Symmetry, Stereochemistry And Application
Prof. Angshuman Roy Choudhury
Department of Chemical Sciences
Indian Institute of Science Education and Research, Mohali

Lecture No-50
Rearrangement Reactions in Organic Chemistry - Part 02

Welcome back to the course entitled symmetric stereochemistry and applications. In the previous lecture we were discussing about various organic rearrangement reactions and in that we have discussed about the Hoffman rearrangement reaction which is a reaction where you can treat an amide and convert it into a corresponding amine by shortening the chain by one carbon.

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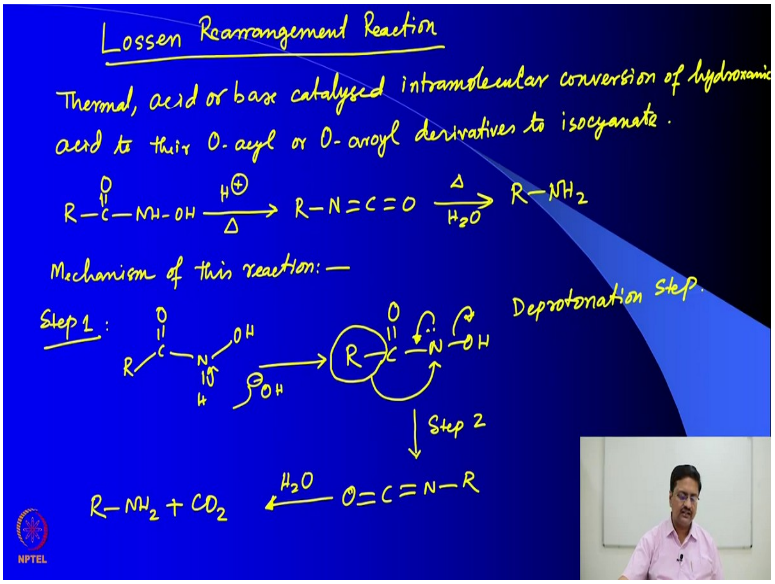

Lossen Rearrangement Reaction

Thermal, acid or base catalysed intramolecular conversion of hydroxamic acid to their O-acyl or O-aroyl derivatives to isocyanate.

$$R-\overset{O}{\overset{\|}{C}}-NH-OH \xrightarrow[\Delta]{H^{\oplus}} R-N=C=O \xrightarrow[H_2O]{\Delta} R-NH_2$$

Mechanism of this reaction:—

Step 1:

Deprotonation step.

Step 2

$$R-NH_2 + CO_2 \xleftarrow{H_2O} O=C=N-R$$

So, in that context we would like to now discuss a couple more similar rearrangement reactions. So, the first one that we would like to discuss now is called the Lossen rearrangement reactions, this reaction is a thermal that means it happens with the influence of heat. Acid or base catalyzed, it is intramolecular conversion of hydroxamine acid to the corresponding O acyl or O aroyl derivatives to corresponding isocyanates.

So here this RCONHOH which is called the hydroxamic acid in acid catalyzed condition under heat forms the isocyanate and the corresponding hydrolysis of this isocyanate leads to the primary amine as we have seen in case of Hoffman rearrangement reaction. So, let us look at the mechanism of this reaction. So, let us see the base catalyze mechanism first. So, this is a deprotonation step, after this deprotonation this alkyl group migrates from carbon to nitrogen and N double bond C is formed in step two with elimination of OH group as well.

So, now this isocyanate as usual and just like in the previous reaction in presence of water releases carbon dioxide and gets converted to the primary amine as we have seen in the previous days class. So, if you could remember this mechanism of the carbonic acid reacting with the corresponding water molecule and it forms the corresponding amine as usual. So, you see here this isocyanate first reacts with water to form the carbonic acid and that carbonic acid releases carbon dioxide to form the corresponding amine. So, this is the Lossen rearrangement reaction that one can use in various organic synthesis.

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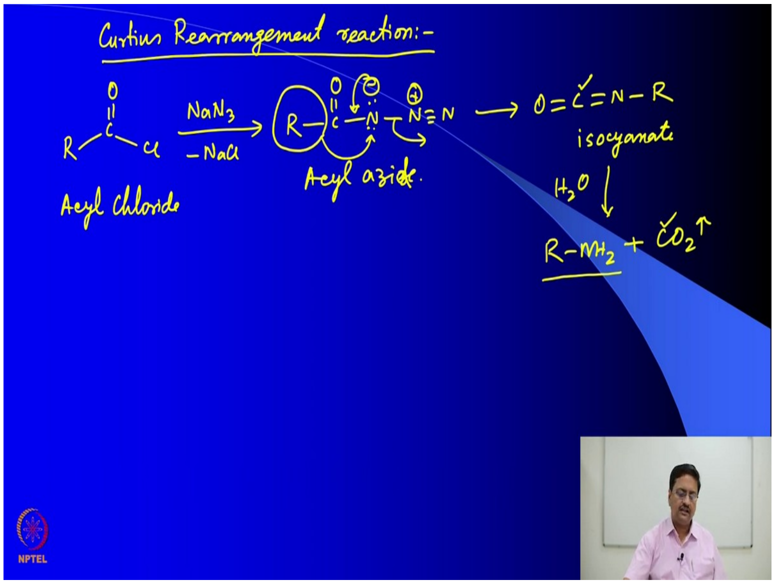
Curtius Rearrangement reaction:-

