Symmetry, Stereochemistry And Application

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Lecture No-39
Dynamic Stereochemistry – Part 01

Welcome back to the course entitle symmetry stereochemistry and applications. In last week we have discussed about stereochemical aspects of various organic reactions involving the carbonyl group and we have seen the reactions are sensitive to different stereochemistry of the carbonyl compound. So in this week we are trying to go through the new portion where we are going to highlight the stereochemical importance of chemical reactions and how the stereochemistry of the reaction can be predicted based on the nature of the substrate and nature of the reagent solvent etc.

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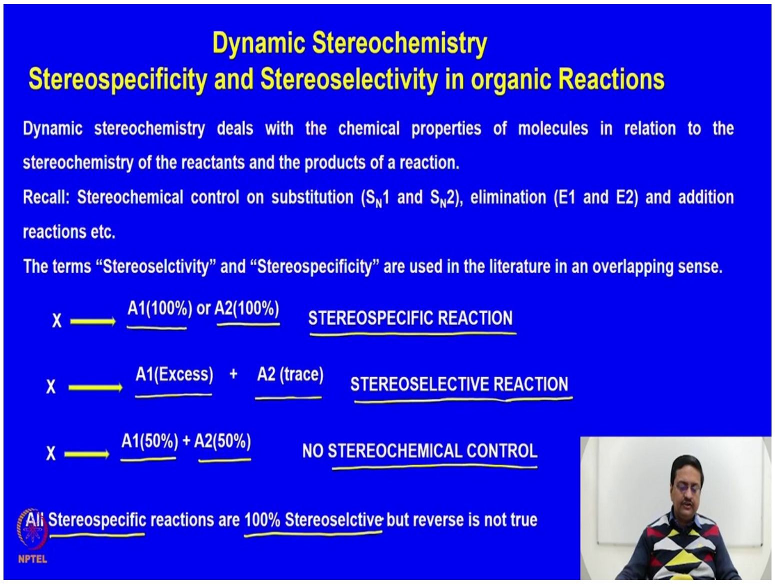

Dynamic Stereochemistry
Stereospecificity and Stereoselectivity in organic Reactions

Dynamic stereochemistry deals with the chemical properties of molecules in relation to the stereochemistry of the reactants and the products of a reaction.

Recall: Stereochemical control on substitution (S_N1 and S_N2), elimination (E1 and E2) and addition reactions etc.

The terms "Stereoselctivity" and "Stereospecificity" are used in the literature in an overlapping sense.

$X \longrightarrow$ A1(100%) or A2(100%) STEREOSPECIFIC REACTION

$X \longrightarrow$ A1(Excess) + A2 (trace) STEREOSELECTIVE REACTION

$X \longrightarrow$ A1(50%) + A2(50%) NO STEREOCHEMICAL CONTROL

All Stereospecific reactions are 100% Stereoselctive but reverse is not true

So, this portion of the stereochemistry is technically termed as dynamics chemistry but we will try to understand the differences and the meaning of stereo specificity and stereo selectivity in organic reactions. So, dynamic stereochemistry deals with the chemical properties of molecules in relation to the stereochemistry of reactants and products of a reaction. So, depending upon on the substrate and reagent and the solvent, the stereochemistry of the product is controlled.

We have discussed this in very brief manner in one of the earlier lecture where we have discussed about the substitution reaction, elimination reaction and then in some lecture where we talking about addition reactions. You may remember that in case of SN1 reaction we encounter the racemisation in case there is a chiral centre associated in the substitution reaction. Whereas in case of SN2 reaction we get to see that the configuration at the chiral centre is inverted and umbrella inversion happens.

Similarly in case of elimination reaction the products that are formed in E1 and E2 reaction may be different because the reaction mechanisms are different in case of E1 and E2 as a result we end up getting 2 different products based on the reaction mechanism whether it is E1 or E2. So, in this lecture and couple of lectures in this week we will discuss more about addition reaction their corresponding stereochemical preferences.

So, when we try to define terms stereo selectivity and stereo specificity these are used in the literature in the overlapping manner. So we too understand these 2 terms very clearly. So, when we have a substance of course X and the substrate gives in a reaction a compound A1 or another compound A2 one of them in 100% abundance the isomer is not formed so that reaction is called stereo specific reactions.

