Introductory Organic Chemistry

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Lecture – 40

Substitution & Elimination Part 2

Let us start discussing the other kind of Substitution reactions. Now, one of the other ways we thought about substituting was such that player on the football field was not playing very well. So, another player, a better player comes in and kicks the current player out right, and this kind of scenario is very similar to an S_N2 type of reaction.

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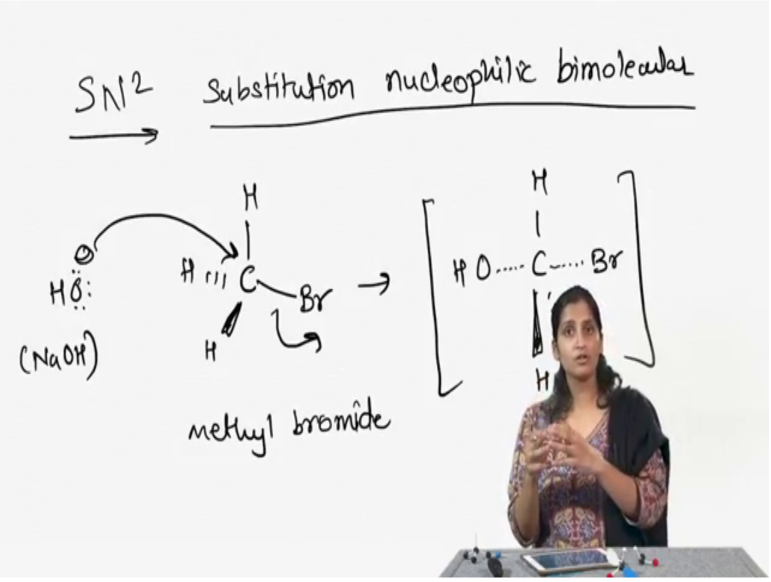

So, this is substitution nucleophilic bimolecular reaction, okay. Now I am going to take an example of an S_N2 reaction and let's see how this really works out to be, okay. I have methyl bromide and in fact, if you think about it when methyl bromide was put with hydroxide it was thought that it will not react, because methyl is not going to create a carbocation, but instead we observed that hydroxide quickly replaces that bromine to do a substitution reaction.

So, it was thought that the reaction mechanism has to be different from what the S_N1 reaction goes through. So, in this reaction what's going to happen is that the hydroxide let's say from NaOH is going to attack the carbon and kick the bromine out, okay. So, what it goes through is a transition state such that the bond between the hydroxide and carbon is starting to form, at the same time the bond between carbon and bromine is starting to break, okay. Really the hydroxide comes in with a full negative charge, slowly it starts putting electrons or giving electrons to the carbon in turn becoming delta negative because it has given up some of its share to the carbon.

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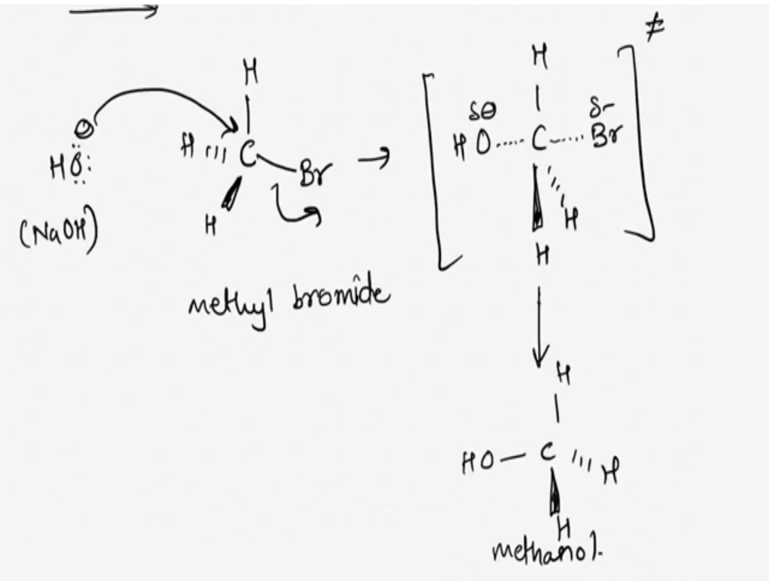

The bromine starts breaking the bond with the carbon and what happens is that the bromine becomes slightly delta negative as well and that's how the transition state of the reaction is going to look like is that a bond is partially formed and the bond is partially broken in the course of the reaction. And then when this reaction ends, it ends such that you end up creating a new bond between carbon and oxygen creating methanol, right.

