Structure, Stereochemistry and Reactivity of Organic Compounds and Intermediates: A Problem-Solving Approach

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Lecture - 07

Axial, Planar and Helical Chirality, Assignment of Absolute Configuration to Such Molecules

Hello. Welcome back to this course on Structure, Stereochemistry and Reactivity of Organic Molecules and Intermediates: A Problem Solving Approach. In the last lecture we have seen that how symmetry elements play an important role in assigning the whether it is chiral and also the how many indistinguishable forms it can take and also the number of symmetry operations that you can perform on a molecule.

Now, 1 important point which was not told that what is importance of this, all these exercise that assigning point group and then finding out all the symmetry operations and the symmetry number. These are important, 1 is definitely chirality because this point group will tell whether a molecule is chiral or not or is it or it is a chiral that is number 1.

Number 2 is, another very important application is that you can draw the molecular orbitals, molecular orbitals for a molecule as well as for even hybrid orbitals you can draw but at that time you have to apply the concept of symmetry. And also you can explain the spectroscopic, the spectroscopic properties like IR spectra and then by applying this symmetry, so by knowing there, so symmetry plays an important role.

Now, this lecture will now depart from that symmetry. They will go to the other aspect, this important aspect of symmetry that is the chirality. And we know that if a molecule is chiral then it can be represented by 2 different formula 3 dimensional formula. 1 will rotate the planar polarized light to the right hand direction to the clockwise, another is anticlockwise, dextro and levorotatory.

However, it is not, it is difficult, actually it is some computational success is there. However, in general it is not possible to predict the absolute configuration by looking at the sign of the rotation, the specific rotation. So absolute configuration is basically the arrangement, the absolute arrangement, the unequivocal arrangement of the substituents or the atoms in 3 dimensional space for a chiral molecule.

Now, we know that chiral molecules can be of different types 1 is having SP3 stereogenic center. The other is that we have discussed in the earlier stereochemistry lecture. The other is that molecules which are having axial chirality.

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So, molecules having axial chirality or planar chirality or helical chirality, helical chirality. So for them how to assign the absolute configuration? What is the notation? The RS notation that you arrive at or is there could be other notations that are possible like p m notation. So today we will just quickly go through this.

In the last stereochemistry course that is there, we have discussed how to assign absolute configuration to allenes, that is the actually chiral molecules or to biphenyls that is another type of actually chiral molecules or spiro systems and also we have, possibly we have not dealt with the planar or the helical chirality at that time.

But today we will cover everything to clarify any doubt regarding axial chirality and then we will introduce the planar chirality and helical chirality and the notation, the absolute, the notation for absolute configuration.

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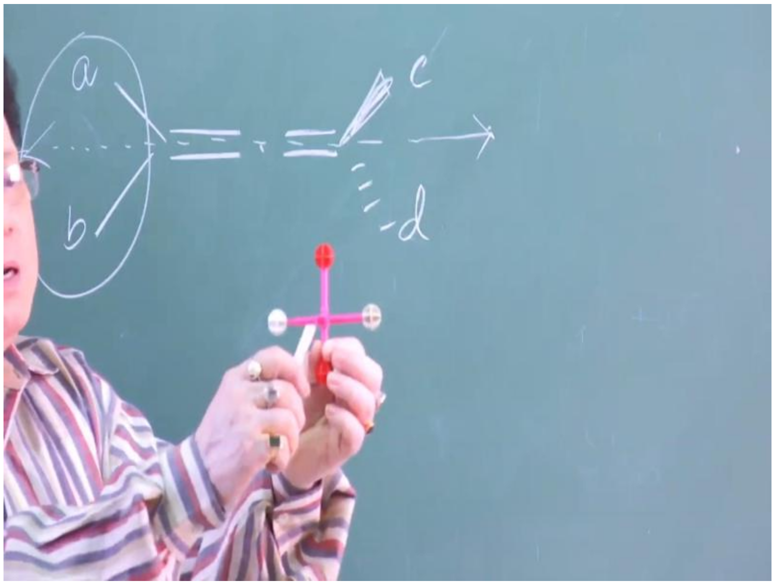

Now, axial chirality we know that if you have axial chirality by definition it says that molecules which are chiral due to the presence of a chiral axis that is what is called axial chirality. That means the presence of a chiral axis like in presence in allenes that you know that these substituents are having this reside in a plane which is orthogonal to the plane of the plane which the other substituents at the other end reside. And so there is we say that there is a chiral axis going through, going through this.

