Course on Stereochemistry
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Module No 03
Lecture 12: Relative Configuration Prochiral Faces and Prochiral Centres

Okay welcome back, and the last time, we had discussed the RS configuration nomenclature system for Allene and biphenyl type of molecules which are actually chiral molecules and also the EZ nomenclature for double bond and then the concept of pseudo-asymmetry. Let us go back and again they inspect the question of relative configuration. There are different nomenclature system. Yesterday, I was telling about Threo Erythreo system and then like and unlike system okay? Now this actually create a, this relative configuration, has created a lot of confusion in the literature. As you will see as I describe in the next half an hour that is where was the confusion?

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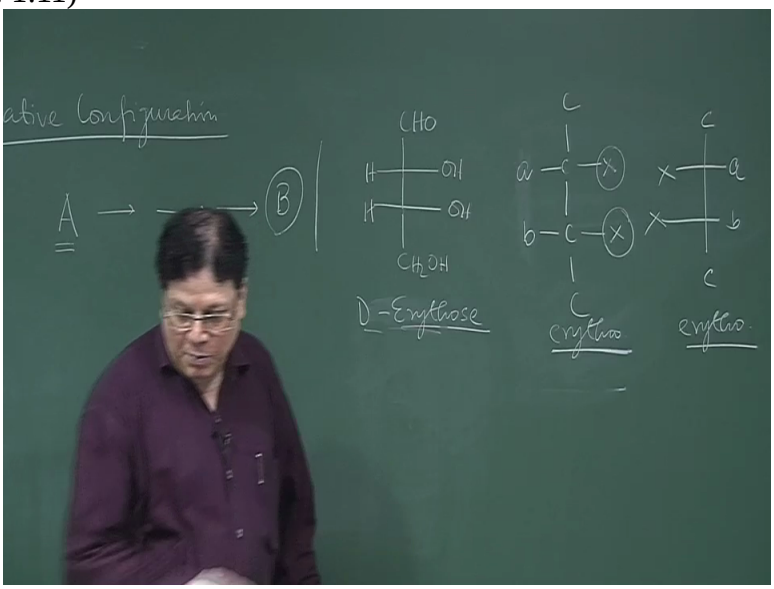

1st of all, this molecule is what is known as an Erythreo molecule okay? Because what is the it it originated from the carbohydrate Erythreos. In Erythreos what happens? The OHes are on the same side. By the way, this is the classical D Erythreos, similarly there will be an L Erythreos where the 2 OHes will be on the left side okay? However, an Erythreo compound of this type where 2 similar groups are present on the asymmetric carbon, the other groups may be same, may not be same.

So the this nomenclature system is applicable for a system where there are 2 similar groups, at least you need 2 similar hetero atoms of these 2 stereogenic centres okay? The other groups may be different okay? And then, this is Erythreo but you have can have another Erythreo compound where the 2 axis are on the left side okay? This is the another Erythreo. In many of the reactions, when we do the reactions in organic chemistry lab, we generate stereogenic centres while we do the reaction.

And sometimes mainly stereogenic centres are created. And in many cases, absolute configuration is difficult to determine because you need x-ray crystallography but the relative configuration, you can determine by NMR spectroscopy and other spectroscopy it means. So most of the time, we land up with describing what we got in terms of Erythreo or Threo okay? That is why relative configuration is is so important concept in stereochemistry because most of the time, we determine the relative configuration and not the absolute configuration.

But nowadays, x-ray crystallography has become much more, has more power now, crystal solvent has becoming more easy, more routine. So absolute configuration can be determined for molecules but in many cases in organic reactions, we have to describe the stereochemistry of the reactions in terms of relative configuration. That is why, I am spending more time on these. Now this is the Erythreo, this is also Erythreo so if I I am asked to write the Erythreos molecule of this formula, then I have to write 2 molecules okay?

