Structure, Stereochemistry and Reactivity of Organic Compounds and Intermediates: A Problem-solving Approach

Professor Amit Basak
Department of Chemistry
Indian Institute of Technology, Kharagpur

Lecture 24

Reactive Functionalities: Chemistry of Alkynes

Hello, everyone. Welcome back to this course on Structure, Stereochemistry and Reactivity of Organic Molecules and Intermediates: A Problem-Solving Approach. In this lecture, we will discuss some of the reactive organic molecules as well as intermediates and then see how they are generated. Some are quite stable, so they can be restored and some are react, they are generated only in C2 because they are too reactive. And then we will see the, discuss their method of generation and then what type of reactions they do.

We will not discuss, will not discuss what is usually covered at the undergraduate course. We will just pick out some of the more interesting or salient features of the class of molecules that we are going to include in our, in this lecture. The class of molecules as I told in general, they are the reactive organic molecules. When I say reactive organic molecules, it depends on the counter partner, reactivity comes if the partner is basically, is the one which the, where the original molecule reacts.

Like if I say benzene is stable, it is very unreactive which is not true. It is reactive, but it is reactive to a particular set of reagents, like if you form a bromine, bromoanime then the bromine, then the benzene undergoes substitution. If you burn, if you burn benzene then also it, it engulfs in fire.

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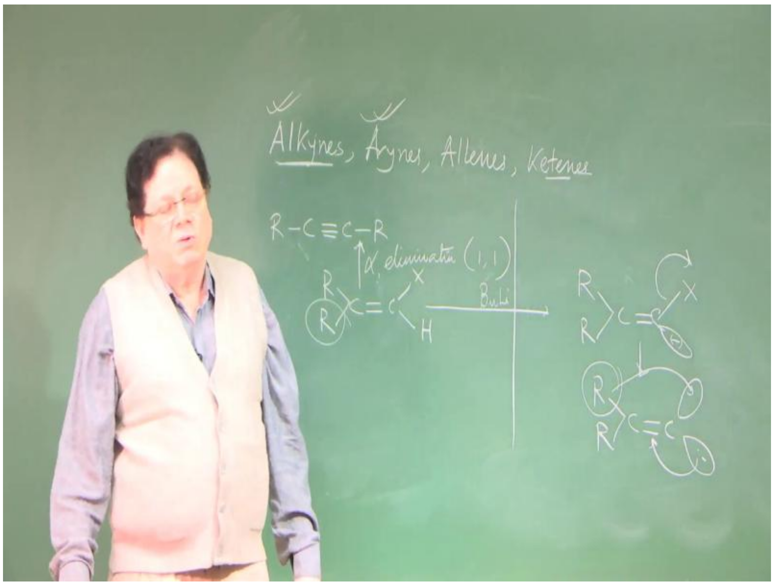

So, let us see the compounds that we are going to include in this lecture are the alkynes, arynes, allenes. So, basically Bi triple ones, alkynes triple one, arynes triple one's, allenes and then ketenes. So, these four we want to include. And let us see that how they are generated as I said only the some of the very salient features of their method of preparation and then their reactivity, out of these we will concentrate more on alkynes and the arynes. These are the very interesting ones, the others, allenes and the ketenes again they have been covered mostly in your undergraduate syllabus.

Now, the alkynes, we know that alkynes generation is basically or historically alkynes have been made by successive one to elimination of dihaloalkynes, successive elimination of dihaloalkynes. Now if you do successive elimination, first you do one elimination, so remove the HX from 1, 2 position. So that creates a double bond. So that double bond, but that is a haloalkene and then you induce the second elimination, but that requires a stronger base because the bond strength now increases because you have a (())(3:42) system now, so you need more for syn condition and it forms the triple bond.

But for 1, 2 elimination that means 1, 2 elimination needs a hydrogen NX at the 1 and 2 positions. But if you have an alkene, if you want to, if you want to have a, have an, have an alkene which looks like this. And you want to convert it into this product and alkyne, this is also an haloalkene but the problem here is that the elimination that it can, it can undergo is an alpha elimination, alpha elimination or you can call 1, 1 elimination, not 1, 2 elimination, 1, 1 elimination.

And that also definite demands that one of the R group must should migrate to the other carbon in order to give this alkyne, and you have this method you already possibly know this that what you do that you add a very strong base like butyl lithium. So, the first it forms the, removes the hydrogen so make the negative the two electrons are here then X and then X leaves so that makes a carbene intermediate, that makes a carbene, so one orbital is free, no electron, another is having two electrons.