That means only one specific compound A1 or A2 is formed and the other one is not formed. The other type of chemical reaction can be considered where your substrate X gives one of the stereo isomer in excess compared to the other stereoisomer which appears as a trace compound and these type reactions are called stereo selective reactions which means this reaction procedure selects one among the two possible products as a preference gives that particular products in excess and other products also forms as minor products or a trace compound.

The Third type of reaction this is something which is already you have encountered is like SN1 reaction where if you started with a chiral substrate, SN1 reactions it goes through a Carbocation is formation and once this carbocation is formed then it is equally probably that carbocation can be attacked by nucleopile from above and below and form 2 different isomers in same abundance. So in that case A1 and A2 is formed in 50% each ratio.

So, 1 is to 1 ratio there will not be any stereochemical control or preference. So, what we can see form these few line is that a stereo specific reaction is essential stereo selective that means a stereo specific reaction yields one particular stereo isomer between the 2 and hence it can also be considered as a stereo specific reaction. But on the other hand when you try to understand the stereo selective reaction it is selective between the 2 particular compound but not specific that which one will be major product or which one will be minor product or it is not a specific that it will only form one of them.

Therefore this concept can be summarised as all stereo specific reactions are 100% stereo selective but stereo selective reactions are not stereo specific.

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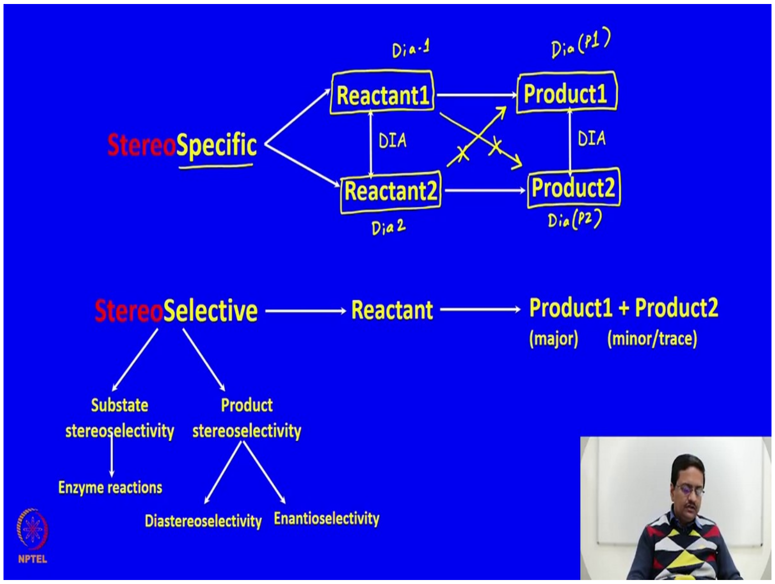

StereoSpecific

Reactant1 → Product1

Reactant2 → Product2

StereoSelective → Reactant → Product1 + Product2
(major) (minor/trace)

Substate stereoselectivity → Enzyme reactions

Product stereoselectivity → Diastereoselectivity, Enantioselectivity

So when we try to understand stereo specificity of a reaction we can simply consider particular reactant which is one of the 2 diastereomer and we do a particular reaction and we get a particular product. And then if we choose a different diastereomer then in the product of the same reaction we get different diastereomer. So, here it is stereo specific a particular diastereomer, suppose diastereomer one gives you diastereomer many product one. And diastereomer two gives you diastereomeric product 2. We do not see formation of any in two cases that it starts with a diastereomer and get a product as diastereomeric product 2 even in trace quantity so we can call it as stereo specific reaction.

And on the other hand stereo selective reactions are such that where one particular reactant can yield 2 products one of them is major product and other one is a minor or trace product. So it may feel like one product is 80% and the other is 20% then we call it as major and minor. Whereas in some reactions it may be case that one forms 98% and the other one is the 2% in that case we would call it as major and trace product.

These stereo selective reactions can be divided into different groups or parts. One can think of substrate stereoselectivity which means the reactant which is the substrate can be a mixture of 2 enantiomer or 2 diastereomers and the reaction is such that one of the two stereo isomers present in the reaction medium reacts and gives you the product and that kind of selectivity is selectivity on substrate. So one of the 2 substrate present in the reaction medium reacts to give you a product and the other substrate does not react and that is called substrate stereoselectivity.

And normally that is observed in enzyme catalyzed reaction. The other possibility is that the product stereoselectivity. So in this case a particular reactant may react with a particular reagent or solvent or catalyst to produce two different products and those two products are produced in two different quantities. And in that those 2 products that we are talking about can be either pair of diastereomers or a pair of enantiomer.

