some these application, you know application.

It does not have to be necessarily these kind of things, but ((Refer Time: 06:31)) something like epoxide or amino substituent depoxide, all kinds of things will proceed, will give more example. Let us take a simple, but tougher example here, this was published in the 2012 and OL and page number is 4528, what is here? You have benzo fural, these case this is mechanistically very simple a benzo fueral all of you can write, and then you have alcohol O H group methane group here, then see other reacting component is a cyclo hexane, and then double bond here and these.

So, all of you can guess, what it is this cyclo hexane phenyl double bond, that would form the dyne part, then you do not have a dynofile, in these case you do not have I means formal dynofile, but in the presence of CSA, what is known as Camphor Sulfonic Acid, which is basically might organic acid. And then this solvent of course, you have to use polar solvent, because your using a sulfuric acid, so polar solvent as temperature is somewhere between 35 degree to 40 degree the centigrade.

So, I mean normally I mean if you did not know the 4 plus 3 cycloaddition reaction, would have expected low reaction in these case. At best in the presence of camphor sulfuric acid, these alcohol undergo dehydration to for the corresponding dying system, but result in these case is remarkable good in the sense I will tell you why is remarkable result is remarkable, you get a 7 number ring. And then the cyclo hexane get fused, and these double bond and the methyl group here, so mechanist do not have to go through this 4 plus 3 cycloaddition reaction, what you can do, you can think about as if this is forming the carbo cat ions here.

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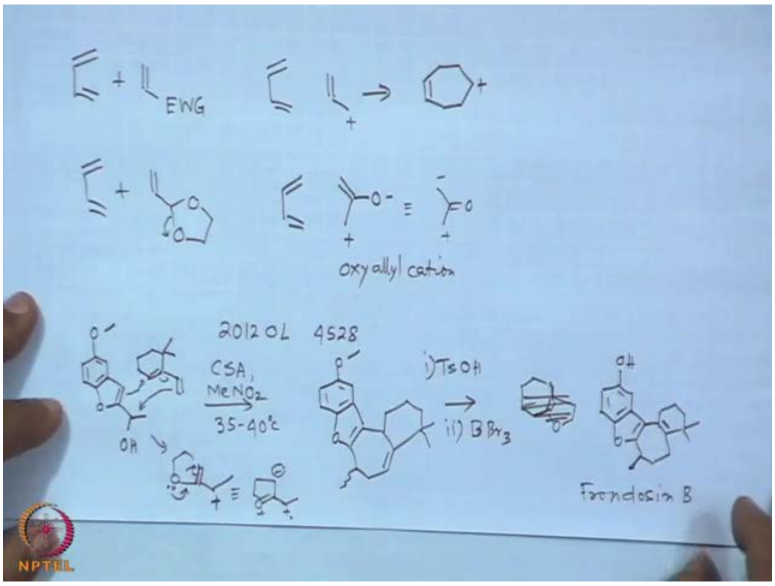

That means, you have a pi system, you have a carbo cat ions here and then what then this middle one the alloy system will have an oxygen here, and all of us know oxygen will in presence of double bond adjust double bond it polarize the electron towards this beta positions. So, that means, a essentially this is equivalent to what you can see, this oxygen here double bond, this is negative charge and then you will have positive charge here then this called methyl group here.

So, then and this is equivalent to carbonyl group and adjacent to they have a plus and they have minus, so all these reaction, so middle one is oxygen it is equivalent to the carbonyl compound. So, will gave and then 1 2 3; that means, three atoms you can say is not truly dipole, but in these case it is a tripole you can say, and then of course, you have this cyclo hexadyne is a part, and that to would undergo reaction as you can see from here double bond would participate this migrate.

And then negative charge would and this negative charge would combined with this other end actually giving this 6 7 membered ring, why it is so important, probably many of you know this reaction is very important reaction. There are for two reasons, firstly, one of the major reasons is that there are few reaction in which you can make 7 membered system, do know many, many standard protocol, there is no standard protocol.

