Symmetry, Stereochemistry And Application

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Lecture No-47
Name Reactions and Their Mechanism - Part 03

Welcome back to the course entitled symmetry stereochemistry and applications. In the last three lectures of tenth week we have discussed about Diels Alder reaction and its applications and different variations. We have discussed about the reaction mechanism of Diels Alder reaction. So, in the next two lectures in this week we are going to talk about a couple of condensation reactions and we will discuss about the reaction mechanism of Aldol condensation and claisen condensation reactions.

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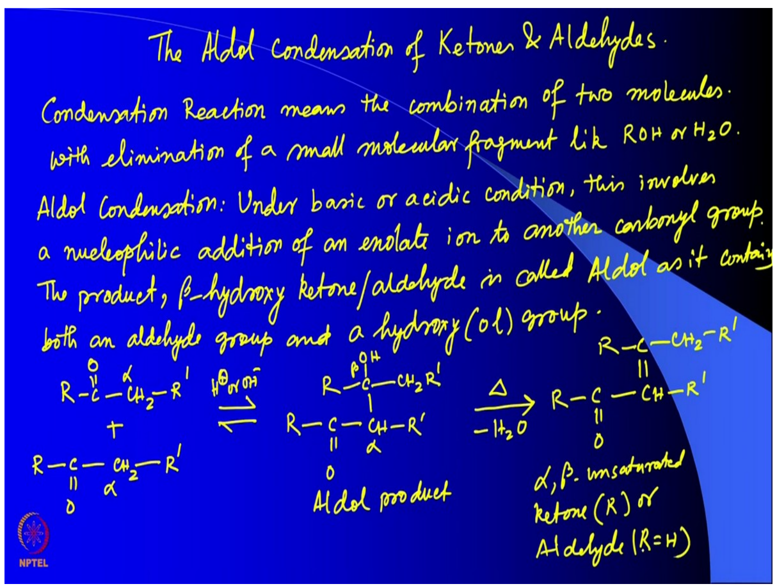

So, let us start with the Aldol condensation of ketones and aldehydes, the Aldol condensation of ketones and aldehydes. In general a condensation reaction means the combination of two molecules with elimination of a small molecular fragment small molecular fragment like alcohol or water. So, the name Aldol condensation comes from the name of the product under basic or acidic condition.

This involves a nucleophilic addition of an enolate ion to another carbonyl group either ketone or aldehyde the product which is generally a beta hydroxyl ketone or aldehyde is called Aldol. As it contains both an aldehyde group and a hydroxy which is also termed as ol group. So, the reaction a general reaction can be written like this plus this carbon is called the alpha carbon in presence of H plus or OH minus you get a product which is this one.

So, this is called the alpha carbon and the second carbon which contains the OH group is called the beta carbon. So, this product is called the Aldol product, if you heat this compound it eliminates a molecule of water and it gives you a new compound which is the alpha beta unsaturated ketone or aldehyde. So, let us try to understand how this reaction happens in a stepwise manner as I have already indicated this reaction can take place in both acidic and basic medium. So, the reaction mechanism should be understood with both the things like acid and the base.

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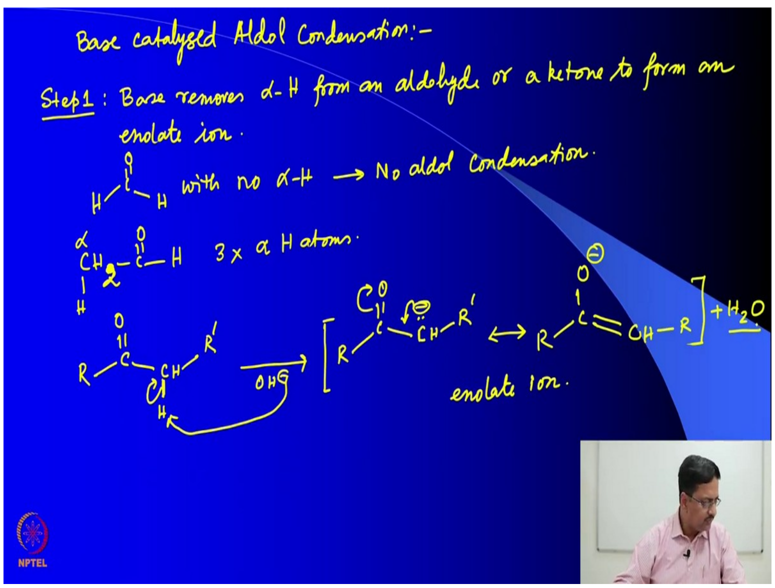

So, let us first try to see the mechanism for base catalyzed Aldol condensation. So, in the reaction mechanism it has several steps. In step one it is the reaction of base which removes the proton. So, base removes the alpha hydrogen from an aldehyde or a ketone to form an enolate ion. So, it clearly indicates that if you use an aldehyde like formaldehyde with no alpha hydrogen you will not get Aldol condensation reaction.