Now, what does it really mean this chiral axis, that it has got a chiral axis? So, it can be easily seen that actually chiral axis is possible for molecules which are, which, where the substituents lying in orthogonal relationship like this is a hypothetical system. Hypothetical system but representing what is present in a biphenyl or what is present in an allene system.

But here what I have done see this thing this carbon-carbon bond as an axis, carbon-carbon bond as an axis. Now we will see that when this axis becomes chiral that means when we change the substituents at the 2 ends and whether we can superimpose those molecules or not. So that will tell you whether this axis has become chiral or not.

So here, this system that I have is basically at 2 ends. I have a white, 2 white substituents and at the other end I have 2 red substituents. So if I now have a mirror image of this which is on my, which is on my right hand in the image and the in the photograph actually that is actually, that got changed. So this is now my, this is my, now this is right, this is right hand and that is the left hand. So that is okay.

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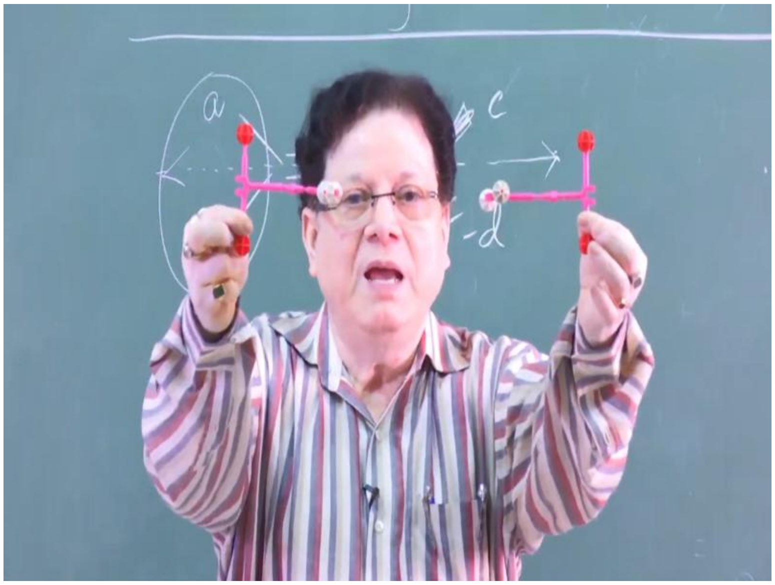

So both these, these are the 2 mirror images of each other. Now the question is, is this axis which is basically this carbon-carbon bond is this axis chiral or not? How to decide on that, that whether these 2 mirror images are super impossible or not? So we can see that these are actually super impossible, no problem, you can superimpose those very quickly.

So, that means this axis now is not a chiral axis. Now suppose I change 1 of the white and go to a green. So I change this and then so this is a molecule where at 1 end I have different substituents. At the other end I have 2 red substituents. So I make the mirror image of this so the mirror image of this so basically I have to hold this so that means there will be a green at this point. So I will just fix it and then show you the mirror image.

So, the mirror image is like this. So they are the mirror images of each other. Again I show to you they are the mirror images of each other. Now the question is, is this axis this carbon-carbon if it is a carbon-carbon-carbon axis whether this is chiral or not? Again, they, how to decide on that? You have to check whether they are super impossible or not.

So, again you see that they are mirror images and they are super impossible on each other. The blue, the white on white and the green on green and reds on the red. Now you change 1 of the red and put a white suppose.

I could have done other colors but I have in my, in my stock I have this, the white. So in 1 case this is white and this is green and in the other case this is white and that is red. Now make the mirror image of this, the mirror image of this. So I have to make this red and this is the white just 1 second let me complete the structure and then show it to you that whether they are mirror image.

You see they are mirror images of each other the green faces green, the white faces white and here the white faces white and red faces red. Now the question is, are they super impossible or not? Now if you try to superimpose on 1 side you have super imposed the green on green and white on white but on the other side white on red and the, this is also white on red. So they are not super imposing here.