One of these to make seven membered system is Deakman reaction, Deakman concentric that is the one of the choice, but all of us also know this is not kinetically favorable thermo dynamical is also not favorable, because they are unstable reaction, any other method. Do you know any other method for a making straight way making 7 membered system, absolutely 7 membered system there are not many, so that is the reason why this reaction is very useful there are plenty of example, and plenty of variations.

And in this case if you treat this with the tartaric solving sulfuric acid, number one and then treat this with boron tri bromide, so what you get, you get I mean the same sorry, I better write this 6 member first, then furan ring system, you have double bond these. And 7 member ring, then you have a 6 member ring, 2 methyl group here, what else you like to see something else what else, this molecule known as Frendosin B this an enzyme eliminator.

As you entered then there is methyl group here, so this methyl group here now it is straightly word defined and you may have to recognized also as you proceed along the start of a hetero cyclic chemistry. It is just aliphatic chemistry now, in first what you expect with the tartaric sulfuric acid, any guess quick feradolic sulfuric acid would induce dehydration, what else. In these case it actually isomerizes the double bond concentrated conjugated with the furan ring system, so the double bond is moved then probably many of you know boron tri bromide famous the agent for de-methilation.

So, that means, if you have let us say phenyl methyl ether, how do generate phenol from phenyl methyl ether quick, classical method phenyl methyl ether, how do you convert phenyl methyl ether corresponding phenol. Na

Student: NaOH

No, you have to know what it is, and this is very standard reaction, B.Sc reaction, Harjic method have you heard of Harjic method, H I, so if just read with H I simple undergo this is even a high school chemistry, problem there you required high temperature. In these case problem can be carried out at minus 78 degree centigrade, so you get this, so and what else what are the other things we learned from here.

Let me simple allylic cat ion is sufficient to activate an allylic activate the substrate to participate in 4 plus 3 cycloaddition, not only that what you can see here although here furan here furan double bond can participate in the 4 plus 3 cycloaddition reaction. Before we have learned furan undergoes Diels Alder reaction as a dying component here furan double bond is in acceptor component means dynofale kind of component. And let us so that, but it is not forming as an hetero cycle, it is forming a carbo cycle, it means carbo cycle ring system, let us look at some other example were you will see, hetero cyclic is being formed and it kind of substitute here.

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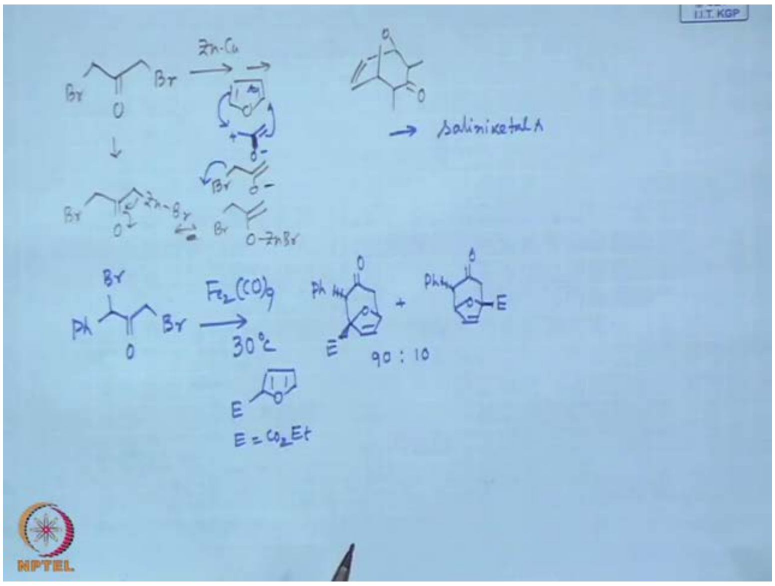

In these case again a kitton write alpha alpha prime, what you do here you treat this with a zinc copper couple, it could be simple also copper bronze this is analary, so basically reducing agent and treat this with now furan. So, if you add furan, so what will you find I mean you will find oxy allyl cat ion, so essentially this is again this is Diels Alder kind of reaction or you can say 4 plus 3 cycloaddition reaction, and these and methyl group here and these.