So, now this is a neutral species but this is a carbene having 6 state of electrons. So, this R group migrates to the vacant orbital and this in turns comes to form the triple bond. So that gives the, this type of alkyne. So that is a very standard way of preparing alkyne.

Recently, actually for quite some time now alkynes are occupying a central position in medicinal chemistry because many of the, of the drugs or the natural products which have got a lot of biological activity, they possess the alkyne. So, methods of generation of alkynes have become very important. This is certainly one of the method, however it has its own limitation because you have to use a very strong base.

So, in a molecule if there is other functionalities which are not, which are susceptible to the strong base so you cannot, you cannot use this methodology without disturbing that functionality. So, what you need is basically orthogonality of the functional groups that is an important concept in organic, organic chemistry, orthogonality that means if there are two functional groups, if you do the reaction at one functional group without disturbing the other that means the two functional groups are orthogonal in their interaction with the reagent. This is also called selectivity, chemo selectivity but a better terminology, general terminology is orthogonality.

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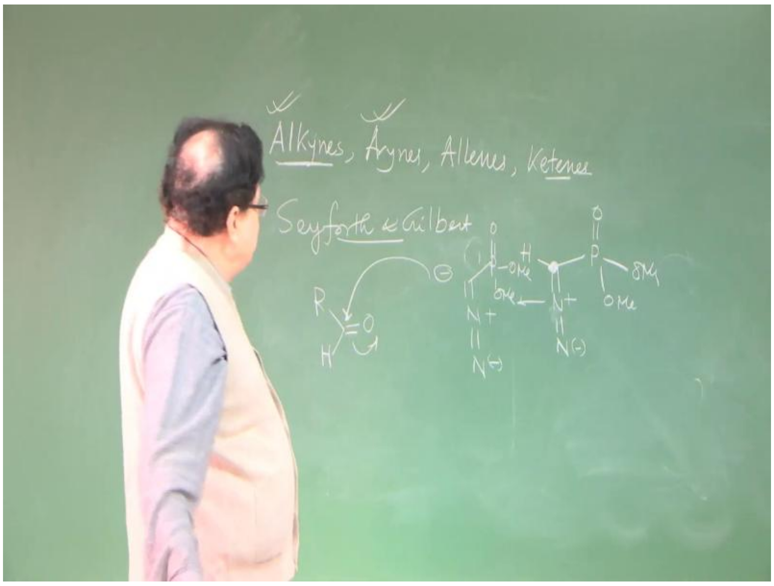

There is another methodwhich is quite similar not, but not exactly similar was, actually the method was given by or developed by two scientists Seyforth and Gilbert, Seyforth and Gilbert they used a reagent, Seyforth and Gilbert they used the reagent which is, a diazo, a diazo compound but this is a phosphonium a diazo phosphonium compound.

See phosphonium means a carbon phosphorus bond, that is called phosphonium. So, it is a phosphonium compound, basically ester and you have a diazo group here. So, this is plus and this is one of the resonating structure, so diazo phosphonium compound. So, this is what is called Seyforth Gilbert reagent. And utilising this reagent you can form a triple bond and that one of the carbon, one of the carbon from the triple bond actually comes from this carbon, the carbon attached to the diazonium functionality.

So, what is your starting material here? The starting material is basically a carbonyl. Suppose an aldehyde, you take an aldehyde and you add this reagent, the Seyforth Gilbert reagent but in presence of a very strong base, quite strong base like say tertiary butoxide, potassium tertiary butoxide.

So, what butoxide will do? Butoxide will make convert this into an anion. So, you have an anion here now the hydrogen is lifted up and OMe, OMe. Now this reacts with this carbonyl, this is the nucleophile so it is basically nucleophilic addition to the carbonyl. So, this is basically the reaction.

So, the reaction is carried out by first forming this anion by utilising a strong base like potassium tertiary butoxide and adding it to the carbonyl system I have taken an aldehyde. And then when it adds, it will add like this, this is the 1, 2 addition to a carbonyl.

