Symmetry, Stereochemistry And Application
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Lecture No-41
Reaction Specificity and Selectivity

Welcome back to the course entitled symmetry stereochemistry and applications. In the last lecture we have discussed about these six different types of differentiation in chemical reactions and we have talked about enantio and diastereo differentiation terminologies.

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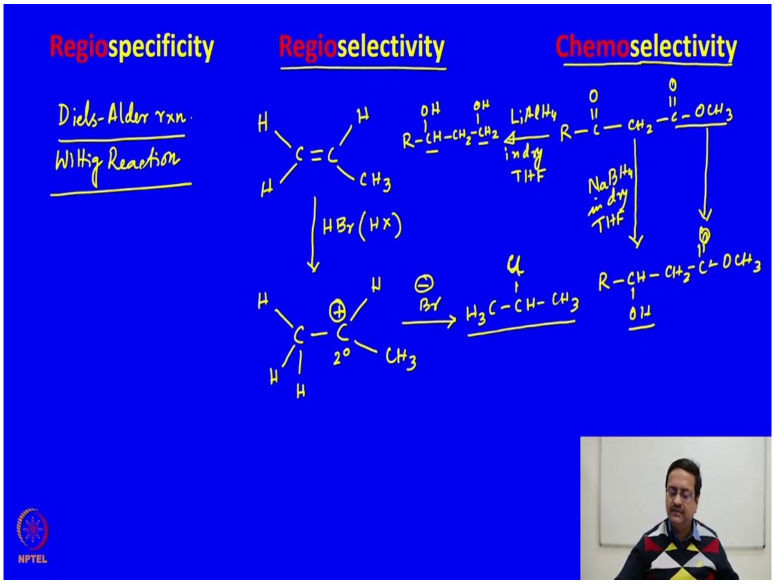

Regiospecificity Regioselectivity Chemoselectivity

So, in that direction we would like to continue in this lecture and introduce you to three more terms which are called regiospecificity, regioselectivity and chemoselectivity. The term regioselectivity indicates that the chemical reaction takes place at a particular region of the substrate and the other possible region is not attacked by the chemical reagent in those reactions. So, there are some region regiospecific reactions like Diels-Alder reaction, then Wittig reaction.

So, we will discuss these reactions in detail in the following week in the coming next week. The regioselectivity has already been discussed in our previous lectures. So, here just I would like to introduce the term and remind you about the previous examples that were discussed but we did not use the term regioselectivity in that case. So, when we have an unsymmetrical alkene, like this and we treat this unsymmetrical alkene with HBr or in general HX, what do we know, this reaction undergoes markovnikov of addition through carbocation formation.

And based on that carbocation stability the product is identified. Now what we need is we need to identify these two groups specifically. So, now when we have this particular molecule, the carbocation that is more stable is this one, right, because this is a two degree carbocation. So, the reaction will proceed in a direction so that the Cl minus or Br minus in this particular case gets added to the two degree carbocation site and produces this particular compound.

So, this is called a regioselective reaction where only one particular compound is formed from the two possible isomers of the compound. We have also established our knowledge on chemoselectivity. If you remember we try to do a set of reduction reactions suppose we take a substrate where you have a ketone and an ester simultaneously in the molecule. So, if you treat this compound using sodium borohydride in dry THF medium this would reduce the ketone to alcohol and produce this particular compound.

But if you treat this compound using lithium aluminium hydride in dry THF medium followed by hydrolysis you would get this compound which is different from the previous one. So, this is here you see that the ester is remaining unchanged and the ketone is reduced to alcohol but in this case both ketone and the ester got reduced to corresponding alcohol. So, here the same substrate has given you two different products based on the reagent that we have used.

So, this reaction is called the chemoselective reaction and you would encounter a large number of such examples when we talked about the oxidation reduction reactions on carbonyl compounds and some of the oxidizing agents or reducing agents are capable of oxidizing or reducing some groups to a definite group and it does not oxidize or reduce other groups to the same chemical entity.

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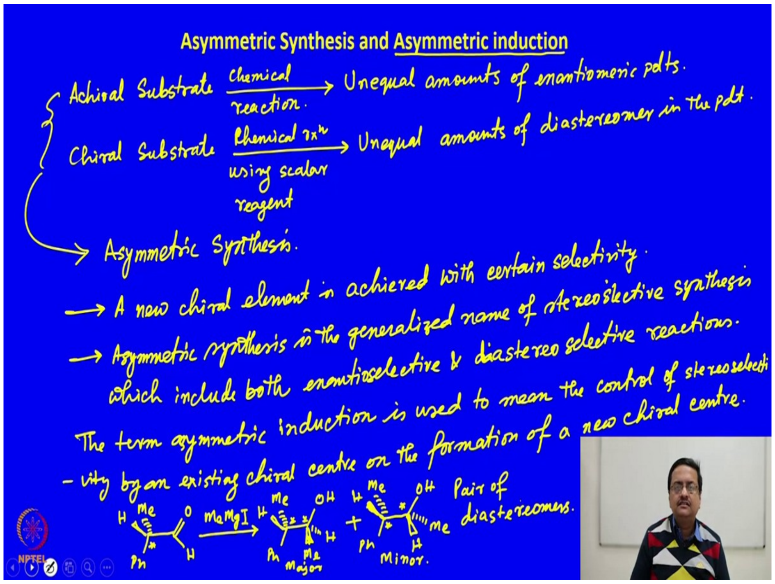