A similar rearrangement reaction is called Curtius rearrangement where RCOCl that is acid chloride is first treated with sodium azide with the elimination of NaCl it forms the acid azide. So, this is acyl chloride forms acyl azide and then the migration of R group takes place from the carbon to the adjacent nitrogen with elimination of nitrogen gas and the corresponding pi bond formation it forms the isocyanate once again.

So, then this isocyanate can easily be hydrolyzed to form the corresponding RNH2 that is the amine with the elimination of CO2 from the reaction medium. So, this particular carbon is released as carbon dioxide in all these reactions and we get a shortened amine. So, what we see is that all the three Hoffmann Lossen and curtius rearrangement reactions take place on three different types of substrates amides hydroxamic acid and the acyl azide to form a shortened amine. So, these reactions can be used to synthesize various organic amines in the laboratory.

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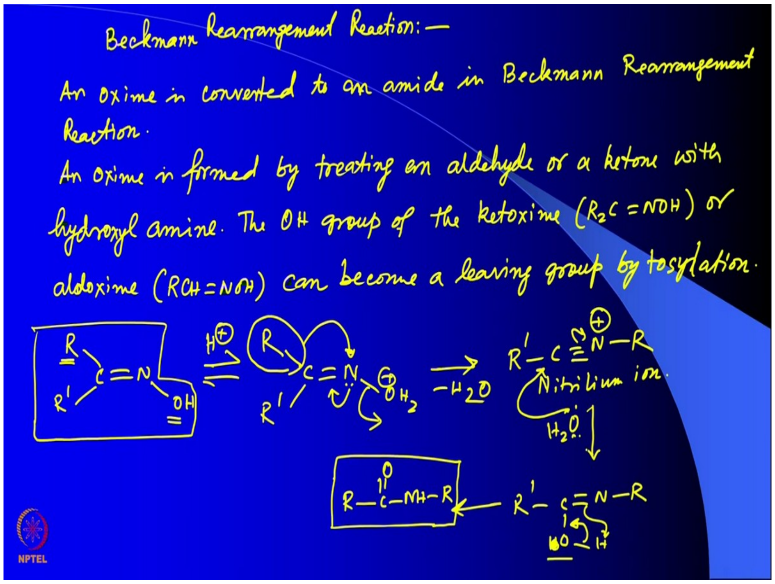

Beckmann Rearrangement Reaction:—

An oxime is converted to an amide in Beckmann Rearrangement Reaction.

An oxime is formed by treating an aldehyde or a ketone with hydroxyl amine. The OH group of the ketoxime ($R_2C=NOH$) or aldoxime ($RCH=NOH$) can become a leaving group by tosylation.

Now let us try to see the reaction mechanism of another very important rearrangement reaction called the Beckmann rearrangement reactions. So, in this case an oxime is converted to an amide in Beckmann rearrangement reaction. An oxime is formed by treating an aldehyde or a ketone with hydroxyl I mean the OH group of the ketoxime that is R2C double NOH or aldoxime that is RCH double bond NOH can become a living group by tosylation.

So, the reaction is like this. So, this R group migrates from the trans position of this leaving water molecule and this nitrilium ion is formed. This nitrilium ion then reacts with water molecule to form this compound which then further rearranges to form the corresponding amide. So, in this reaction the product that is formed is an amide from a particular oxime. So, this OH group becomes a leaving group after taking up a proton and then the nitrilium ion reacts with water that is present in the medium to form this intermediate which then easily rearranges to form the corresponding amide.

So, this amide is formed from the ketoxime. So, what happened is the group which is trans to the oxime is found to move or found to migrate from one carbon to the adjacent nitrogen and we will see some application of this reaction mechanism.