And one of the things to pay attention here is that the mechanism is such that the nucleophile attacks from the backside of the carbon-bromine bond. So, the way I have written it, it attacks from this backside of this carbon-bromine bond, okay. And why is that important? Because this backside attack is really going to govern the way the product is going to look like, okay.

Now, one thing to know is that the backside attack by the nucleophile is really facilitated by in kind of two ways, the first one is that the polarization of the carbon-bromine bond is such that the carbon atom will have a delta positive, right and the bromine will have a delta negative. And that is the nucleophile which is going to be really looking for nucleus, looking for a positive charge is going to attack that partially positive carbon, right.

The other reason the structure facilitates a backside attack is that if you really think about it bromine which is a very bulky group, right, so, when the hydroxide wants to attack instead of attacking from the same side of bromine and facing a lot of steric hindrance from that side. It prefers attacking from the backside such that it can really reach that carbon that is partially positive very effectively and facilitate in the leaving of the leaving group; that is the leaving of the bromide ion.

If we want to talk about in terms of the molecular orbital theory remember that one of the ways to break the carbon-bromine bond is to populate its anti-bonding molecular orbital. So, the anti-bonding molecular orbital is currently empty, the bonding molecular orbital for the carbon-bromine bond in the beginning is occupied. But, as the oxygen attacks it puts the electrons from its lone pair in that anti-bonding molecular orbital, really making the bond between carbon and bromine break.

And if you think about it, the anti-bonding molecular orbital is oriented in the back side of the carbon-bromine bond, right. So, if we really look at the anti-bonding molecular orbital, that's where the anti-bonding molecular orbital is going to be and the hydroxide is going to put its electrons in there really resulting the bond to break. The other ways for the hydroxide to put its electrons into the anti-bonding molecular orbital are not going to be effective, because they are not going to provide the most efficient orbital overlap.

And this is the only way that you get a very efficient orbital overlap in order to weaken the carbon and the leaving group bond. And this backside attack has some particular stereochemical consequences, but we will go to it when we discuss the stereochemistry of the reaction.

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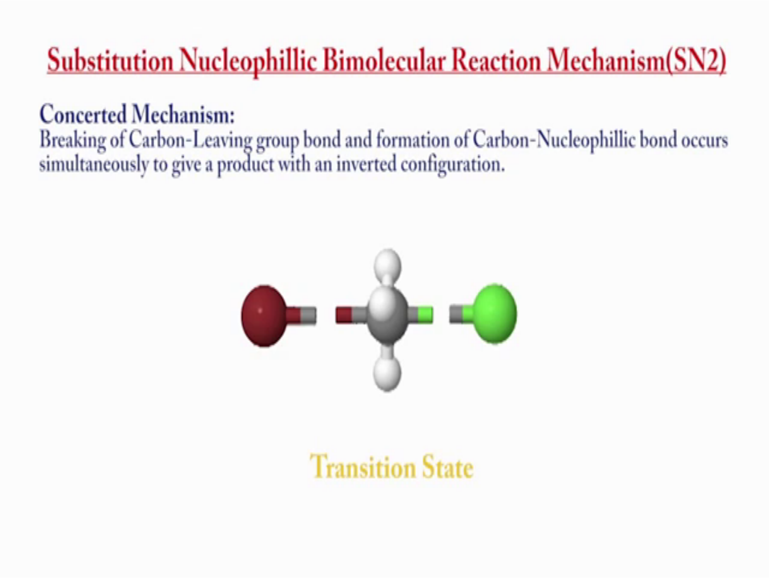

Substitution Nucleophillic Bimolecular Reaction Mechanism(SN2)

Concerted Mechanism:
Breaking of Carbon-Leaving group bond and formation of Carbon-Nucleophillic bond occurs simultaneously to give a product with an inverted configuration.

Transition State

So, now we will look at the animation of this reaction. Let’s discuss the energy profile diagram of the reaction. So, as the reaction is happening in the beginning what we have is your starting material.

