Course on Stereochemistry
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Module No 02
Lecture 08: Absolute Configuration (Contd.)

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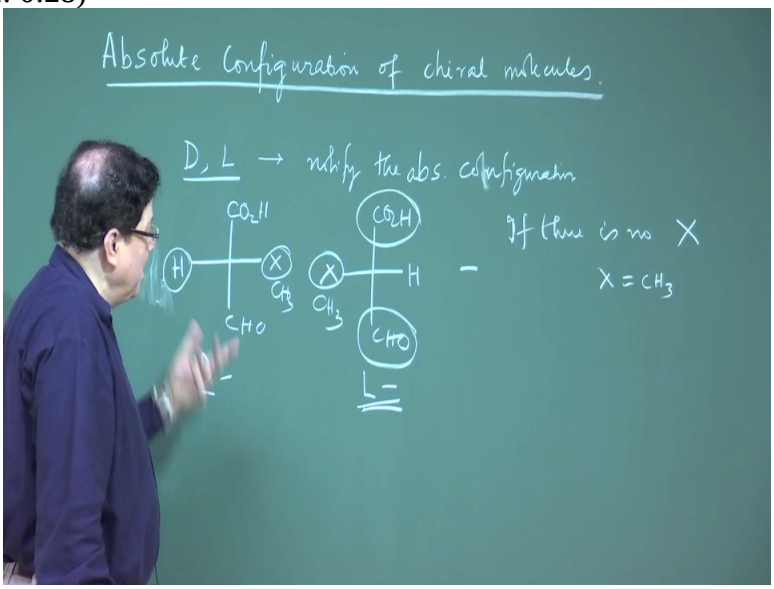

Okay last time we have discussed the absolute configuration of chiral molecules and we have introduced to you the 1st system that was introduced earlier and that was called the D and L, capital D and capital L system. This is a system to notify the absolute configuration. I again reminded what is absolute configuration. It is the absolute arrangement of the groups in the three-dimensional space okay?

So DL was the starting point. It was based on the carbohydrates, configuration of carbohydrates which Professor Emile Fisher started okay? He assumed that the + glucose had the D configuration. That means the lowest possible chiral centre, the hydroxy group is at the OH at the right. And the that was he assumed to be D + glucose and it started then onwards. Now the problem with this configuration.

I just repeat what is this configuration that if you have a chiral molecule and if you write it in the Fisher projection formula, that means the two-dimensional formula and you should write it in the proper way so that the carbon, there are 2 carbons suppose. So the one, the top one should be at

the highest oxidation level. Suppose it is between CO2H and CHO, so the CO2H is a higher oxidation level than CHO. The CO2H at the top.

Now if you have a heteroatom on the right and a hydrogen on the left, we call this as the D isomer, capital D. And the opposite one where X is on the left and CO2H on the right, CHO at the bottom then that will be called L. Remember, this is very important, the positioning of the of the carbon in the vertical axis, that actually decides whether your X will be on the right or on the left. Now the this system could not be applicable in case of where there is many cases.

1st if there is no heteroatom, then what are you going to do? If there is no X that means the heteroatom, then this will fall apart. If X is suppose methyl then this will be replaced by a methyl that cannot be regarded as the heteroatom. So sorry not this one, this X should be replaced by methyl but it is still chiral but you cannot have a DL nomenclature system for this okay? So it fails when X is an alkyl group, X is a different, I gave a nice example.

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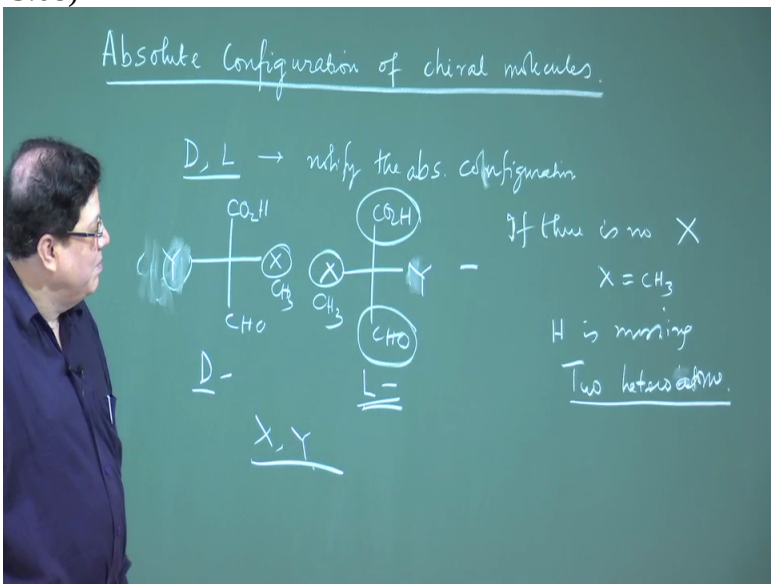

The most important thing is X is not containing a heteroatom and the other is that if there is no hydrogen, if hydrogen is missing, and if you have if you have that is replaced by 2 heteroatoms, 2 heteroatoms, hydrogen is replaced by a heteroatom and X is already there. So then there is a situation that you have 2 heteroatoms, maybe different, Y and Y here. So both X and Y are

heteroatoms. Then also, the problem is, which one is now the which one I should get a preference so that I can consider right or left.

So in these cases, it fails. That means, it is not a general, absolute configuration. So there must be something, some better way of looking at these molecules and name them accordingly. Okay? So the next one was developed by the developed and was accepted by the International union of pure and applied chemistry. You know the IUPAC is the our organisation which provides all the rules how to name a compound and then how to name is Stereochemical compound.