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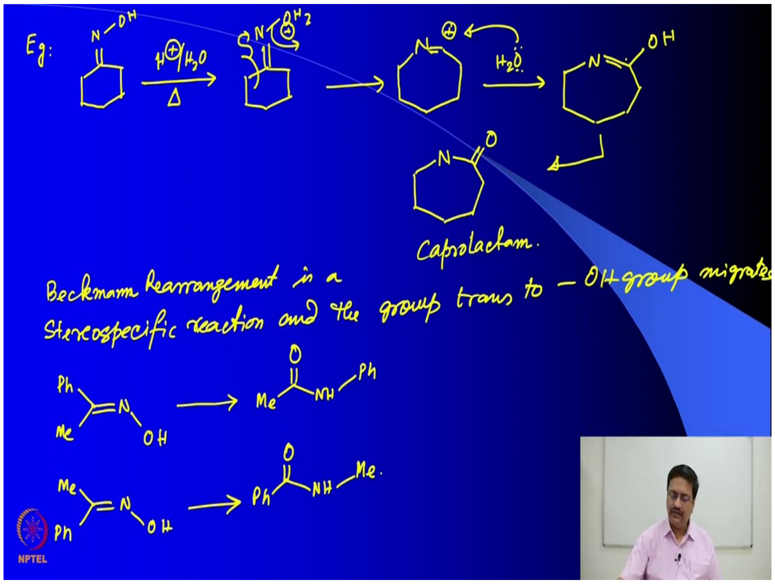

Beckmann Rearrangement is a Stereospecific reaction and the group trans to – OH group migrates

The first example is this one, suppose you have an oxime which is like this. So, you do an acid catalyzed reaction under heating condition. So, what it have does is it protonates the OH group first and forms OH2 plus then this group from the transposition moves to nitrogen and water is eliminated as a result the ring expansion takes place and a double bond is formed here with a plus sign.

So, then the water molecule gets attached here and it forms this intermediate which then rearranges to form the 7 membered ring which is called the caprolactam. So, here what we see is a ring expansion reaction taking place through a rearrangement reaction. So, what we understand about this Beckman rearrangement is a stereo specific reaction and the group trans to the OH group migrates.

So, if we have a compound where Ph and methyl groups are present and the oxime is such that the Ph is in the trans position with respect to the OH group then the product would be this one and if the methyl group is in trans position with respect to the OH group then this will be the product. So, what is seen in case of a Beckman rearrangement starting from a ketone. Let us see what happens.

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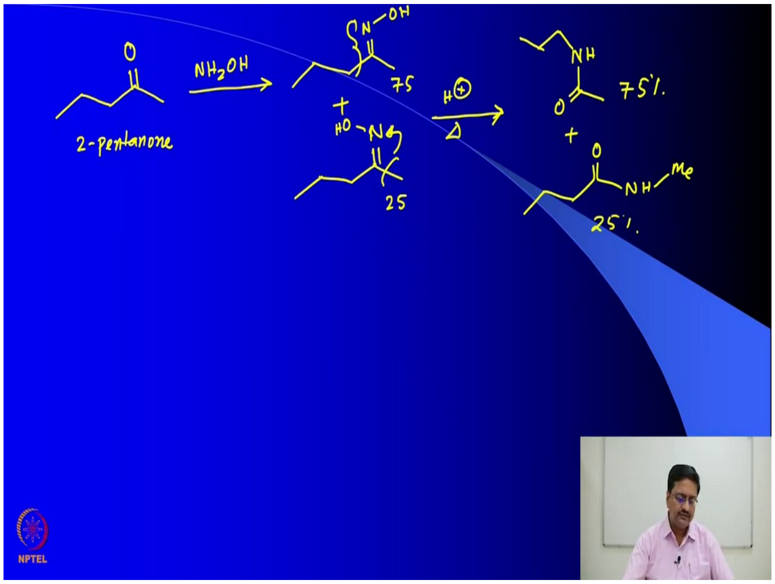

If you start doing a reaction from this particular ketone that is 2-pentanone if we treat this with hydroxyl amine what we would get are two different oximes in a ratio of 75 is to 25. And then when we do Beckman rearrangement we would get a product which is this one when this group migrates there we have three carbon atoms there and this will seem to 75% of that product in addition when this methyl group migrates one would get this as a minor product.

So, by looking at the ratio of the products one can identify what was the preference for the formation of hydroxyl amine the formation of the oxygen with the reaction of hydroxyl amine on the corresponding ketone. So, the ratio of the product tells you the procedure of reaction mechanism.