So, is bicyclic compound, now it is truly hetero cyclic molecule, what was the function how does it proceed, you can simply this one you can think of all of us know zinc undergo oxylatory addition in between this halogen and the carbon bond. So, and you will have bromine here then this undergoes once the shift of the zinc, so result would be oxygen and zinc here and the bromine here and then you have this. Now, also all of us know this oxygen zinc means basically oxy anion, so it is equivalent to oxy anion here, and then you have a bromine which is bromine which is equivalent to now you can see now, you have oxy anion now, so oxy anion.

So, it called then on these reaction conditions, if you have polar solvent, so you likely to cat ions of these kind and this is now sorry this is oxygen minus and is double bond, and so and then this electron polarize towards the cat ion here and then negative charge goes to this oxygen there were moves, so essentially you get to this kind of molecule. So, as again 7 membering, now in this case oxygen, because you started with an hetero cycle is furan and this can this has been recently been used.

For again a synthesis of a natural products called Saliniketal A which is nothing, but highly heavily oxygen substituted natural product. So, what does it tell you this example has many, I means things to be learned, number one di bro alpha alpha di bro compounds can be an oxy allyl cat ions precursor. Number two the zinc can be used zinc copper couple and then that is restricted to this dynofile, which is sorry dyne which is fural, for other example otherwise to make this oxy allyl cat ion.

The methods that is commonly used is something very uncommon, and it is resume that is use of allyl carbonyl gives this carbon bromine bond, little more higher covalent collector, so that is why the reactions is quiet phasyl. If you are react with this di iron flono carbonyl and this reaction temperature is very little 30 degree centigrade, and if you treat this with ferron and E, in this case E stands for ester.

So, once again, so non carbonyl is very safe compound is a liquid, partially available and photolysis it becomes aryl penta carbonyl that is also a liquid, and it is basically solve the purpose of zinc, and it undergo iron tetra carbon means that iron plus carbon monoxide, so it is basically iron 0. So, it undergo it insertion between carbon bromine bond like zinc, so that is ((Refer Time: 20:54)) and then this iron also activate the carbon bromine bond that means take a, this bromine to produce carbon cat ions here.

And the reaction product in this case so; that means, you will have ketone here that is basically all these reaction is equivalent to the reaction of the acetone at alpha positional alpha prime position as plus and minus that it. And so furan here double bond know moves and these fleuron ends are connected to the acetone ends alpha alpha primes, and these case this is something you have to sit down that actually this phenyl part of alpha position of the phenyl gets the positive character and the other part gets the negative character.

So, these one is produce a 90 percent and other one is 10 percent other one means other riju isomer, and which is again is fleuron then the ester part is on the right, between the two difference is that ester is one case ester is the on the phenyl side other side. Now, but what I did not tell you in the first example is there are other things here, that you have to be little worried about the steve of chemistry by virtue of phenyl and ethyl being on the same side and acidity.

One can just quickly say that if this is phenyl is alpha and ester is beta, because of these simple studied reason and in these case also this is alpha this is beta, so that is not a problem, but most other cases you get the mixture of the compound. That means, will have alpha; that means, this method for example, in the previous case you methyl group can be alpha to the oxygen beta to the oxygen, similarly this one; that means, then both the alpha, both beta, all kind of formulas and combinations would be possible for these.

That is the drawback of the 4 plus 3 cycloaddition reaction, in most cases they produce mixture of unlike, Diels Alder reaction is variation de selective and many cases various specific, but in these case these reactions are not well defined with respect to the Steve chemistry. So, result is that you get mixture, but there are cases you get just single isomer simply, because of the satiric reasons simply by the satiric reasons, what does it tell you, you get mixture of stereo isomer, what is it mean is not a truly a ferry cyclic reaction number one.

Number two that methods I mean this methods or the reaction could be stepwise while this; that means, when there is no defined chemistry of the product, one can just simply conclude the reaction is not very specific reaction. So, infect the truly this reactions are not a stereo specific reaction, and then let us look at other reaction of other examples here, that is mean in these case you have produce this oxygen hetero cycles.