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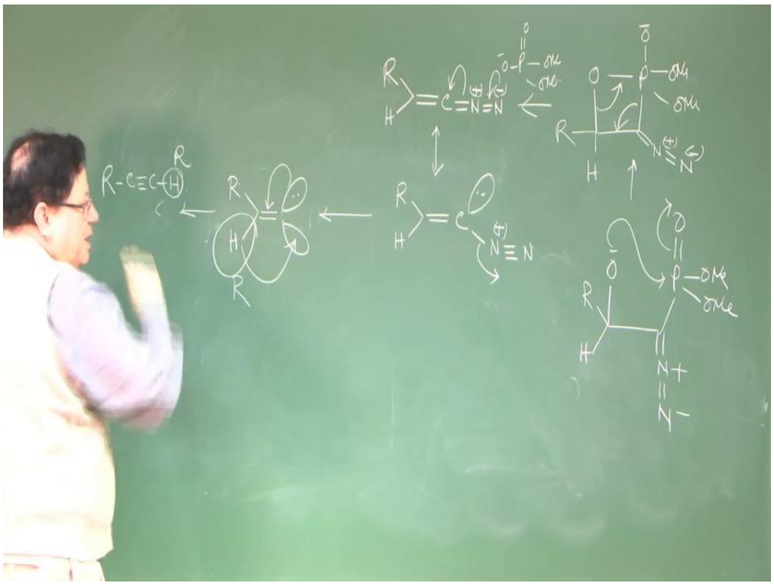

So, that will form now R CO minus, this is hydrogen and then you have and here is the, that phosphonate functionality. So, this is the intermediate, the first intermediate that is formed and then you know that there is a oxygen is or oxygen and phosphorus, they like each other and the it is like you have seen that in the Wittig reaction, the formation of this type of four membered ring.

So, the oxygen will attack the phosphorus and this goes, the electron pair goes to the oxygen, the phosphorus oxygen double bond that undergoes this electron shift and then you get a four membered ring like this OMe, OMe and then oxygen, this is R, this is your hydrogen and you have this is the N double bond we are drawing, we are taking actually one type of resonating structure here. So, this is the scenario.

Now, this will break in a similar fashion like the Wittig reaction. So, these four membered ring breaks and you get this type of another intermediate but the phosphorus is gone. That is the forming the dimethyl phosphate. So dimethyl phosphate comes out. So, P double bond O and then O minus OMe OMe that comes out and what is left is basically this and then the carbon with this type of structure.

Now, we have to look carefully into this structure. This is, we will draw another resonating form of that. So, I will erase this part. So, up till now, the steps are basically formed the anion from the Gilbert's Seyforth reagent or Seyforth Gilbert reagent, that anion adds to the carbonyl and then it forms a four membered ring and then that collapses into this compound.

Now, let us try to draw other resonating form of these R CH C double bond then the carbon and then you can write it as, you can write another resonating form which is like this. So, you have a negative charge on the carbon and the positive charge on the nitrogen. That is, you know, already, the structure of diazo, any diazo structure can be represented in several resonating structures and one of them is this.

Now, this nitrogen can leave and when it leaves, you see that you are actually getting a very very similar sort of intermediate that I showed you earlier about the alpha elimination the formation of alkyne via alpha elimination, where there is a migration of one of the alkyl group. So, the same thing will happen.

So, basically, ultimately you are involving a very similar type of intermediate carbon, one orbital is vacant and the other orbital is filled. So, this is the, this is your carbene state. Now, the hydrogen can migrate if it is alkyl then alkyl will migrate and this comes back and forms that triple bond.

So, ultimately what you will get is R C triple bond CH and if it is another R then you will get R here. So, this is a very good, very good reagent developed by Seyforth and Gilbert and the mechanism I have shown you, but the final step ultimately is basically what was obtained by alpha elimination of a haloalkene and so, that involves the carbene and then migration takes place and the formation with concomitant formation of the triple bond.

Now, there is some limitation of this methodology. The limitation is basically you are using again the same thing, you are using a strong base. So, we have now basically if you look at this methodology it is now more improved than the previous one that 1,1 elimination of an haloalkene. It is, it has been improved by, earlier you had to use the butyl lithium which is even stronger basis, now you are using potassium tertiary butoxide. So, you have lowered the requirement of the strength, requirement of a strong base. So, you have used a, this tertiary butoxide.

Now, what will happen? Still tertiary butoxide is quite strong base, so there may be functionalities which are not amenable to the use of tertiary butoxide which may react tertiary butoxide may disturb those type of functional roles, so people try to lower the basis, the requirement of a stronger base. So, you, whether a weaker base can serve this purpose.

However, for this Seyforth Gilbert methodology you cannot generate the anion and remember the first step is the generation of the anion from the diazo phosphonium compound that is not possible utilising a weaker base like say potassium, only say methanol, methanol and potassium carbonate, that is even weaker but that was not possible but then there are people who tried to develop, further develop it for a better way so that the requirement of a very strong base is minimised.

