Symmetry, Stereochemistry And Application
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Lecture No-40
Dynamic Stereochemistry - Part 02

Welcome back to the course entitled symmetric stereochemistry and applications. We have just started discussing about the dynamic stereochemistry and aspects of stereo selectivity and stereo specificity and in the last lecture, we have discussed a couple of examples and try to understand what is called stereo specific and what are called stereo selective reactions.

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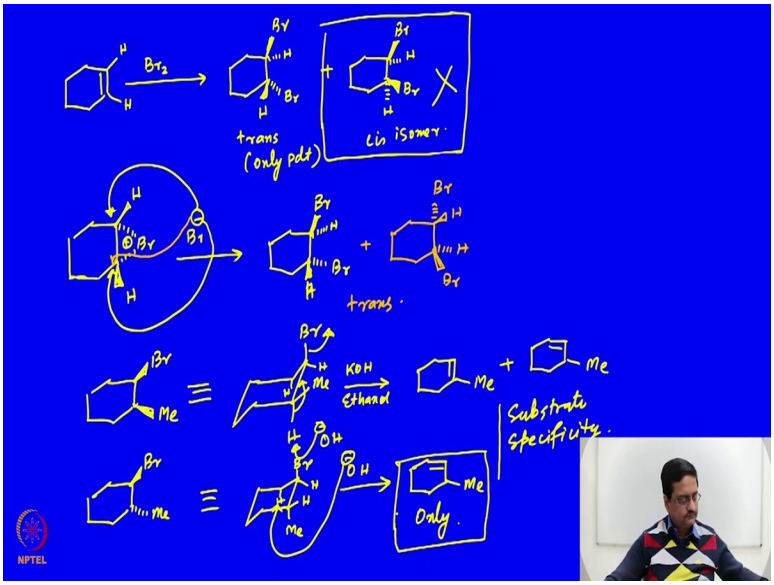

So, we continue our discussion in this direction with some more examples. Suppose if we have a cyclohexene and we try to do a bromination reaction what we know for a bromination reaction is when we have done in the previous class for the alkene the bromonium ion could be broken from either side and formed 2 different compounds. But, here when We do the reaction in the same way we only end up getting a compound which is the trans dibromocyclohexane and we do not get the corresponding cis dibromocyclohexane.

Because as we know the reaction mechanism does not allow the formation of this Cis isomer, no formation of this compound, why is that so, if we try to understand using the formation of bromonium ion in the mechanistic path, the bromonium ion that may have formed in this

reaction is this one and then on this bromonium ion, if this br minus comes from top you would get a product where the br will be up the hydrogen will be down and here the hydrogen will remain up and the bromo will go down.

So, it is trans. If the bromine attacks from the bottom here then also you get the same product. If bromine attacks from the top on this carbon what you would get is bromine up hydrogen down and in that case the bromine on this carbon will be down. So, this is always it forms the trans isomer. On the other hand if we try to see what happens when you try to do an elimination reaction with a cis compound which is this Cis 1 bromo 2 methyl cyclohexane.

The conformation of this molecule should be identified for an elimination reaction to happen. So, if you do elimination reaction on this compound using KOH in ethanol medium OH minus will take away this proton as a result a double bond will form here and bromine will be eliminated. So, we will end up getting a product which would be this one, along with this there is a possibility that the other product which can form from that particular proton also forms as a second alternative product.

But, if we had done the reaction with the corresponding trans isomer which if we try to write down the corresponding chair form of this cyclohexane the trans isomer will have the methyl in the anti position. So, when you do the same reaction with OH minus there is no hydrogen in the anti periplanar orientation with respect to the bromine on the first carbon. So, the elimination happens from the third carbon and you end up getting a product which is this one the only product.

This reaction is producing 2 different compounds whereas this particular reaction is producing only one compound. So, here it is the substrate specific reaction. So, what we see here is substrate specificity and in this particular case it is highly selective for this particular compound formation.