On the other hand, if you try to superimpose at this position then you will see that they were not going to superimpose fall on each other on the other side. So that means now we have generated a chiral axis. Now 1 more point is that let us change this green and make it on both sides white and red. So what happens to this axis? I have to hold it properly so that they look like mirror image see this is, now this is not the mirror image sorry.

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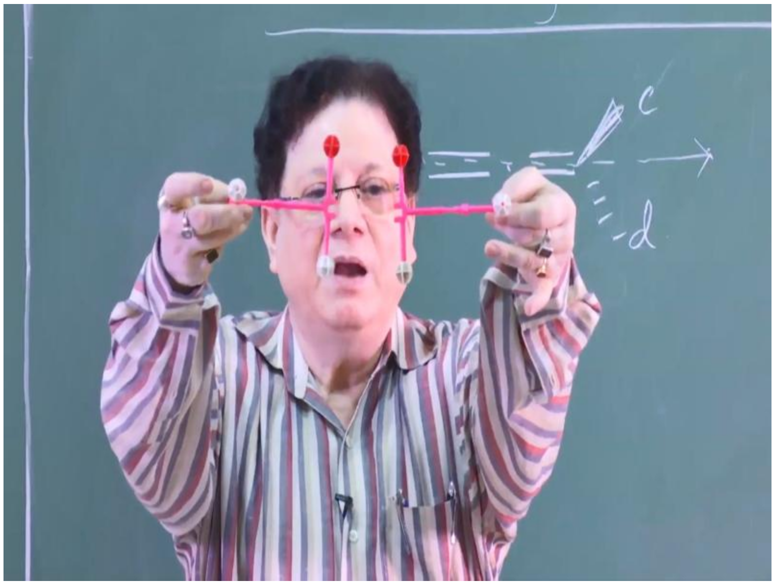

This is, so this is the mirror image of each other and now if you try to superimpose again the same problem is there, the same problem that on 1 side you can super impose, on the other side you cannot. So now it has become the axis has become we said that the axis has become chiral. So these groups are arranged around the axis in such a way that they generate chirality that is why this is called axial chirality.

Axial chirality is basically existence of an axis where the substituents are spaced in such a way, are attached in such a way that the 2 forms are not super impossible on each other. So that is why this the allene or the biphenyls because 1 might be confused with planar chirality because in biphenyls we are considering 2 planes, in allenes also we are considering 2 planes but it is actually the axis going through in case of biphenyls, this is the, the biphenyl.

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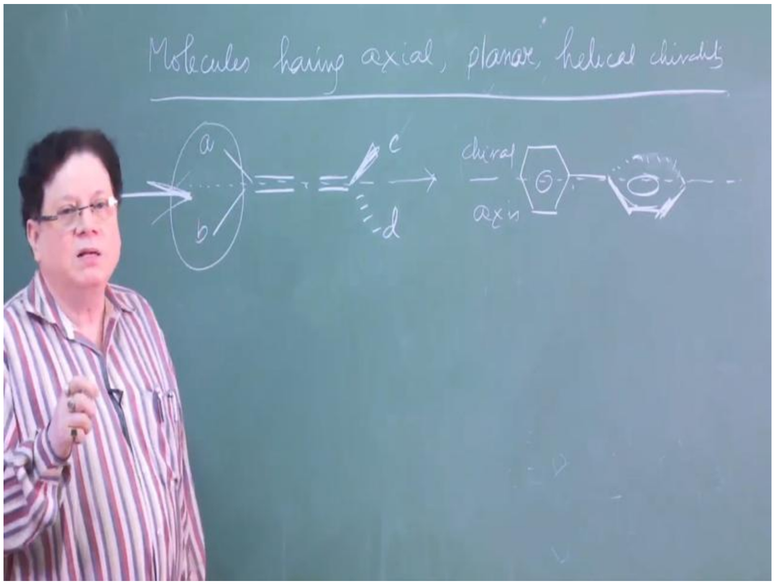

So, in biphenyl the chiral axis is going through this. This is the chiral axis, chiral axis, so that is why these are axially chiral molecules. Now how do you assign the stereochemistry here? I think you know for the allenes very sure, that you actually lo from any direction. However, you have to remember the zeroth, the rule zero of assigning absolute configuration and that says that the near groups precedes the groups at the further end.

