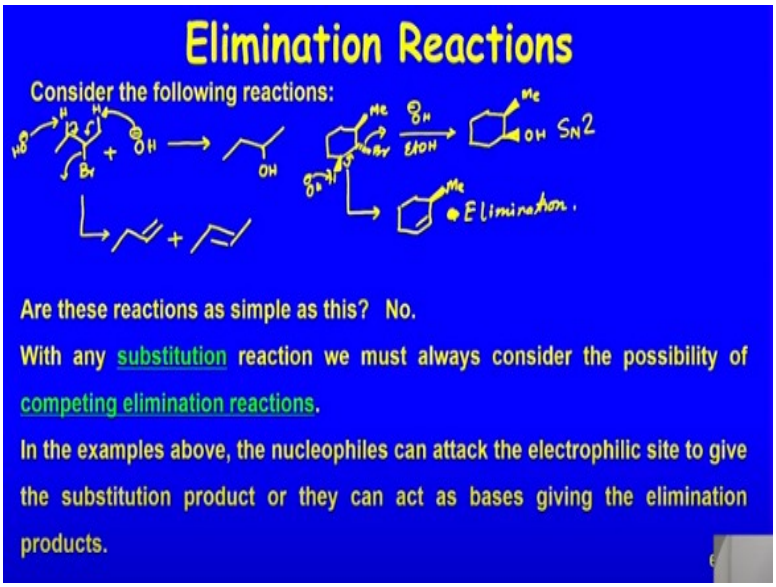
Symmetry, Stereochemistry and Applications
Prof. Angshuman Roy Choudhury
Department of Chemical Sciences
Indian Institute of Science Education and Research, Mohali

Lecture - 33
Elimination Reactions

Welcome to the course entitled Symmetry, Stereochemistry and Applications. In the last few lectures, we have discussed about the substitution reactions and stereochemical aspects of SN1 and SN2 reactions.

(Refer Slide Time: 00:32)



So today, we will start the next part of this course, where we will try to understand the stereochemistry of elimination reactions. So let us consider a few reactions which we have already seen in our previous few classes. Suppose, we are trying to do a reaction where this alkyl halide is treated with OH- and following a substitution pathway we can write the product could be this.

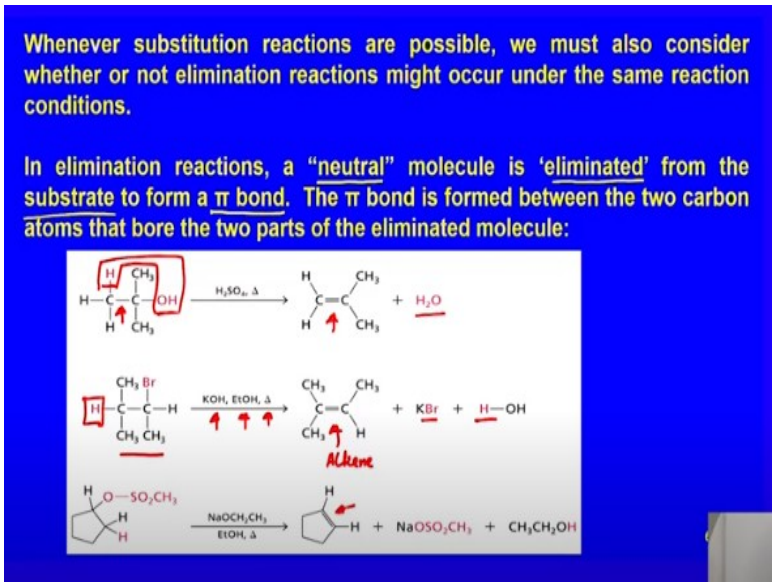
Similarly, if we take a cyclohexane derivative like this and do the same treatment, OH- in say ethanol, very easily you will be able to write that the product would be a substitution product and which maybe SN2 which would mean that the OH would come from the top and form these product. Now the question is does the reaction is so simple, does it happen in such a simple way?

So these reactions are not so simple. Always with any substitution reaction, we must consider the possibility of competing elimination reactions. In the examples above the nucleophile can attack the electrophilic site to give the substitution product as they are giving or they can act as base by giving the elimination product. So what is the elimination product you may think of?

What we may think of in this case is that this molecule has two hydrogens on two adjacent carbon atoms. So this OH- can abstract the proton and Br- can get removed and we may form an alkene like this. Or the OH- can attack the other proton, a double bond may form there and we may end up getting a product like that.

Similarly, in this case, if the OH- attacks this proton and this double bond forms and the bromine is eliminated, you will get a product which would be this one. So it is possible to get some SN2 product like this and some elimination product in this type of reactions. So we need to see what are the factors that influence the formation of elimination products and that we will go through in next few slides.

(Refer Slide Time: 04:19)

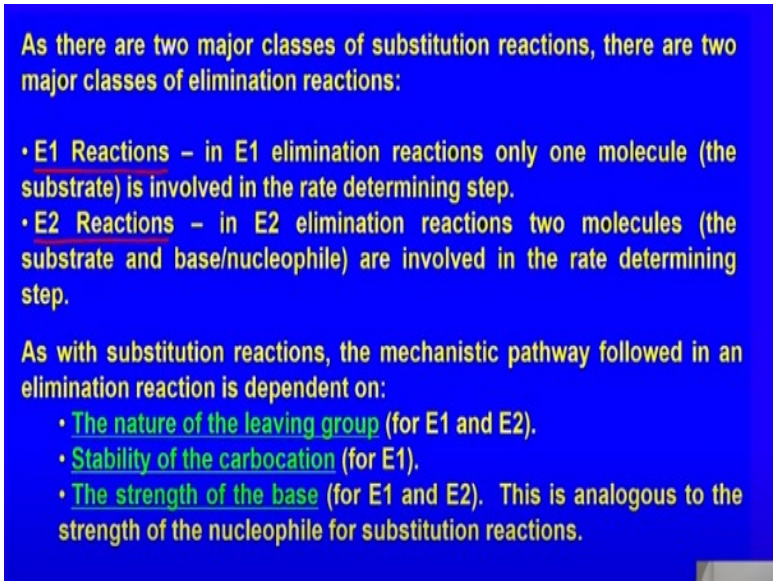


So whenever the substitution reactions are possible, we must consider whether or not elimination reactions may occur under the same conditions. So in elimination reaction always a neutral molecule is eliminated. If you remember in the previous example that we talked about it is HBr elimination from the substrate and it forms a double bond or a pi bond.

