Introductory Organic Chemistry
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Lecture - 42
Substitution & Elimination Part 4

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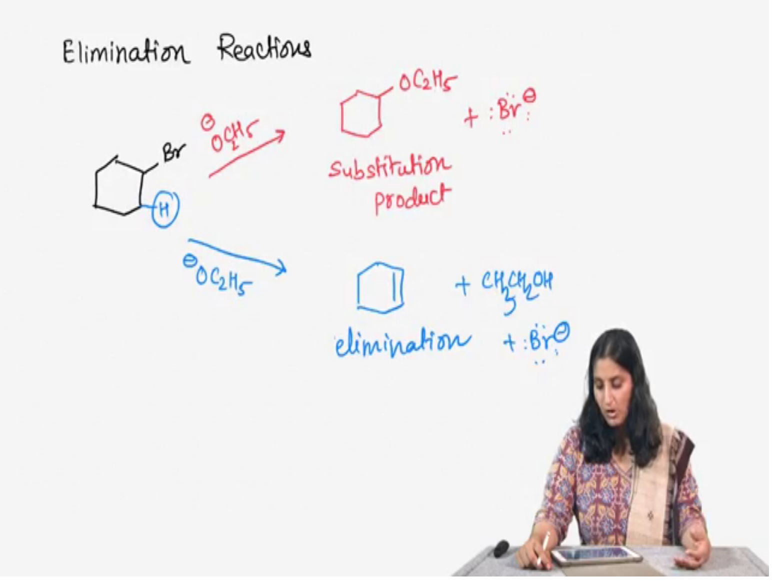

So far, we have looked at substitution reactions and typical reaction like this one here on the screen, you have a bromocyclohexane and then ethoxide acts as a nucleophile and kicks off the bromine as a leaving group, right. So, that's the kind of S_N2 type of reaction that we have seen so far; but remember nucleophiles also come with the property of corresponding basicity with them. So, good nucleophiles can be sometimes even good bases or rather what we have seen is that good bases are good nucleophiles, right.

Since the basicity and nucleophilicity of the compound goes hand in hand, this particular nucleophile here ethoxide, for example, can also do something called as a Beta- Elimination reaction. And before we go ahead and look at what the reaction is, remember that, the product of this reaction when Bromo cyclohexane reacting with ethoxide, it can come as a substitution product. So, something that we have written here or it can also come as an elimination product. So, what will the elimination product look like?

The elimination product is the formation of an alkene, a carbon-carbon double bond, okay. And that forms because ethoxide attacks on the hydrogen that is beta to the alkyl halide, okay. And it results into the formation of this carbon-carbon double bond. We will go ahead and look at the mechanism in detail, but before we go ahead, I want to point out that the substitution and elimination reactions are such that they go hand in hand; in the sense they are competing with each other in order to form the product.

Depending on the reaction conditions, depending on the type of compounds that are doing the reaction, so for example, depending on how strong the nucleophile is or how strong the base is or what kind of substrate we are using. Depending on all of these, whether substitution product will predominate or whether elimination product will predominate will really be governed by various conditions, okay. And we are also gonna go over that, but before that let’s first look at what beta-elimination reactions are, okay.

So, let me just complete this reaction on screen here. So, for example, in this particular beta elimination reaction, it forms a carbon-carbon double bond along with alcohol molecule and bromide as the leaving group.

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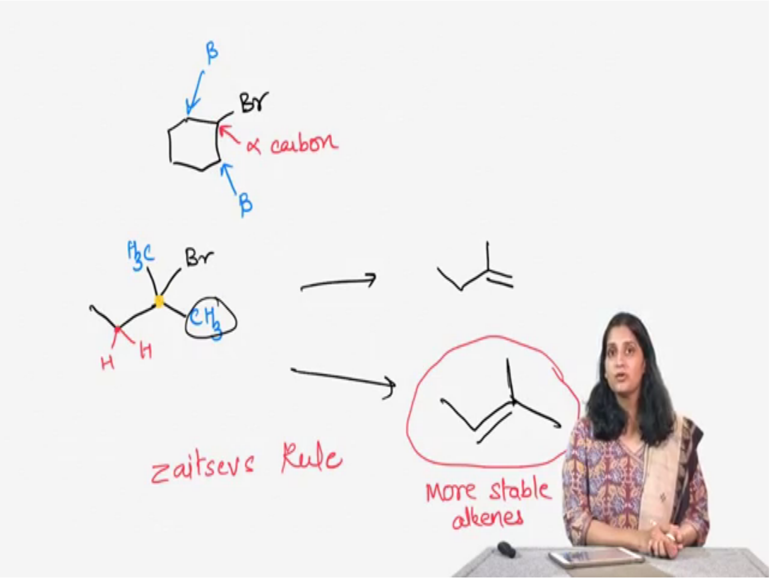

First, let us understand what beta-elimination mean? So, let us look at this Bromo cyclohexane; the carbon that is attached to the bromine is the alpha carbon. The carbon that is attached next to the alpha carbon, so, anything that is next to the alpha carbon is a beta carbon. So, here in I have 2 beta carbons, right. And both of these beta carbons are going to have hydrogens that are present on them. And when we do a beta-elimination reaction, the base comes in, abstracts the beta hydrogen and kicks out the leaving group in a type of beta-elimination reaction.