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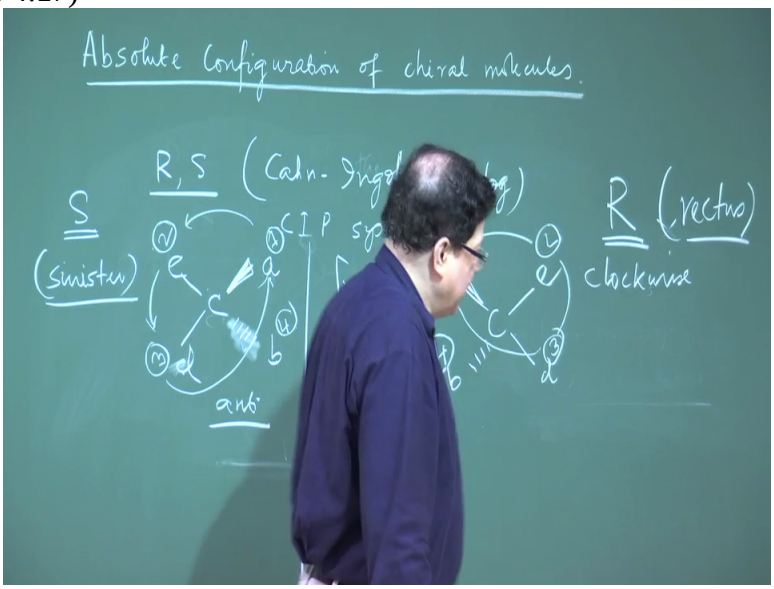

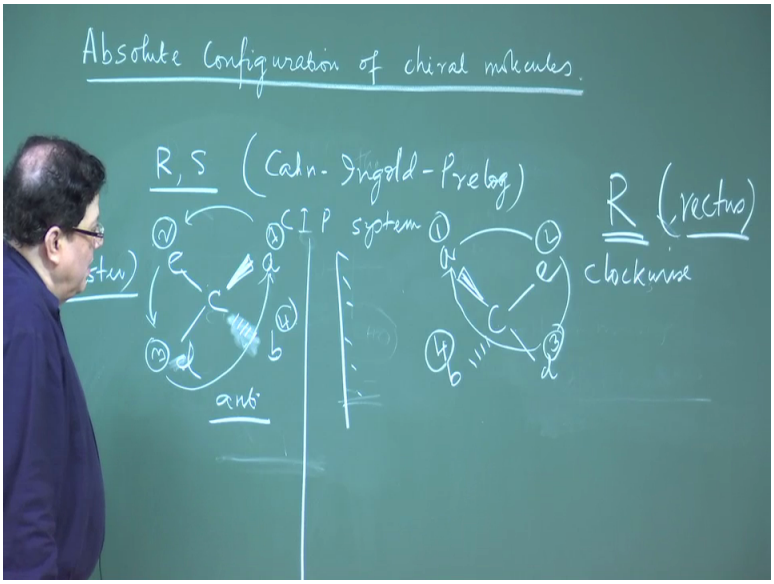

So they accepted and they proposed whatever was the proposal by 3 scientists, very famous scientists, one is Cahn, another is Ingold and that 3rd one is Prelog and sometimes this is called Cahn Ingold, CIP system. CIP system is nothing but Cahn Ingold Prelog system. So whatever they proposed, IUPAC have accepted and it is a very general way of giving absolute configuration to a molecule. Now what you do in the in this CIP system?

Suppose you have the carbon, now I am writing it in the tetrahedral fashion, you know that in the tetrahedral fashion, 2 bonds, all 4 bonds cannot be in the same plane. So if one bond is up, then one bond has to be down and the these 2 bonds can be in plain. So 3 bonds cannot be in a plane in it a Tetrahedron. There are there can be 3 bonds which are up, there can be 3 bonds which are down. One bond can be in the plane, but number, 3 bonds can never be in a plane in a tetrahedron okay? Now this is a carbon which is a tetrahedron and suppose this has got 4 ligands, A, B, and in order to avoid carbon, I put D and E.

So if this is the scenario, D, B, E, D then what this IUPAC system, this RS system tells is that you assign a what is called a priority sequence of the groups, of the ligands, priority sequence okay? And also there must be a way to give priority to these atoms. So the rules actually are two basically. 1st of all, after giving the priority sequence, how you should look at this molecule and and then should see what are the sequence of priority when you grow form 1 to 2 to 3.

Okay let me clarify it a little better. Suppose by priority sequence rule, I will come to the priority sequence rule later. Suppose that this becomes number 1 carbon and this becomes number 2 carbon, this becomes number 3 carbon and this becomes number 4 carbon okay? So this is 1, that is 2, that is 3 and that is 4. So now the rule says that you should view this molecule in such a way that the number 4 carbon is away from you, away from the observer.

So here, the number 4 carbon is actually behind the plane of this board. So it is not difficult, the face that we are having here, so we are actually in the front of the board and this group, the B group which is having the 4th priority so the least priority that is at the back. So whatever I see from here, that is correct, that is according to the rule. The rule says you look at the carbon away from the 4th group.

So I am looking at the carbon away from the 4th group and then you see what is the sequence order if you go from 1 to 2 to 3. What is the direction order? What is the direction? That if you go starting from 1 to 2 to 3, what is this order? Is it clockwise or this is anticlockwise? So in this case you can see that a 1, 2 and 3 are arranged in an anticlockwise direction okay?

So in in other systems like if I draw the mirror of the suppose, I draw the mirror image of the same molecule. So A will be now here, D will be now here, A will be here,, B will be there. Still alpha, this is a lateral image I am taking. And then D is here and E is here okay? So these are the 2 systems that I get. Now the priority sequence remain the same. So 1 is here, then E was 2, 3 is D and this is 4.

Now if you look at this molecule at the system at the carbon, stereogenic carbon, again the is is you are following the CIP norms, that is we are observing the carbon away from the 4th group because the 4th group is now behind the plane of the board. Now you see what is the direction between if you go from 1 to 2 to 3 and back to 1. So now you see, this is clockwise. This is clockwise. So this is what is called now if this 1 to 2 to 3 direction is clockwise, then you view a molecule away from the 4th group, then that will be called R molecule if it is clockwise.