The pi bond is formed between the two carbon atoms, which has lost two elements like hydrogen and bromine. So here is in this particular example, what I am trying to show here you have OH and H. When we heat this compound in concentrated sulphuric acid, we generate this alkene by elimination of water. So this H and that OH gets eliminated and a double bond is formed in between.

Similarly, if we have a substrate like this, it is possible to abstract this proton by this base potassium hydroxide in presence of ethanol under heating condition and give rise to an alkene with the elimination of H and Br from the substrate. Similarly, the cyclic compound also can give a cyclic alkene in an elimination reaction pathway.

(Refer Slide Time: 06:05)

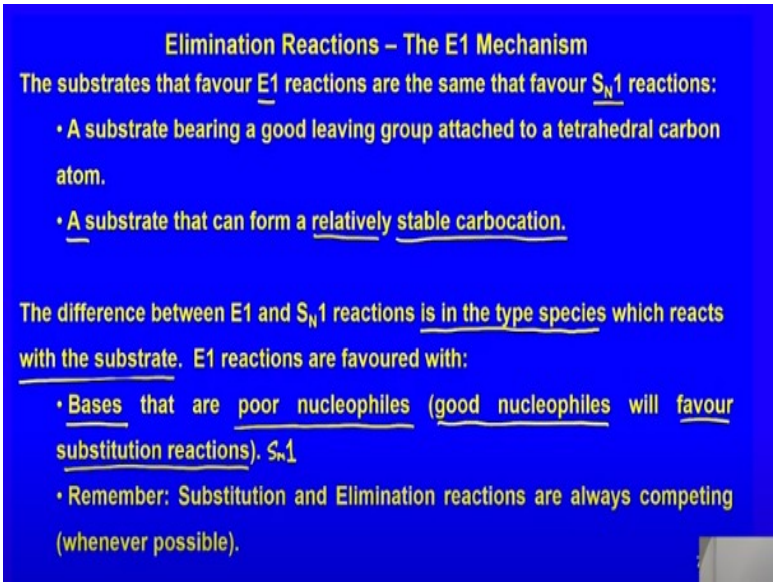


So as there are two major classes of substitution reactions, there are two major classes of elimination reactions as well. So the reaction which we call as E1, that means elimination reaction unimolecular that where in E1 elimination reaction only one molecule is involved in the rate determining step that is the substrate.

E2 reactions where the elimination reaction occurs where two molecules are involved in the rate determining step. So we will see these one by one. As with substitution reaction, the mechanistic pathway followed in an elimination reaction depends on a few things, the nature of the leaving group which is important for both E1 and E2. That means the nature of the alkyl halide is important here.

The stability of the carbocation for E1 mechanism where a carbocation is formed. And the strength of the base for both E1 and E2. This is analogous to the strength of the nucleophile for substitution reaction.

(Refer Slide Time: 07:22)

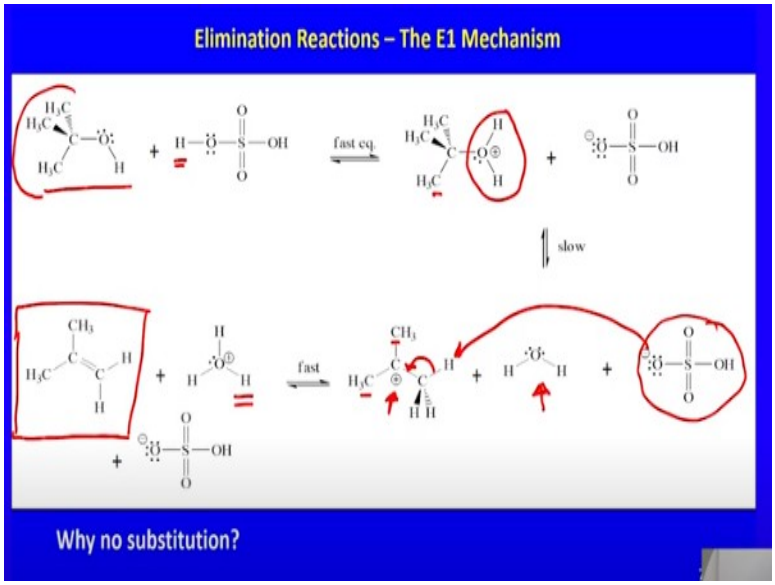


So let us first try to understand the E1 mechanism stepwise. The substrate that favor E1 reactions are the same as that of SN1 reactions. So which are the substrates that preferred SN1 reaction? The substrates which are connected to a good leaving group to a tetrahedral carbon atom and the group these substrates which are sterically hindered are favored for SN1 reaction.

So a substrate that can form relatively stable carbocation favors SN1 reaction. Similarly, in E1 mechanism, a carbocation is formed and hence the stability of that carbocation determines the suitability or feasibility of E1 mechanism for that particular substrate. The difference between E1 and S1 reaction is in the type of species which reacts with the substrate. E1 reactions are favored with bases that are poor nucleophiles.

Good nucleophiles will favor the substitution reaction or SN1 reaction. Remember substitutions and elimination reactions are always competing. So whenever there is a possibility of elimination and substitution reaction happening together, there will be a certain percentage of elimination product along with a certain percentage of substitution product present in your reaction mixture.

(Refer Slide Time: 09:13)



So let us see the elimination reaction mechanism using a standard example. Here what we have is tertiary butyl alcohol. You see this, this molecule is sterically hindered. The back side is bulky. Therefore SN2 reaction would not go through in this particular molecule. Similarly, here this group OH is not a good leaving group. So what we do is when we are treating this with sulphuric acid it protonates the OH group and makes it a positively charged OH2+ group.