And whenever we do a beta-elimination reaction, the base abstracts the beta hydrogen in one of the steps of the reactions and which results into the formation of carbon-carbon double bond, okay. Now, herein, in this particular example it doesn't matter which beta hydrogen takes part in the reaction, right. But there would be conditions or situations when a particular beta hydrogen will be abstracted, right.

And typically it is seen that, the beta-elimination reactions follow something called as a Zaitsev's rule. So now, let us look at, what Zaitsev's rule is? Just to give you an example, I am going to start from 2-bromo-2-methylbutane, okay. Now, if this particular compound were to undergo beta-elimination reactions; first of all we need to identify, where are the beta hydrogens.

So, if I look at it, I have 2 methyl groups here which are beta to the alpha carbon and also this particular ethyl group you can call it which is this particular carbon here, is beta to this alpha carbon. So, I will point the alpha carbon with this yellow dot. Now if you think about it; there are two types of beta hydrogens or rather two non-equivalent beta hydrogens, which are present on the two non-equivalent carbons.

And the formation of the corresponding carbon-carbon double bond will be different, if one of these take part in the reaction versus the other, right. So, for example, I can form a beta-elimination product if this particular methyl group takes part in the reaction or the hydrogen on that methyl group really takes part in the reaction. Or you can form a product that looks like this, okay.

And if you think about it both of these alkenes are two different alkenes. What is seen is that more often in these kind of reactions? The formation of the more substituted double bond is preferred; the more substituted double bonded compounds or more substituted alkenes are also more stable alkenes. And so, this particular rule or Zaitsev's rule is followed whenever beta-eliminations take place because they favour the formation of more stable compounds.

I would like to point out that, it is not always that the Zaitsev's rule is followed. In fact, we will go over conditions or we will go over situations, when Zaitsev's product is not possible. And those are special conditions or special considerations that we have to give. But for more often, we see that the more substituted carbon-carbon double bond is formed and more substituted alkene, thus takes place at the end of a beta-elimination reaction.

To begin with the understanding of the mechanism of these reactions; we are going to take a step back and remember that, for substitution reactions there were two types of mechanism. One was S_N1 and one was S_N2. The same way here for elimination reactions as well, we are going to have two types of elimination reactions. One is E1, that is elimination unimolecular; the other one is E2, elimination biomolecular reaction. So, to go over the E1 type of reactions or elimination unimolecular reactions, okay.

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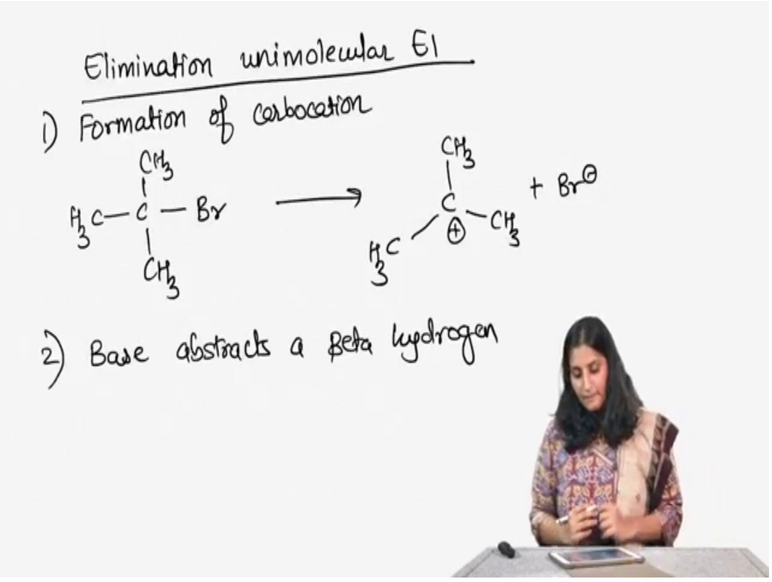

Elimination unimolecular E1

1) Formation of carbocation

2) Base abstracts a beta hydrogen

I am going to take the example of tertiary butyl bromide, okay. Again just like S_N1, E1 will also be preferred for some substrates as compared to another, okay. And we will go over those considerations very soon. But for now, let’s look at the first step of this elimination reaction. The first step of an elimination E1 type of reaction is that it breaks a bond between the carbon and the leaving group to form a carbocation. So, this should sound very similar, because in S_N1 also, the first step was breaking a bond between the carbon and the leaving group to form the carbocation.