That actually has come from the Greek word, rectus means right. And anti, when this 1 to 2 to 3 direction is anti when jobs of the molecule, when you observe the carbon specifically away from the 4th ligand, the ligand of the least priority and if the direction is anticlockwise, then that will be called as compound and that is called sinister. Sinister is means left in in Latin. Okay? These are Latin words, rectus and sinister.

Okay? So you know the at least you know what to do in a if you have a three-dimensional molecule you have to assign priority sequence and then observed it from a direction. So there are 2 things, assignment of priority, that is one important issue and the 2nd issue is the the direction of view, which direction you should from which direction you should see the stereogenic carbon okay? So we have to now go to the sequence rules. How do we know that whether A is one, whether B is 2 or B is 4, how do we know that, so what are the rules?

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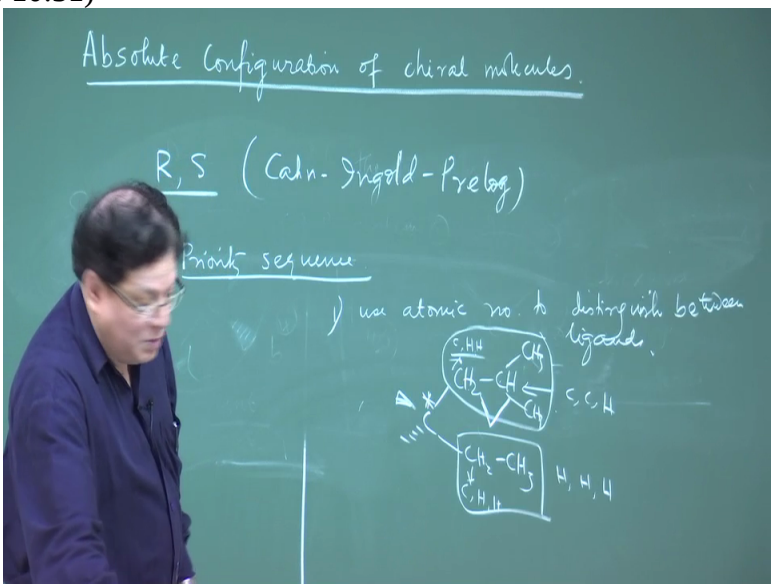

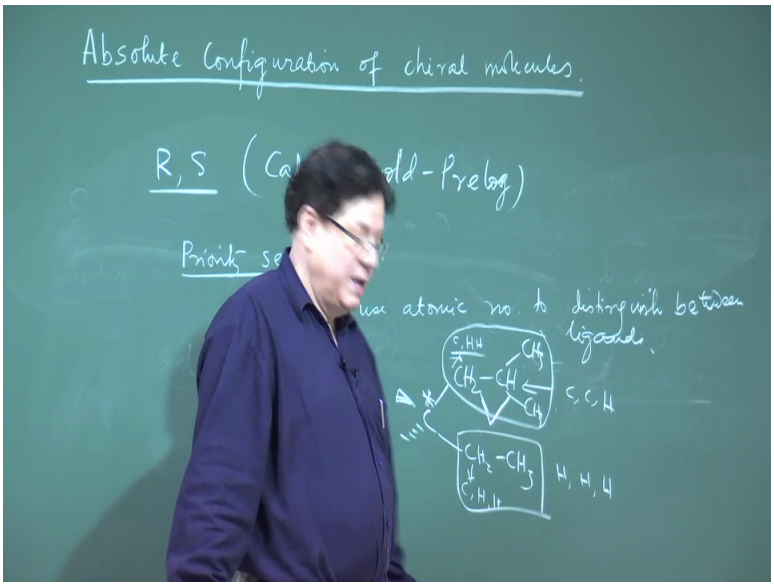

The rules say that you your priority sequence, to assign priority sequence, you 1st check, use atomic number to distinguish between the ligands okay? So what does it mean? It means, if a carbon has a fluorine and a chlorine, then fluorine chlorine has a ironic number, so. chlorine will get better preference than fluorine okay? Now the things we become more complicated later on I will tell you because the 1st atom that is attached to the stereogenic Centre, maybe the same but the 2nd atom may be different.

That means, suppose this is CH 2, then CH CH 3 and CH 3 and you have CH 2 and then CH 3. So if I if you are asked to distinguish between these 2, then what you do? You check the 1st carbon, 1st ligand which is attached to this stereogenic Centre and you you see what are the other ligands that are attached. So what are the other ligands? One is carbon, another are 2 hydrogens. So this is this scenario of this carbon. Okay?

Here is also one carbon attached, hydrogen attached, another hydrogen attached for this carbon. So there is no difference. So the now Cahn Ingold Prelog says that you continue proceeding towards the outerwards, towards the chain, outerwards away from the stereogenic Centre and then away from the stereogenic Centre and then see where is the difference. Once you find a difference, you stop there and and then assign the priority.

So 1st carbon did not do any showed no difference. What about the 2nd carbon? Here, this is a carbon which is attached to 2 carbons and 1 hydrogen. And this is a carbon which is attached to 3 hydrogens. So obviously, carbon being a higher atomic number atom, so this one gets ultimately, so this group wins over this one. So this will be then have we are not, we are discovering these groups, that means this will get high rate of preference over this. This will be greater than this okay?

So if it is 1, then that is 2. Now this type of work you have to continue in many cases. In many cases, you have to continue this going away from the stereogenic Centre to find the difference okay? Once you find the difference, then you stop and then assign the priority. Okay? So what we use? We use the atomic number as the criteria to do the discrimination. Once you are finished with the atomic number criteria and that is clearly does not give any difference, so it appears that the ligands may be same. But we are dealing with a chiral carbon.