The minimum requirement is CH3 CHO that is acetaldehyde which has the alpha carbon and contains three numbers of alpha hydrogen atom. So, the first step involves the removal of this alpha hydrogen. So, in case of a general reaction that can be written like this we write it as RCO CHHR that is CH2R prime and we are treating this with OH minus which attacks this alpha hydrogen and extracts this and the double single bond of this hydrogen breaks and a carbon ion is formed. This carbon ion has two resonating structures.

As I am drawing here. This is called the enolate ion and of course this reaction eliminates water because this OH minus when it abstracts the proton that is eliminated as water molecule.

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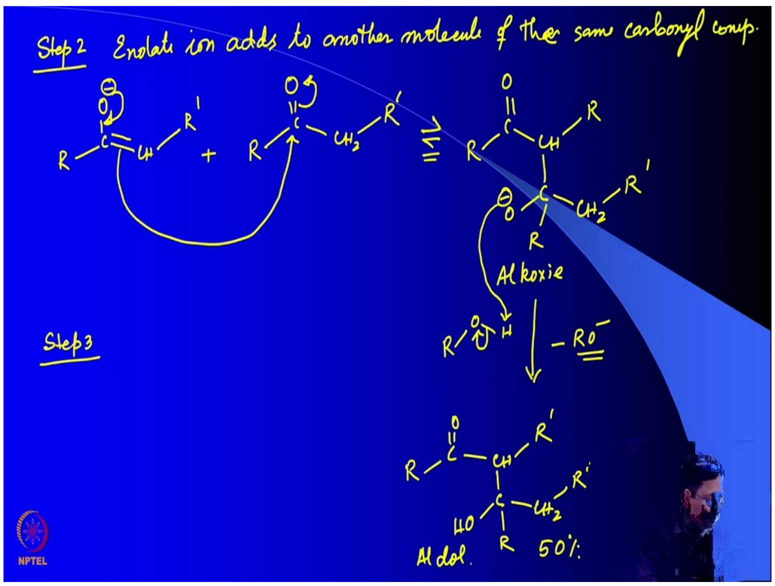

So, in this step two this enolate ion adds to another molecule of the same carbonyl compound. So, what we end up getting is this compound. So, this compound is called the alkoxide ion. So, now this step three is the reaction of this alkoxide ion with the alcohol that is present in the medium because if you remember in the first step it eliminated a particular alcohol. So, what we have in the reaction medium is this ROH.

So, this O minus abstract the proton from alcohol and RO minus is released and we get the product of this reaction which is the corresponding Aldol and it releases this RO minus which is the corresponding base which then continues the reaction further and reacts with further molecule of carbonyl compound that we started with. So, this reaction continues with a very little amount of catalytic amount of the base and proceeds towards formation of Aldol.

But remember all these steps are technically reversible and hence always you get a 50% yield at the end of an Aldol condensation reaction.

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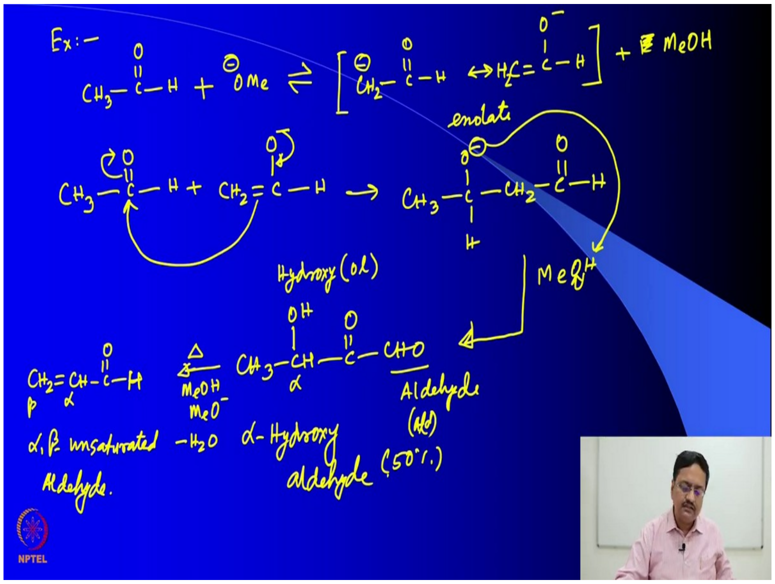

So, let us try to see with a real example if we have taken acetaldehyde as I indicated in the second slide today you take acetaldehyde and treat this with OMe in a reversible reaction it generates the carbon ion which resonates to form the enolate ion and forms methanol as the elimination product. Then this inolate ion reacts with one more molecule of acetaldehyde as shown in the previous slide it forms the alkoxide.