And now you will understand why we took tertiary butyl bromide as our first substrate? That is because, tertiary butyl carbocation is going to be more stable, right. So, remember this particular step the formation of the carbocation is going to be a tough step. It’s going to be a slow rate determining step of the reaction. And so, more stable the carbocation is the more easier it will be for it to get formed, right.

So, once the carbocation is formed it is like any other carbocation. So, it could rearrange, it could do substitution reaction, right. So, there are various pathways that this particular carbocation can do. But now, the next step of elimination reaction happens when a base abstracts a beta hydrogen, okay. Now what does it mean? So, let's look at our tertiary butyl carbocation again.

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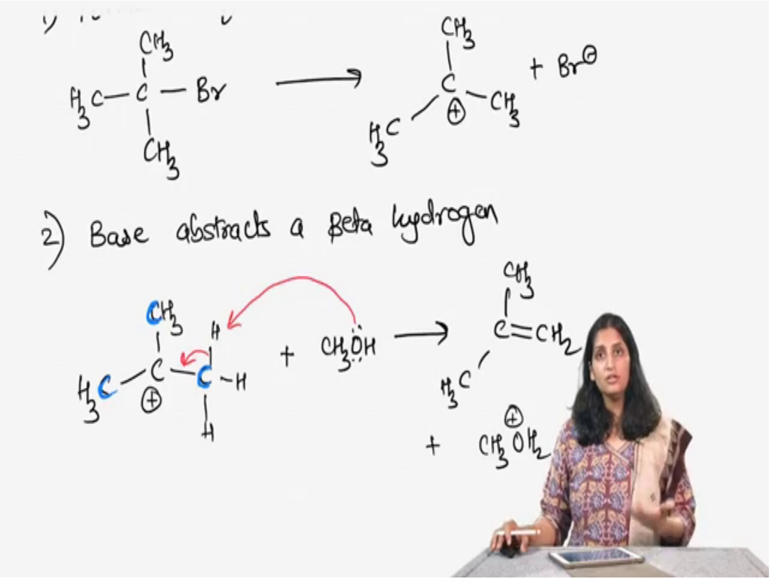

And I am writing one of the methyl groups completely, so, that we can see that beta hydrogen. Now the carbon that has the carbocation or the positive charge is the alpha carbon. The carbon next to it so, all of these will be the corresponding beta carbons and the corresponding hydrogens on them will be the beta hydrogens, right.

So, the second step is taking the proton away; here nucleophile is going to act as a base and it's going to grab that proton, right. So, I am going to take methanol here as my base. And what it does is, it attacks the beta hydrogen. So, the oxygen's lone pair are going to go and grab that proton. Now that proton does not want to form two bonds at the same time. So, what it does is it puts the electrons between the carbon-carbon bond, okay. That is favourable because you have a deficiency on that middle carbon, right. So, it's electron deficient; it is a carbocation.

So, this kind of reaction is favourable because, it forms an alkene at the end of it, right. And this kind of reaction is the elimination unimolecular reaction.

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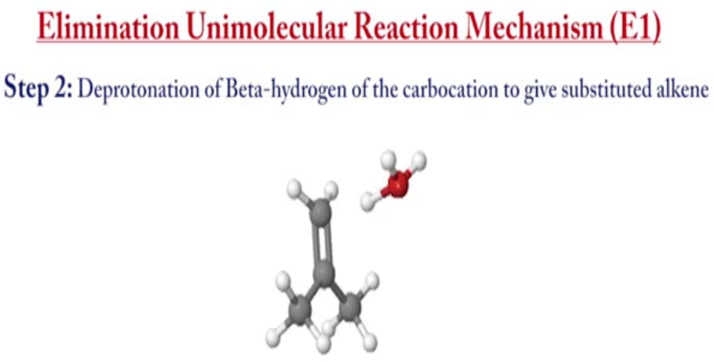

Elimination Unimolecular Reaction Mechanism (E1)

Step 2: Deprotonation of Beta-hydrogen of the carbocation to give substituted alkene

So, now we will look at the animation of this reaction. So, in the case of E1 mechanisms for example, the first step where the bond between the carbon and the leaving group breaks in order to form a carbocation is the rate determining step; that is the step, that is gonna take the maximum amount of energy or activation energy, right.