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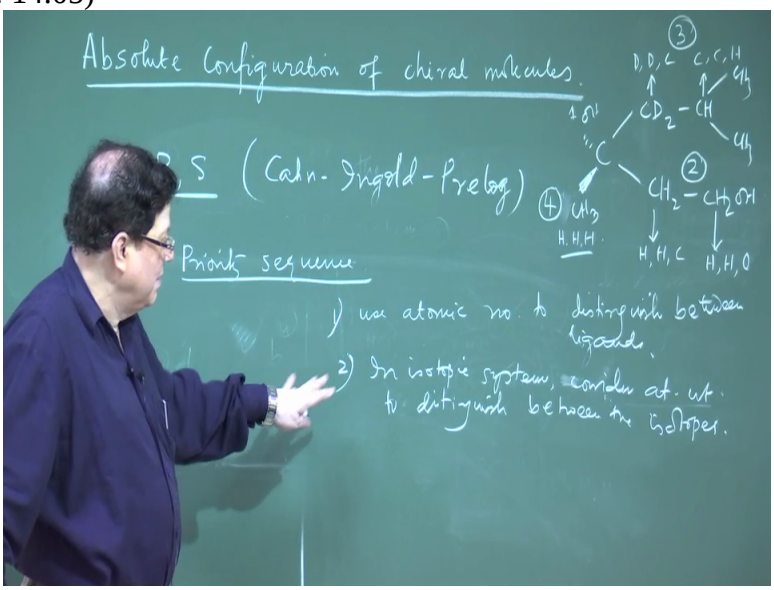

That will help in in case of in isotopic systems, consider atomic weight to distinguish between the isotopes okay? So to distinguish between the isotopes what the rule now the important thing here is the number 1 rule has to be used 1st and then followed by the number 2 rule. Number 2 rule is the atomic weight you use. Here, you use the atomic number. Now I will give you an example to stress this point.

What I am saying that suppose if a deuterium is attached and a hydrogen is attached, and suppose a OH and a methyl, then assigning priority sequence will be, this will be if you go by atomic number, 1st you have to go by atomic number. So atomic number wise, this is number 1, then this is number 2 and then you are stuck. Atomic number cannot be distinguished between deuterium and hydrogen because both have same atomic number.

So now you have to use once this rule cannot distinguish between the groups, then you distinguish these 2, use your 2nd criteria, that is the atomic weight criteria. So based on the comic weight criteria, this becomes 3 and that becomes 4. Okay? Another case may happen that you have CD2, then CH CH 3 CH 3 and you have CH 2 CH 2 OH okay? So in this case, okay this is one that is now that is no longer 2 methyl because this gets higher priority over this.

Okay? Because that is only attached to hydrogen, hydrogen, hydrogen. No substitution. So we write this. In case of this carbon, there is deuterium, deuterium and carbon. For this carbon, there

is a carbon, there is a carbon, there is a hydrogen okay? For this carbon, there is hydrogen hydrogen carbon. For this carbon, there is hydrogen hydrogen oxygen okay? Now according to the atomic number rule, this is number 1, then you apply the atomic number, continue atomic number until it falls apart that it cannot distinguish.

So you see after this, this group there is hydrogen hydrogen carbon, there is deuterium deuterium carbon. But at this stage, the rule 1 says that deuterium is equivalent to 1 hydrogen because they have both atomic number. So you have to use your atomic number rule 1st and based on that, this becomes you cannot distinguish at this stage. Then you go to the next carbon and you see there is a difference.

Hydrogen hydrogen oxygen has come, atomic number is more. Here it is all carbon. So which one is is now number 2? So this becomes number 2 and this becomes number 3 and methyl becomes number 4. So you see, in spite of having the deuterium here, you could not give higher preference to this to this because your 1st atomic number rule can distinguish between the 2, 1st atomic rule does not care whether there is isotopes. Isotopes are regarded as the same atomic number rule. Once that falls apart, then only you can utilise the isotope role. That means the 2nd distinguish between the isotopes okay?

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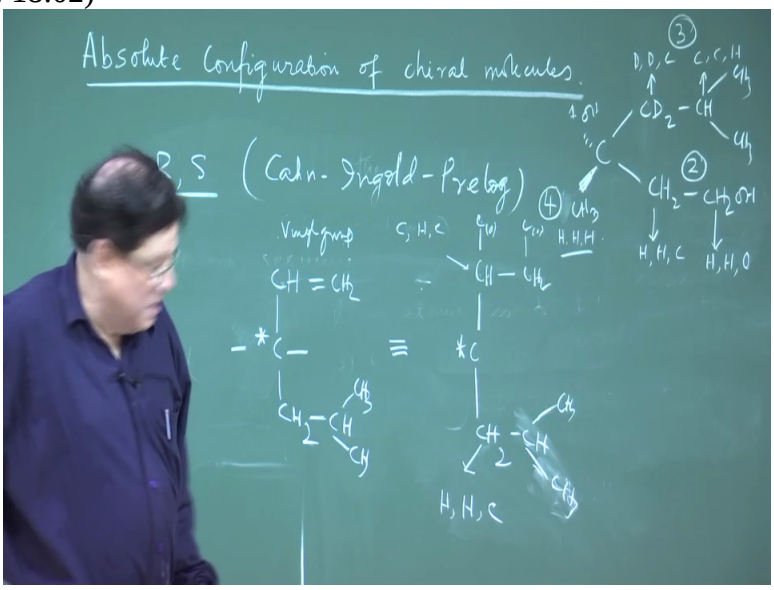

The 3rd rule, this is the 2nd rule, the 3rd rule says that in case of a double bond suppose you have a double bond attached to a stereogenic Centre, okay? And you have an isopropyl group so how the isopropyl group is compared with a with a vinyl group? This is called a vinyl group. So what you do? It has been suggested that because there is a double bond present between these 2 carbons, so you think as if 2 carbons, 2 extra carbons, one extra carbon is attached to this carbon, and one extra carbon is attached to this carbon because they are connected by a double bond.