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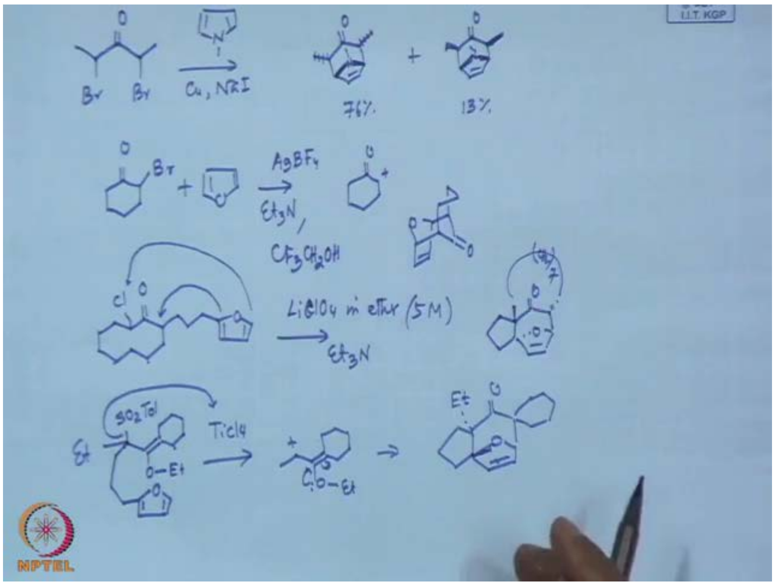

Similarly, if you begin with once again with a bromide here, and read this with payroll malty and then copper normally copper bronze is used and the sodium iodide, so sodium iodide what will you find a basically again you get a 7 membered ring. And this case have nitrogen and double bond just like fleuron the reaction takes place and both the methyl group is in these case nitrogen carbon bond is beta.

That means, transe to each other, other possibilities could be simply again 7 membered ring is carbonyl is nitrogen making beta here of nitrogen double bond this methyl group, what else; that means, this is beta carbon nitrogen bond beta this methyl group also is beta. Now, I mean anybody can guess you know which one be the major product the transformed the major product infect, this is found in 76 percent, this is found 13 percent.

So, this is a just case of nitrogen hetero cycle; that means, what it means the spiral also participate in the 4 plus 3 cycloaddition reaction, now let us look at one more example were will have unlike the previous example, you will have just alpha bromoketon and than fleuron, now it is whether it is possible or not. This reactions to so; that means, now you have to whether first of all you have to do a visibility test whether this reaction would occur or not, at least we knowing about the at dying part you know dying is electron range that is not a problem at all.

We do not have many options infect the dying either fleuron payroll, now and in previous example we have see dying system, simple beta dyne phenyl cyclo hexine; that means, we do not have much options it has to be electron reach dying. And then we have now pricurs in principle it could be an oxy allyl cat ion, but you have to choose right reaction condition what is the reaction condition could be, so to pull out the bromine the standard protocol is guess to pull out the bromine from is reaction mixture to format a carbon cat ion see normally formulas of carbon cat ions adjacent to a carbonyl group is little tough.

So, how do you do, so you have to have a halophilic reagent, and what is halophilic reagent silver so; that means, these example people have use silver tetra fluoride, that takes care of these; that means, that would pull out this, then these then at the same time you have to form a anion here. So, how do you do just use a base in these case tri ethyl ammine that is enough, and then solvent because your using inorganic compound silver tetra fluoride, so you have to a polar solvent.

What polar solvent used, methanol ethanol, no you cannot use simply because methalone, ethanol is sufficient in nucleu filling, if you take fleur acetone alpha fleur acetone put it in ethanol. After one day will come and just will see undergo how will mixes to form the methe oxy acetone so; that means, sufficient in nucleo filling, so what you can do you can use this ethanol analog tri fluero ethanol and difference between the just simple ethanol and tri fluero ethanol is that this is less nucleo filling.

As, the reaction proceeds two gave once again this portion is acetone cyclo hexine and so this is acetone cyclo hexnol portion, the this other portion on this one is a fleuron portion. You get a nice architecture of organic molecule, you can see here this is tricycle molecule can be made with the very simple methods alpha bromine acetone cyclo hexonal easy to make.