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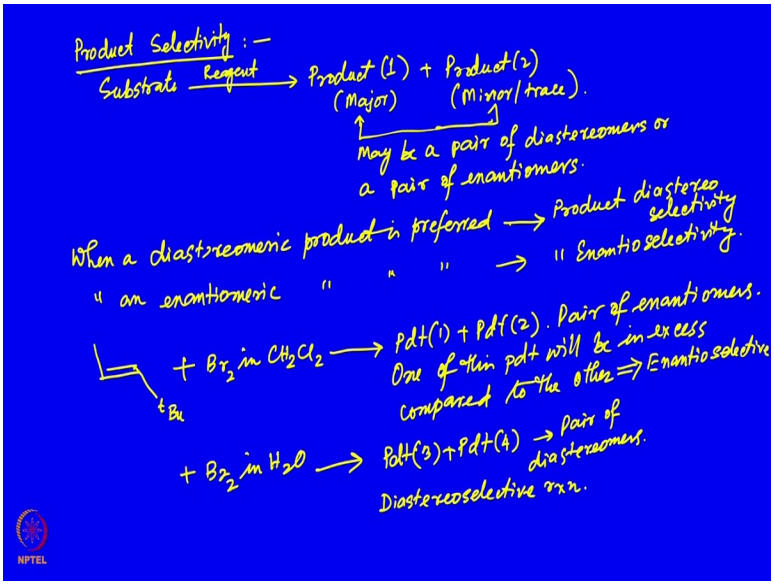

So, let us try to see the case of product selectivity. So, here what does it mean is that you start with the substrate and perform a reaction with a given reagent you get 2 products one and product 2 and what you see is that the product one is a major product and product 2 is a minor or trace product. And these 2 products may be a pair of diastereomers or a pair of enantiomers. So, when a diastereomeric product is preferred then the reaction is called product diastereoselectivity.

And when an enantiomeric product is preferred then we call it as product enantioselectivity. Let us try to understand this with a couple of examples, Suppose we are doing a reaction with a t-butyl group present on a C-C double bond and we are doing a reaction with bromine in dichloromethene. So, I will show you in the next slide that it forms 2 products and these 2 products are a pair of enantiomers.

But then one of this product will be in excess compared to the other that means we will see that this reaction is enantioselective but, when we do the same reaction with bromine in water, we will again get 2 different products that is product 3 and product 4 and we will see that these products are pair of diastereomers and we will see a selectivity among these 2 products. So, this reaction will be a diastereoselective reaction.

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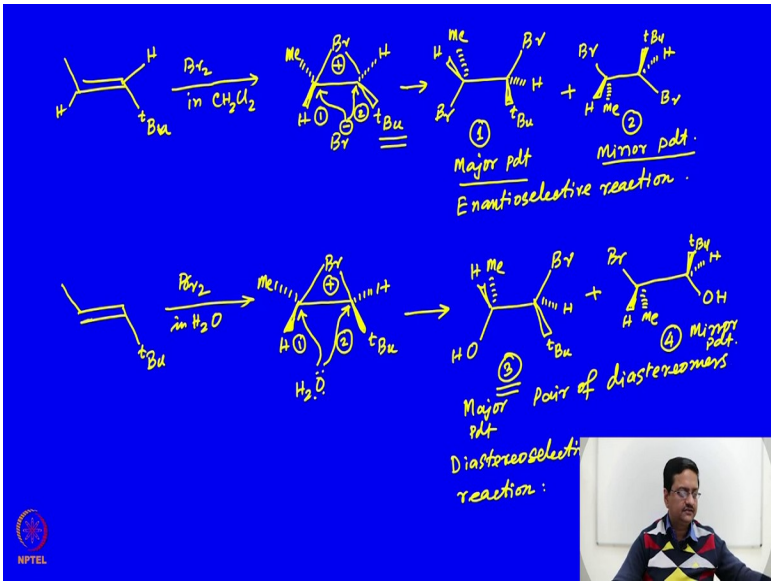

So, let us see how this reaction proceeds, as we all know that the addition of bromine in a C-C double bond goes through a cyclic intermediate called the bromonium ion; the first step of this reaction is the formation of bromonium ion as I am trying to show here. So, now, in this particular bromonium ion intermediate what we see is that the br minus that attacks has now, a preference for this center which is less crowded, the center one and the center 2 is more crowded because of bulky tertiary butyl group.

So, when the br minus attacks the first carbon the product that we get is this one and when the br minus attacks the second carbon the product we get is this one and this is the major product because br minus when it attacks one it has more preference because of less hinderance in reacting. So, this enantiomer gets preference over the other enantiomer. So, the enantiomer 2 is the minor product.

So, here 2 enantiomers are formed and these 2 enantiomers are formed in unequal amount. So, we can term this as the enantioselective reaction. Now, if we see the second reaction where we are trying to treat the same alkene with bromine in water. What we know is that bromine in water gives forms the halohydrin. But, that halohydrin formation also goes through the formation of bromonium ion to start with.