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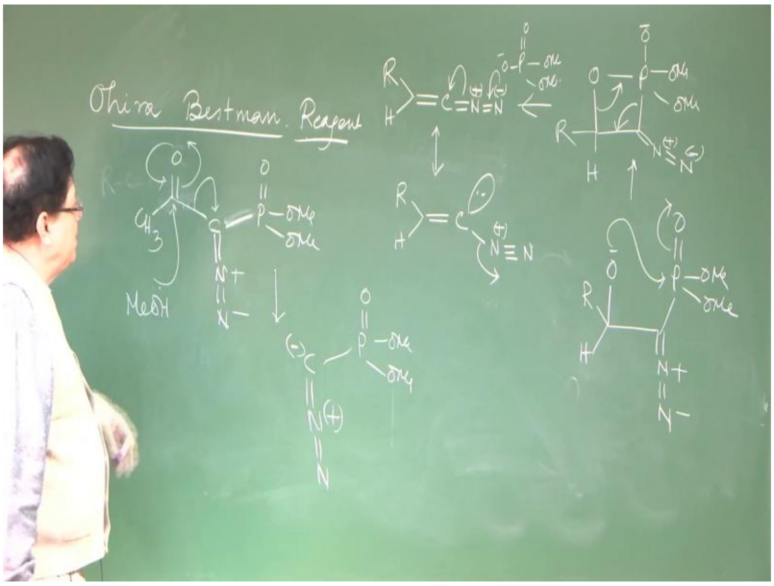

And what happened that there are again two scientists Ohira and Bestman, they introduced another modified reagent which is, which does not require the employment of a strong base like butoxide, only methanol potassium carbonate those type of bases will do.

Now, what they have done? Earlier the Gilbert this Seyforth method was this phosphonium compound. Now these two gentlemen, what they did? They put an acetyl group at this position. So, an acetyl diazonium phosphonium salt. So, this acetal group is quite reactive.

So, if you add say methanol in potassium carbonate methanol, so your methanol is the nucleophile or so that attacks, basically you do not need a base here, here it is a nucleophile, it is a nucleophile mediated generation of the same carbon anion that was introduced or that was made from the Seyforth reagent. So, methanol in presence of potassium carbonate will attack this carbonyl that goes in this direction, then comes back and this breaks.

So, the driving force is the weakening, is a weak this carbon carbon bond. You know that it is basically, basically as if having two very electron deficient carbon, which is not a very good system they are extremely vulnerable. So, it breaks and then generates the same carbon anion same carbon anion which was generated from the Seyforth Gilbert reagent. So then the same mechanistic pathway will follow and you will ultimately get the alkyne.

So, this is a very nice way that Ohira Bestman reagent is a very nice way just a simple modification of Seyforth reagent by putting this acetyl group and now you do not basically say that it is a base mediated generation of an anion, it is not, it is a nucleophile mediated generation of the anion. So that is the difference. So, these are some some of the approaches of making the triple bond.

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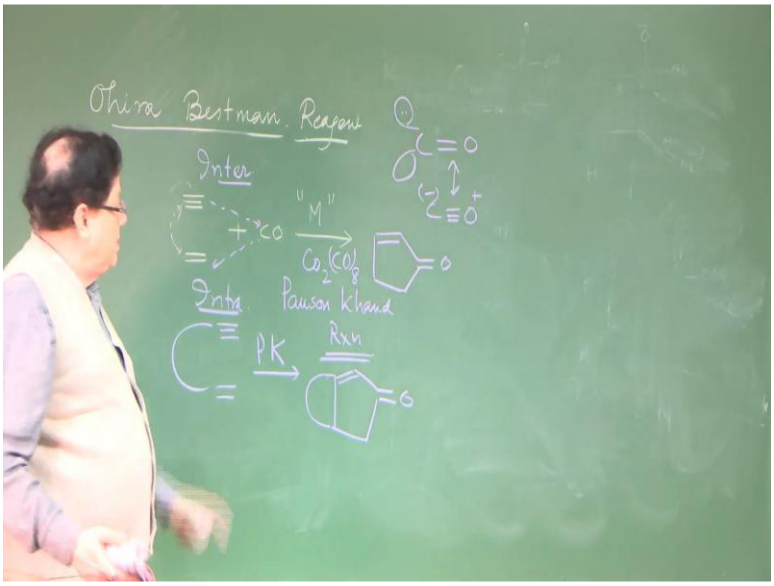

Now, let us talk about some reactions, some typical reactions of the alkynes which are very specific for alkynes. One is that, one is a reaction which is like this, that you have a triple bond and you have an alkene and you have carbon monoxide. If you take these three, triple bond supplies two carbons, double bond also supplies two carbons and the carbon monoxide supplies one carbon.