The near groups are given higher priority over the groups which are further apart, which are at a distance far, which are the far groups. So and in allene interestingly whatever direction you take it remains the, the absolute configuration is the same. 1 important point is that many students get confused that whether when you look at from this direction.

So because this is the nearer group so that will be 1, that will be 2 and this will be 3. Suppose this is 3 C gets preference over D, so A gets preference over B. So if you do that you end up with something which will look like see the vertical 1s are 1 and 2, and the horizontal 1s are actually on the right side is 3 and on the left side is 4.

Sometimes you get confused with the fisher projection formula of a molecule where you are told that if the 4th group lies in the horizontal position then your absolute configuration whatever you see you have to change the direction. But that is not true here. This is nothing but what is a Newman projection.

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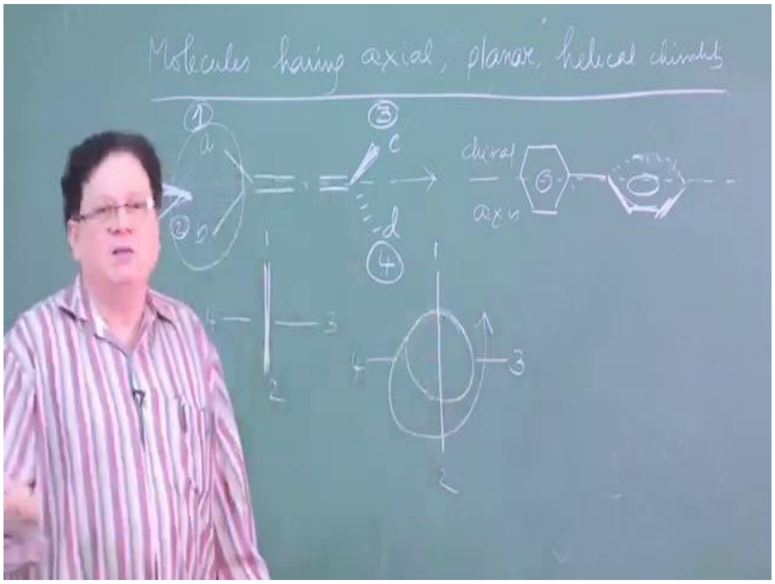

It is nothing but what is a Newman projection. If you draw it in a Newman projection then this is 1, that is 2 and this is your you can do that rather than drawing this you draw this 4 and 3. So this is the Newman projection. Now you would assign the absolute configuration. So whatever you see that is your actual direction because your 4th group are always away from the observer. So that is 1 important point for allene.

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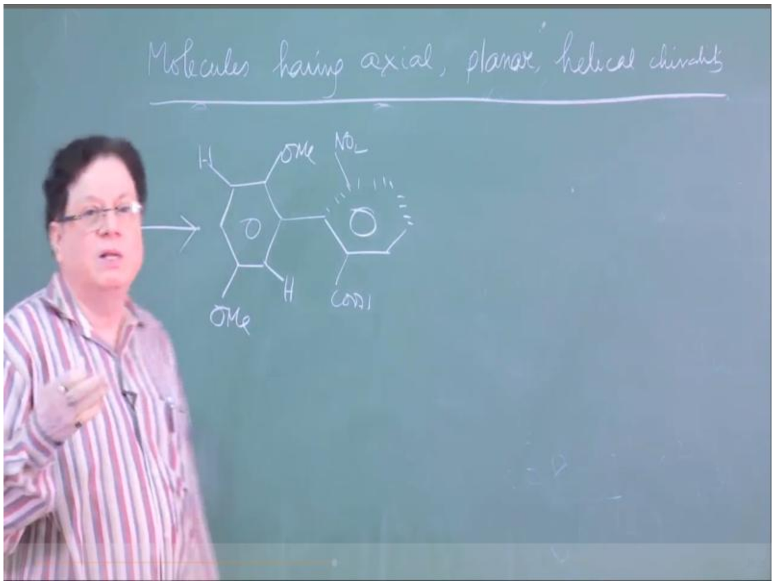

For biphenyl for biphenyl there is a slight change in the rule later on because initially what happened that if you have sorry if you have groups here, suppose this is OME and this is H suppose here is nitro and here is Co2H and suppose there is another OME here. Now if you want to assign the absolute configuration to this you look from any side suppose I look from this side and there is the old rule which is based on this that the near group, nearer group gets precedes over the groups at the further end.