And then of course, fleuron’s now similarly reactions as been performed with again just a monochloro, so far we had discuss about this di bromo acetone etc, now you see a single bromine is sufficient to produce this oxy allyl cat ion here. Let us look at one more example this is now macro cycle with keton with halogen at the alpha position here, there are tricks where you can make this, now you have substituent containing this fleuron link system.

And the so once again basically the purpose is to engage the furan unit in the reaction, so is to alpha fleuro unit alpha fleuro acetone unit in a 4 plus 3 cyclo addition reaction. So, you can think about previous reaction, you can think out the previous reaction condition; that means, you have ((Refer Time: 31:32)) extra, extra this is sufficient, but while exactly it is difficult to say why it is not been used, but in these case there has been trick has been used and this trick here is lithium par chloride in ether.

And of course, the tri thealamine, so why suddenly lithium par chloride, normally it actually pipe molar lithium par chloride, any idea no halofalic reagent now, base is there to form the carbon ion at the alpha position, other side of the carbonyl go. And lithium par chloride is to again this to pull out chlorine here, this lithium par chloride actually was long back used unknown scientist as a polar solvent; that means, ether is a solvent flectro light if you put little bit of lithium par chloride; that means, to the extent of 5 molar.

Actually, saturated solution lithium par chloride ether is 5 molar solution, this becomes very, very polar solvent becomes very polar, so once you have a polar solvent; that means, carbon chloride bond undergoes salborieses means carbon cat ions formation facilated. And essentially so what will find again, again if you sit down if will see there is an intra molecular cycloaddition technique base and so fleuron is now; that means, this unit is reacting here this sorry this end, reacting to this.

So, essentially you will get to this molecule and then you have by virtue of geometry this is beta and this is alpha then you have this carbon cycle this other; that means, you have these three here 1 2 3 4 5 6 7. So, basically C H 2 and it should be 7 so you will have now micro cycle produced then you can do all kind of things you can do all kind of things here. So, from dibromo to monobromo, then to monochloro now, let us see then basically your go to peter sizes how many O H you can produce carbon cat ion. How many of you can recall, there are I mean almost 10 different methods one can make how do you make carbon cat ion just summarize.

So, that is what people would do so long we removed chlorine from this; that means, hetero atom and substrate and hetero atom, then hetero atom could be many you can have nitrogen, you can have sulfur, you can have oxygen, and all kinds of things here. That is what we will see and in the next example, you will see that sulfur oxygen all kind nitrogen may be depending on the situation for example, if you have amine group and treat with nitric acid, so it automatically released nitric acid.

So, you have this right and then there some certain tricks all you do not now there is group called sulphone S O 2 P H extra, the sulphone also form the nice living room in the presence of acid. That is not known most of us know sulphone is an activating group to produce a carbon ion. If you have a C H adjacent to sulphone, it is forms carbon ion in the strong base, at the same time if you have sulphone in presence of luyies acid aluminum chloride extra, extra it conforms also a carbon cat ion.

So, we will see the one of the example there with sulfur for example, this sub studies again, again variation of; that means, intervaled reaction. In these case the substrate would look like this down; that means, minimum requirement is double bond, that is for sure and you have to allylic substituent, in these case is a sulphone then allyl group. And these particular example you have cyclo hexine unit, then you have three different carbons, then you have a again fleuron unit, and obviously sorry, this one is ethyl now.

So, once we write this you can make out, I guess which one is allylic cat ion portion, which one this portion so; that means, basically what have you do your attention should be focused on the double bond. Once you identify the double bond you recognize which allylic portion, these and these and nothing portion this and you have dying portion, in built dying portion.

So, it should be intervaled reaction, and now is to know the reaction condition. So, you to form the cat ion first another portion is very easy, so in these case carbon cat ion being form the sulphone is particularly reactive towards titanium tetrachloride. And then di ethyl aluminum chloride; that means, one single chlodyne dimethyle aluminum chloride this kind of molecule compound, and these examples and it has been used as titanium tetra chloride.