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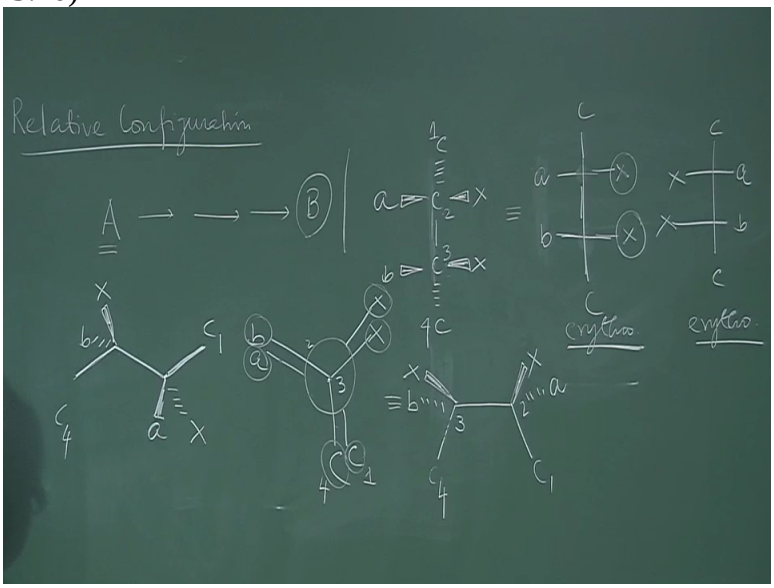

And the what is the Threo? you know what is the Threo. Threo is when the 2 axis are on the opposite sides okay? And because it is a Fisher projection formula, actually it is not wise to show then customary is that you do not show the carbon is okay? So the carbons are not shown on the axis, these 2, the stereogenic scentre carbons are not shown. So this these are the 2 Erythreo forms okay? So now you have also been introduced to the different, other different projection formula okay?

What are the other different projection formula? One is new man projection formula. Now if you convert this into the new man projection, what happens? Better see for as you are a beginner, so better you do the OH formula, convert it into the OH formula 1st. So this is X, this is X and this is B and this is B Jack sorry this is A and this is the alpha carbon and this is the alpha carbon okay? That is the OH formula.

You also number it. Suppose this is your number 1 carbon, this is 2, this is 3, and this is 4. Now how do you convert it into the new man? We look along the C2C3 axis or C3C2 vice versa. Either you look from this side or from this side. Now if you look from this side, that is a little bit easier to visualize because the molecules are usually held at the top of the board. So it is easy to look from the backside.

If you look from the backside, the way to write thewrite the new man projection formula of this is that 1st of all, you know that the front carbon is shown by a dot and the back carbon is by this circle as if the front carbon is blanking the back carbon and the substituents are shown in 3 lines okay, 120 degree angle with each other. So when you look at this from this side, this carbon definitely you can visualise and realise that this carbon is at the back.

And this X will now be on this side and this B on this side okay? And what will be the C1 carbon? So C1 carbon is also is in the same side of this C4. So this is the C4 carbon. So C1 carbon is actually eclipsed by the C4 carbon and the X at C3, this is the C3 carbon, this is the 2 carbon, the back carbon and this is the number 1 carbon. So the other X is here and this is the, now the A.

So this is the correct new man projection formula of this feature, starting from this Fisher, Erythreo molecule okay? Now the problem is that this is a molecule where all the bonds are

eclipsed in are in the eclipsed form. Today, later on we will do the confirmation of a sigh click system when we will discuss we will see what is the stability of this. Obviously, it is not very stable because there will be repulsion between the, stErythreo repulsion between these groups which are eclipsing each other and also there is what is called bond opposition strain.

Because the bonds are made up of electrons so they repel each other. So this will be, actually this will have the highest energy, highest energy. So in order to Jack so there is a criticism of Fisher projection formula that the molecule actually does not exist in this form. It because that is the form which is the fully eclipsed form as we see here.

So you better you have to convert it into the form where which is the more table form and that is why, what happens that there is another rule that came which says that write the molecule in a zigzag fashion where the carbon carbon bonds, these carbon carbon bonds, that means, the C2C1 and C3C4 are anti to each other because that will be the stable form okay? And then you have 2 groups, the other 2 groups okay?