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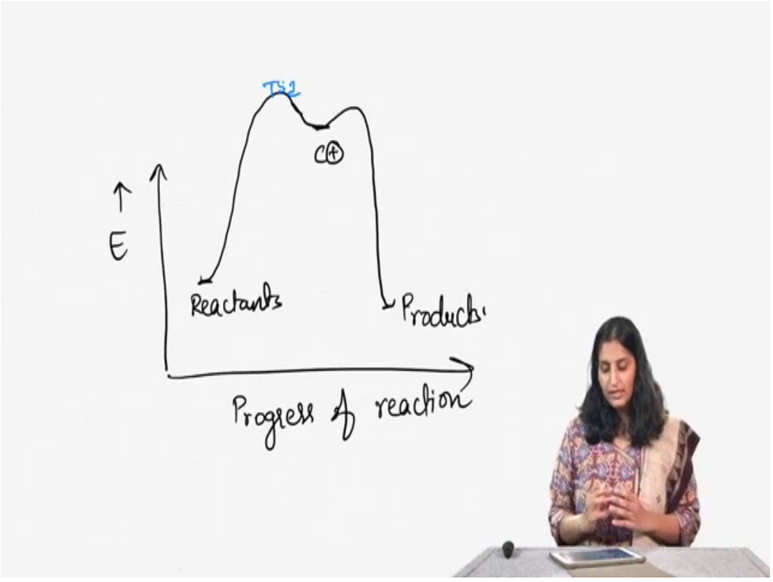

So in this case, when we want to draw the energy profile diagram of this reaction. What we see is that from the starting materials or reactants the energy goes up, as we start drawing this progress of reaction. The energy goes up towards the formation of carbocation, right. And carbocation is gonna be the highly energetic intermediate of the reaction, okay. And this particular hill for example, here will be our transition state 1, right.

Now, once the carbocation is formed, the base is going to come abstract the beta hydrogen and really form the products, okay. Now one question to ask is how do we know that the first step will require maximum amount of energy? So, you can take it as a rule of thumb that whenever you are forming a carbocation, that particular step is going to be the slowest step. And in fact, it is going to be the rate determining step of the reaction as well, okay.

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So, the rate of this E1 reaction is going to be, if I have to write down the rate equation it will be proportional to the concentration of substrate. Because, as you can clearly see that, only the substrate's concentration will matter in the rate determining step of the reaction, right. The concentration of the base in this case methanol will not play any role on the rate of this reaction. So, this particular reaction is called as E1, because the rate solely depends on only one type of compound that is the substrate.

More often, because even reactions undergo formation of a carbocation, more often we see that they follows Zaitsev's rule, okay. And after the carbocation is formed, remember that it is just like any other carbocation. So, it will may directly lose a hydrogen to form the beta-elimination product or it may rearrange to form a more stable carbocation and then lose a hydrogen.

So, there is, just treat that carbocation like any other carbocation that you have seen before, okay. So, this was one kind of a reaction E1 now just like in substitution you have S_N2, in the case of elimination reactions we have E2 reactions, okay.

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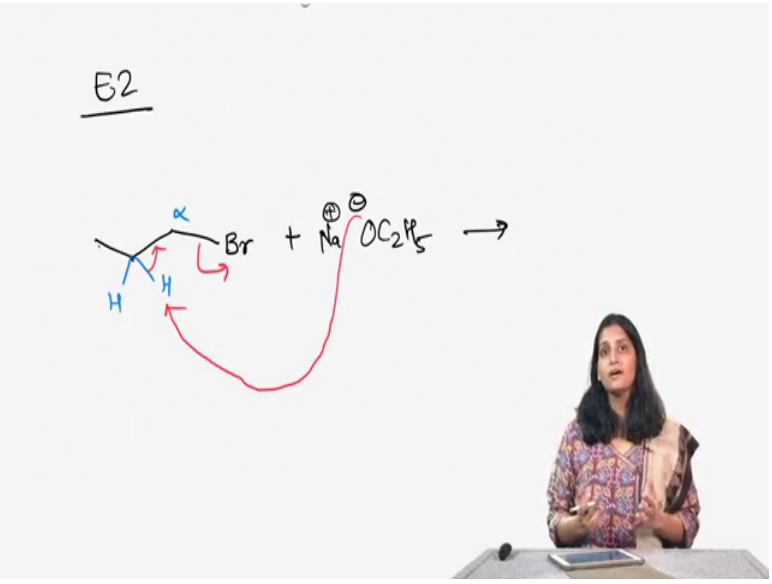

For E2 reactions; I am going to take the example of 1-bromopropane along with a compound like ethoxide, right. So, if I use sodium ethoxide for example and along with 1-bromopropane; what would be the product? Now remember that, ethoxide is also a good nucleophile. So, it may result into S_N2 reaction, right. But if it wants to do an elimination reaction. Now it cannot do this particular substrate here will not form a really stable carbocation, right.