Mechanistically, what will you see this should undergo coordination with lithium actually coordination take place at the oxygen end, so what you will find, this becomes the carbon cat ion and now this is ethyl here. Now, obviously all of us know this anion is not required, because oxygen is sufficiently nucleus to polarize the electrons towards the ring system. So, product would be again a 5 member ring because you have 3 carbon then you have fleuron and this is the keton here.

And then cyclo hexine part and there is I missed one point here, there was ethyl group here in these case this ethyl group would be resulting in these E z and by virtue of these satiric effect, again once again this carbon oxygen bond is beta and you have the double bond. So, this kind of success you know, then there are other variation of the sulfur substituent, let me just give me the example try to see whether anybody can make out this is somewhat like true problem for you see what here write here double bond first.

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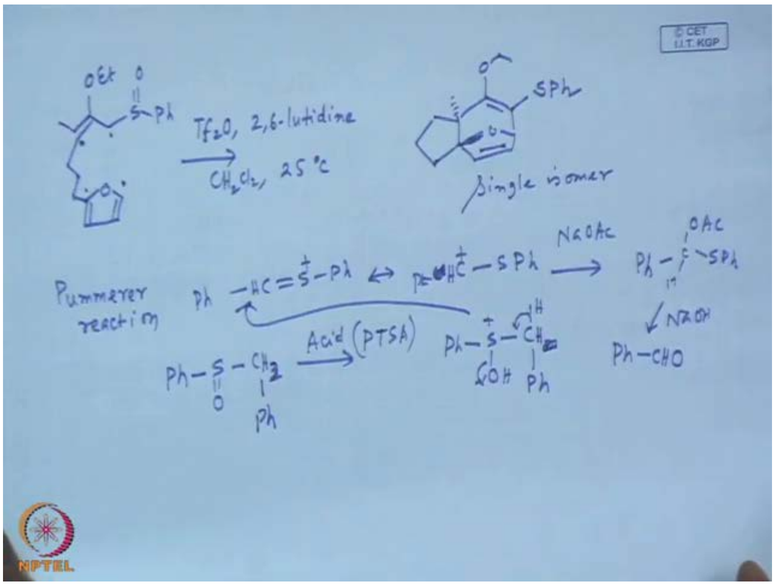

Once again a oxygen the middle one, then you have now is different move, it is this is not a sulphone, sulfoxide then you have three carbon and fleuron unit again so; that means, fleuron is pretty popular dying for this kind of molecule. And in these case difference is that the allelic position is that the having a substituent like known, as what is that name of the functional group sulfoxide and that mean sulphon would not work and it is trifoliate trifling hydrate.

And then 2 6 lutidine, what is it 2 6 lutidine, and solvent is methyline chloride here see here you do not have any harsh condition for the reaction, just very I mean this is a kind of room temperature kind of thing. So, what do you see, now you have to basically recognize the substituent now you have to see the agent 2 6 lutidine is a basically peridin derivative, 2 and 6 position 2 6 di-methyl peridin. So, it is a hindered kind of a base and tiffany anhydride all of you know trifloro acidic anhydride and so what do you expect these reaction, in these case again a very similar reaction, intermolecular you have 1 2 3 and 4 5, so it is a 5 membered right because this end would react.

So, that means, you count from here 1 2 3 4 and 5, so it is a 5 membered ring and then you will have this phenor part, and other part have again connection here, and as usual would be in other as previous example, you have this here. And the methyl substituent, so methyl substituent now is alpha here it has to be beta here, but what else what you will see here, this is something quite interesting. You will see now not a sulpoxide, what is it sulphide, and in this example you get a single isomer out of many possible isomers, you will get only single isomer.

Once again it is a outcome of studies and reactivites and all these things, it is very difficult to explain people have tried to explain, reactivites with calculations extra, but they are not really manageable. But, so we have to, but mostly it is ((Refer Time: 43:21)) and you are forming bicyclic compond, tricyclic compound, so these rings all other things should be involved to define the ((Refer Time: 43:29)). So, but once again there is a trick new trick produces carbo cat ion, what is this carbo cation, it is a carbo cation something like this, it is a system like this if you draw the resonance structure.