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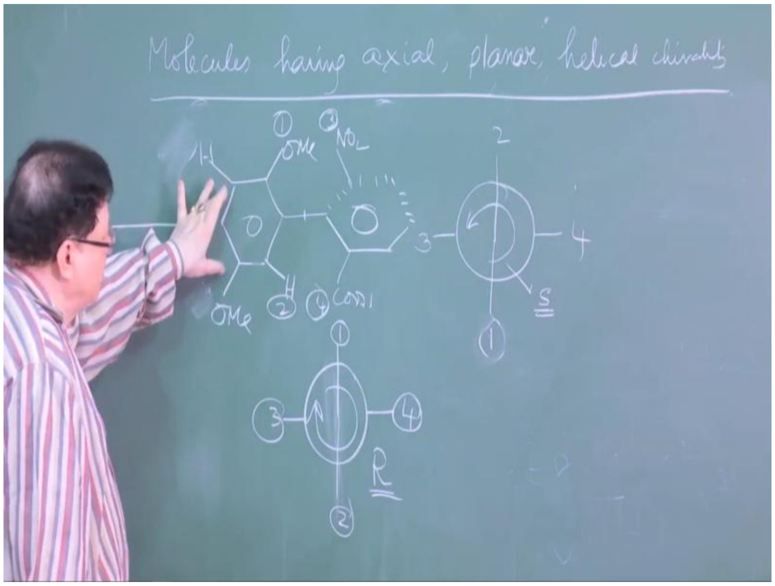

According to that rule so these are the nearer to the observer the H and the OME. So that will be 1 and that will be 2 and this will be your 3 and that will be your 4. Now if you draw the, draw the Newman projection that I am looking from this side, so your 2 will be at the top and 1 will be at the bottom, sorry and then this will be, so on the right side will be 4 and on the left side will be 3.

Remember again this is the Newman projection. So 1, 2, 3, so that is basically this direction. So that will be S configuration, this is the older nomenclature system. The new nomenclature system that was developed, now it is not new, it is actually, it is also quite old, but the rule got changed, possibly during the 80s that what it says now that rather than seeing from outside in, it is said that you better check from inside out.

That means from this direction if you see then they are the nearer groups and behind groups are the are this nitro and CO2H. So when you decide between 1 and 2 so you have to now go by this, the nearer, this inside out you have to do, inside out if you do then what will happen you have again draw the Newman projection.

So, now this will be your 1 and that will be your 2. So if that is the situation then your 1 here and 2 you have here and then 3, 4 remaining the same so that is your 4, and that is your 3. So now the rotation then the absolute configuration becomes R. So there is a change of the rule somewhere in the 80s that earlier it was outside in that was the approach, now inside out.

So, if you do inside out then this becomes the nearer groups and if that is the nearer group so they have to be given 1 and 2 rather than the substituents at the 3 5 position. Let us consider what is called the what is called planar chirality. The planar chirality let us do some other, other examples like the before we go to planar chirality suppose the spiro system.

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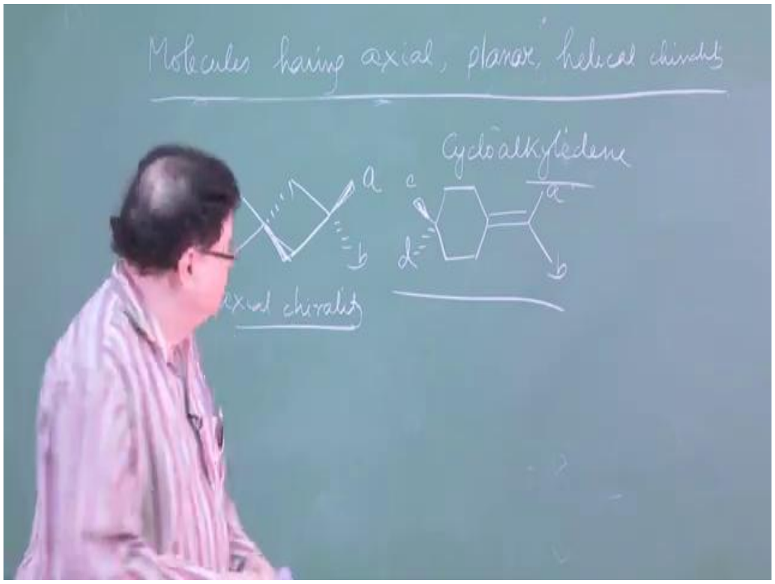