So the products are diastereomers then that particular reaction is called diastereoselective reaction whereas if the products are a pair of enantiomers then we call that as enantioselective reaction.

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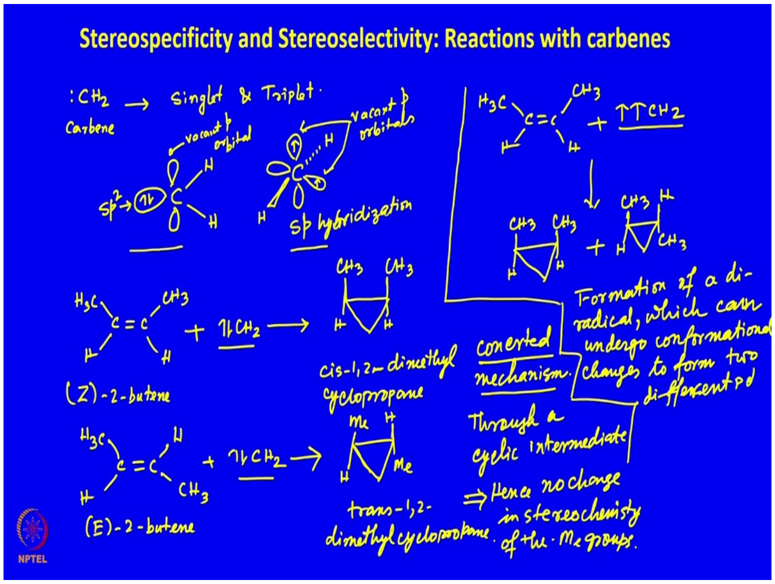

Stereospecificity and Stereoselectivity: Reactions with carbenes

Formation of a di-radical, which can undergo conformational changes to form two different pd

concerted mechanism.

Through a cyclic intermediate

⇒ Hence no change in stereochemistry of the Me groups.

Let us try to see the stereospecificity and stereoselectivity in some common reactions. So let us start with the reaction with carbenes. We have discussed in one of the previous lecture that the species CH2 double dot is called the carbene or methylene carbene. This methylene carbene can exist in two different forms singlet and triplet. So these two different forms of this carbene are different in terms of their bonding.

So this singlet carbene, the carbon is in sp2 hybridized state and the 2 electrons, the lone pair of electrons resides in sp2 hybridized orbitals and you have a vacant p orbital present in the singlet carbene, whereas the triplet carbene exist as a sp hybridised carbon. So in that you have 2 vacant p orbitals each one of those contains one electron each sp hybridization. So you see the 2 carbene are structurally different.

And as the result of the structural difference these 2 carbenes reacts differently with the alkenes so if we use a Cis compound, rather Cis 2 butene using the singlet carbene it forms the CH3 CH3 Cis compound. So these we started as Z 2 butene we get here the Cis 1,2 diemethyl cyclopropane. Similarly if we start with corresponding trans variety, that is the E 2 butene to the same reaction with the singlet carbene we would end up getting corresponding trans dimethyl cyclopropane derivatives.

On the other hand if we had done this reaction with triplet carbene, we would have got a mixture of Cis and the corresponding trans isomer. Form this observation one can conclude that the reaction with singlet carbene happens in a concerted mechanism, so that this happens through a cyclic intermediate and hence no change in stereo chemistry of the methyl groups. But then, when triplet carbene reactions goes through a different mechanistic pathway and in that case it is believed that the reaction proceeds through the formation of di radical which can undergo conformational changes to form different products.

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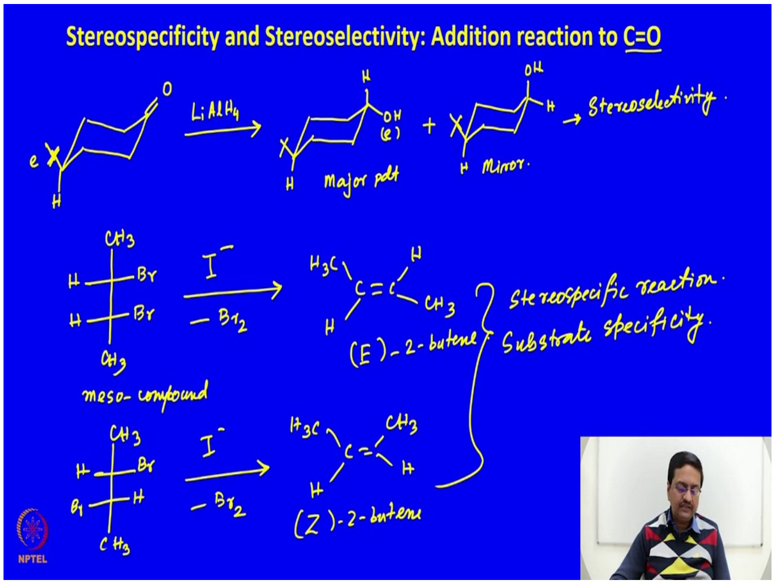

