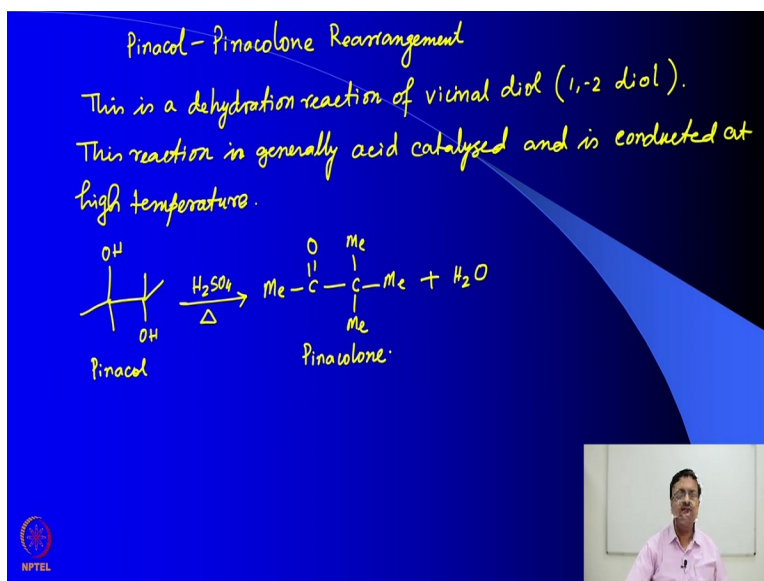


Symmetry, Stereochemistry And Application
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Lecture No-49
Rearrangement Reactions in Organic Chemistry - Part 01

Welcome back to the course entitled symmetric stereochemistry and applications. This is the 11th week of this course and we are supposed to discuss about a few well known rearrangement reactions in organic chemistry. And we would like to discuss about their corresponding stereochemistry and from that you will understand in various organic reactions how these rearrangement reactions can be utilized.

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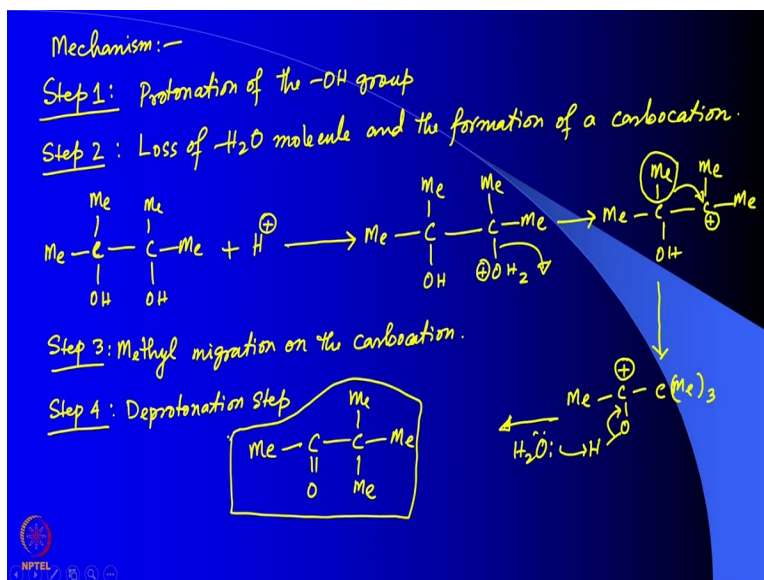


So, let us start with the reaction called Pinacol Pinacolone rearrangement. This rearrangement reaction is formally a dehydration reaction. So, what we can write here is this is a dehydration reaction of vicinal diol that means 1 2 diol kind of compounds where you have two hydroxy groups on adjacent carbon and this reaction is generally acid catalyzed and is conducted at high temperature. So, the general reaction that one can write is this one.

So, when you start with vicinal diol which means 1 2 kind of a diol where two hydroxyl groups are there on two corresponding carbon atoms in presence of strong acid and heat, this gets converted to a ketone. So, this starting material is called Pinacol and the product is called

Pinacolone. So, this reaction takes place through four steps. So, let us see what are those four steps of this reaction.