So, it will be so; that means, the now carbo cat ion adjacent to s p h and how do you make it by now monolisa should have known, in your lab this reaction is done what is this. Some says fumier rearrangement and fumier rearrangement is nothing, but you say let us say if you begin with p h next sulfuoxide and C H 3 of here and just any acid either luies acid or bounced acid whatever the acid used. Just take an acid basically, even simple iodine also sometimes involves, what is let us we begin with say commonest one let us say para toluene sulfonic acid.

For example, paratolin sulphonic acid what is expected here oxygen get sportnated sulphonium ion or then now what you see this one, now loss of water if you give loss of water, what will find. This will be a C H previous example, p h here, so if you loose water if essentially forms sulphonium kind of these things, and then these of course, if you have nuclo file in this system for example, let us you have a sodium acid for example, so what you expect you will expect p h, then c and hydrogen here s p h.

So, then if you just p h let us say alkali, what you can guess it will give you benzyl dihyde; that means, starting from sorry I think I made mistake somewhere, I need a phenyl group here. So, it should be a phenyl group here, the only you can get this, it should be a phenyl group and to essentially; that means, the phenyl sulfuoxide can give you benzyl dihyde, this is a very useful reaction to form a new carbon carbon bond.

The product here of course, I think I should admis this, there is double bond here, so this is essentially example, where you can do I mean. Now, just look at one more very similar example; that means, basically what we are trying to see we have to an allylic system, middle carbon as an oxygen ion, then this adjacent should have a group that would form a carbo cat ion, so sulphone, sulfuoxide previously halogen this thing that thing.

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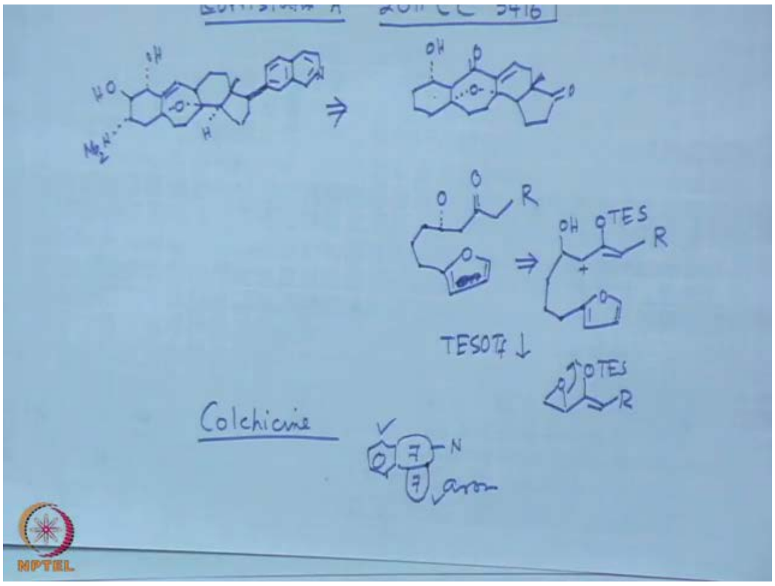

Now, just will see an application this type of reaction in the synthesis of natural product, this is big molecule I will be writing here just have passion to see this is known as cortistatin A molecule very recently as been isolated. And structure wise it is looks like a kind of strides it is not a strides, it is not exactly strides, but what will you see it just made for 4 plus 3 cycloaddition reaction, because you have 7 member ring system and also what will see you will have oxygen here, exact what will you want from it 4 plus 3 cycloaddition reaction.

And then there are so many other things here O H group, then here another O H group then this n me group then like stride last ring is a 5 member ring then angular methyl group and this hydrogen here. And then addition to that there is something here, so an hetero cyclic class, so you have to an hetero cyclic nucleolus write, and these case it is an iso chlorine nucleus, and this has a beta position.