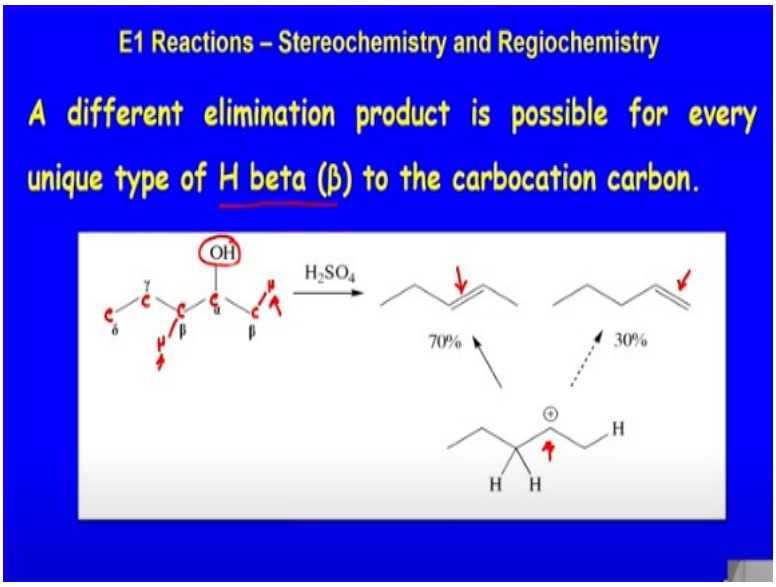
And now that OH2+ group is a good leaving group. So immediately as a slow reaction process, water is eliminated and the carbocation can be written now like this. Two methyl groups are written as it is. The third methyl group is written with three hydrogens as a tetrahedral group like that. So now we have in solution, the bisulphate anions which abstract one of those hydrogen atoms and the double bond forms because it takes the H+.

The electron pair present on the bond is now forming the double bond and hence the product forms. But as soon as it abstracts the H+, it transferred that proton to the water molecule that is present by protonating it H3O+. So what we see is the elimination product is formed in this particular reaction. Why there is no substitution reaction?

Because, as soon as this carbocation is formed, this becomes a sterically hindered carbocation and it becomes very difficult for this bulky bisulphate anion to come here and get attached to this carbocation. Rather it is easier to eliminate this proton and

form the double bond. So therefore, we do not have any substitution reaction taking place in this particular case.

(Refer Slide Time: 11:47)

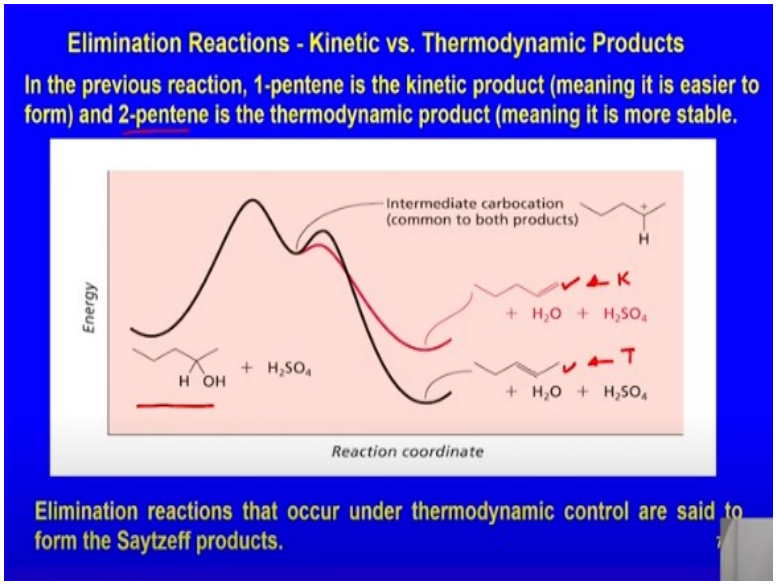


So in case of this E1 reactions, we need to talk about the stereochemistry and regiochemistry. A different elimination product is possible for every unique type of beta hydrogen to the carbon atom. So when we are talking about a particular compound which is drawn here with respect to this OH group, the first carbon that we have here is the alpha carbon. The second carbon on either side is called the beta carbon, third carbon is called gamma carbon and fourth carbon is called delta carbon.

So when the elimination reaction occurs, the elimination reaction can occur from this hydrogen or from that hydrogen. So once this hydrogen is abstracted, the double bond is formed here, when the terminal hydrogen is abstracted, the double bond is found at the terminus. And both of them are generated from this particular carbocation which is generated at the alpha carbon on which you have the OH group.

So when we have the possibility of two products, it must be a case where one of them is more stable compared to the other and one of them will form faster and the other will form slower.

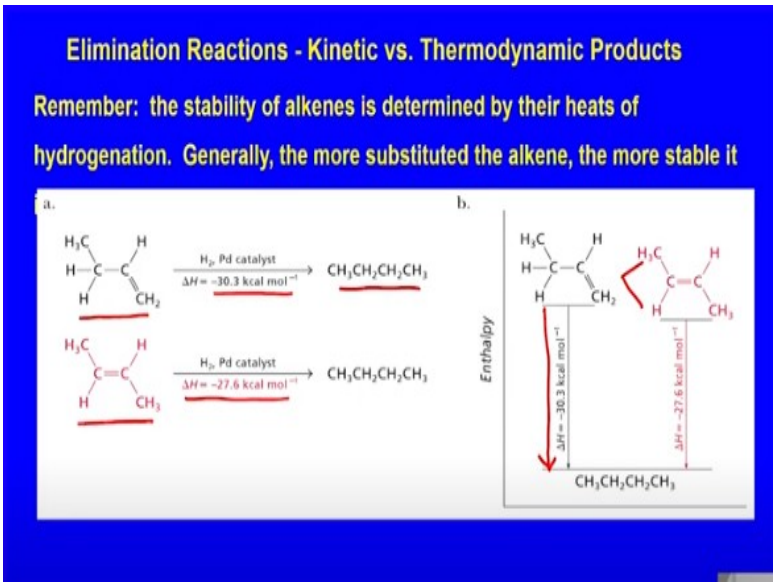
(Refer Slide Time: 13:15)



So in this particular reaction 1-pentene that is this one is a kinetic product meaning it is easier to form because it directly forms from the carbocation that was formed and the hydrogen that is eliminated is from the terminal carbon, which is less in that carbon. Therefore, it is easy to eliminate hydrogen from there and it forms faster.