Other 2 groups which will be if you Jack better 1st you convert it into directly into the kind of OH formula. So if you directly convert it into the OH formula, what happens? It will look like this. This is the C1 and this is the C4. I am actually turning it on this side little bit. So now this X will be beta, will be towards me and we talk about the say the back carbon, C2, so this X will be towards me and Jack the A so we are not talking about hydrogen, here we are talking about this is 1, that is 2, so let us talk complete the 1.

1 has this X, so as I turn it from this side, so X comes in front and B X is attached to A, so A goes to the backside and the same thing happens here also. X in the front, and now it is instead of B, you have A. So this is the 3 carbon. So that is the OH formula of this, the OH formula of this. Now if you want to make it in a zigzag fashion, that means your C4 remains here okay on this side. So you turn the C1 to the top to make it zigzag.

And if you do that, C1 goes to the top and here, everything remains the same. So X is beta and your this is the alpha but here as we put a 180 degree rotation, so X will become alpha and A will become beta because it is a 180 degree operation. So C1 goes to that side, X will become alpha,

A becomes beta okay? So this will be the situation. Now this is a more preferred form of this molecule because this is more stable.

Now you are not eclipsing X, you are not eclipsing B or A, you are not eclipsing more important, the C1 and C4. So another nomenclature system which says that forget about the Fisher projection because it is in the eclipsed form, so you better write the molecule in the zigzag fashion , the carbon chain in the zigzag fashion. And then you look at the atoms which are similar, which are the heteroatoms.

That is X and X. If these two Xes on the same side, in this case it is not, this is beta, this is the alpha. If they are on the same side, that is called Erythreo like this. And if they are on the opposite side, that is called Threo okay?

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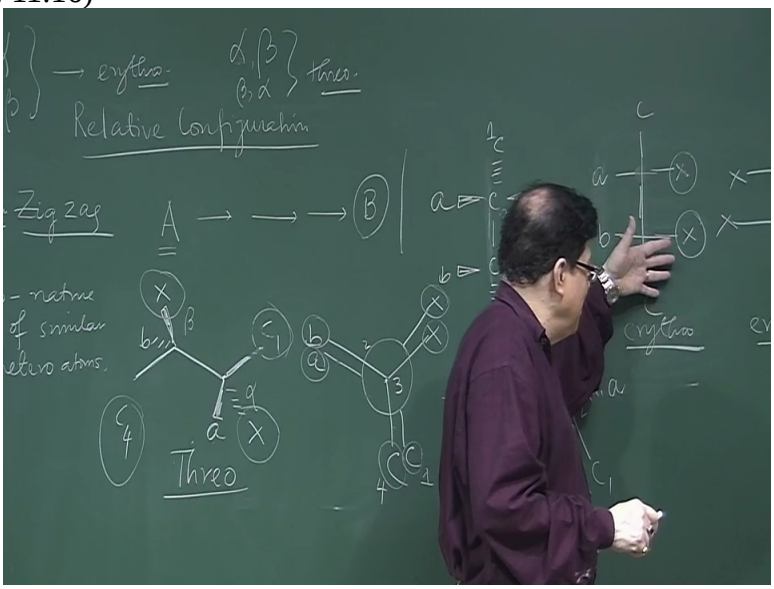

So based on that, that write that in the zigzag, this is the carbon chain, the C chain in the zigzag and then you look at the alpha beta nature of the heteroatoms of similar heteroatoms. If both are alpha or both are beta, if both are alpha or both beta then that will be called Erythreo or if both are, one is alpha, one is beta or vice versa then that is called Threo. Okay? Now you see, this will be according to this definition, this X is beta and this X is alpha. So this will be according to this definition, this should be Threo okay? Now you see, we started with the Erythreo form in the hair projection, so if you follow the Fisher projection formula rule then this molecule, the molecule

which is Erythreo, that becomes Threo in the zigzag rule which was by the way proposed by a scientist whose name was Heathcock.