And this alkoxide is then reacts with methanol to abstract the proton from methanol and the methoxide ion alkoxide that is methoxide sodium methoxide methoxide ion is generated back. So, we have both aldehyde functionality and hydroxy functionality which is written as ol. So, it comes from here as ald and ol from there and what we can see is this forms as alpha hydroxy aldehyde as a product and always we get this as a 50% reaction mixed reaction product.

If you heat this product in methanol in presence of the MeO minus base then what we get is a very well known elimination reaction and it eliminates a molecule of water and it forms CH2 CH COH which is alpha beta unsaturated aldehyde. So, in following reactions after this with alpha beta unsaturated aldehyde one can proceed for various different organic compounds from this particular reaction product.

So, the Aldol condensation does not only limit to the synthesis of alpha hydroxy aldehyde, one can convert it into alpha beta unsaturated ketone or aldehyde and then take that compound for further reaction.

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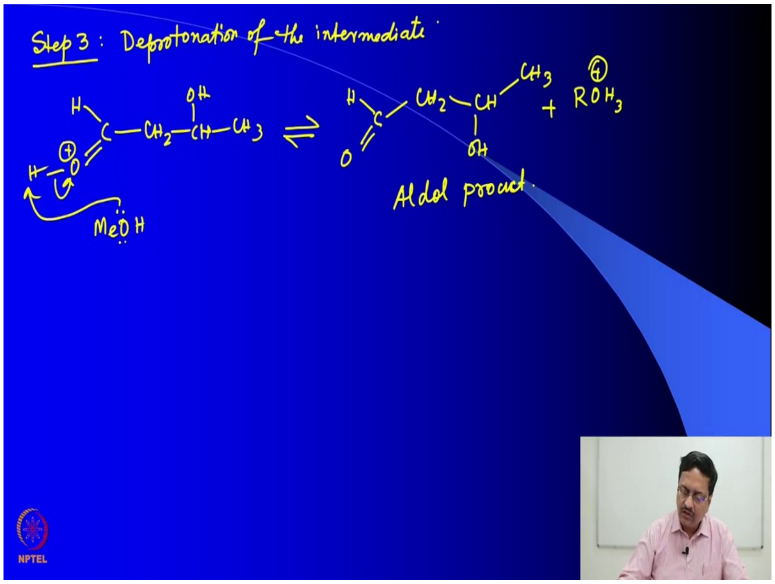

Now as I indicated this Aldol condensation can be catalyzed by the acid as well; acid catalyzed Aldol condensation. So, here in also there are three steps in step one it forms protonation of an aldehyde or ketone leads to the formation of an enol. So, again we take the example of acetaldehyde and treat this with acidic solution so H3O plus what we get in equilibrium is this one which essentially has a resonating structure as I am drawing here. And then in acidic aqueous medium this proton can be abstracted and the corresponding enolate can be formed.

So, then in step two this enol adds to another molecule of protonated carbonyl compound. So, what happens is the following this is again resonance stabilized you can understand the resonating structure from here. In step 3 it happens as a deprotonation reaction of the intermediate. So, when you have this intermediate as I had drawn in the previous slide you see that there is OH plus and in the medium we have methanol to abstract the proton what we get now is the corresponding Aldol condensation product.

So, the medium still remains acidic and this is the Aldol product at the end of the acid catalyzed Aldol condensation reaction. So, what we have seen is that both acid and base can be used to catalyze an Aldol condensation reaction and in all these cases what we have shown here is that the same aldehyde or ketone reacts to form the Aldol product.

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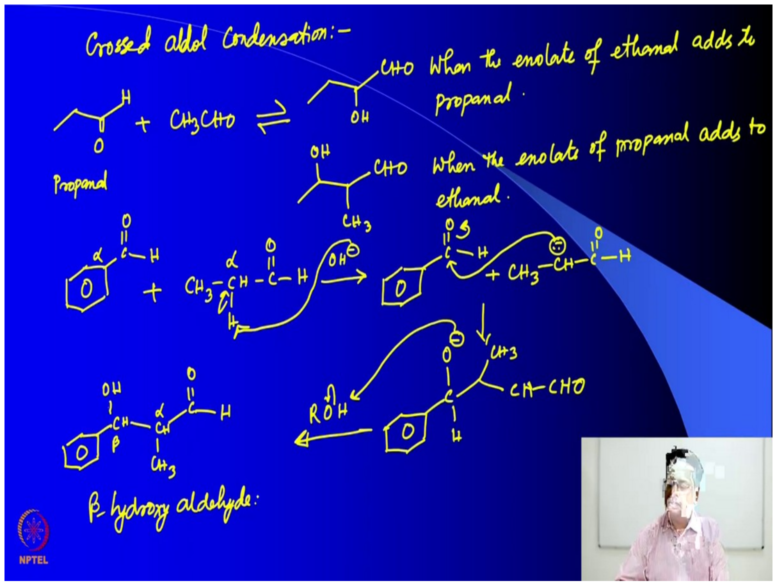

But it may be possible to do a crossed Aldol condensation. For example you can treat this aldehyde with the acetaldehyde you can expect two different products one can be this one and the other one can be this one. So, the first one can form when the enolate of ethanal adds to propanol. So, this is propanal sorry this is yeah propanal this is hydrogen. And this second product appears when the enolate of propanal adds to ethanal right.