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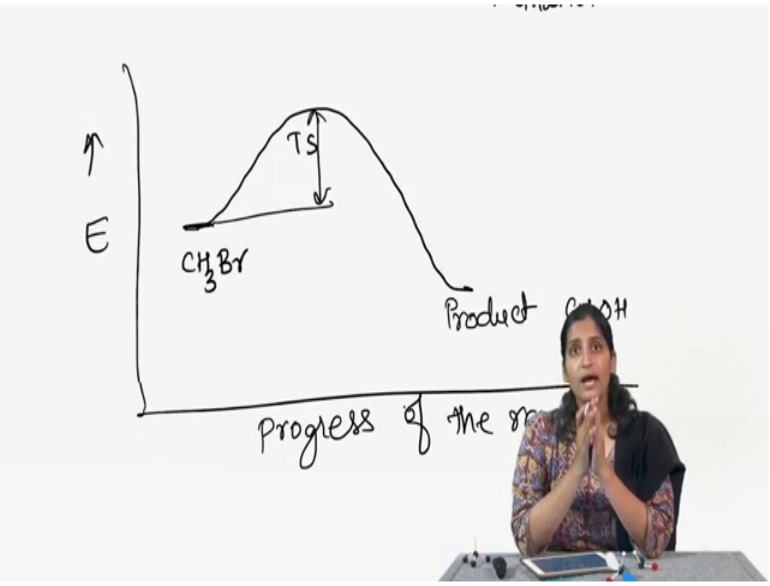

So this is the energy of the reaction, this is the progress of the reaction and in the beginning this is our methyl bromide. If you look at the mechanism we are not creating any intermediate, it goes through a transition state, but there are no intermediates created in this reaction.

So, what happens is that it goes over just one single hill, right or one single transition state that happens in the reaction. In fact, we have drawn this transition state over here, this is our transition state and then you end up forming the products which is our methanol molecule, okay. So, in S_N2 reaction you don't have any intermediate form. So, there are no valleys in the energy profile diagram; it is just one single hill.

Now, remember how we talked about the rate equation for S_N1 reaction. If I want to talk the same way about S_N2 reaction we want to think about what is the slowest step of the reaction. Now, in this case the slowest step is of course, climbing this one hill that is to achieve the transition state, right and what all species are playing a role in this particular transition state, I do see the methyl bromide playing a role I also see a hydroxide molecule playing a role.

So, both the species need to collide, I must collide, and are present in that transition state and thus the reaction is bimolecular; it's not a unimolecular reaction. You need both the species the hydroxide as well as the methyl bromide for the slowest step of the reaction to happen and thus the rate of the reaction if I want to write down.

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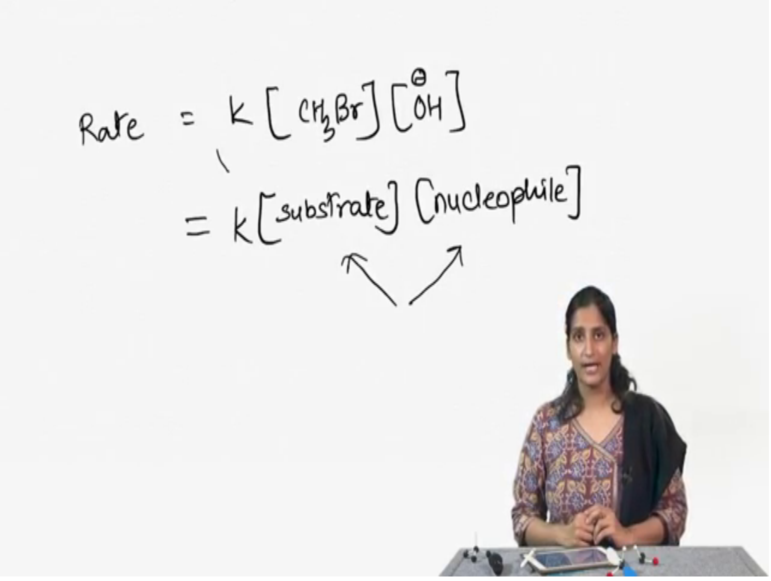

$$\text{Rate} = k\,[CH_3Br]\,[\overset{\ominus}{O}H]$$
$$= k\,[\text{substrate}]\,[\text{nucleophile}]$$

I will draw this particular rate equation as if it is concentration of the methyl bromide and concentration of hydroxide, right. And if I want to generalize this, I will generalize it as it is the some rate constant K into the concentration of substrate and the concentration of nucleophile, right.

So, it is bimolecular S_N2 because I see two species playing a role in the rate equation of the reaction. In this case if I increase the concentration of hydroxide and double it, the rate of the reaction will also get doubled; if I double the concentration of substrate, the rate of the reaction will also get doubled. And if I double the concentration of both substrate as well as nucleophile, the rate of the reaction will be quadrupled at the end of the reaction, okay.