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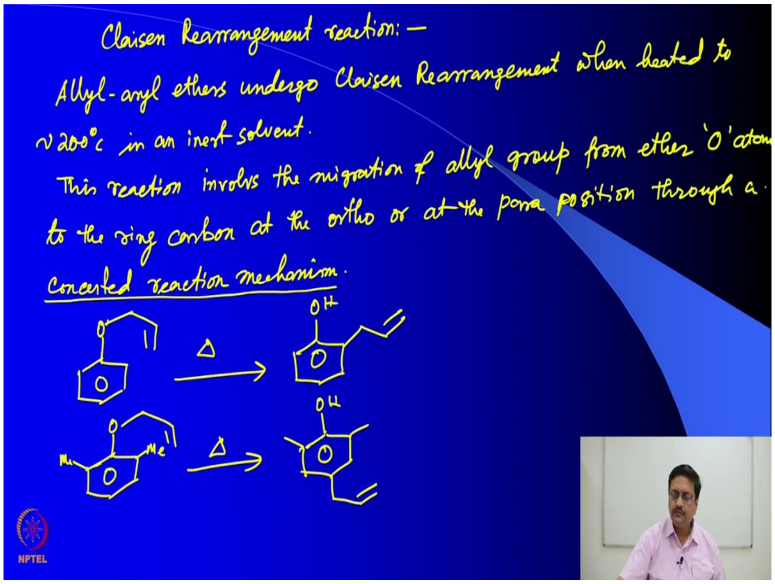

Claisen Rearrangement reaction:—

Allyl-aryl ethers undergo Claisen Rearrangement when heated to ~200°c in an inert solvent.

This reaction involves the migration of allyl group from ether 'O' atom to the ring carbon at the ortho or at the para position through a concerted reaction mechanism.

Let us now try to see a different type of rearrangement reaction called Claisen rearrangement reaction, here allyl-aryl ethers undergo Claisen rearrangement when heated to about 200 degree centigrade in an inert high boiling solvent. This reaction involves the migration of allyl group from ether oxygen atom to the ring carbon at the ortho or at the para position through a concerted reaction mechanism.

So, the reaction is this one, in case the ortho position is blocked. Suppose for this type of substrate where the ortho position is blocked by methyl groups then in this reaction the para product is also formed right. So, one can see ortho migration if the ortho position is free if the ortho position is blocked then one can expect a para migration product to form. In this particular reaction i have indicated that it is a concerted reaction mechanism.

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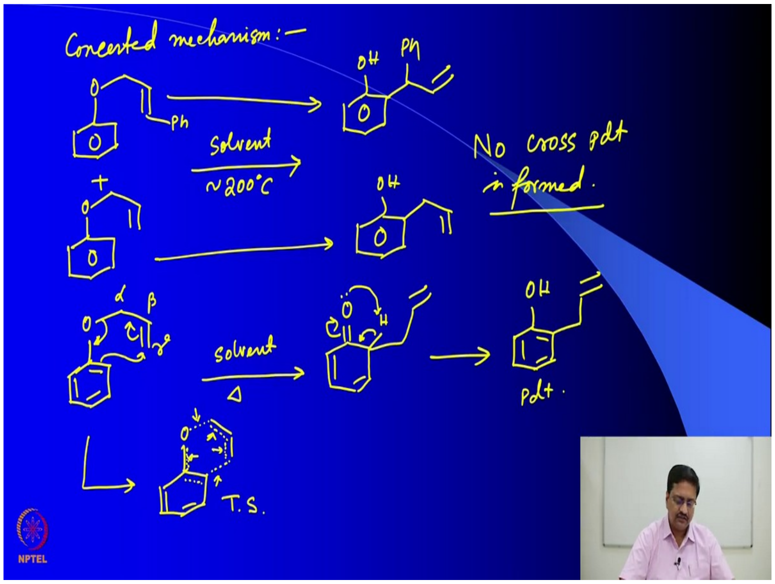

The proof of such statement is the following. Suppose if we had taken a mixture of two compounds one with a phenyl substitution and other without any substitution and had taken a mixture of these two compounds in a given solvent at about 200 degree centigrade. The product that would form are these two. So from this, this is the product from this, this is the product. No cross product is formed which indicates the reaction takes place through a concerted mechanism through a cyclic intermediate reaction intermediate.

So, one can think of writing the reaction mechanism like this. So, this is the alpha carbon this is beta that is gamma when we heat in a solvent the bond formation takes place from there to this bond moves here and that forms a double bond. So, what we end up getting is this reaction intermediate which then further rearranges to give you the final product. So, this is a concerted reaction mechanism and one can draw the corresponding transition state of this reaction as this which essentially means the dotted lines are bonds that are either in the process of formation or in the process of breaking.

So, this bond is forming this bond is breaking this bond is forming this bond is breaking and again this bond is forming. So, alternate bonds are either forming or breaking. So, this is a very well known rearrangement reaction in organic chemistry. And one can use these reactions to convert the ethers to corresponding phenols with a simple reaction just by heating the reagent in a solvent at high temperature. So, we will continue from here in the next class.