Heathcock, he proposed this system, this Threo Erythreo nomenclature and base on the zigzag confirmation, that means the actual, that is the confirmation which the molecule mostly resides. However, that creates a lot of problem because what is Erythreo in the Fisher projection, that becomes Threo in the zigzag confirmation and vice versa what will be you can practice, what is Threo in the Fisher projection, that becomes Erythreo in the zigzag confirmation.

So seeing all these confusions, there was another scientist who is at MIT, USA, his name was Mussaimune. So Mussaimune said that let us forget about Threo Erythreo system, let us have a unified name which does not complicate the scenario of further. So do not call this alpha alpha beta beta Erythreo. He says that better call these as syn and when it is alpha beta or beta alpha, you call it as anti okay? So according to Mussaimune that you still follow what Heathcock said that write it in the zigzag form.

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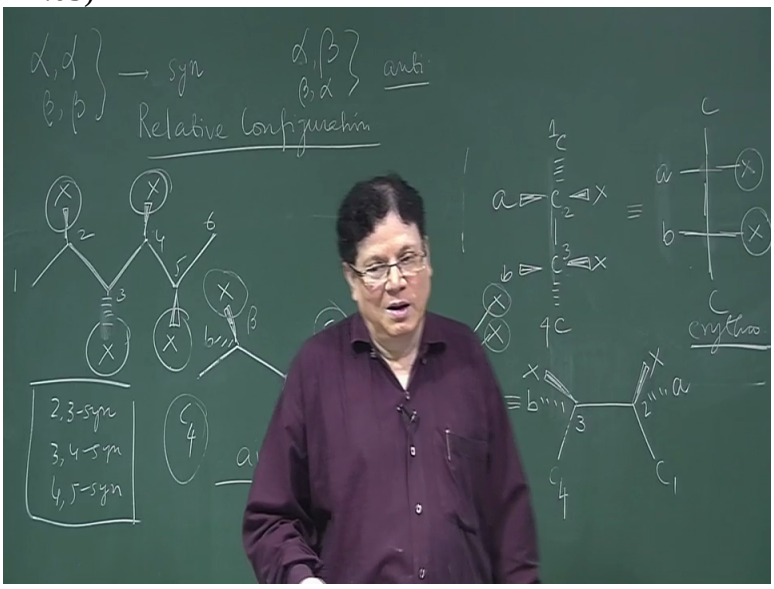

And now if you see that the similar hetero atoms have beta alpha configuration or alpha beta configuration, then you call that as anti. Okay? And if both are beta, then you call that as syn are both are alpha, you call that as syn. So that is the present-day nomenclature for the relative configuration in case of Jack molecules with a multi-stereogenic Centre. You can actually this

was extended later for even compounds which are having more than 1 more than 2 asymmetry centres.

Suppose you have a molecule like this. You write the carbon chain in the zigzag fashion and see what is the alpha beta status of this axis okay? Suppose this is the number 1 carbon, 2, 3, 4, 5, 6. So this molecule will be called syn, 23 syn and then 34 syn and also 34 and 45 syn. So to describe this molecule, you can say that this is 23 this is just say syn syn syn. Okay? That will of course take care but it is better to mention the the carbons that you are considering okay?

If you change the mid suppose the middle carbon I change now, this I will make alpha so then what will happen? C2 C3 anti and then C3 C4 anti and C4 C5 syn okay? So that is the modern day nomenclature. So Threo Erythreo is a very dangerous thing not to consider because that as I said, that becomes exactly opposite. What is Threo in this Fisher position formula, becomes Erythreo in the zigzag formula okay? So now our modern-day practice is to use the syn and anti relative confirmation nomenclature for these type of molecules okay?