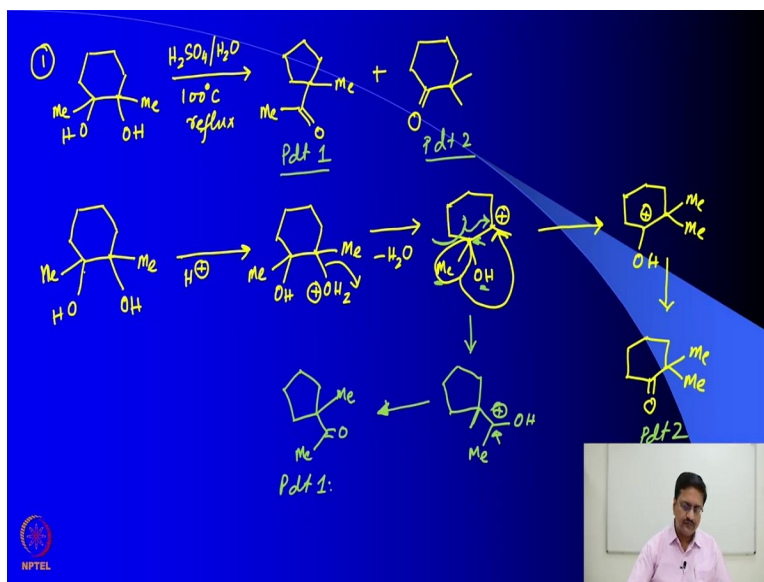
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So in this step one of reaction mechanism, protonation of the OH group is the first step and the second step is loss of water molecule and the formation of a carbocation. So, if we try to write these two steps for our starting material, this is the first step, the protonation step and the second step is removal of this water molecule to form a carbocation step three is methyl migration on the carbocation.

So, this methyl group then migrates from this carbon to that carbon and generates a new carbocation at the adjacent site. And then step four is a deprotonation step where this OH group loses the proton and a C double bond O is formed. So, this reaction gives you a ketone from a diol. So, this is a standard reaction called the Pinacol Pinacolone rearrangement reaction.

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So, let us try to see what happens if you try to do this reaction on different substrates suppose in the first example we have a cyclic diol like this. So, when you do this Pinacol Pinacolone rearrangement in the presence of sulphuric acid in aqueous medium at about 100 degree centigrade in reflux condition what is the product that one can expect what we see are two different products that are formed in this reaction.

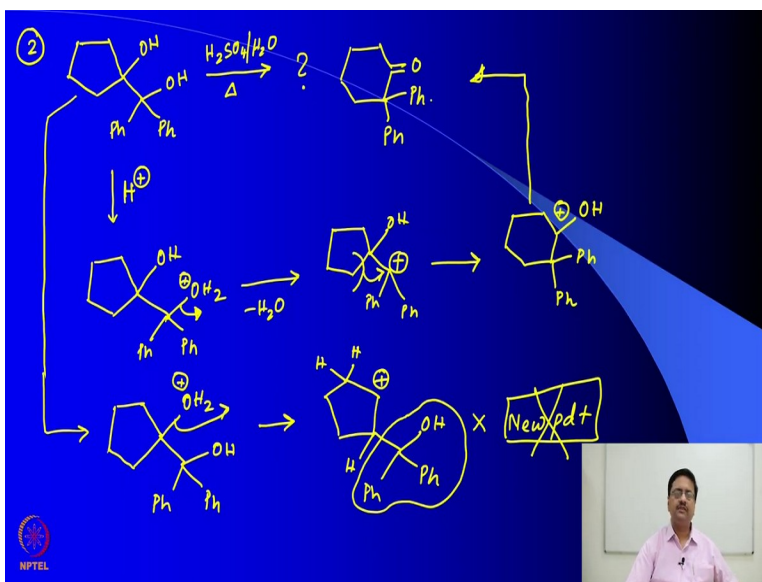
This is one product and the other product is this one. So, one may ask how this does this reaction takes place to give you these two different types of products. So, let us try to understand the mechanism of this reaction, when you add H plus one of the OH groups get protonated as usual and the corresponding methyl groups are there as usual as it is. So, then when the loss of water takes place it forms a carbocation a cyclic carbocation at this point.