Because it will be a primary carbocation; that's not going to be a greatly stable carbocation. It may rearrange to form a secondary carbocation, but the very first formation of that carbocation will be a troubling case; also in the presence of strong bases like sodium ethoxide the stability of carbocations is very low. So, forming a carbocation in this case is gonna be very-very tough. Instead what happens is, as you can see this is the alpha carbon and this is the beta carbon, right.

So, what happens is this ethoxide the oxygen with its lone pair comes and grabs the beta hydrogen, okay. Now, this particular beta hydrogen here, does not want to form bonds with two things that is oxygen and carbon. So, it puts its electrons, the bond electrons between the two carbon atoms, okay. And since, carbon doesn't want to hold on to new pair of electrons, right, otherwise it will break its octet rule, what happens is in order to sustain the octet it kicks off bromine as a leaving group.

So, what is happening; three things are happening, but all three things are happening at the same time. That is, the base is going to abstract the beta hydrogen; the beta hydrogen is going to put the bond electrons between the hydrogen and the carbon in between the carbon-carbon bond to form the carbon-carbon double bond, but the other carbon will start breaking a bond with the leaving group because it wants to form this new carbon-carbon double bond.

So, all these three things are going to happen in sync, okay. All the three steps are happening at the same time, okay. So, I am going to draw the transition state for this particular reaction here.

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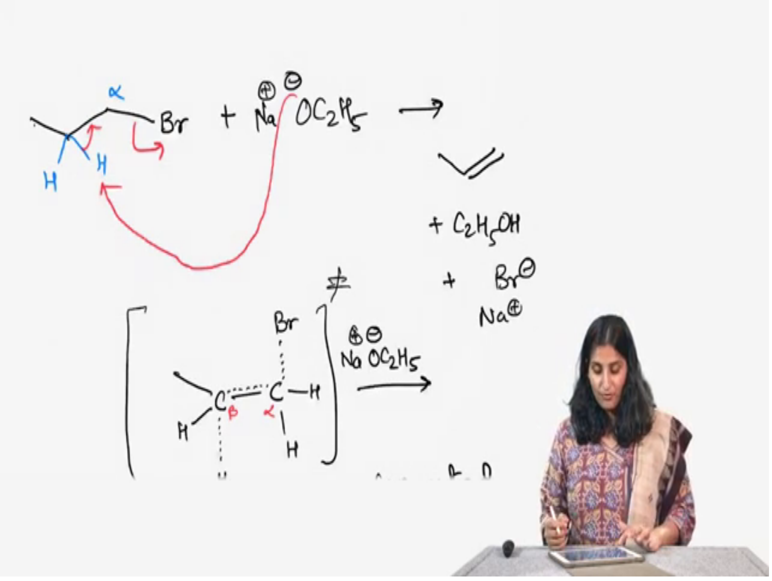

So, now let us start drawing the transition state. In the first step, the bond between the beta hydrogen and ethoxide will start forming, as the ethoxide starts grabbing that proton, the bond between the hydrogen and the carbon starts breaking, okay. So, that bond is going to start breaking and as that bond breaks, those electrons are going to go in between the alpha and the beta carbon. So, what we see here is, a new bond will start forming between the alpha and the beta carbons.

As a result of which, the bond between carbon and bromine is going to start breaking, right. So, as you can see in the same step, couple of bonds are forming and a couple of bonds are breaking, okay. And, this kind of synchronous steps are needed for E2 kind of reaction or this is also called as a concerted mechanism. Because, everything happens at the same time, okay.

In fact, this particular transition state, that we have drawn here has considerable double bond character; that is the bond between the alpha and beta carbon has formed considerably, because everything is happening in a concerted manner. Now, if I have to draw the final product of this reaction, of course, as these two things will form what I have end up forming is a double bond between the alpha and the beta carbon.

And we will form C_2H_5OH along with Br^- and Na^+, right. So, that would be the complete reaction. If we were to draw the energy profile diagram of this reaction.

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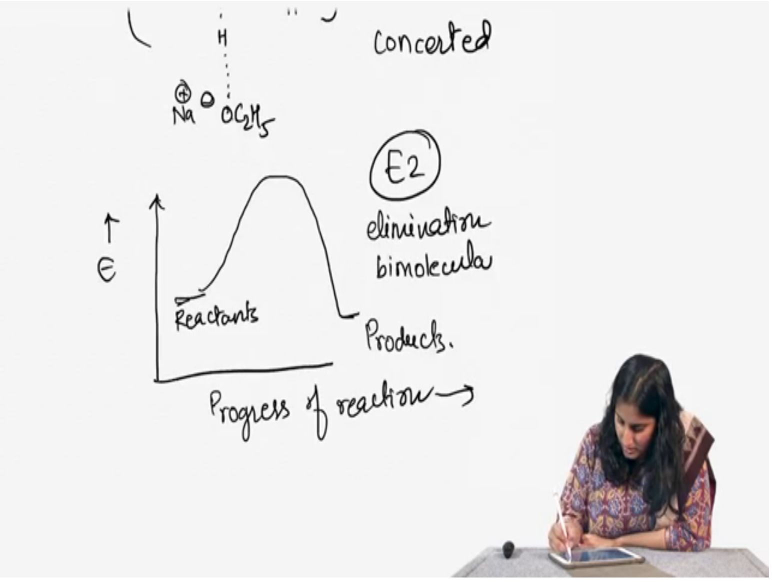