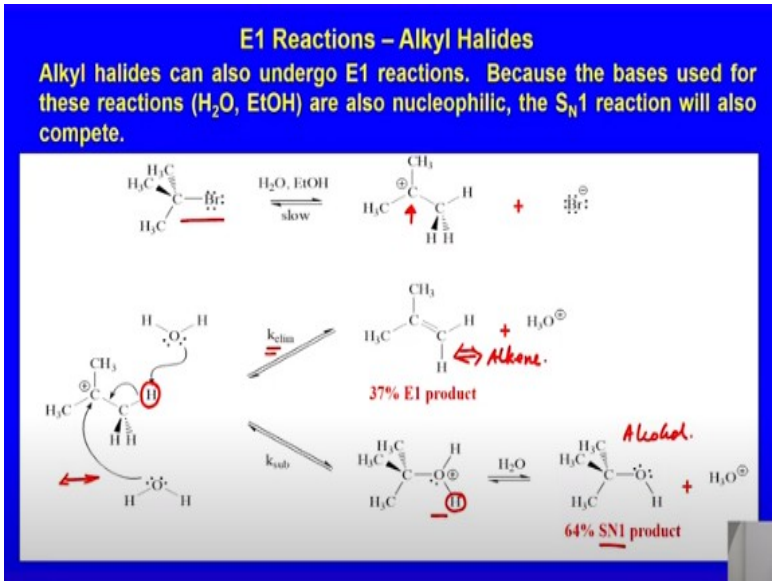
But 2-pentene which is this one is the thermodynamic product, meaning it is more stable because more substituted hydrocarbon, more substituted alkene is more stable. So starting from one compound, we are getting two different products and one of them is kinetically controlled, the other one is thermodynamically controlled product. And this thermodynamically controlled product is more stable compared to the kinetically controlled product.

(Refer Slide Time: 14:27)



Remember the stability of these alkanes is determined by their heat of hydrogenation. Generally the more substituted alkene the more stable it is. So if you try to hydrogenate this molecule to that, the energy released is 30.3 kilocalories per mole. That means this one and when you try to hydrogen this one which is more substituted in the sense that it is not terminal alkene like that it is alkene is in between the molecule the delta H is -27, this is more stable compared to the terminal alkene.

(Refer Slide Time: 15:15)

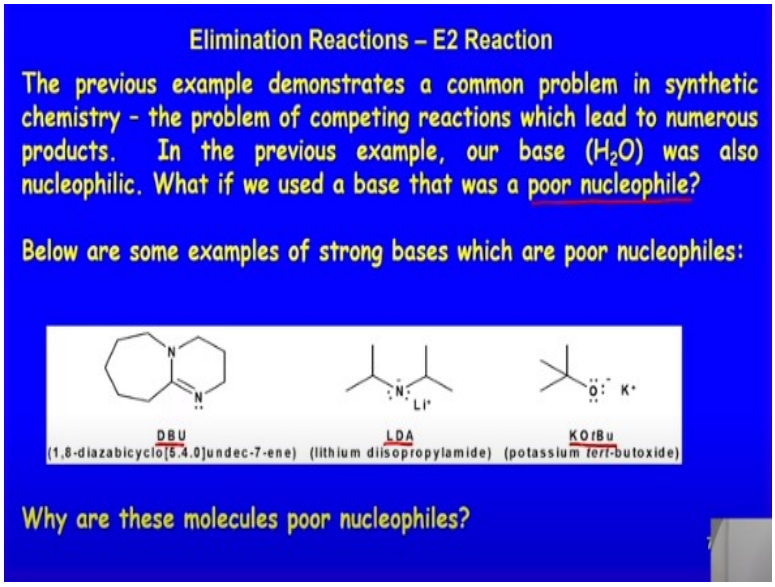


As we have already seen that alkyl halides also undergo reaction of the E1 reaction, because the bases used in these reactions are water, ethanol are also nucleophile. So the SN1 reaction will also compete in those cases. So when we have a tertiary butyl bromide like this, in presence of water and ethanol the reaction is slow, but it generates a carbocation. This is the first step of the reaction when the Br- ion is released.

And then this carbocation can undergo two types of reactions. One reaction is the elimination reaction where this proton is abstracted by water and the rate constant is identified by k elimination you get the elimination product here which is an alkene. But, if the water molecule comes and attacks the carbocation site, it forms these positively charged species and upon the elimination of one of those hydrogens, it forms an alcohol which is nothing but an SN1 product.

So in this particular case, when we use ethanol in water medium, we may expect to get both the products, the alkene and the alcohol when treated with a tertiary alkyl bromide.

(Refer Slide Time: 17:01)

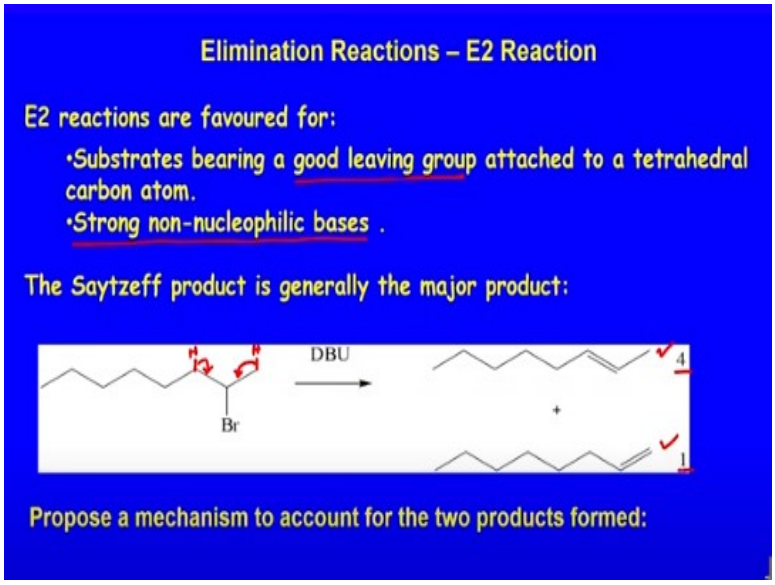


Now let us try to see what are the factors that favor E2 reactions. The previous example demonstrates a common problem in synthetic chemistry, the problem of competing reactions, which lead to numerous products. You will see when we talk about the cyclohexane derivatives and SN1 versus SN2, E1 versus E2 reactions. In those we will see there are possibilities of multiple products in case of different substrates.