Asymmetric Synthesis and Asymmetric induction

Achiral Substrate $\xrightarrow[\text{reaction.}]{\text{Chemical}}$ Unequal amounts of enantiomeric pdts.

Chiral Substrate $\xrightarrow[\text{using scalar reagent}]{\text{Chemical rxn}}$ Unequal amounts of diastereomer in the pdt.

→ Asymmetric Synthesis.

→ A new chiral element is achieved with certain selectivity.

→ Asymmetric synthesis is the generalized name of stereoselective synthesis which include both enantioselective & diastereo selective reactions.

The term asymmetric induction is used to mean the control of stereoselectivity by an existing chiral centre on the formation of a new chiral centre.

So, when we are talking about this asymmetric synthesis a term always gets associated is called the asymmetric induction. So what it means? It means, suppose if we start with some achiral substrate and we conduct a particular chemical reaction on this and we generate unequal amounts of enantiomeric products or we can start with a chiral substrate and do a chemical reaction using scalar reagent which means using some reagent which is not essentially a chiral substrate.

So still we end up getting unequal amounts of diastereomers in the product. So, this type of reactions in which you generate preferentially one enantiomer in excess or one diastereomine in excess these type of reactions are termed as asymmetric synthesis and you must be knowing that this asymmetric synthesis is very important in organic chemistry to make one particular enantiomer of a given compound which may have a certain biological activity which may have some medicinal activity and the corresponding other isomer may be biologically or medicinally inactive.

So, in these reactions one common thing is that a new chiral element is achieved with certain selectivity and this asymmetric synthesis is the generalized name of stereoselective synthesis which include both enantioselective and diastereoselective reactions. The term asymmetric induction is used to mean the control of stereo selectivity by an existing chiral center on the formation of a new chiral center.

So, if we try to visualize this using some example I would like to cite one example here when this aldehyde with a chiral center here is treated with methyl magnesium iodide we get two products which are these two which has two chiral centers. So, the other isomer is this one which also has two chiral centers it is observed that it generates these two compounds in two different amounts and it is observed that this compound is a major product and this one is minor product.

So, these two compounds are diastereomers and we see here the induction of diastereomeric differentiation or diastereomeric stereo selectivity is taking place. And we need to identify we need to find out how this diastereomeric selectivity can be controlled or can be predicted.

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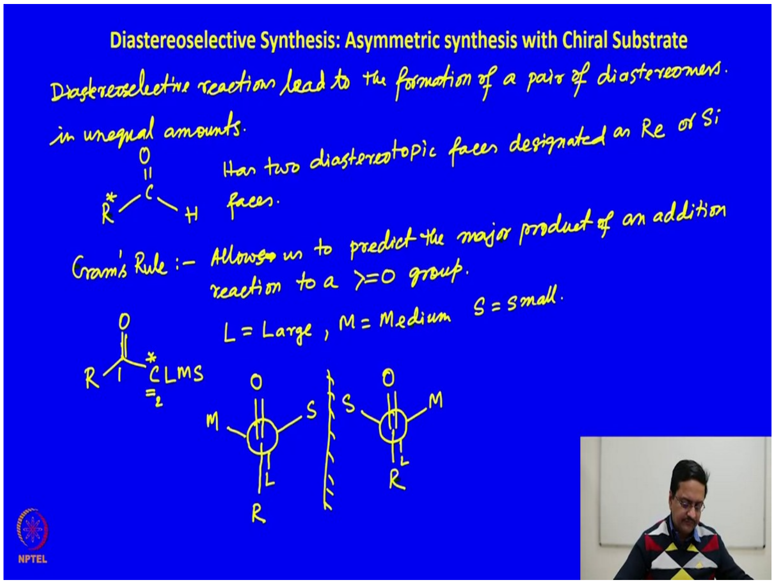

Diastereoselective Synthesis: Asymmetric synthesis with Chiral Substrate

Diastereoselective reaction lead to the formation of a pair of diastereomers in unequal amounts.

Has two diastereotopic faces designated as Re or Si faces.

Cram's Rule :- Allows us to predict the major product of an addition reaction to a >=O group.

L = Large , M = Medium S = Small.