So, this reaction can lead to two different products if you use two different aldehydes or ketones. So, if somebody wants to use it efficiently and effectively then one has to choose this aldehyde judiciously such that only one aldehyde or ketone can generate the enolate ion and the other one cannot that means you should use one of the aldehyde or ketone which does not have the alpha hydrogen for the formation of enolate and the other aldehyde or ketone should contain an alpha hydrogen atom.

Let us take benzaldehyde as one of the aldehydes. You see this benzaldehyde does not have any alpha hydrogen. So, this benzaldehyde cannot form the enolate ion and we treat this benzaldehyde with CH3CH2CHO which has an alpha hydrogen which has which has two alpha hydrogens present. So, if you do this reaction in the presence of a base what will happen is it will abstract a proton from this alpha hydrogen and the carbonanion will form here and that carbonanion can attack this carbonyl group of benzaldehyde leading to this intermediate.

And then this intermediate further reacts with alcohol abstracts the proton from alcohol and forms the beta hydroxy aldehyde. So, this is alpha this is beta. So, in this case you have got a mixed aldehyde reacting to form a combined Aldol which has two different starting materials.

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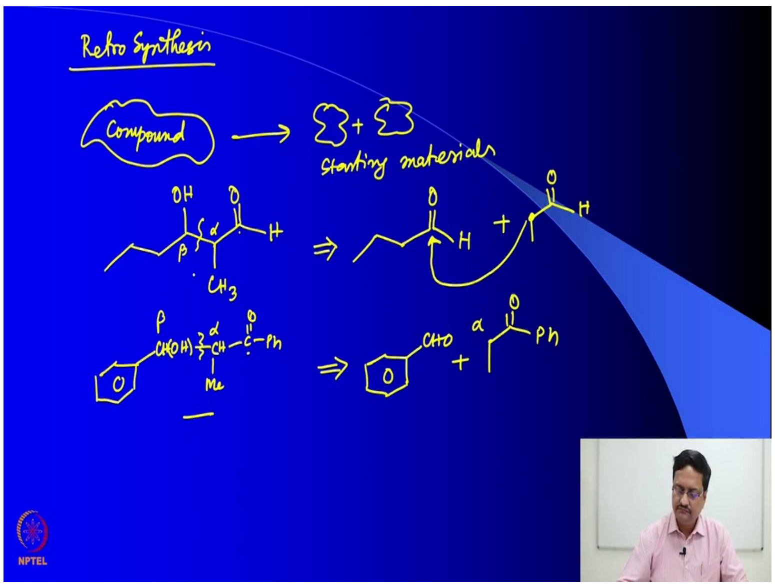

So, when we try to use this concept and try to see how one particular beta hydroxy aldehyde can or ketone can be formed then we can think of something which is called a retrosynthesis. Retrosynthesis is a process where when you are given a compound and you are asked to find out what were the two starting materials which were supposed to be combined to get this final product if I ask you to give me a reaction mechanism to form this compound and identify the starting materials for this compound what should be your approach?

You see from this first carbon C1 this is alpha that is beta and what we know is the bond between alpha and beta is the bond which is formed by aldol condensation. So, the two components that you can think of should be this rather it should be aldehyde and the other component should be this one. So, what has happened is the proton of this carbon is abstracted and then it reacts here to give you this particular product similarly if I give you the compound like this phenol with CH OHCHCOPh then what we see with respect to this carbon this is the alpha and that is the beta hydroxy.

So, this bond is supposed to be made during the Aldol condensation. So, in a retrosynthetic approach this bond should be broken and converted to the corresponding aldehyde or ketone in this case it is aldehyde and here this should become ethyl phenyl ketone. So, this one is simple because here you have only one aldehyde or one ketone which has the alpha hydrogen present. So, it is obvious that these two compound will combine and give this product.

But here you remember that this particular compound also has alpha hydrogen as a result this will not be the unique product for that particular reaction. So, here I have shown you that how a crossed Aldol condensation can be used to make various compounds. So, we will continue from here in the next class and discuss about Claisen and Dieckmann condensation reactions, thank you.