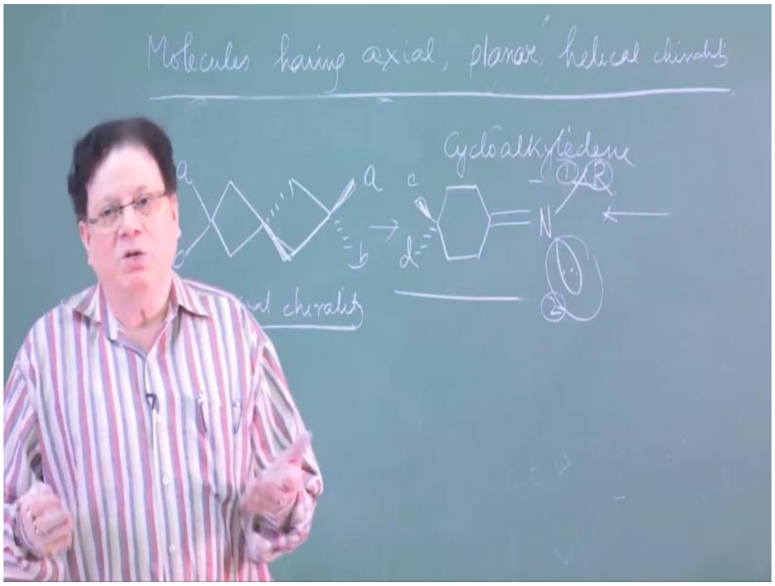

So, I draw a spiro system like this and then it will be chiral only when like when allene system like these 2 cycles basically are can be considered as replacement of double bonds, 2 double bonds the 2, 2 cycles. So here suppose there is a group a and here is b and then this is a and this is b. So that is another example of axial chirality, axial chirality and then the other systems are it could be that 1 cyclic network and another double bond.

So, do not replace the 1 double bond. So here it is basically you are replacing the allene with 2 cycles both the double bonds are replaced by a cyclic system. On the other hand, here it is alkylidene system that means 1 cycle a cycloalkylidene, I can say cycloalkylidene cycloalkylidene alkylidene I think cycloalkylidene, cycloalkylidene. And then also the same sort of scenario will happen.

So, this is a, this is b, this is c, this is d and at the rule for absolute configuration assignment remains the same like what was applied for the allene system. Sometimes you can replace it by a nitrogen that is also possible because the nitrogen lone pair is there and suppose this is R so that also makes it chiral. Because now you have different substituents at these ends and you know the lone pair is the always gets the 4th priority provided you are looking from this direction.

If you look from that direction then this will be 1 that will be 2. So you have to remember that. So the important points are that 1, 2 basically is decided from where you are seeing and the other point is that it is not a fisher projection whatever you are drawing is nothing but a Newman projection. So you do not have to be worried about the 4th group, 4th group is always behind the observer. Now let us come to what is called a planar chirality.

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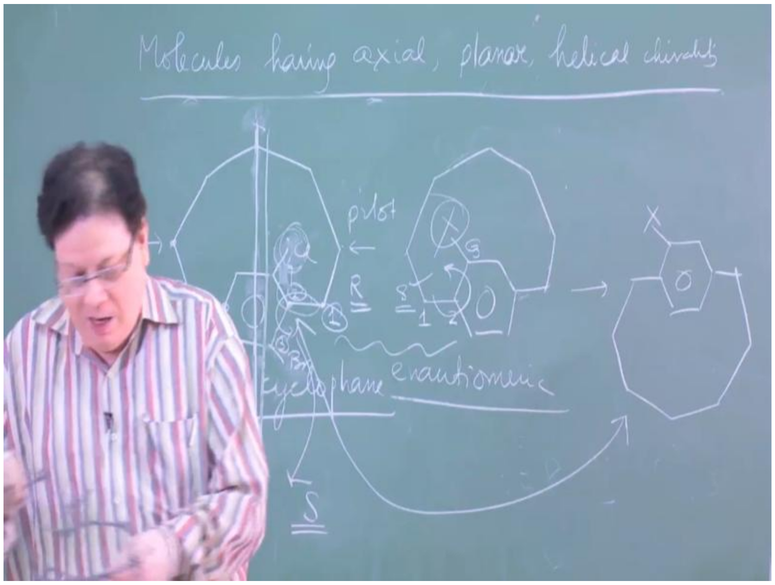