Now there are two possibilities one possibility is migration of this methyl group to the adjacent carbocation site to form this new carbocation which certainly in turn would give the second product on deprotonation in the step four. The other possibility of this reaction is the movement of this group which is the larger group from this carbon to the carbocation side. So, as a result of this movement what will happen is the size of the ring will be reduced from a 6 membered ring it will become a 5 membered ring there will be a methyl group.

And this group will have OH and plus and methyl here because this methyl and OH is hanging now from that particular carbon which is here. So, a following deprotonation step from this carbocation will lead to sorry I made a mistake here this, methyl group should come at this position because the bond moves there and both the groups are hanging from the same carbon atom. So, methyl there and C double bond OMe there gives you the first product.

So, this is product one and this is product two and these two products can be formed by migration of two different groups one time the methyl migration gives you product two. And the other time the migration of the larger alkyl group which is the part of the ring when it moves it gives you a 5 membered ring as product one. So, you can see that by following the reaction mechanism very carefully we can predict and one can also show how two different products can be formed from a particular reaction.

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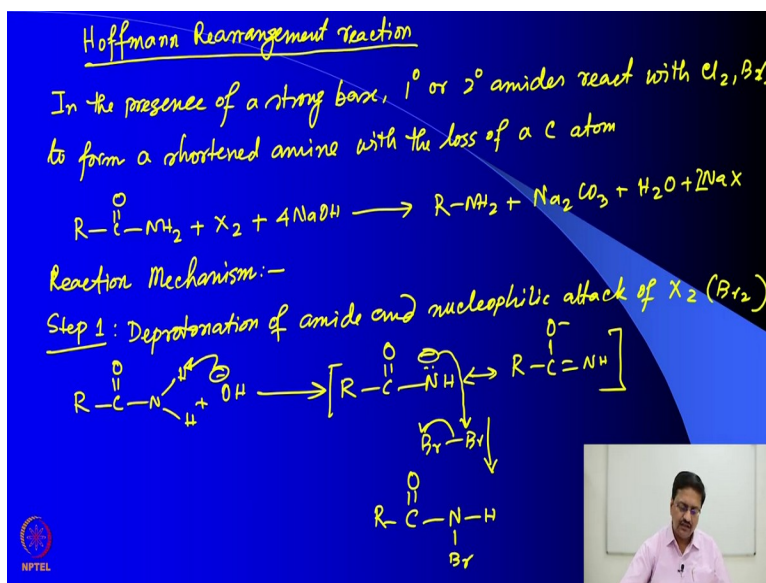
So, let us take one more example here we have a five membered ring with OH and then another OH in the side chain with two phenyl groups associated with that. So, if we add H_2SO_4 and heat in aqueous medium what will be the product. So, let us try to follow the mechanistic path and see how we can predict this particular product. So, the first step of this reaction as usual is addition of H plus.

So if the addition of proton takes place in the OH group outside it will form this compound this protonated molecule. So, in the second step when water molecule is eliminated it forms a carbocation. So, now this group the entire group from the cyclopentane ring moves from the first carbon to the last end carbon the carbocation carbon and forms this compound or rather a carbocation. This is the migration of the larger group to form a new carbocation and a deprotonation step would give you this product right is there any other possibility.

The answer is certainly, yes if the other OH group gets protonated what will happen so then elimination of water molecule will lead to this carbocation which contains OH Ph Ph. Now what can happen? See we have only hydrogens here and in this we have one hydrogen and this large group. So, this large group migration is not always possible and hence this will not lead to any Pinacol Pinacolone rearrangement product.

So, there will not be any; no new product will be formed in this particular reaction. So, we have seen a couple of examples using Pinacol Pinacolone rearrangement how one can predict different products of a given reaction.