So you have to break it into, so this is a stereogenic carbon. You have to break it into CH CH2 write single bond and then both and then on both the carbons, you attach an extra carbon. Why? Because this attached to that by a double bond. So it should have a double hand, 2 carbon atoms and on the same argument, this carbon is attached to this carbon by a double bond. So now you have attached a single bond. So you make a, you add another extra carbon.

Some, these are called phantom atoms and in some books you will find, just to distinguish between the normal carbons attached 0, but this has really no significance if they are behaving like the normal carbon, they are behaviour like the normal carbon, only thing they do not have any substitution, that is the difference. Okay, let us continue. So these are normal carbon. And then, you have this isopropyl, CH CH CH 3 and CH 3.

Now let us see, the 1st carbon you have, look at the 1st carbon, you have this is attached to the carbon, hydrogen and a carbon. Carbon, hydrogen and a carbon. This carbon is attached to hydrogen. Sorry, CH 2. This was CH 2, sorry this was CH 2 CH CH CH 3. Now we we better compare this one with, they continue with this HHC. The 1st one is HHC HHC okay? The 2nd one HHC, so this wins over wins over that one because this is HHC and this is CCH okay? So that has the that has the higher preference than this.

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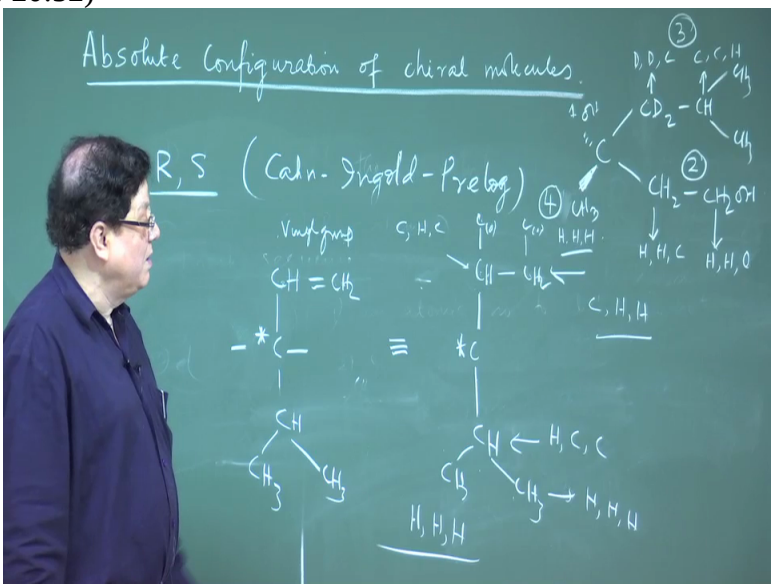

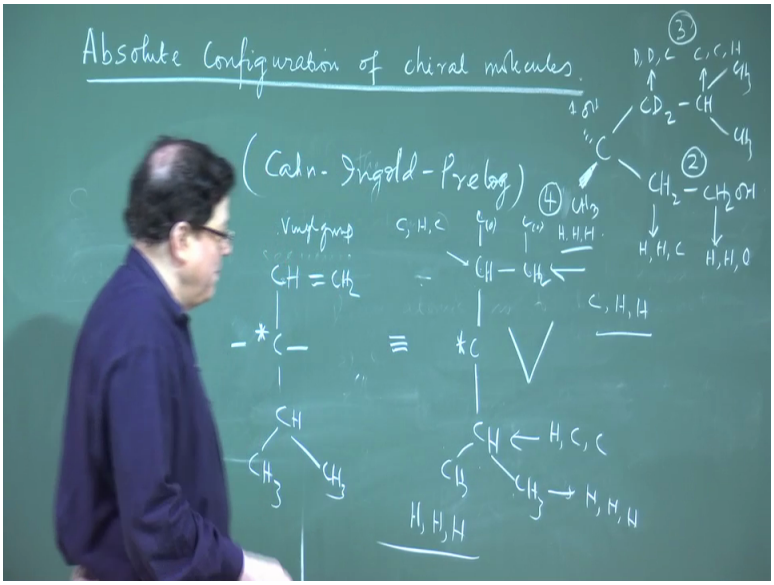

If we change it, suppose I change it to isopropyl, earlier it was isobutyl okay? So if I make it to isopropyl, then what will happen? This carbon is attached to this carbon is attached to what? Hydrogen carbon carbon. So there is no difference here. Hydrogen carbon carbon. This is the same way as hydrogen carbon carbon okay? But the next carbon, now you have to go to the next carbon.

The next carbon if you see, this is carbon attached to a carbon, then two hydrogens. But what about this one? This one is attached to hydrogen hydrogen hydrogen. What about this one? You

have to check everywhere. This one is attached also to hydrogen hydrogen hydrogen. So now you see, there is a difference here because this carbon is attached to a carbon whereas this carbon or that carbon is not attached to a carbon, it is attached to only hydrogens.

So which one wins over the which one wins? Make sure that that means this is this has got higher priority over this. Okay? We can talk about the triple bond. So the same case that what is going on with the double bond, the same case is with the triple bond.