Planar chirality is I have a model I will show you, planar chirality is shown by some interesting class of molecules which is called cyclophanes. Cyclophanes are basically an aromatic ring like a benzene ring which is connected where 2 positions of the ring like here it is the 1 4 positions are connected to a bridge of alkyl groups, bridge containing alkyl groups like this.

So, this is what is called paracyclophane. You can say 1 4 cyclophane but popularly known as paracyclophane. So this cyclophanes there could be meta cyclophanes also. And they are interesting compounds because they can show chirality provided, provided here, provided you destroy, see here if it is the way it is written here, now if you draw a vertical plane here going through this and divided into 2 you will see that that plane is a plane of symmetry.

Now, this plane of symmetry, this plane of symmetry is disturbed the moment you put a group here like x. Then your plane of symmetry is gone basically the plane of symmetry that what you are thinking is gone. So now this molecule if you draw the mirror image of this they become non super impossible. If you draw the mirror image of this so then x is here now. So now these are, so now this plane of symmetry is gone because of the substituent x.

And these are now enantiomeric pairs. However, there is a catch here. What is the catch? First of all why this is called planar chirality? Because when you did not have x, when you did not have x then what was happening, that you had a plane of symmetry, you have a plane going through the middle of this ring and that is a plane of symmetry. And that plane of symmetry is disturbed the moment you put a substituent here.

So, that is why this, we say that this is basically the plane is becoming a chiral plane. So, that is why this is, this is said that this molecule is having axial, sorry, planar chirality. Like axial chirality what happens in the this type of system, what happens? That the axis which was earlier not chiral becomes chiral as soon as you have differences in the substituents at the 2 ends.

Then the axis becomes chiral how do you know because you make the mirror image of this and then you see that the mirror image is not super impossible on it. So that is axial chirality. Planar chirality is originally you had a plane of symmetry but now once you put the x now this plane has lost its plane of symmetry character. So now it is no longer dividing the molecule into 2 halves which are mirror images of each other.

So, these 2 are now basically non super impossible. However, what happens that if this linker, which is linking this 1 and 4 positions making the paracyclophane, if this linker is very big then it is possible for this whole, the whole thing at the top which is like a, this whole thing is like a, like a your helmet kind of thing. So that can now flip over and come to this side, the down side.

So, basically what I am saying that there is a possibility that this whole thing now can come down at the bottom, below the, below this plane of the benzene ring. If that happens then this becomes same as that 1 if that happens, that means whether a paracyclophane with a suitable substitution in the benzene ring to generate axial chirality will show, will be resolvable provided you have sufficient, you have introduced sufficient strain in the system so that this type of flip over does not take place.

So, it cannot flip to the other side that whole chain at the top, the link are at the top cannot flip to the downside. So that means with longer linkers you will not be able to resolve these molecules. So that is the beauty of the, of this planar chirality. There are other examples of planar chirality, you have trans cyclooctene that can also exist in chiral forms and that also shows planar chirality.

Now, the question is how to assign RS configuration into these molecules showing planar chirality. The rule says that basically you take an atom first of all you have to there are 2 ends of the benzene ring where this linker is attached. So you, when you decide on the RS nomenclature on this system you have to first take a pilot atom something what is called a pilot atom.

Pilot atom is basically the atom which is nearest to the plane of the aromatic ring that you are considering, plane of this, in this case in paracyclophane this carbon is the nearest to the plane of this benzene ring. Now you can say that this is also same because it is also just 1 carbon away from the plane of the benzene ring.

But we will consider this as the pilot atom because from that side your the substituent that is basically present and that is creating the actual chirality that is near to the, that is near to the pilot atom. So basically you have to select a pilot atom which is not only nearest to the plane of the aromatic ring in case of this cyclophane but it is also nearest to the substituent that is basically generating the planar chirality.