So this diastereoselective reactions lead to the formation of a pair of diastereomers in unequal amounts. So, for this type of unequal amounts of the pair of diastereomers, need to be understood and we need to find out the reason for such differentiation. So, as we have already seen already understood in our previous lecture that if you have a carbonyl compound like this it has two diastereotopic faces designated as Re or Si faces, this diastereoface differentiation is very common in carbonyl addition reaction.

So, to address this issue which diastereomer will be preferred in a given reaction we have Cram's rule which is essentially based on a large number of experimental observations. So, this Cram's rule allows us to predict the major product of an addition reaction to a carbonyl group. So, suppose a carbonyl group is associated with a chiral center which contains three substitutions which makes this center as chiral, the L is a large group, M means a medium group and S means a small group.

So, large medium and small are three different designations of three different types of groups associated with this chiral center. So, then what is done is that the Newman projection of this compound is drawn using the front carbon as the carbonyl carbon and the chiral carbon as the back carbon. So, this C1 C2 bond is used to draw the Newman projection of this molecule. So, if we draw this the Newman projection of this molecule as per Cram's rule we are drawing the carbonyl and the corresponding R.

Now the Cram's rule says that when we draw this Newman projection then the bond between the second back carbon with the large group should be opposite to the carbonyl group that is it should be eclipsed with the other substitution in the aldehyde and the other two groups should be drawn as per its stereochemistry. So, this can be one enantiomer of this particular compound and the other enantiomer of the same compound should look like this.

These two are a pair of enantiomers because these two compounds have only one chiral center. So, as per Cram's rule we first should draw the molecule in this orientation and then allow the reaction to take place.

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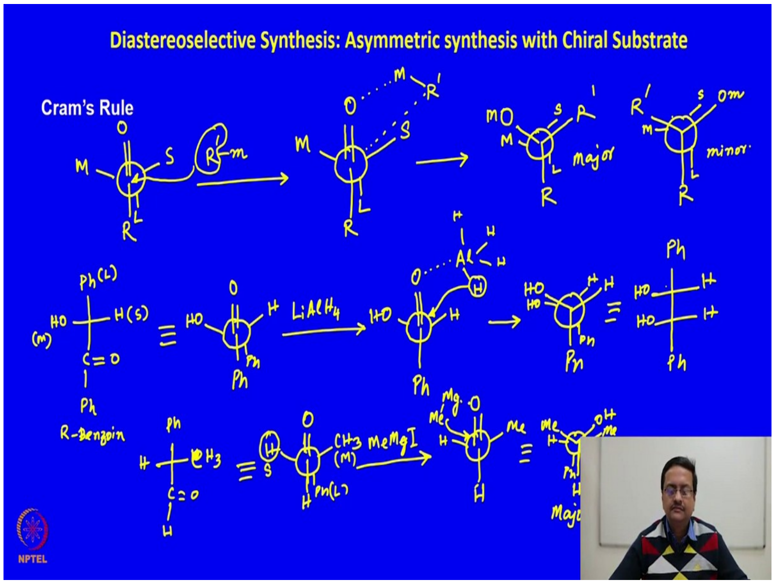

Diastereoselective Synthesis: Asymmetric synthesis with Chiral Substrate

Cram's Rule

So, when we allow the reaction to take place by once again draw the molecule here in its form in which the original proposal of Cram is used. So, when we are trying to do a reaction on this molecule with some R prime m compound this reaction will proceed in such a way that the R group would approach the chiral center from the side of the smaller group and the product that forms through this reaction will be the major product.

So, when you do this reaction the reaction intermediate would look like this and the final product according to Cram's rule the major product will be this one and the minor product should be this one. So, let us try to see this with a couple of real examples. So, here this is called R Benzoin and in this case this phenyl group is the large group OH group is the medium group and hydrogen is the small group. So, when we try to draw the molecule in Newman projection following Cram's recommendation.

We should draw the molecule like this and when we try to do the reaction with lithium aluminium hydride what we would get is a transition state which would be like this and then the major product from this reaction should be this one which is equivalent to the meso compound. So, this is how the major product of this has to be identified. Similarly let us try to see with one more example where you have a chiral center which is containing Ph CH3 H and C double bond O Ph.

Now C double bond OH so, if we draw this molecule in the correct orientation like in Cram's rule it would form, it would look like this and when we try to draw a Grignard reaction methylmagnesium iodide. So, what will happen is this is the smaller group this is the medium group and that is the large group. So, the reaction will proceed in a way where the oxygen will hold magnesium this side and the corresponding methyl will attack the carbon center from the side of the hydrogen and hence we would get a product of the reaction as this one as the major product.

So, using Cram's rule one can easily identify which product will be the major product in case of the reaction to carbonyl double bond and you can identify which diastereomer will be formed. So, from here we will continue in the next class, thank you.