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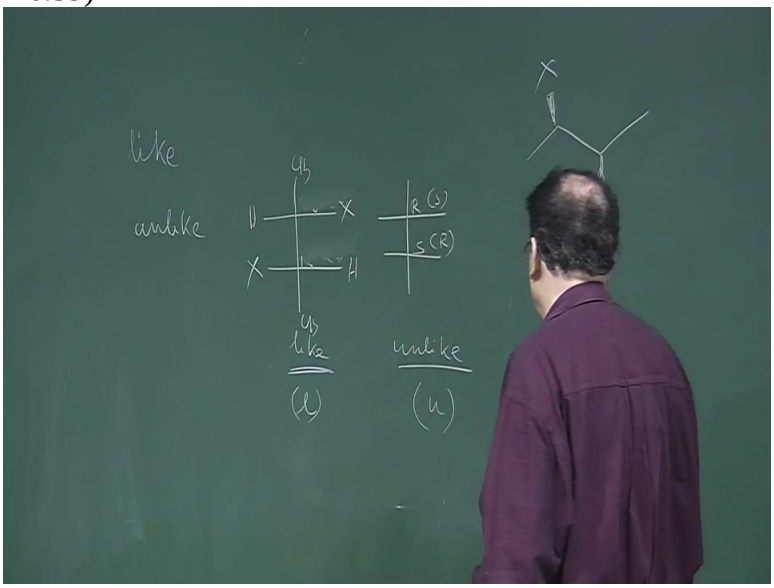

Yesterday, I was telling about like and unlike and like and unlike arrows little confused at the time that what is the, how do you say like, abbreviate like and unlike? What was again I repeat, what was like and unlike? That if you have 2 centres, you determine the configuration at each

centre, suppose this is R and this is R, so that is a like system or suppose this is X and this is S, that is also a like system. And for unlike system, this is R, this is S or this is S and this R. Okay?

This was was proposed by Sevak at the University of ETH, a famous university in Switzerland. He proposed this. So this is your like and this is your unlike but as I said, you want to abbreviate this. Then I looked at the books. I thought that maybe this is LK but then I found in Roche Pure's book that this is written as L and this is written as U okay? So that is the abbreviated.

So just to dispel the confusion which we landed in last time that what is the universal practice of writing this like and unlike confirmation. Remember, this is applicable for all systems. There is no confusion at all. Only problem is, by looking at the molecule, you cannot see the Threo, Erythreo, you can by looking at the molecule you can immediately tell whether it is syn or anti, immediately.

But assigning relative configuration for this molecule, you cannot really immediately say that whether it is like or unlike. Why? Because you have to do the configurational assignment, R and S. Then you can tell whether it is like or unlike. So it is lot of work. So that is why, Sevak Systems was criticised that like unlike although it is not so much problem, that was there earlier Threo Erythreo but it has the criticism that you have to do this R and S in order to assign the relative configuration.

So that is a kind of little extra work. In this case, the advantage is, by seeing it, you can immediately tell that what is the relative confirmation, relative configuration in the molecule okay? So so far we have discussed the last 2-3 lectures, we have discussed 1st the chiral environment, how to assign nomenclature for the chiral environment around a stereogenic Centre. Then we went, how to assign the the the configurational nomenclature for molecules without any stereogenic Centre which has got which are axially chiral okay?

And then Jack also we we we try to determine what is this relationship between the ligands. See so far, we concentrated on the carbon. So there are 2 ways of looking at stereochemistry. Look at the carbon which is the main cause for giving the chirality. That is one approach, the other is what happens to the groups? Do not forget the the surrounding groups, okay. Usually stereochemistry started concentrating all on this carbon but then people started thinking of the

groups attached to the, what is relationship between the group, not the switch between the carbons.

Like in relative configuration, what is the relationship between the conservation of this carbon vs the other carbon? We are not seeing, we are not looking at the inter relationship between the ligands but yesterday we we have shown that the interrelationship between the ligands are what are called topicity, the geometric relationship between the ligands in a chiral environment is what is called a what is called topicity.

And we have identified different types of topicity. Homo topic which are connected by C2 symmetry and then heterotopic, heterotopic has 2 types, one is Enantiotopic, another is diastereotopic. And this heterotopic we are talking about stereo heterotopicity, not constitutional heterotopicity yes? Stereo heterotopicity we have discussed and then we have identified they are Enantiotopic ligands and then diastereotopic ligands.