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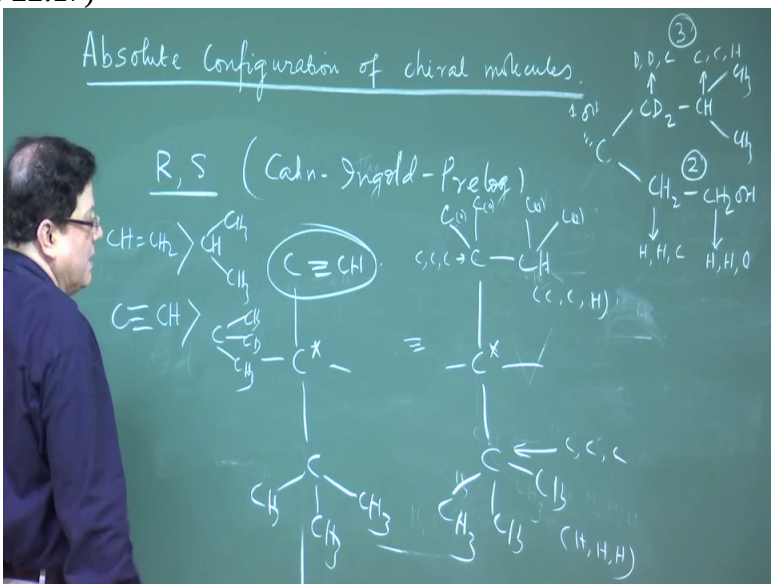

So if you have CH vs you are comparing with tertiary butyl suppose C CH 3 CH 3 CH 3, so what is done? As I said, now you have to say this, view this as a carbon attached to the single carbon because there is a, there are triple bonds so break the both of the bonds, make it a single bond, but while doing so as you have broken two bonds, so now this carbon will be will be regarded as having 2 ghost carbon atoms okay? You can write 0 as you wish and you can, you have to do the same thing.

A ghost carbon atom have both the carbons. Okay? And here, there is no ghost because it is just normally attached. So this is your stereogenic Centre and this is your C CH 3 CH 3 CH 3. So now what will happen? Now you have this you check what is the where is the difference? The 1st is that this carbon is attached to 3 carbon atoms.

So there is virtually no difference. This carbon is also attached to 3 carbon atoms but the next carbon whichever you take, is attached to only hydrogen hydrogen hydrogen and here, they are attached to carbon carbon hydrogen okay? So ultimately, acetylene wins over T butyl. So we can write CH double bond CH 2 has higher preference than CH CH 3 CH 3, acetylene has higher preference over tertiary butyl okay? So in many cases, you have to do this.

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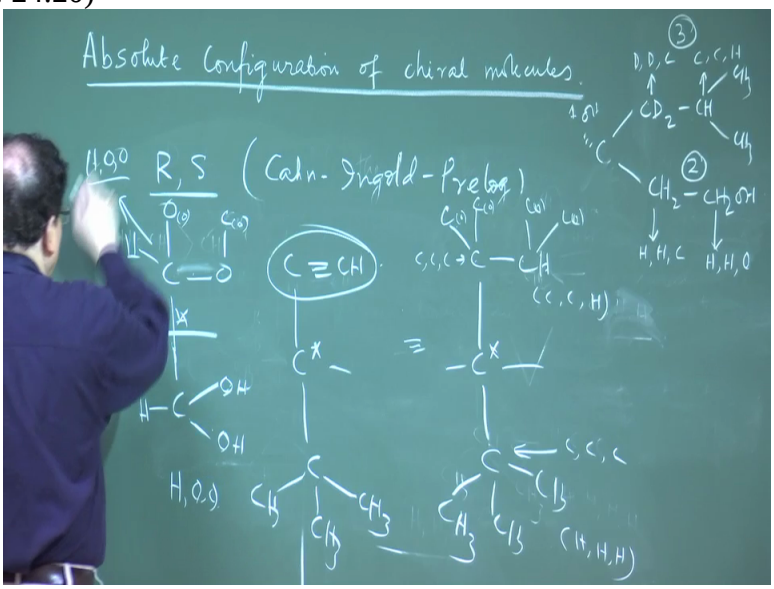

This addition of of ghost atoms like in aldehyde, that is the same thing. That if you have an aldehyde versus, so this is your stereogenic Centre, versus C OH, a carbon bearing 2 OHes which are usually not there but electron withdrawing groups can make a carbon forced to have 2 OHes okay vs this? Now here what you have to do, you have to again do the same thing that there is a, now this is a carbon double bond to oxygen, you have broken a bond.

So now you have to have two oxygens here. One of them is the phantom atom. For the oxygen, it was attached to a carbon by a double bond. So now you have to put a carbon here okay? So carbon host. Now you compare these 2. So here, this carbon is attached to hydrogen oxygen oxygen, this carbon is attached also like that, hydrogen and oxygen oxygen. So there is no difference. Now the next oxygen is attached to a carbon and this next oxygen is attached to a hydrogen. So this wins over that.

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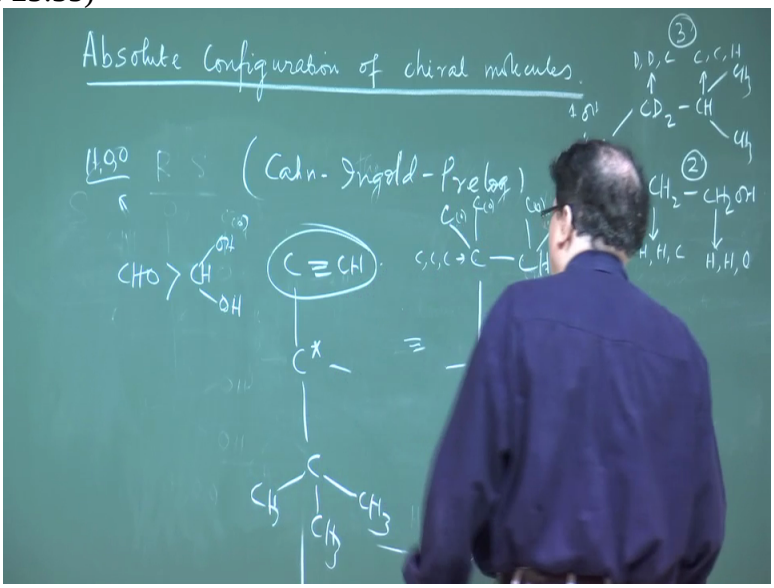

So CHO so the rules says CHO greater than CH OH OH okay? So like that, I hope you will be able to sort out several things. So the rule as I said, the rule is based on 1st of all atomic number. Once the atomic number issue is gone, if it fails to establish between 2 ligands, then you apply the atomic way to distinguish between isotopes, and then for the whole want systems, triple bond systems, you consider as if there is a single bond between between the 2 atoms but in addition these 2 atoms are attached to what are called ghost atoms.