Then, we would start with reactants. And then the energy would go up in the transition state and then we will form the products, right. As you can see, there is no intermediate formed, right. It only goes through one single transition state. Since there is no intermediate, there are no valleys in the energy profile diagram and it just has one transition state in the reaction.

Since, the base as well as the substrate, both of them are playing a role in the rate determining step of the reactions, right.

As you can see there is only one step everything is concerted the base as well as the substrate are playing a role together, since both of them are playing a role, it's a bimolecular reaction or it is also called as E2 reaction or elimination bimolecular reaction. So now, we will look at the animation of this reaction.

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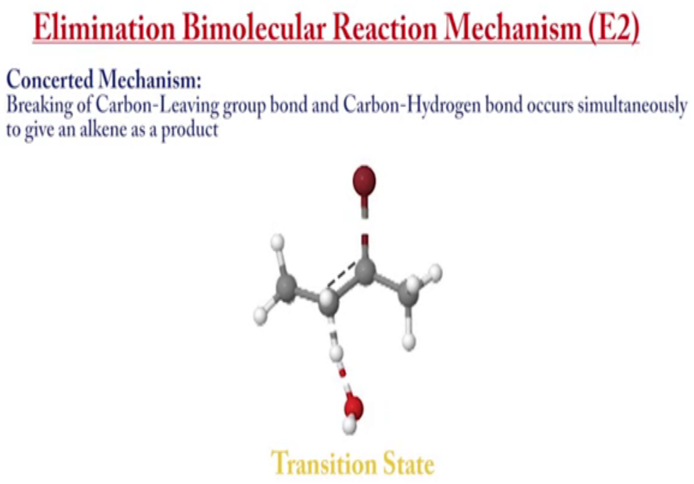

Elimination Bimolecular Reaction Mechanism (E2)

Concerted Mechanism:
Breaking of Carbon-Leaving group bond and Carbon-Hydrogen bond occurs simultaneously to give an alkene as a product

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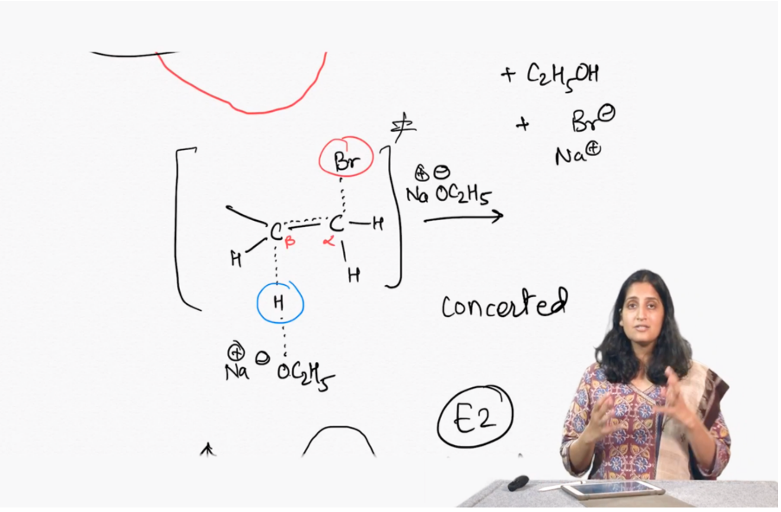

Now, in the case of E2 reactions; we use really strong bases, okay. And more often E2 reactions will also form Zaitsev's rule. Unless we have some really specific steric relations that are to be considered. Other than that really most of the reactions will undergo Zaitsev's product, okay. Now what is this really specific steric relations or the stereochemistry of E2 reaction, okay. Now for that, we need to understand this particular process of bond forming and bond breaking, okay.

In order for the base to grab the beta proton and the beta proton to put the electrons in between the carbon-carbon bond, a particular type of conformation is needed, okay. And in fact, the stereochemistry of E2 reaction is strongly controlled by the conformational effect, okay. The transition state of the E2 reaction is such that, the leaving group, okay, so, in this case the bromine and the beta hydrogen. So, this particular hydrogen has to be such that they are anti-periplanar to each other, okay.