Enantiotopic against were the were connected by the by either I or Sigma or S and diastereotopic ligands because the molecule is chiral, entirely you started with a chiral centre somewhere, so the molecule does not have any of these any of these symmetry elements, improper proper okay? So that is the relationship between the groups. There is a 3rd now scenario where you have the chiral molecule and then what happens to the space surrounding the chiral molecule Sharma

What is the relationship between the the faces of a molecule? Suppose you have a, suppose I have this double bond compound okay? Suppose this is an aldehyde, this is suppose a hydrogen, this is another group and this is an oxygen. Now, if I place it in the horizontal, then it actually it is dividing this entire space into 2, one is above this, above this plane, this is a planar molecule and the other is below the plane.

So there is, there are faces, there are 2 faces and these 2 faces may be same, may not be the same in stereochemical sense. How to know that? So if I add something now onto this carbon, because carbon is susceptible to nucleophilic attack. So the nucleophile can come from the top or come from the bottom. The question is, will it lead to the same compound or not? So that means, if if they lead different compounds, that means, to faces, these 2space on the top and the bottom are different okay?

Or if they lead to the same compound, that means these 2 faces are same. There is no difference. So that is another one. So we have done the relationship between the carbons, the relationship between the ligands, that is the topicity and now what we are, we will discuss, the relationship between the on the on the between the spaces that the molecule is divided. The three-dimensional space that is being divided into 2. Now what happens?

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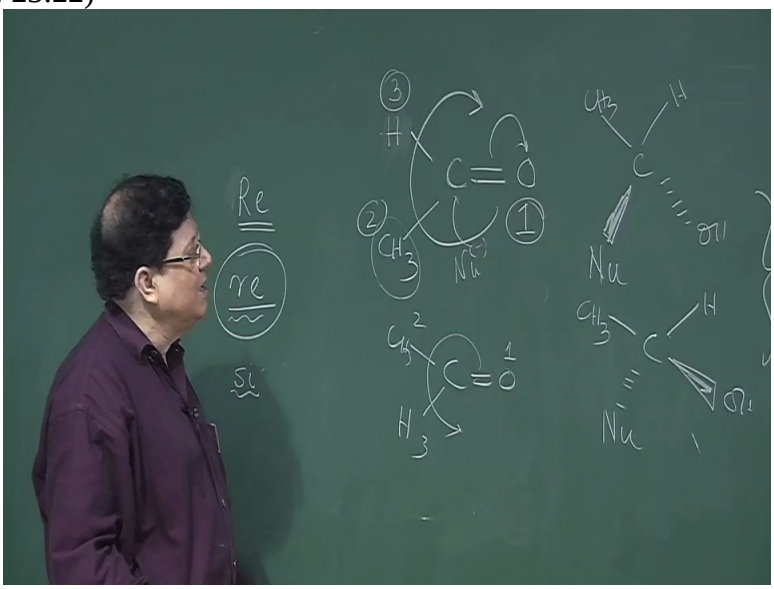

Suppose I take again back to this example, say hydrogen and methyl. Now this is a planar molecule, this is in the plane of the of the board. Now so this is dividing, this space, three-dimensional space into into 2 halves basically. One is towards this side, another is the space we cannot see because this is a room, behind the this this board, that is the other space okay? Now if you add, because these 2 groups are different, if you add a nucleophile from the top, so what you will get? The nucleophile will definitely will take up the a beta position.

Because it is coming from this side, it is above the plane of the board and what goes, so this will be the Jack as it comes from the side, so the OH will go down, so OH that this double bond breaks, the nucleophile comes from the top, the double bond breaks and becomes OH. So that and these 2 remain the same, the hydrogen and the methyl. So this is one compound that you will get if it comes from the top face, the pace on this side.