So you have duplicated or triplicated the system. Like in double bond, the carbon double bond is thought to be attached to the normal carbon and you have to duplicate to add another carbon. Okay? So that is the that is what is the Cahn Ingold Prelog rules okay about the double bond. Sometimes what happens?

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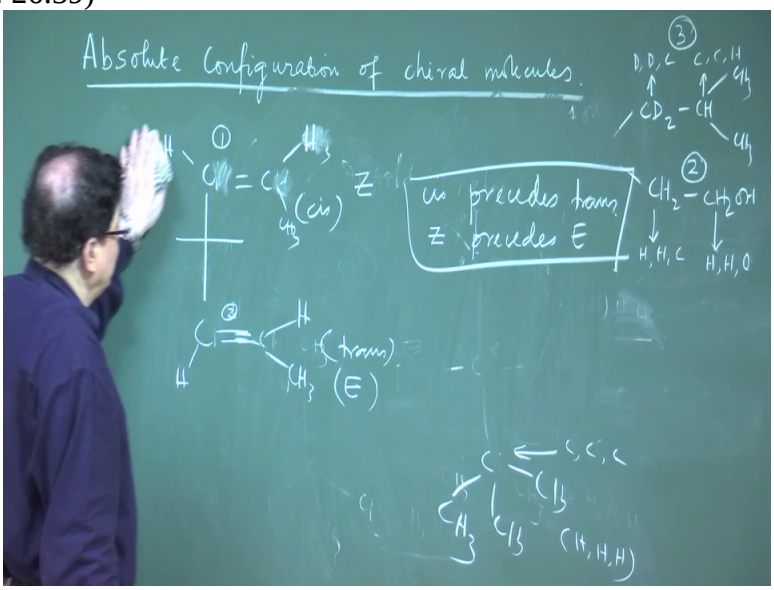

That there is a, there are, see there is a double bond here which is in the cis confirmation and there is a double bond here which is in the trans-confirmation. Suppose this is in the cis, if it is in the cis, that means this hydrogen is on this side, this hydrogen is on this side, methyl is on this side, that is cis. And if it is trans, that means this hydrogen is on this side, this hydrogen is on that side, sorry this hydrogen now you would have to make trans.

So this hydrogen is here, this methyl is there, okay? So in this case, this is your trans. Later on I think you you or you have already known that this is what is called a Z, cis is called a Z isomer in absolute (config) similar to RS nomenclature and trans is called the E isomer okay? So here the rule is, cis precedes trans. That means, between these 2 groups, this one will be will be having higher priority. If it is 1, then this is 2 okay? Cis precedes trans, so you can say Z precedes E. So same thing, cis precedes trans, Z precedes E.

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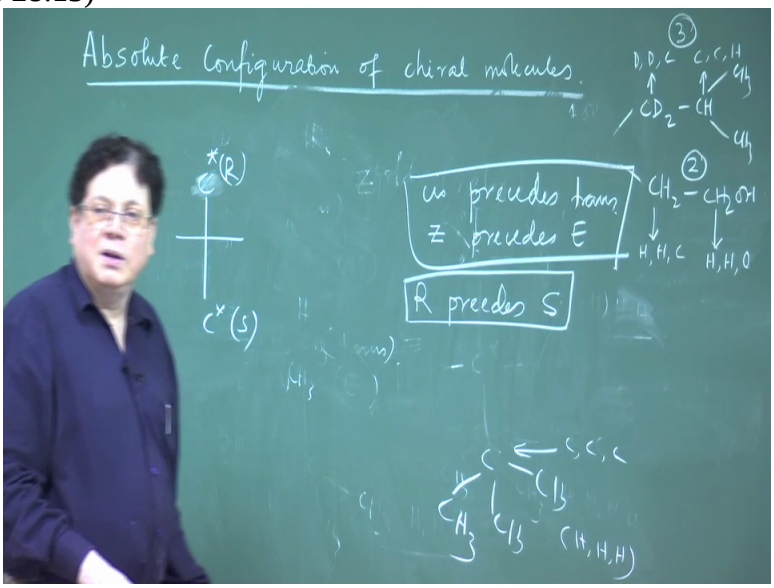

On the same token, if you have, if you have groups which are chiral here, a carbon which is chiral and which is having R configuration suppose and on this ligand, you have the same group, but in the S configuration okay? If that be the case, then also, see atomic number, atomic weight, nothing can distinguish between these groups.

Only the absolute configurations are different. So here the rule is that R precedes, precedes meals R is favoured over S, R precedes S okay? So that is the, this is the rule. So if you face this type of situation, then you can do that okay? I can give you just to end the I can do one problem where this RS is involved.

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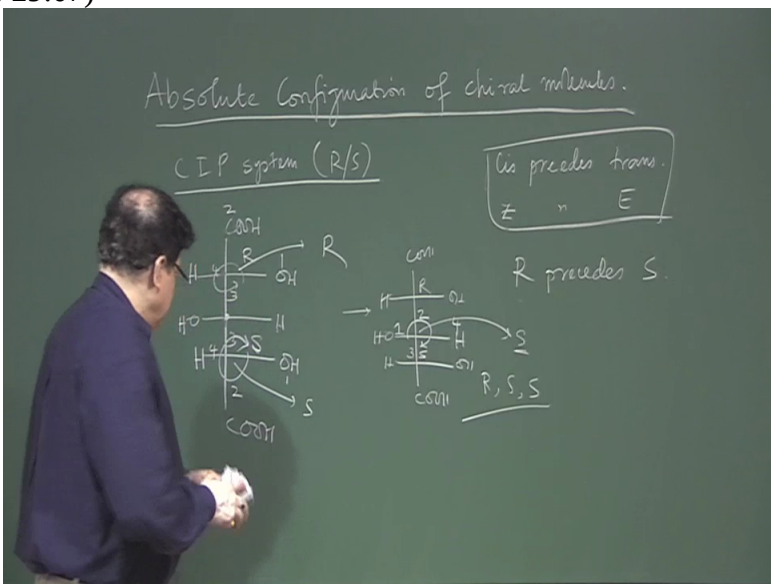

So let us do a problem on these sub rules. Cis precedes trans or Z precedes E and then R precedes S. Okay? So if we draw a molecule which has got a, a 5 carbon molecule, suppose this OH is to the right. It is a tri-hydroxy compound. Then you have OH and you have OH here okay? H H H. Now there are 3 carbon atoms and 3 carbon atoms, this is definitely stereogenic, this is stereogenic and this, we are not very sure whether it is stereogenic or not because that will be depending on the the configuration of this and configuration of this.