Now anti-periplanar meaning that the dihedral angle between them, okay, is 180 degrees. So, they are going opposite to each other, okay. And the reason why this particular dihedral angle is favoured is because, it allows for the proper orbital overlap. It allows for the orbital overlap effectively such that the carbon-carbon double bond can be formed. Now, more often you will see that the anti-periplanar geometry is required, okay.

And what you will see is that more often it can be achieved, because carbon-carbon bonds can be rotated and you can really get to this anti-periplanar geometry where the hydrogen, the beta hydrogen and the leaving group are going directly opposite to each other. And that will really form the major product or more often the Zaitsev's product, in the case of E2 reaction.

But, there are some cases, when this particular geometry cannot be achieved, okay. First we will look at some of the examples of how this anti-periplanar geometry plays a role? And then, we will go to these specific examples.

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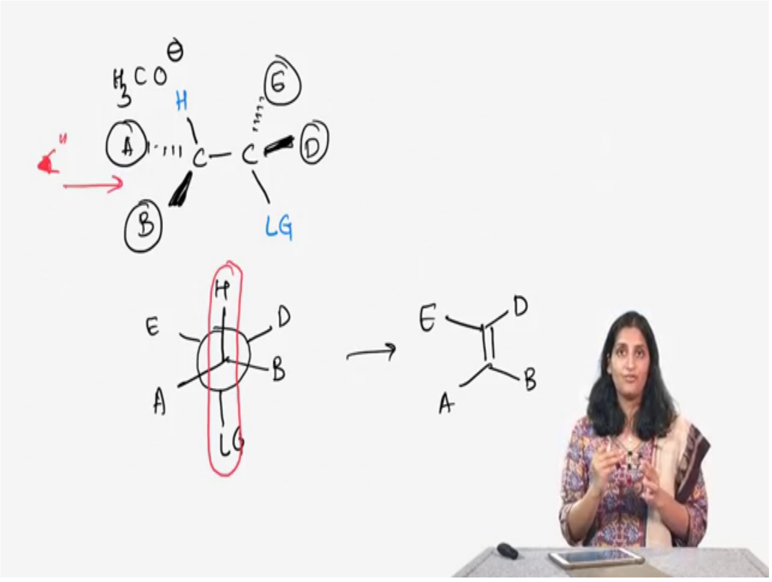

So now, let’s take this particular example here, okay. I am going to take methoxide as the ion as my base, okay. And I am just naming some random groups on this particular carbon A, B, D and E.

Now the anti-periplanar geometry is such that, when the hydrogen and the leaving group are having a dihedral angle of 180 degrees, right. And this will be more, better seen, if we can look at it via a Newman projection. So, let me explain first of all what the dihedral angle means here, okay. Imagine that this is the leaving group, okay. Imagine that, this is the bromide, then this particular carbon here becomes the alpha carbon. A carbon next to it will be the beta carbon, right.

Now for the elimination to take place the incoming base will come and grab this proton, put the electrons in between the carbon-carbon double bond and kick off the bromide, right. And this can be achieved when the hydrogen and the bromine are going directly opposite to each other. Remember, this molecule is gonna be constantly rotating, but the transition state will involve the formation of an anti-periplanar geometry.

For example, this molecule will not eliminate in this particular geometry when the hydrogen and the leaving group are not at 180 degrees, okay. So, we want to make sure that, the hydrogen and the leaving group are directly opposite to each other in the anti-periplanar geometry to do this elimination reaction. So, in order to explain this concept better, I am going to look at this particular molecule, okay. As you can see, when you start imagining yourself looking at this molecule in this particular fashion.

If I start drawing the Newman projection, what I see is, I have B here, A here and the hydrogen is going up and at the back carbon, the leaving group is going down and on this side you have a D and E, okay. And as you can see, since this particular anti-periplanar geometry is fixed, such that the molecule will have a specific conformation as it does the elimination reaction the particular geometry of the corresponding alkene also gets fixed.

So, for example, here this will result into the formation of this alkene. Where B and D are going to be on the same side of each other whereas, E and A are going to be on the same side, right. And right now, we have not taken a particular example, but we can take a particular example now and go through this process. What it means is that it will result into the formation of E or Z alkenes selectively because, the geometry of the transition state is fixed, okay. So, now let's look at a particular example.