If it comes from the bottom face, you get exactly the opposite compound, enantiomer of this okay? So these are Enantiomers so now because addition leads to a set of enantiomers, addition from one side leads to one enantiomer, addition from the other side leads to the other enantiomer, so these faces are 1st of all these faces are now no longer similar and they now have a you have to assign a name to this because like we have to we will also go for ligands also + just like we have assigned absolute configuration of this carbon which are having attached to 4 different groups, similarly this space has to be given a name.

Suppose I have some restrictions that this is a wall, the reagent cannot come from the bottom side. The nucleophile has to come from this site. Then I will only get this compound and not that compound. Okay? So there must be a descriptor for the cases that we have. We cannot just say top face and bottom face because the same compound can be obtained if I write it in a different way, the methyl at the top and the hydrogen at the bottom.

Now to get to this compound, the nucleophile has to come from the backside because it is written just in a reverse fashion. So the backside now becomes identical to the front side if you write it in this fashion okay? So we need to describe the the topicity of the face, the two relate, the relationship between the the faces okay? So again there is a a nomenclature system very simple, this is a remember another point, that if this is no longer a hydrogen, suppose this is a methyl, then addition of the nucleophile does not create any asymmetric centre.

Okay? So then the question of the 2 faces are same. Because it does not matter whether nucleophile comes from top or bottom, at leads to the same molecule. So there is no question of topicity of the face okay? It is there once these 2 groups are different, that is the thing. Now how to assign the the descriptor for the 2 faces? This is done by again giving priority. Now we have 3 ligands to this carbon.

So giving priority according to the atomic number, so this is number 1, this is number 2 and this is number 3. So 1, 2 and 3. So you see what is the direction for going 1 to 2 to 3. So this is now clockwise. So the space, that is when I see from this space, this looks clockwise, so this space will be called a Re face. Some books write it capital and a small. Both both are okay but I prefer the the small one, the re face. Remember? This is actually, again it should be written in italics because these are again coming from Latin word.

Okay? So this is now becomes the red Jack Jack the re face and if I say what is the face which is behind this board? If you look from that side, the direction I I told you that if a fan is rotating in a clockwise direction, if I see from bottom side, it is clockwise, then from the other side, it will be anticlockwise. So because I cannot go into the backside and see the molecule because there is a wall now which is preventing me to do that.

So I will if I look from the backside, the same direction will now be anticlockwise. That means, the other face is what is called a Si face. So now the face, faces are also have these descriptors, the re face and the si face. So if there is a reaction and if I tell that the nucleophile is adding from the re face, so you can immediately figure out that what is the re face and you can draw the geometry of the product.

Interestingly, as I said that when you write these 2 systems, these methyl and hydrogen, if you write in the opposite way, so now what will happen? This is 1 this is 2, this is 3, not the site becomes the si face and the backside becomes the re face. And I told you that if you ride this way, if the nucleophile comes from here, it gives this product. It is the same product from this confirmation, from this form is the nucleophile comes from the back but that means you are, you might be confused that back and front.

As I said, back and front does not have any meaning, we have to assign the re and si descriptors for the faces. So if I write it in this fashion, this site is the re face, backside is the si face. If I write this molecule in this fashion, known the backside will be the the backside will be the re face, and the front side will be the si face okay? So from now on, the faces should not be front or back. If you want to give stereochemical descriptors, you have to say re and si okay?

That will be very important when we discuss reactions, the reactions involving stereochemistry, chemical assignments that you generate a new chiral centre. Now by the way, this carbon is called a it is a pro chiral centre because this is not a chiral centre but as soon as you do one transformation, you converted into a chiral centre. So if by one transformation, you can convert a carbon into a chiral centre, that carbon will be called a pro chiral centre.