This will become stereogenic when the configuration of this is not the same as the configuration of the stereogenic Centre. Then it becomes stereogenic. If they become same, suppose this is R, that is R, or that is S, that is S, then this carbon is not stereogenic. So this type of carbon is actually called pseudo-chiral centre or pseudo-stereogenic Centre okay? Sometimes stereogenic, sometimes not. Let us see what is the status of this.

Now 1st you have to assign be RS configuration of this carbon. So if this is 1, that is 2, that is 3 and that is 4, so it will be 1, 2, 3, looks like anticlockwise but since the hydrogen is in the horizontal side and that means it is towards you, so actually you have to see behind the board and if you look at from behind the board, so this should be in the clockwise direction. So whatever you see here, you just reverse it.

So actually this will be in the R configuration okay? Because the hydrogen is towards you. So whatever you see again I repeat, you change it to the other direction. So what about this one? This is number 1, that is number 2, this is number 3 and this is number 4. The same thing, hydrogen is in the horizontal position, so you have to be careful. So this shows that this is looks like a R configuration clockwise but you have to see from the backside.

And from the backside, it will look like just the opposite. So it is in the S configuration. So this is S and that is R. So now this carbon has become a stereogenic Centre because it is now attached with 4 different 4 different groups okay? The difference here is basically different items and here the difference is because there are different configurations of the chiral centres attached to it okay?

Now what is the configuration of this? Now this is the carbon where this group is R and that that group is S. So if you now do the priority sequence, maybe I can just do it here because that figure looks complicated now cumbersome. So this is R, OH is on the right, this is CO2H. So if it is and this is in the S configuration, OH is on the right and H is on the left, CO2 H and this is OH and this is sorry, this is H and that is OH.

So now what is the configuration of this? This will be your number 1, that is the highest atomic number. Then comes either this or that but since R precedes S, R gets preference over S so this will be 2 and that will be 3 and the hydrogen will be 4. So 1, 2, 3 looks like R but because the hydrogen is on the horizontal side, so the configuration is S okay? So this is a R, S, S compound.

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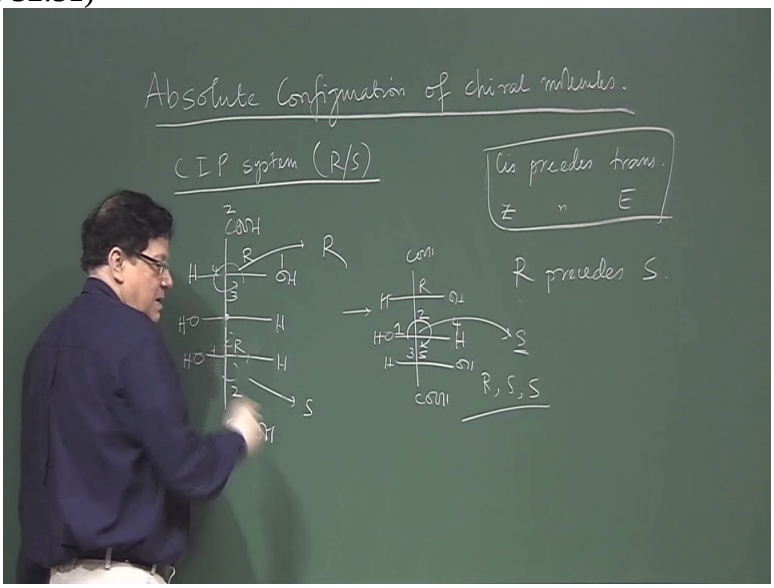

Interestingly, if you change the change this OH into this side, so what will happen now? So this will become also R. Because you have remember, in Fisher projection, if you interchange the position of 2 groups, then the configuration gets inverted. So this becomes also R. So now this loses its stereogenicity, it is no longer stereogenic because this is attached to the same, it is attached to the chiral centre, same chiral centre with same configuration okay?

So you have to be careful. So this is what is as I said, that it is sometimes chiral, sometimes not chiral. So this is called pseudo-chiral centre. Some books prefer to write small R or small S for this to to distinguish between the normal stereo centre vs the this type of pseudo-stereo centre. They write small S, small R notation they use okay? So we have now gone through the this absolute configuration, the Cahn Ingold Prelog system.

And we have seen that how to assign the RS nomenclature into a compound which is written in a three-dimensional formula or inefficient projection formula and there are certain rules, you always remember those rules and then just one more thing is left and that is sometimes there are compounds where the 4th ligand is a lone pair. So if like nitrogen, if the 4th ligand is a lone pair, then because the lone pair has no atomic number, it is only electrons, so lone pair takes take the least lone pair is the least priored group followed by hydrogen and then followed by your carbon, then nitrogen, then fluorine, oxygen, then fluorine.

Sorry, it is the other way around. Less. So this is less preferred. An oxygen is less preferred than fluorine. So this is the priority. So always if there is a lone pair, so you have to take into account the lone pair is the 4^{th} group and that is the group of least priority because it has no atomic number okay? So lone pair less than H less than carbon less then nitrogen less than oxygen less than fluorine. Thank you.