So, when they combine in presence of some metal catalyst, what will happen? That basically you have a connection between this and that and then you have a connection between, because carbonyl carbon you have a, in carbon monoxide the carbon can assume a very similar role like a carbene, that it is, it can accept electrons, it can also donate electrons. Because one of the structure will be like this and then you have the other resonating structure because people do not like this.

So, they draw this type of resonating structure, but anyway if you look at this structure, it is a donor, it can attack an electrophilic centre and it can also be attacked by a nucleophilic centre. So, that is why it can form two bonds involving the same carbon. So, that is ultimately the product from this reaction will be a cyclic compound, a cyclopentenone.

By the way cyclopentenone are very important entities. Many of the natural molecules, drug molecules they contain this type of moiety. This is a famous reaction, this is a name reaction, reaction between an alkyne, alkene and carbon monoxide is what is called Pauson Khand reaction.

It originated basically utilising cobalt catalyst, cobalt octacarbonyl, that is the catalyst and but there are many modifications later on, that it was, earlier there was a requirement of carbon monoxide itself, but then by utilising this type of organometallic compounds you can form the, you can utilise this and bypass the requirement of the carbon monoxide in Pauson Khand reaction.

Now, this reaction can be also, this is an intermolecular reaction that I have said, but there are many examples where it can be. So, if you do this PK reactions then the product will be ultimately that then you have the double bond, you have the carbonyl and this is the ultimate product. So, you can have both inter and intramolecular, both are possible.

The reaction looks simple like this, but the mechanism if you try to draw in detail that is quite complicated but quite complicated but we can simplify that mechanistic details. The simplify the mechanistic details like this. What is happening here is basically you have this cobalt octacarbonyl.

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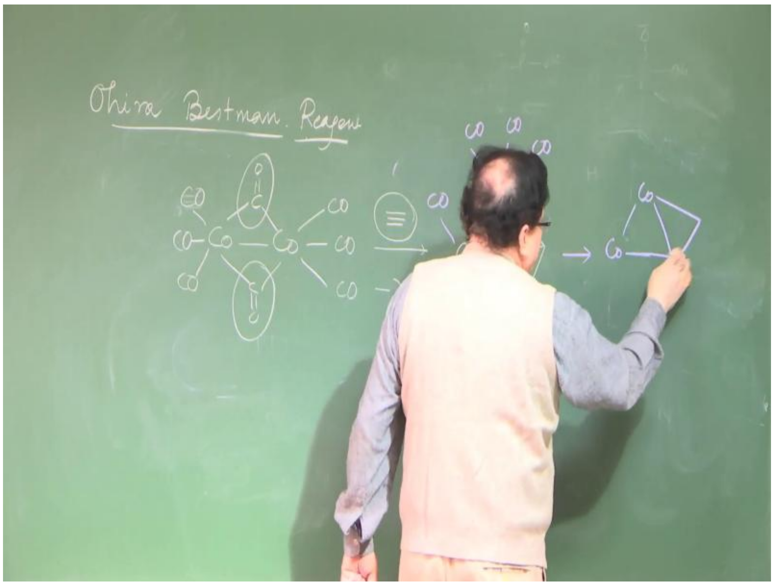