So in the previous example, our base was water which was also a nucleophile. So if we use a poor nucleophile what will happen? You will use some nucleophiles which are like DBU, LDA, potassium tertiary butoxide. These molecules have bases, these are good bases, but they are poor nucleophile. Why? Because they are bulky in nature.

Therefore, they are not easy, they cannot easily form a bond with the carbocation site or a site where there is one halogen atom you want to do any substitution reaction. So because of that, they are poor nucleophiles. So therefore in this cases if you use this kind of bases, then the elimination reaction will be favored over the substitution reaction.

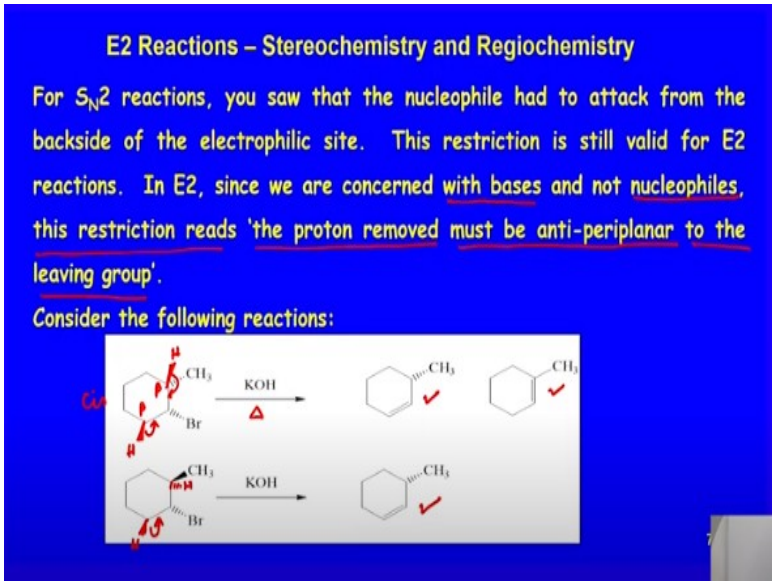
(Refer Slide Time: 18:33)



So E2 reactions are favored for substrates bearing good leaving group. Of course, the leaving group is important and strong non-nucleophilic bases that like this DBU. If you have remembered the names of these compounds, DBU, LDA or potassium tert-butoxide, these are all non-nucleophilic bases. And when you apply such non nucleophilic bases, you do not get any substitution product, rather you get elimination product.

But then again you have the possibility of elimination of hydrogen from this beta carbon or the other beta carbon and you end up getting two different products. One product is elimination from here, which gives you this product. One elimination from here that gives you this product. And this is the ratio of the two products, 1:4 in which it will form. So I would like you to propose a suitable mechanism for the formation of these two products yourself.

(Refer Slide Time: 19:48)



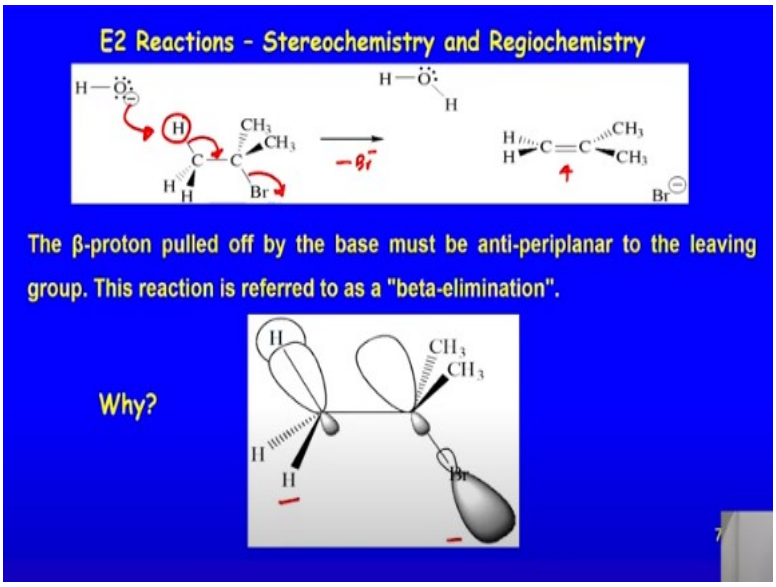
So let us see what happens when we talk about SN2 reactions. You saw that the nucleophile had to attack from the back side of the electrophilic site, in case of SN2 reaction. The restriction is still valid in E2 mechanism as well. In E2, since we are concerned with bases and not nucleophiles, this restriction reads as the proton removed must be anti-periplanar to the leaving group. What does anti-periplanar mean?

It means that the orientation of proton and orientation of the alkyl group sorry orientation of the bromide should be anti. So if there is a hydrogen exactly in anti-position with respect to the bromine then only the elimination reaction can happen. Let us see what in these two reactions below. In case of this cis compound, we have a proton here and let us write the cis separately. We have a proton here.

So as we know that these protons which are on the beta carbon are anti to that bromine. So by elimination reaction using KOH and possibly heat, if you can abstract this proton, this double bond is formed to give you this product. Or this double bond is formed to give you the second product. But if this is trans, then you have the hydrogen which is here. Therefore, this hydrogen and that bromine are not anti, they are on the same side of the C-C bond.

So the only anti-hydrogen is present here. So this anti-hydrogen is eliminated to give you a single product. So therefore, in this particular case, the E2 reaction gives you only one elimination product.