Now, what you now there are two actually hetero cyclic unit, one is the iso chlorine, another is fleuron ring system a bended in 7 ring system, now how can you make this, this was first attempted with target to make this only the stride part. That means, is that is model study, what you study via accumulate O H here and then 7 member ring and then 6 member ring with double bond keton and there is 5 membered ring, this is angular dymethyl.

This was the primary target then this fleuron ring part, now what will you do you start with actually what you have to do sort of model study, what should be the model study. That means, you have to choose right substrate; that means, first of all you have to concentrate this part; that means, you have to have cyclo heptanes this fleuron ring and a O H group. That means, you have to create oh group up here at the beta position if you very closely look at just look at the structure here, that means at the one end you should have fleuron part right that sorry fleuron part.

Then you have to have an how many carbons, you have to have 1 2 3 4; that means, 1 2 3 and one more, and then will have to have oxygen there, 1 2 3 is skip the fourth will have an oxygen. Fourth will have an oxygen, which will have this, like this structure then you will have a carbon, again carbon here then this carbonyl and then this. And then of course, other should be there and let us say I put r here, you have to fill in the blanks here what type of group should be require; that means, to bring in this sort of backbone.

That means, basically what I am trying to say we are just cutting down this complexity of the molecule making, it as a simpler substance and we have identified that these portion should come from fleuron, and then this other part. So, all of us know this oxygen normally this oxygen minus or an oxyethen, so maybe we can get it from this kiton here, and let us say oxygen here. And in this case it is TES trithene sinide group and r then this one is not having any thing so but the other position will have the O H group, and then we have 1 2 3 and this fluron part.

So, you have to produce a carbo cat ion basically here, that is right, so how do you produce you all know the answer how do you produce a carbo cat ion that is a trick. So, far we had only the given example and how in this case we have get the carbo cat ion, once again they emerge go to the chapter of carbo cat ion how to produce a carbo cation. Actually, you can produce carbo cat ion from any organic material, methyl carbo hydrogen molecule we for example, hydro carbon also carbon can also react with super acid to produce a carbo cation through hydrant transfer.

Similarly, but commonest one we have to look for first the commonest one, we have removed halogen extra, siphon, shipoxide, nitrogen you have not talked about, so in this case let us say digonium. We are not talked about, what else alcohol, plane alcohol if you have diaol let us say if you have let us say in this case, if you have an O H group, you can think about, but you cannot think about. See if you 2 O H group then you will have computations, you can expect, what sort of reaction expect, if you have 2 O H group a side by side.

If you are trying phinochord reaction so; that means, you have to do a little bit of manuplication to skip the phinocol arrangement, so what have to do you form epoxide; that means, what you have to do u have to have an expoxide up here that is it. So, if you havean expoxite here all of us know under the influence of acid here, is T E S and triplate, so and this is the reaction and has been used, when you are interested I will give you the reference, this is taken 2011 chemical communication page number 3416. Those who are especially organic chemistry, study this interesting reaction chemical communication.

So; that means, you see here I mean if just see here rightly matches with the target molecules, and there are other molecules very similarly has been made, and naturally hydro cyclic molecule, but they are used intra molecular 4 plus 3 cyclo addition reaction to produce a very use full molecule. If you can make a synthesis of these molecule simpler, you will be rich over night, very rich anybody know the name of the molecule, it is a colchicines, what is colchicines.

I will briefly write 6 membered then you will have 7 membered and then another 7 membered ring system here, this is a aromatic and this is non aromatic and you have a nitrogen. If you just basically type Google, you will find colchicine as a nice structure, it has two stave chemistry two center, one is a kinal center itself and exle kinality. Basically, have 4 possibilities, the molecules is has been approved in 2009, as a drug for acute goute, did you understand what is the meaning of goute.

I know that is why I asked you what about Madhavan know you Vasudevan, pain in joints all these things, in [FL], it is a seviour know believe me or not, at least people like me or like elderly people like me you know have siviour problem. Sometimes, people would just cry, it is a very old molecule it was isolated in 1800 some thing from a small flowery plant, and people have tried to develop synthesis of this method. I mean they are about some 10 to 15 different methods how to make it, but all of them are equally lousy not possible, if you can make a good synthesis in 10 steps you can make money.