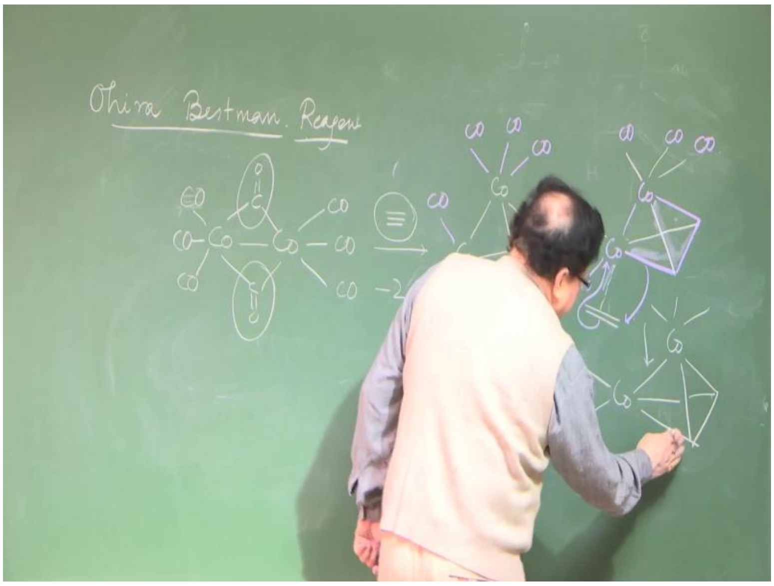

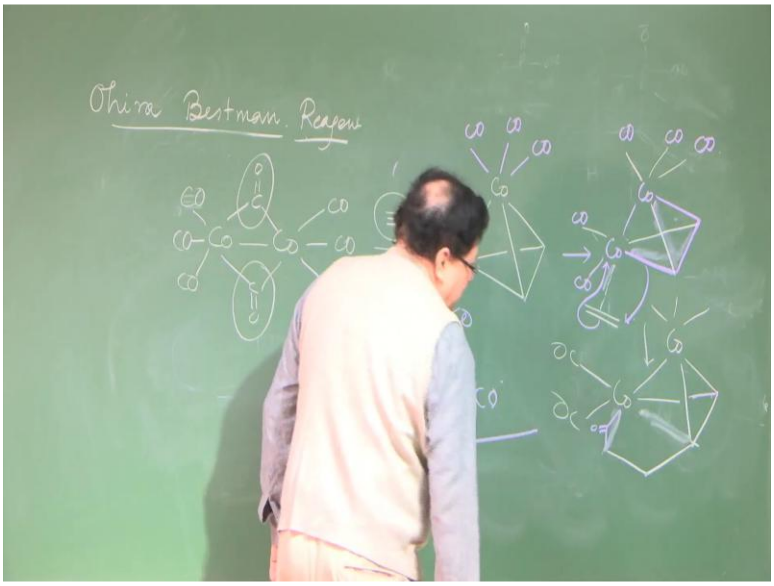

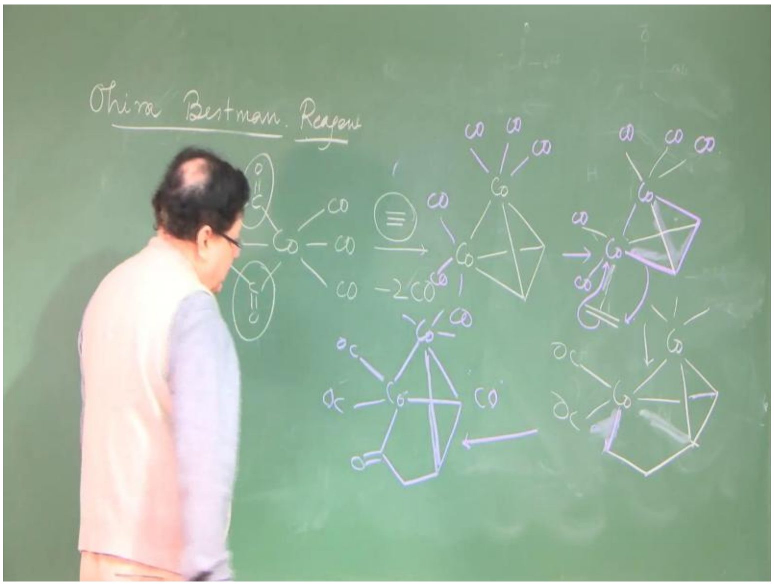

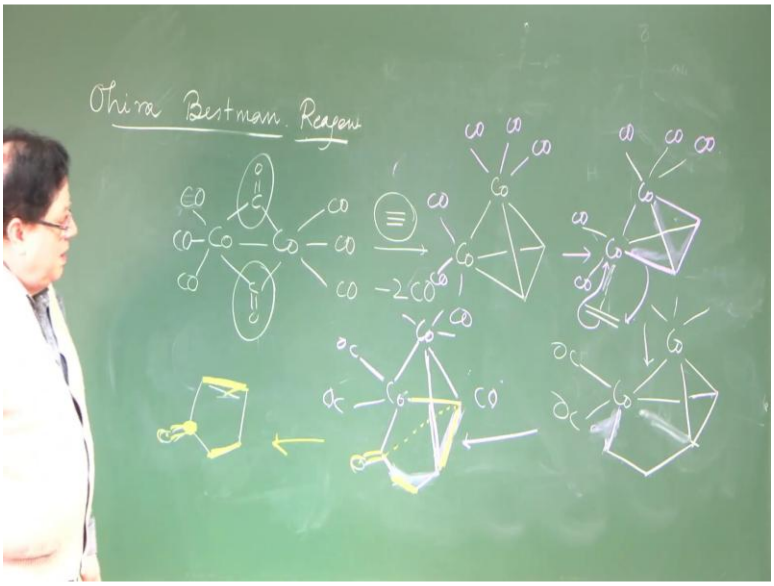

What is the structure of cobalt octacarbonyl? You have CO here, you have CO and then you have three CO attached to both the cobalts. So, this is cobalt octacarbonyl, if we put the CO, CO, CO, and CO. So, first it is the alkyne which reacts with this cobalt octacarbonyl dicobalt octacarbonyl system.

And what it forms is basically like this, this cobalt cobalt bond remains and these carbon monoxide ligands that is the bridging ligands, they leave and they are replaced by the alkene. One double bond, one bond replaces one carbon monoxide and the other bond also replaces another carbon monoxide. So, the product is like this. So, this is the alkyne part and so, this is the kind of intermediate that you will get, these are having the CO, CO, CO carbon monoxide, carbon monoxide and carbon monoxide.

So, it it has got two organo, this is a various organometallic bonds like this is a carbon cobalt bond, carbon cobalt. So, all these are quite weak bonds so, they can be manipulated. Now, next step this is the first component of the reaction that is the alkyne. What is the second component? The second component is your the double bond the alkene. So, the alkene now comes, the alkene removes one carbon monoxide, one ligand and then gets complexed with the, with one of the cobalt. Sorry let me see try to.

So, now, this is the, this is loosely complex with the alkene. So, this is the scenario, five minutes. This is the, this is the scenario. So, this is CO, this is CO all are carbon monoxide. Now, what will happen? Now, it will be, this bond, this as I say these are very vulnerable bonds carbon metal like carbon iron, carbon cobalt, carbon nickel these bonds are quite vulnerable and they can be manipulated.

So, now, as the alkene is loosely complexed to the cobalt. So, now this bond and a carbon carbon bond formation takes place. The resulting is this type of migration. So, now you have, so, basically what you have now is a cobalt and then you have another cobalt CO, CO, and then you have a, you have this but this bond is not there sorry this one is not there this is now attached to the alkene and this is the scenario. Is it clear?