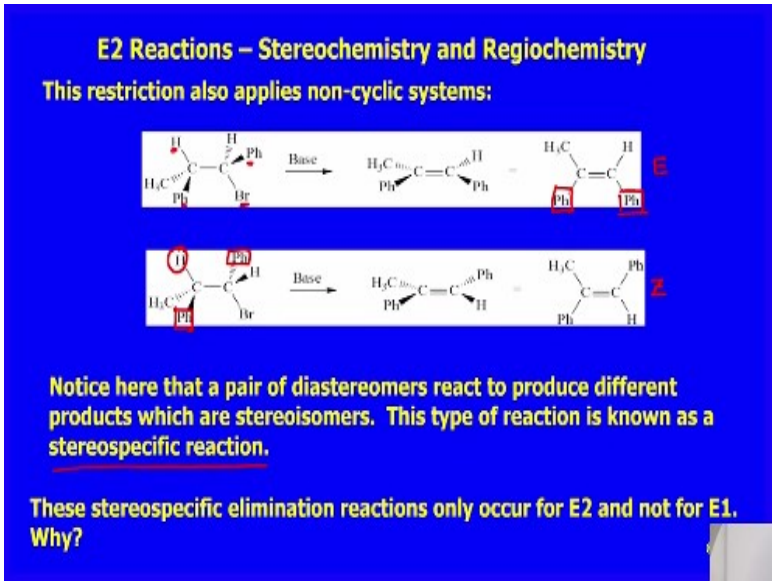
(Refer Slide Time: 22:20)



In case of E2 reaction, here we have drawn a molecule in the sawhorse projection, with the wedge projection rather, not sawhorse. We have drawn the molecule in wedge projection and if the hydrogen here is in anti position. So OH- abstract this proton, this bonded electron forms the corresponding double bond and Br- is eliminated as the anion and you get the alkene that you have.

So beta proton is pulled off by the base and must be at anti-periplanar orientation as you can see here in the orbital diagram. So this reaction is referred to as a beta elimination reaction, okay.

(Refer Slide Time: 23:20)



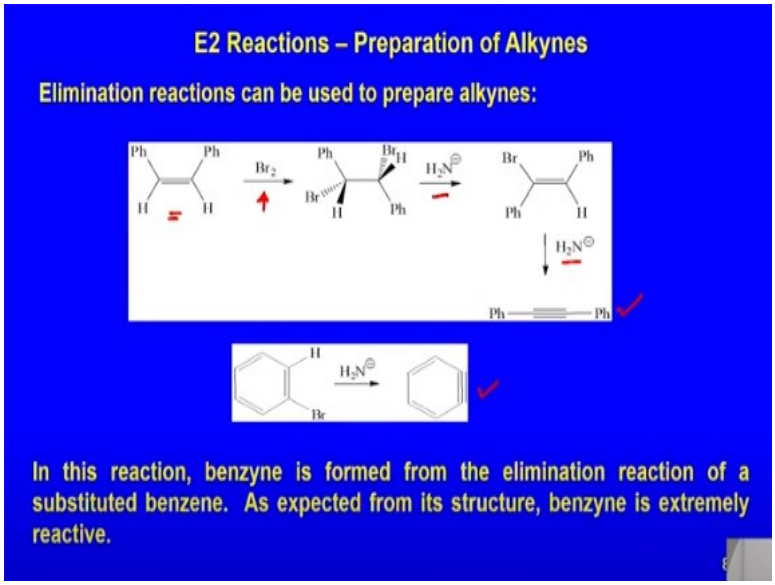
So similar reactions we can talk about where we have a compound. You can see here that the bromine and hydrogen are anti. These two phenyl groups are on one side of the C-C bond and the methyl and hydrogen are on the other side of the C-C bond. So when you use a base for any elimination reaction on the substrate, you always get a product which is both the more priority groups on one side.

So it is the E isomer. Whereas, if the substrate was such that when the phenyl rings were on the opposite side of the C-C bond and methyl and hydrogen were on the opposite side, the elimination reaction takes up that proton and forms the corresponding Z isomer. So this elimination reaction can specifically produce either E or Z isomer depending on the substrate that we are using, because this always goes through a beta elimination and the elimination occurs in an anti-periplanar arrangement.

So what happen in this reaction is that we generated two different diastereomers, a pair of diastereomers from two different starting materials. So this type of reaction is also known as a stereospecific reaction. We will have a few classes on this stereospecific, stereoselective, regiospecific and regioselective reactions at a later stage of this course.

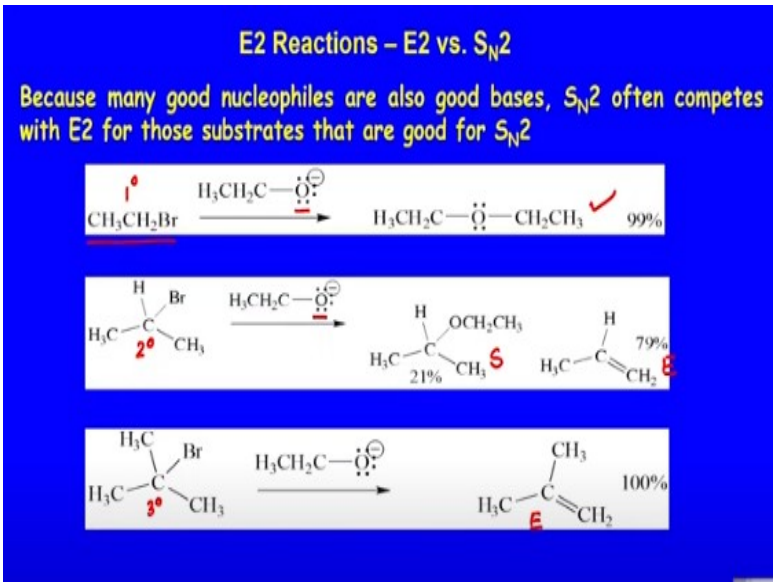
Now I am going to ask you a question these stereospecific elimination reaction only occur for E2 and not for E1 mechanism. Can you explain that? It is your responsibility to think about it, go to the textbook and find out the answer to this question, why in E1 reaction you do not see any stereospecificity.

(Refer Slide Time: 25:34)



Similarly, elimination reactions can be used to prepare alkynes. So if you start with an alkene we use bromine to make a Dibromo compound and then stepwise we can do two steps of elimination reaction to produce one alkyne. So here in the same way one can generate benzyne as well.