Stereospecificity and Stereoselectivity: Addition reaction to C=O

What happens when di radical forms it is possible to have rotation about single CC bond and the Cis isomer also gets twisted through CC single bond and the ring closure happens as a result we get to see two different products Cis and trans isomers. So here it is clear that these reaction of the alkenes with carbenes give you 2 types of reaction one is a concerted step which is also called a pericyclic reaction and other one proceeds through a di radical formation and results into two different product which form in equal quantities.

Let us see one more example of this stereospecificity and selectivity in case of additional reaction to CC double bond. So, let us take the example of a cyclohexanone derivative which contains tertiary butyl group in the 4th position with respect to the C double bond O and as you know the tertbutyl group is more stable at the equatorial position compare to the axial position. So, this compound is treated with Lithium aluminium hydrate.

What happens you have already seen that carbonyl groups gets reduced to form the alcohol so the product is cyclohexanol derivative and what we see in this reaction that OH in the equatorial position this the major product while the other possibility that OH is in the axial position is the minor product. So here, what we see is called the stereoslectivity. On the other hand if we try to look at the elimination reaction offered by these 2 particular compound that I am drawing.

Which is this one is the meso compound but when you treat this compound with iodine what happens is bromine elimination happens and it produces the trans isomer of the double bond. But when we use a different substrate where the bromines opposite side which means it is one of the 2 optically active form of dibromobutane in the same reaction the elimination of bromine leads to the formation of the corresponding Cis isomer that is the Z 2 butene.

So these 2 reactions are called the stereospecific reactions where we see the substrate specificity. So, here it is possible to choose different substrate to get target molecule through this stereoslective or stereospecific synthesis groups.

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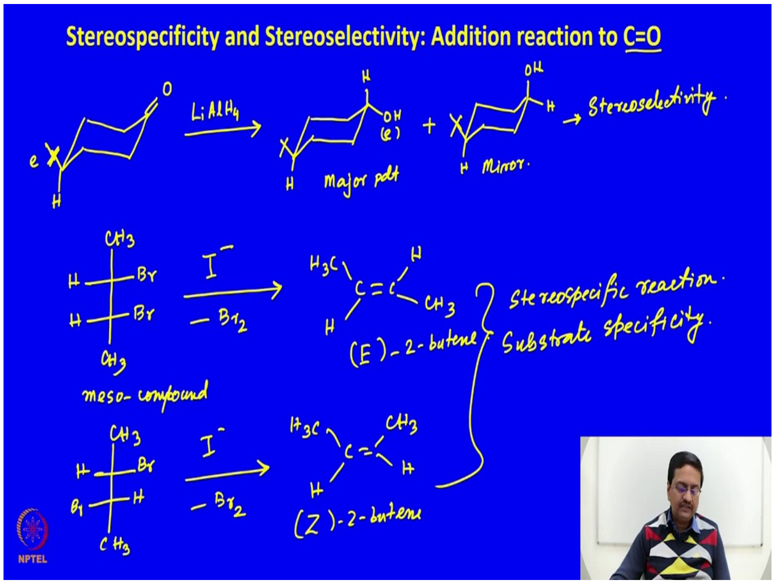

Stereospecificity and Stereoselectivity: Addition reaction to C=O

When we try to do reaction with double bonds what we have already seen is I am going to repeat that again. If we start with a trans product and do a bromination reaction we could end up making compounds where there will not be any stereo chemical preference, both the isomers will be formed so we do not see any specificity or selectivity. You can say that no specificity or selectivity in this reaction.

So here what we know is that the reaction proceeds through the formation of bromonian ion which would look like this and Br minus can equally attack by that carbon to give rise to 2 products which are pairs of enantiomers therefore these reactions do not have any stereospecificity or stereoselective control as we have seen in our previous lecture. So, from here we will continue in the next class.