So, let me again just explain, first of all this is the structure of the, this cobalt octacarbonyl. The alkene comes, removes the two bridging carbon monoxide ligands and then form this type of organometallic complex. And then the alkene comes and alkene is basically inserting, if you look at this reaction inserting between this carbon cobalt bond. So, that is the reaction that we are talking about. And in the process one of the carbon monoxide is removed. So, you have got now this type of organometallic complex.

Now, basically carbon monoxide, carbon monoxide which was eliminated or earlier as I said carbon monoxide was used as an external source. So, carbon monoxide comes and, that gets inserted because this is another carbon cobalt bond, that gets inserted in that between that carbon cobalt bond.

So, cobalt and then carbon monoxide and then you have CO this is basically you can, if you break this, so, you have a CO and this. So, that is the scenario. So, we are drawing this here CO and then and the other part remains and these are the carbon monoxide ones, the ligands. So, this is almost, we are almost there.

We have one, two and maybe there is some mistake here 1, 2, 3, 4. So, carbon monoxide there is another CH2 here 1, 2, 3, 4, 5 because now you have added all the components, the first two carbons came from the. So, this is the, this is this has come from the alkyne part, this is the alkyne part, this is the alkene part and this is the carbon monoxide.

So, now, you can say that basically what you have, what you have to do, you have to just break this bond and form the five membered, five membered ring and then removal of the, finally removal of this the cobalt from this which is tied up to the, to this the carbons which belong to the alkyne. So, you have to remove that and, in the process, you will form the double bond here.

So, that is the mechanism of this reaction. Again, just starting from this side. So, first it is the addition of the alkyne and then addition of the alkene basically addition means it is insertion between a carbon cobalt bond. So, and then finally, another insertion of the carbon monoxide again between a carbon cobalt bond. And finally, removal of all the cobalt. So, you get the cyclopentenone. So, you get the cyclopentenone, again this part came from the alkyne. This is the alkene part and this is the carbon monoxide. So, this is carbon from the carbon monoxide.

So, basically several insertions, first it is removal of the carbon bridging ligands and forming a complex with the alkyne and then it is basically insertion of the alkene into a carbon cobalt bond and then followed by insertion of carbon monoxide and then removal of the entire cobalt from the system and release of this cyclopentenone moiety.