So, if that be the case this should be your pilot atom and not this 1 because this is further away from the substituent. So then you assign basically this will be your number 1 atom. This will be your number 2 and then then the other there are 2 carbon atoms attached to this C2. But you know that because there is a substituent here so that will be your number 3 according to the rank.

So, here the rank does not follow at least 1 and 2 is basically is a compulsion that the number 1 is attached to the pilot atom that is why that is number 1, then the next 1 is 2 and then the differentiation that this is branched into either this direction and branched in this direction and that direction but this will get higher priority because suppose x is say CL so that will be a carbon having CL that is the carbon having H.

So, that will be your number 3. So now if you look from this side of the pilot atom so that will be coming 1 to 2 to 3 so that is a clockwise direction, so this belongs to an R molecule. This is suppose there is a CL here and there is a bromine here, because that molecule is also having axial, planar chirality. So in that case obviously the 3 will be on this side because CBR will be preferred over CCL.

So, you apply your, the rules for assigning the priority, the priority rules after crossing your C2. C1 C2 is fixed and then the number 3 you decide based on the substituents on the 2 sides. So that will be number 3. So if that the case then 1 to 2 to 3 so that becomes an S molecule. So this is an S molecule and if you do this, this is the mirror image of that so that will be your number 1, that will be your number 2 and that will be your number 3. So, now it will be anticlockwise so that will be S molecule. So this is how it is done.

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I can show you in the model I have tried to make a model of this paracyclophane, see this paracyclophane let me, so this is your linker. Now you can say that Sir, the linker is the linker, so this is the, if it is clear to you so this is the benzene ring and this is the linker the methylene bridge at the top.

Now, what happens, because there is a substituent here, because there is a substituent, if you can see the substituent, this is the substituent. So that makes this, that makes this, disturbs this plane. Now you can say that Sir, this is not lying in a 1 plane but what happens, remember I told you in the first or the second lecture that in a methylene bridge although this is zigzag but there will be a conformation when they change from 1 conformation to the other.

There will be a conformation where they are all, they will be all in a symmetrical form like this it is a symmetrical form now. I have made it in a symmetrical form and now the plane of symmetry is apparent. However, because of this substituent at this point because of this substituent it is no longer a symmetrical, it is a symmetrical molecule.

So, now it is assuming axial chirality. So this is your pilot atom. This is your number 1, this is your number 2 and this is your number 3, so 1 to 2 to 3. So you have to see from the side of the pilot atom that is also important you have to see from the side of the pilot atom and then 1, 2 and 3 so that becomes R configuration. So that is basically 1 of the example of planar chirality.

Now, if you want to as I said that there is a possibility that this whole chain can flip over and come to this side this is only possible provided the length of the chain is quite big. Otherwise you see that there is lot of distortion as you want to do this there is lot of distortion that is happening but I can still do it in this form where the bridge is actually 1, 2, 3, 4, 5, 6, 7, 8. So this is 8 carbon, 8 methylene bridges.

So, that will decide whether this is isolable in a particular chiral form or not. So that actually says about the axial chirality. So we have done the planar chirality and the axial chirality and the helical chirality is very simple that you have to see whether the helix runs in clockwise direction or it is, that is the right handed helix or it is running as you go from 1 end to the other end whether you are following an anti-clockwise direction that is a left handed helix.

So 1 is called plus that is the p and the other is m the minus the minus is the left handed 1. So p helix and the m helix. So that is helical chirality. So nothing very extraordinary in helical chirality but some people may think that going from 1 direction if it is going in a clockwise turn then looking from the other side in case of helix it is again the same it is, it will be clockwise.

So, it is p helix irrespective of whether you see from 1 side or from the other side. So remember that fact because this is important when you study the structure of proteins or which can exist in right handed alpha helix or you can also the right handed the double helix of the DNA.

So, here the helical chirality becomes very important. So we have done through the absolute configuration of these molecules where this chirality is not due to the presence of an SP3 stereogenic center but it is due to the presence of either chiral axis or chiral plane or helical or a helix, so that takes care and how to know the, how to determine the absolute configuration. Thank you.