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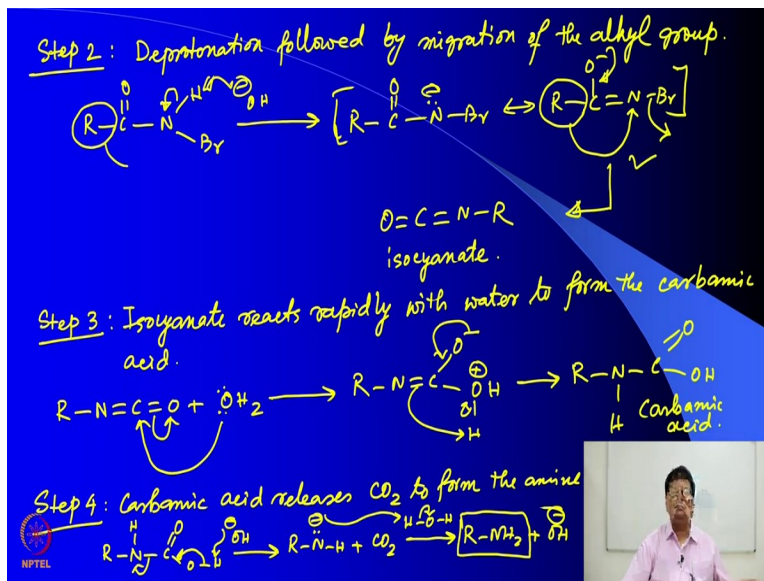


Now let us try to see a new reaction which is called new rearrangement reaction which is called the Hoffmann rearrangement reactions; in the presence of strong base one degree or two degree amides react with halogens like chlorine and bromine to form a shortened amine with the loss of

a carbon atom. So, in this process the reaction of $RCONH_2$ plus X_2 plus four $NaOH$ we get a product RNH_2 with the loss of carbon as Na_2CO_3 plus water plus NaX .

So, let us see how this reaction happens the reaction mechanism. So, step one is deprotonation of amide and nucleophilic attack of X_2 here I am taking example of bromine. So, the reaction is like this. So, this is the first step in which this $NHBr$ compound is formed.

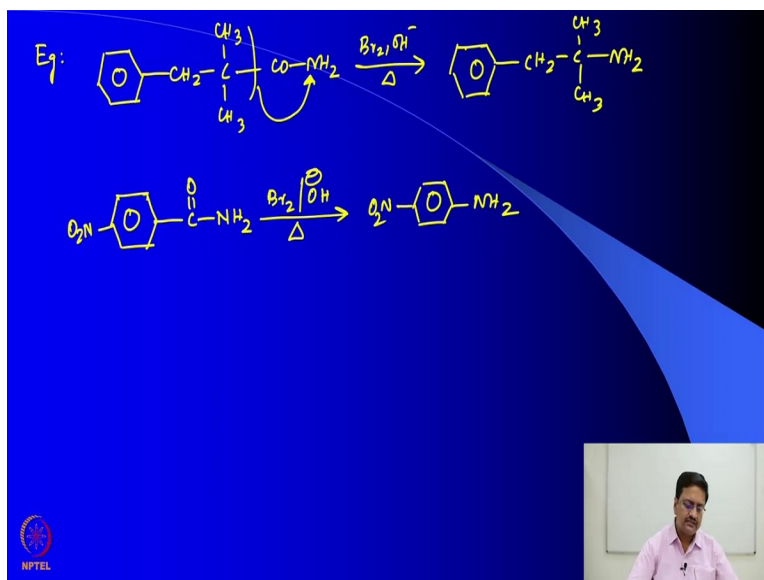
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The step two is another step of deprotonation followed by migration of the alkyl group. So, here what happens is the product of the previous step $RCONHBr$ reacts with one more molecule of base and it forms the intermediate like this which is again resonance stabilized as before, this R group then migrates from carbon to nitrogen and bromine is eliminated in this step. So, we end up getting a compound which is this one this compound is called isocyanate.

So, the step three is the step where isocyanate reacts rapidly with water to form the carbonic acid. So, in step four, carbonic acid releases CO_2 to form the amine. So this product is formed by a rearrangement of this alkyl group from the carbon to nitrogen which took place in this step. So, this is called the Hoffman rearrangement reaction.

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So, let us see quickly a couple of examples of Hoffmann rearrangement reaction. So, from this reaction this group migrates from here to the nitrogen in step 3 and forms this shortened amine. In another similar reaction benzamide with a nitro substitution. In this similar reaction medium bromine in alkaline medium with heat reduces to this nitro aniline para nitro aniline. So, this is the reaction which is used to make amine from the amides by doing a shortening step.

So, in the next lecture we will discuss about a couple of similar reactions where the similar type of mechanism will be discussed.