Remember in the case of S_N1 reaction that was not the case; in the case of S_N1 reaction doubling the rate of or increasing the concentration of nucleophile did not really play any effect on the rate of the reaction, but in this case the nucleophiles concentration is going to play a role. So, what kind of substrates would do S_N2 type of reaction? If we think about it we want to think about the way the mechanism happens.

So, for the reaction to happen the nucleophile should be able to approach the substitution centre that is the carbon that attaches to the leaving group right and it needs to start forming a bond, a new bond with the carbon and the nucleophile. But it also needs to start breaking the carbon-leaving group bond, okay. And if we compare the ease of this approach, the nucleophile approaching that carbon, the centre, a substitution centre we will see that the methyl alkyl halides are the best followed by primary followed by secondary; and it is almost difficult to approach that tertiary alkyl halides carbon centre, because the alkyl groups present on the tertiary alkyl halide are going to create a lot of steric hindrance for the nucleophile to attack.

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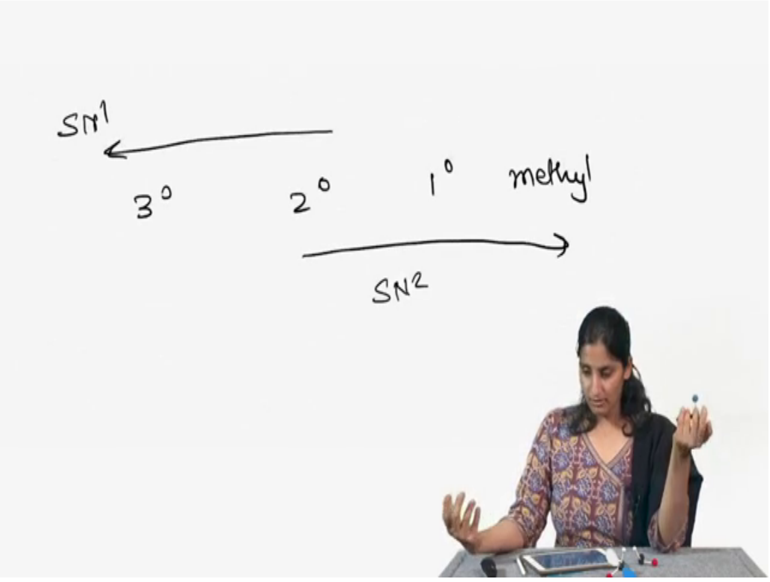

So, here in if you want to summarize let's take our tertiary alkyl halide, secondary, primary and methyl alkyl halides. The rate of S_N1 goes on increasing in this way, but the rate of S_N2 goes on increasing such that when we go towards the methyl alkyl halides and that is kind of easier to see because if the incoming nucleophile is going to face a lot of steric hindrance from these alkyl group it won't not be able to approach that carbon centre, whereas if these are hydrogens it's much easier for the nucleophile to find that centre to attack.

In fact, we see a similar effect of steric hindrance on S_N2 reaction in the molecules that have a branching, okay and in fact, I have some data here.

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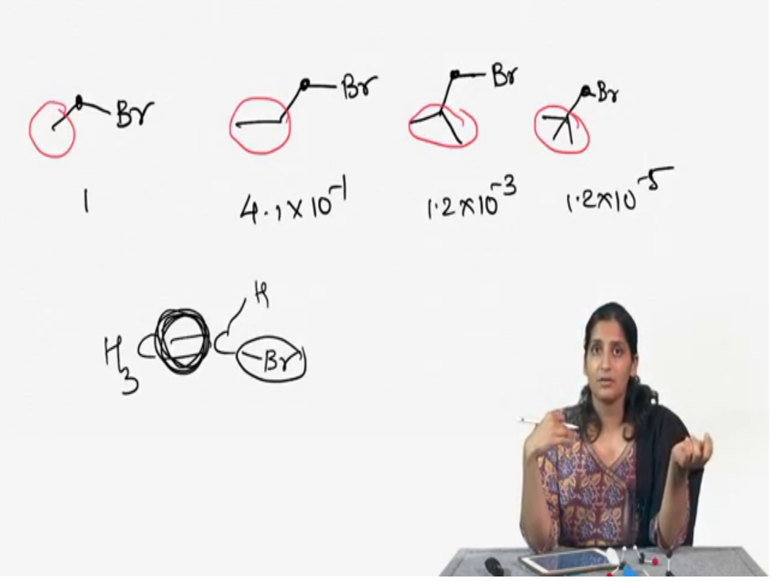

Let's take ethyl bromide versus propyl bromide versus this versus this. Now, remember in all of these cases the carbon that is attached to the bromine is still a primary carbon, right.