(Refer Slide Time: 26:05)

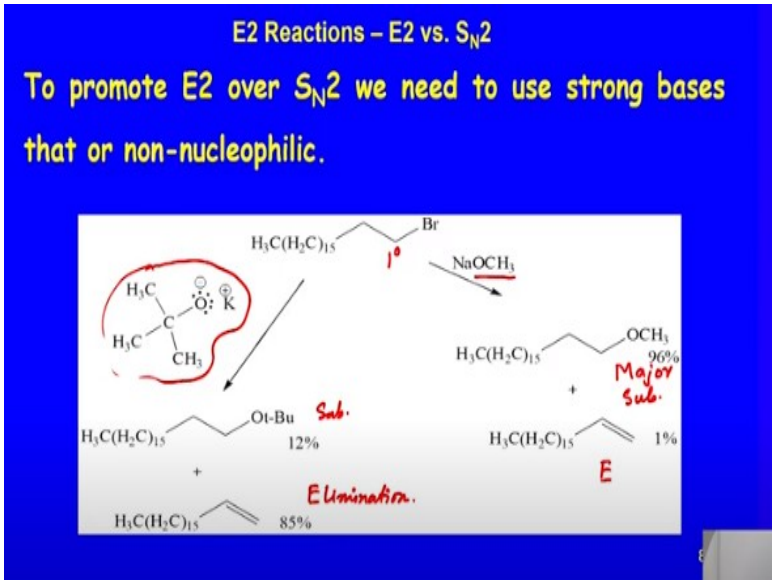


So when we are having E2 reactions, always there will be a competition with SN2 reaction because many good nucleophiles are also good bases. SN2 often competes with E2 for those substrates that are good for SN2 reactions as well. So therefore, if you react this ethyl bromide with this base, you would get the substitution product 99%. Because this is nothing but 1 degree.

But when you go for a 2 degree alkyl bromide, use the same base, it is possible to have this substitution product with the elimination product as well. And if you go for a 3 degree alkyl halide, you only get the elimination product and not the substitution product.

Therefore, depending on the nature of the substrate, the same base can generate or can produce different products depending on what kind of substrate it is, whether it is 1 degree, 2 degree or 3 degree alkyl halide.

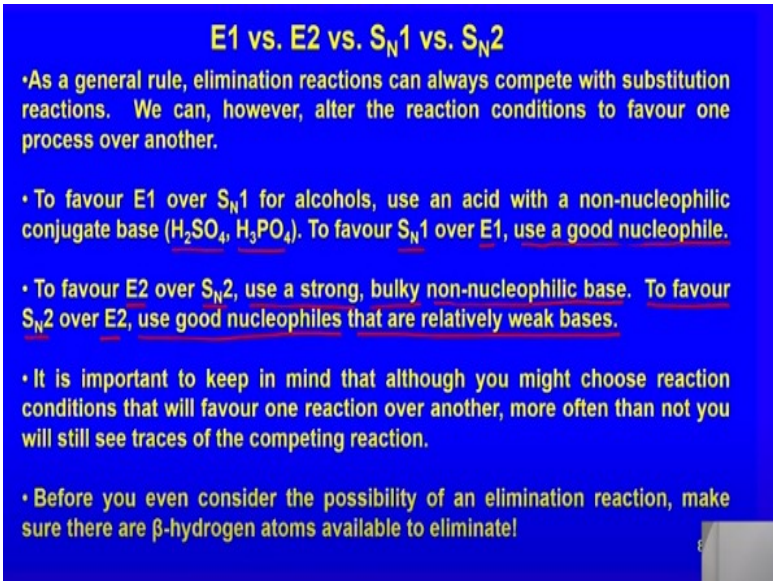
(Refer Slide Time: 27:24)



To promote E2 over SN2, we need to use a strong base or a non-nucleophilic base. So if you have a compound which is 1 degree alkyl halide, if you use the sodium methoxide as a base, you would get majority of the product as a substitution product and a very little amount of the elimination product.

Whereas if you use a bulky non-nucleophilic base like this, your substitution product is less and the elimination product is in major quantity. So this is how we can modulate these type of reactions and try to drive these reactions to form a particular desired product.

(Refer Slide Time: 28:24)

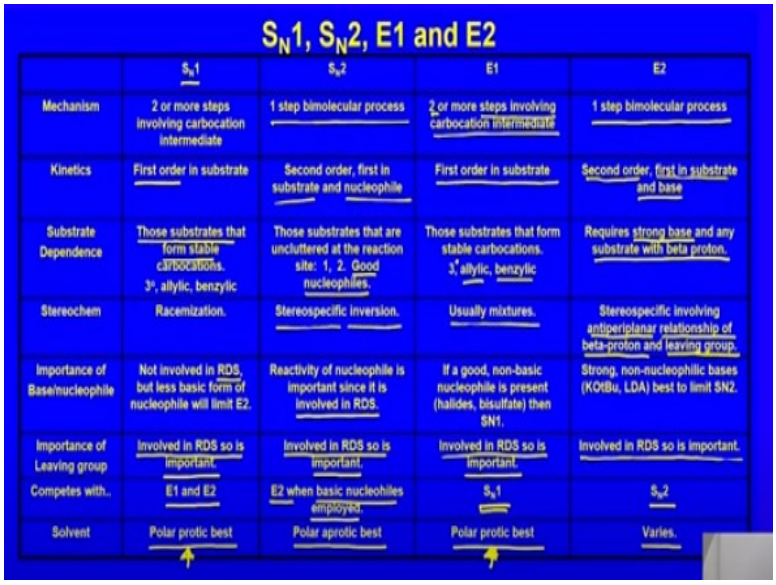


So let us now consider the differences between E1 versus E2 versus SN1 versus SN2 reactions. As a general rule, the elimination reactions can always compete with substitution reaction. We can however, alter the reaction conditions to favor one process over another. To favor E1 and SN1 for alcohols we use an acid with a non-nucleophilic conjugate base like the acids, sulphuric acid, phosphoric acid etc.

To favor SN1 over E1, we use a good nucleophile. To favor E2 over SN2, use a strong bulky non-nucleophilic base. To favor SN2 over E2, if you use a good nucleophiles that are relatively weak bases. It is important to keep in mind that although you might choose reaction conditions that will favor our reactions over another.

More often than not, you will still see traces of the competing reaction products. Before you even consider the possibility of an elimination reaction, make sure there are beta hydrogen atoms available to favor elimination reaction.