So, this brominium ion is first formed and then the water molecule has possibility of attacking the carbon center one or the possibility of attacking carbon center 2. So, now, again what we see is carbon center one is less sterically hindered as a result the product that will form by the attack of water on carbon center one is going to be the major product and the one which attacks the carbon center 2 will be the minor product.

So, let us try to draw the 2 compounds that are going to form after elimination of H plus obviously in this particular reaction. So, here the product three and 4 are a pair of diastereomers and preferentially this product three forms as a major product while this forms as a minor product. And hence what we see is this particular reaction is a diastereoselective reaction, hope you can understand the difference between the enantio selectivity and diastereoselectivity from these 2 examples.

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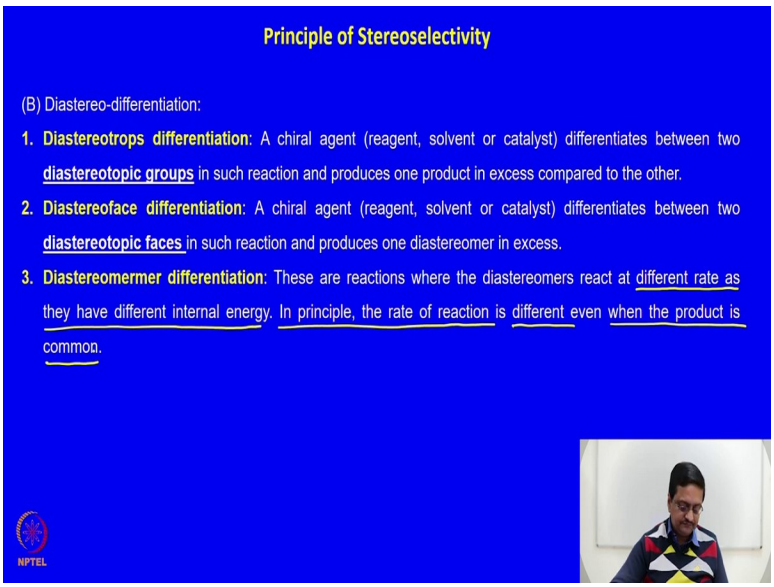

Let us try to now see what is called the substrate selectivity. So, in a substrate selective reaction suppose you have 2 different stereoisomers substrate one and substrate 2 you do a reaction, you get a product one which is coming from substrate one and the substrate 2 remains unreacted. So, this reaction is called a substrate selective reaction and this substrate selectivity or substrate selective reaction happens in case of enzyme catalyzed reactions.

So, now, let us try to understand the principle of stereo selectivity. Principle of stereoselectivity means that stereoselective reactions are essentially stereo differentiation reaction where one of the 2 stereoisomer is differentiated by the reagent in a given chemical reaction. So, there are in general six categories of stereo differentiation under 2 general classes which are called enantio differentiation and diastereo differentiation.

So, let us see what are called enantio differentiation, under enantio differentiation there are three types of differentiation reactions. The first one is called the enantiotrops differentiation where a chiral reagent or chiral agent which can be a reagent solvent or a catalyst differentiates between 2 enantiotropic groups present in a molecule in a given reaction. So when the enantiotropic groups are differentiated by a chiral reagent then we call it as enantiotrop differentiation.

The second type is called the enantioface differentiation where a chiral agent a reagent solvent or a catalyst differentiates between 2 enantiotropic faces that means the faces of a double bond it can be a C-C double bond or a C-O double bond. So, when the chiral reagent differentiates between those 2 phases and gives you different products with different amounts one of them being in the major product then it is called the enantioface differentiation. The third type is the enantiomer differentiation.

Here a chiral reagent differentiates between the 2 enantiomers in the process and this process is not necessarily an chemical reaction as it includes chiral separation of a pure enantiomers from their racemic mixture using a chiral column. So, that chiral column has a chiral reagent which interacts with one of the 2 enantiomers and blocks the passage of that enantiomer and allows the passage of the other enantiomer through the column and one can separate a mixture of enantiomers using this kind of column chromatography.

The other type of differentiation is called the diastereo differentiation, diastereotops differentiation means a chiral reagent, the solvent catalyst differentiates between 2 diastereotopic groups in such a reaction and produces one product in excess compared to the other is called the diastereotops differentiation. Diastereoface differentiation in is a case where a chiral reagent a

solvent or a catalyst differentiates between the 2 diastereotopic phases in a reaction and produces one diastereoisomer in excess.

The last type of diastereomer differentiation happens when the at both the diastereomers react at different rate as they have different internal energy. In principle the rate of reaction is different when the product is common in both the reactions. So, this is very important for you to understand. We will continue from here in the next class, thank you.