But, we will see that the rate of the reaction, the S_N2 reaction, will change as we go from one end to the other. So, why is that? That even though the primary carbon is playing a role the bulkiness of the attached group will hinder the nucleophile from attacking and we know that the tertiary butyl is the most bulky group in this case. What we see is that if the initial rate for ethyl bromide is 1, okay; this one is around 4.1 x 10^{-1}, this is 1.2 x10^{-3} and this is 1.2 x 10^{-5}, right.

So, the rate is slowing down as we go on adding that bulkiness in the branch chain. So, for S_N2 reaction, the lesser bulky the carbon the better it is, for S_N1 reaction the more stable the carbocation the better it is. One thing to note is that the S_N2 reactions can never occur on sp^2 or sp hybridized carbons, why? Let’s take for example, this particular compound, the backside of the carbon-bromine bond is the pi bond, right and the nucleophile cannot attack from where the pi bond is.

So, you almost never ever see an S_N2 reaction happening on an sp^2 or sp hybridized carbon.

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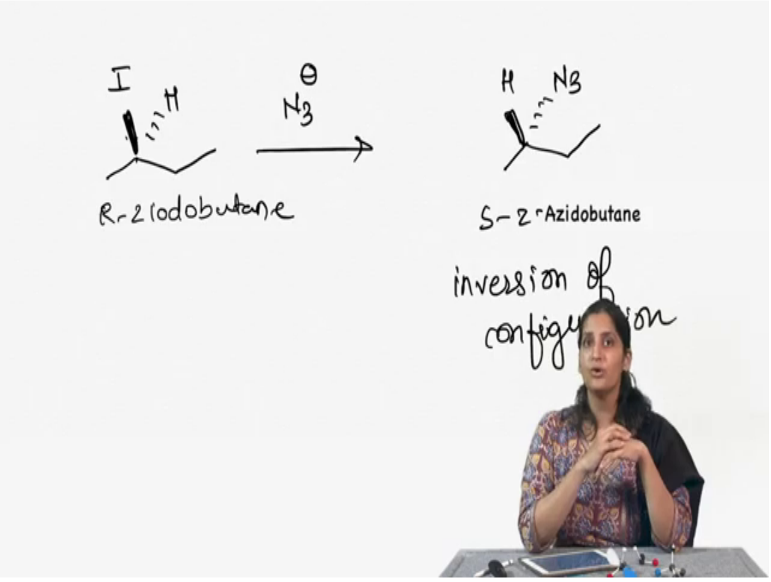

Now, what kind of nucleophiles will prefer S_N2 reaction or what kind of nucleophiles are required for the mechanism to be S_N2. Remember that the nucleophile does play a role in the rate of the reaction; it does play a role in the rate determining step of the reaction. So, the nucleophile here cannot be a weak nucleophile like in the case of S_N1 reaction and the better the nucleophile the easier it is for it to perform the S_N2 type of reaction.

So, strong nucleophiles kind of favour doing this S_N2 type of reaction rather than S_N1 type reaction. If we think about the stereochemistry of the reaction, as I said that the nucleophile has to attack from the backside of the carbon bromine bond. So, in order to see the effect of the reaction mechanism on the stereochemistry of the final product what we are going to do is we are going to react this particular iodobutane with this azide, okay

Now, in this case azide is a very good nucleophile because if you think about it, it bears a negative charge. So, it has a strong charge it’s going to attack on that carbon, it is also a very tiny nucleophile in the sense it is not bulky. So, it is like an arrow that can easily go and approach that carbon, right. So, the azide is going to be our good nucleophile here and what we observe is that when we start from this (R)-2-iodobutane and when the azide does this reaction we end up with (S)-2-azidobutane, which means that the reaction proceeds with inversion of configuration, right.

And in fact, if you think about it because the incoming nucleophile is going to attack from the opposite side of the leaving group you are going to almost always see that inversion of configuration taking place, because the new bond of the carbon nucleophile is going to be opposite to that of the carbon leaving group bond, okay. So, for S_N2 reactions we always almost seen full inversion of configuration as the reaction happens. Whereas, for S_N1 reactions it was partial inversion partial retention of configuration or a mixture of compounds was formed; in the case of S_N2 you have full inversion of configuration.