(Refer Slide Time: 29:53)



So in the tabular form if we summarize these four different reaction mechanisms SN1, SN2, E1 and E2, we can make a very nice table as I have done here. When we talk about SN1 reaction, the mechanism has two or more steps involving the carbocation as intermediate. It is a first order kinetics. It favors those substrates that forms stable carbocations that is 3 degree alkyl halides, allylic or benzylic halides will favor SN1 reaction.

Stereochemistry indicates the racemization because it goes through carbocation formation. Therefore, the substitution product can be formed from the either side of the carbocation as a result to make it a racemic mixture. Importance of base or nucleophile, it is not involved in the rate determining step because the rate determining step is the bond breaking step. But less basic form of nucleophile will lead it to E2.

Importance of leaving group, it is very much important because it is involved in the rate determining step. So it is very important. SN1 always competes with E1 and E2 reaction. And for solvent we already have seen that polar protic solvents like ethanol, methanol, water are best solvent for SN1 reaction. On the other hand, the SN2 reaction, it is a one-step process.

It is a second order kinetics and first order in substrate and nucleophile. Those substrates that are uncluttered at the reaction site, that is one or two, they are good nucleophiles. It always gives you the inversion of stereochemistry, that is a

stereospecific reaction and you always get a stereo inversion of chiral center during the SN2 reaction. The reactivity of nucleophile is important since it is involved in the rate determining step.

Because the nucleophile attacks the carbon and the removal of halide happens simultaneously. Leaving group is also important because it is involved in the rate determining step. It competes with E2 when basic nucleophiles are involved. SN2 reaction is favored in polar aprotic solvents, for example acetonitriles, acetone, dichloromethane and so on.

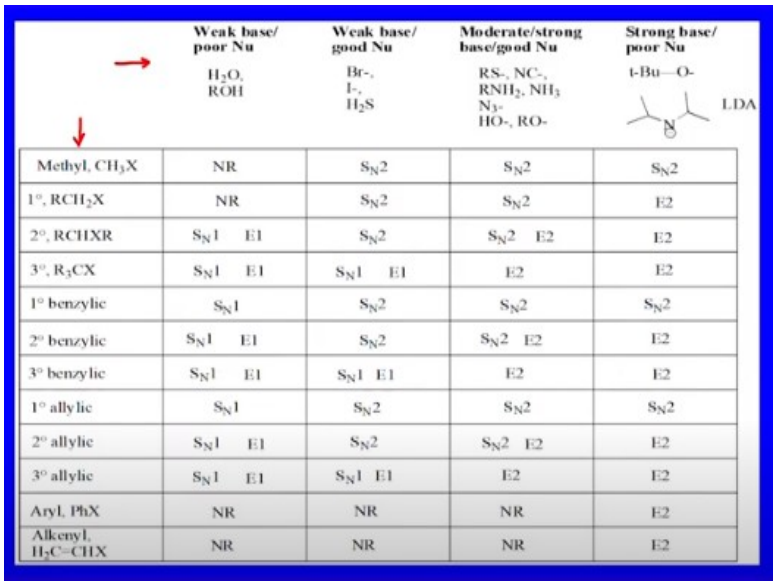
When we go to E1 reaction two or more steps involving carbocation as intermediate, it is again first order with respect to substrate. Those substrates that forms stable carbocations, that is 3 degree allylic or benzylic, those kind of alkyl halides favor E1 reaction. It gives mixture of products usually. Because as you have seen, it can eliminate the terminal hydrogen and form a terminal double bond.

Or it can eliminate a proton from the inner part of the carbon chain and form a more substituted alkene. If a good non basic nucleophile is present, then halides, bisulfate etc., then SN1 is the reaction with which it competes. Involving rate determining step, so it is important. That is leaving group is important. It competes with SN1 and it happens in polar protic solvent.

So if you note that, the solvent choice is similar for SN1 and E1 and that is why they always compete. In case of E2 reaction, the first step is a bimolecular process just like SN2. It is a second order reaction and first order with respect to both substrate and the base. It requires strong base and any substrate with a beta proton is very important for this elimination reaction.

This reaction is stereospecific involving the anti-periplanar relationship of the beta proton anti leaving group So this stereochemistry is absolutely important in E2 elimination reaction. Once again the leaving group is very important because it is involved in the rate determining step. Since these conditions are very similar to SN2 reaction, E2 always competes with SN2, but the choice of solvent varies for various E2 reactions depending on what the substrate that you are using.

(Refer Slide Time: 35:24)



	Weak base/ poor Nu H_2O, ROH	Weak base/ good Nu Br-, I-, H_2S	Moderate/strong base/good Nu RS-, NC-, RNH_2, NH_3, N_3-, HO-, RO-	Strong base/ poor Nu t-Bu—O-, LDA
Methyl, CH_3X	NR	S_N2	S_N2	S_N2
1°, RCH_2X	NR	S_N2	S_N2	E2
2°, RCHXR	S_N1 E1	S_N2	S_N2 E2	E2
3°, R_3CX	S_N1 E1	S_N1 E1	E2	E2
1° benzylic	S_N1	S_N2	S_N2	S_N2
2° benzylic	S_N1 E1	S_N2	S_N2 E2	E2
3° benzylic	S_N1 E1	S_N1 E1	E2	E2
1° allylic	S_N1	S_N2	S_N2	S_N2
2° allylic	S_N1 E1	S_N2	S_N2 E2	E2
3° allylic	S_N1 E1	S_N1 E1	E2	E2
Aryl, PhX	NR	NR	NR	E2
Alkenyl, H_2C=CHX	NR	NR	NR	E2

So in this particular table, I have summarized the possibility of different types of reactions for different types of alkyl halides. So on the first column here I have the substrate. And here I have different types of nucleophiles or bases. So this chart is giving you an overview which combination gives you what kind of reaction product.

So this chart will be very important for you to understand the reaction mechanism or to predict the products for various substrates that you may encounter in this course. So I would like you to go through this table very carefully and understand the basics along with what I have discussed in last couple of few lectures.

In the next lecture, we will discuss a few problems in which we will use this table and demonstrate how these reactions are favored, which reaction favors and which reaction gives you what kind of product using various substrates and base and nucleophile combination.