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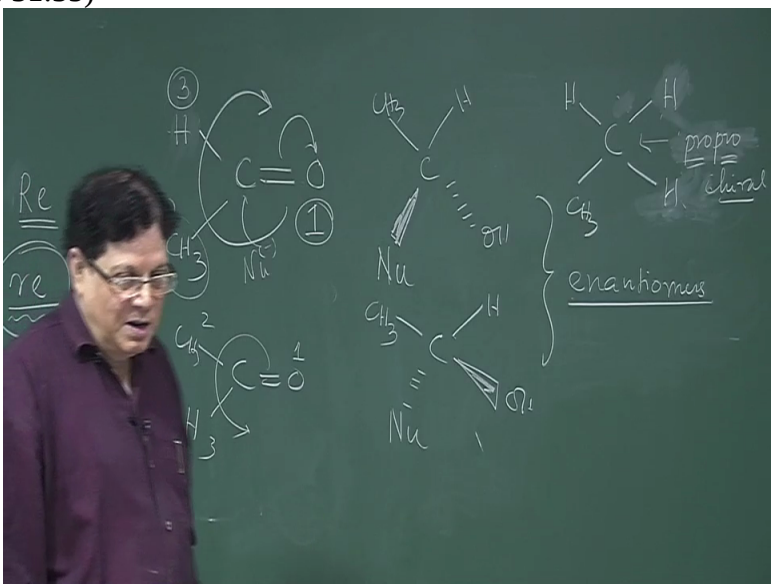

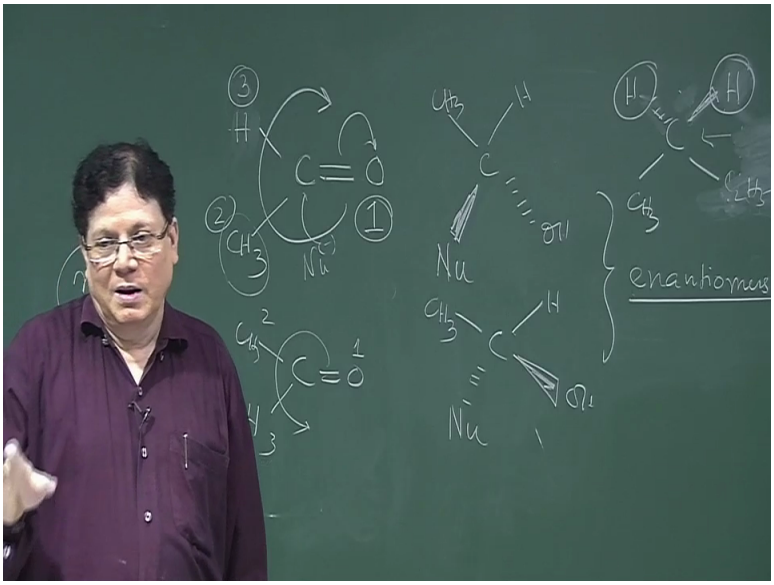

Now this is not only restricted to a carbonil, it is restricted it is also it is applied to systems like this. Yesterday, we have seen this molecule. These 2 hydrogens are Enantiotopic okay? So here also, this carbon is a pro chiral centre. This is not chiral because all the 4 groups are not same. These 2 hydrogens are same. But if you replace, if you by one transformation you can replace it by X, it immediately convert into a chiral centre.

So this is called so that will be a pro chiral centre okay? So by one transformation if you can convert a centre into a chiral centre, then the Central will be called a pro chiral centre. And so

then what will be the centre were there are 2 transformations needed to make it chiral? Like if you have this compound, CH 3 CH 3 and if I ask you what is this carbon, see by one transformation, you cannot get a chiral centre.

You have to make two transformations. This hydrogen has to be replaced by X and this hydrogen has to be replaced by Y. Then only you can get a chiral centre. So so there are 2 transformations needed. So this will be so when you have this all hydrogens, this is called pro prochiral centre from there are 2 pros because you need to transformations to convert into a chiral centre okay?

So we have seen that there will be that faces how to how to give stereochemical descriptors to the faces which are basically attached to the 2 sides of a pro chiral centre and the re and the si 1st, si face have been introduced. Indie, you can also assign because it is a when there are 2 groups, C2H5 and CH 3, when this carbon is okay, when this carbon is a pro chiral centre, these 2 hydrogens are Enantiotopic and you can again assign stereochemical descriptor to this hydrogen okay? That we will do in the next lecture. Thank you.