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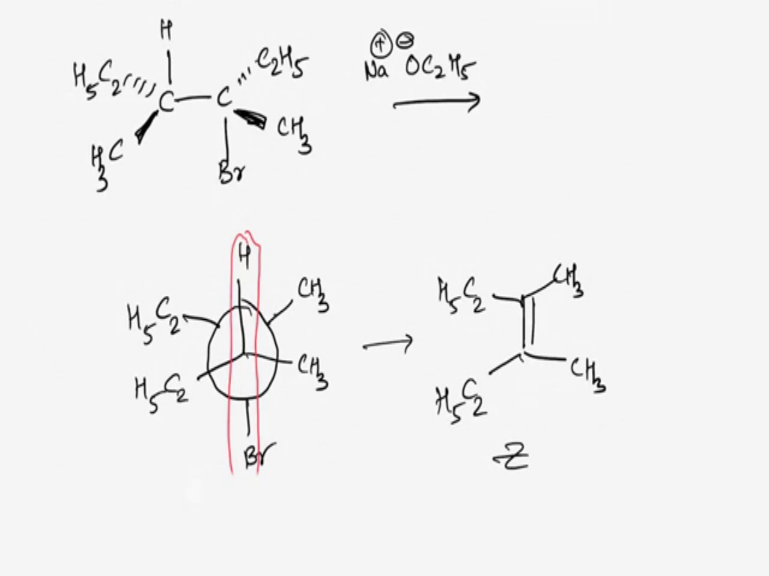

When this molecule will undergo an E2 reaction like this, first we need to determine what is the transition state geometry like. And in fact, in order to do that the best thing to always do is draw a Newman projection. Now the Newman projection will look like this, right. And when this particular elimination happens when the hydrogen and bromine are directly 180 degrees away from each other or with a dihedral angle of 180 degrees, what should happen is, the resulting alkene will look like this.

So, is this a Z or an E alkene, since the higher priority group are on the same side, this will be a Z alkene, okay. And in fact, this molecule will not eliminate ever to form an E alkene. So more often, we observe that the anti-periplanar geometry is needed for E2 reactions. Very few times the E2 reaction really deviates from this anti-periplanar geometry and under very-very specific conditions you can also see something called as an anti-coplanar geometry that can really happen.

But that is very negligible amount of time; more often you will see a dihedral angle of 180 degrees being required. So, very often we see that the anti-periplanar geometry is required for the E2 reaction to happen where the dihedral angle is 180 degrees. Very-very few times, depending on the reaction conditions and the substrate you might see that the elimination can happen when it is such that the leaving group and the hydrogen, the beta hydrogen, have a dihedral angle of 0 degrees.

But again I will stress that, that is very few number of times and that is not the major case. The major case is such that you always need that dihedral angle of 180 degrees, right. And one of the major reasons or one of the good explanations why this particular dihedral angle is needed, is that there is a orbital based reason for it, okay.

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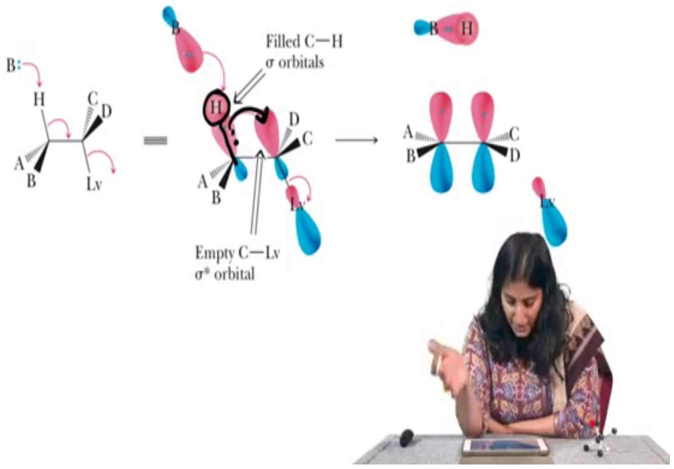

Now, if you really see this diagram here what you can see is that, the base will come in and grab the proton, right. So, it is going to grab this particular proton here and the bond electrons of this carbon-hydrogen bond need to overlap with the empty sigma star (σ^*) orbital of carbon and the leaving group. And why it needs to go in the sigma star orbital is because as this overlap happens, as the sigma star orbital gets filled, the carbon and the leaving group bond can break, right.

So, one of the good ways to break the bond is to put electrons in the anti-bonding orbital, right. So, as this hydrogen puts electrons into this anti-bonding orbital of the carbon-leaving group bond, the carbon-leaving group bond breaks, right. Now, if you see the right orientation, since the sigma star orbital of that carbon-leaving group bond is going to be opposite to it, it's good to have it such that this particular hydrogen can put its electrons right across this particular carbon-carbon bond in order to fill the empty sigma star orbital that lies here, okay.

And that's why this particular geometry is needed for elimination reactions to happen or E2 type of reactions to happen. Now, in the case of E1 reactions, it becomes easier because in the case of E1 reactions you have formed the carbocation. And the carbocation is going to be flat and planar and it's going to have its empty p-orbital such that it goes above and below the plane for example.

So, it's gonna be easier for the base to come and grab the proton and for the proton to put its electrons such that it results into the formation of carbon-carbon double bond. But for the case here for E2 reactions for the orbital overlap to be successful it needs to be aligned in a particular manner.