So, it is a little bit complicated in the sense that because the structure of the your reagent is quite complicated. That is why, otherwise and you are handling two cobalt at the same time and alkyne can bridge both the cobalts also at the same time. So, that is why that structure looks like little complicated otherwise, things are can be rationalised as I said by just simple addition and then insertion, two insertion reactions and finally removal of the cobalt, that gives you the product. So, that is what is the Pauson Khand reaction.

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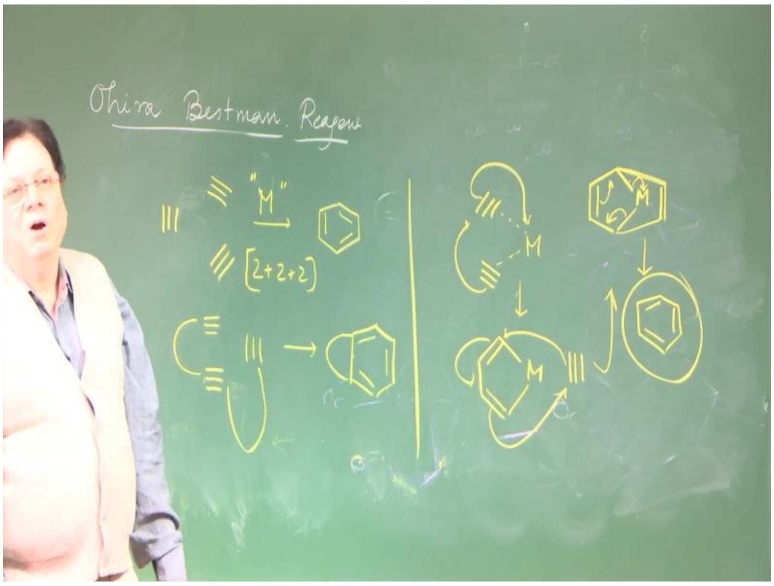

There are other reactions of alkyne, very quickly, I will just tell you that these are the some of the important reactions one is the cyclotrimerization. This is a very historically very famous reaction that three acetylenes can combine to give a benzene but the yield was originally very low, but now by use of the transition metal catalyst these reactions are now made proceeding through quite good yields, acceptable yields.

This is nothing but 2 plus 2 plus 2 again you can use cobalt here, but there are many other metals that have been used and you can use it also in intramolecular or semi-intramolecular that two alkynes are in the same molecule and then another alkyne that gives this type of product or the other way that you have all the alkynes coming from the same molecule. So, then the, then this it is purely intramolecular reaction, intramolecular 2 plus 2 plus 2 cycloaddition and all these are possible and there is considerable development in this case.

The mechanism is means, can be simplified like this that basically you have the two triple bonds which is first chelated to the metal. So, when it is chelated the final then there is this carbon carbon bond formation. So, you have a metalo cycle. So, first the metal was having a lot of ligands, some are replaceable ligands. So, ligands are replaced and then it forms the metalo cycle like this.

Now, the another acetylene will come the, third one. So, that undergoes a very a type of Diels-Alder type of reaction 4 plus 2 cycloaddition, 4 plus 2 cycloaddition and that will give what, double bond here and then the metal and then you have this, there is a double bond here. Now, it is the expulsion of the metal that you have to do. So, this bond goes there, that goes to the metal ion, this comes here.

So, the metal ion leaves and you get the benzene in the process double bond, double bond, double bond. That is a very simplified version of the mechanism. I think in this case it is much simpler unlike the Pausond Khand. So, the as I said, now, these reactions are routinely used in synthetic organic chemistry. The beauty of this that the aromatic ring can be made from a non-aromatic system, non-cyclic system only from the three triple bonds you can do it.

So, I think these are some of the reactions I wanted to tell you this. So, we have done the Gilbert's Seyforth method of formation of the alkyne, then the subsequent improvement by Ohira Bestman procedure and then we have done, we have discussed two reactions one is formation of cyclopentenone by Pausond Khand reaction utilising this dicobalt octacarbonyl and subsequently this considerable improvement of the earlier observed this 2 plus 2 plus 2 cycloaddition of three alkynes forming the benzene ring.

So, we will talk about alkynes later on again, right now, this is the, these are the things that I wanted to include in this lecture. And the next lecture we will talk about the, will bring the arynes also in picture, that alkyne, this triple bond aromatic compounds and with alkyne functionality. That also creates a lot of interesting chemistry to talk about. Thank you very much.