Symmetry, Stereochemistry and Applications
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Module No # 04
Lecture No # 16
Stereoisomerism

Welcome back to the course on symmetric stereochemistry and applications. In the previous lecture we were discussing about isomerism. And we started with talking about various different types of isomers and we were trying to understand what are chiral compounds?

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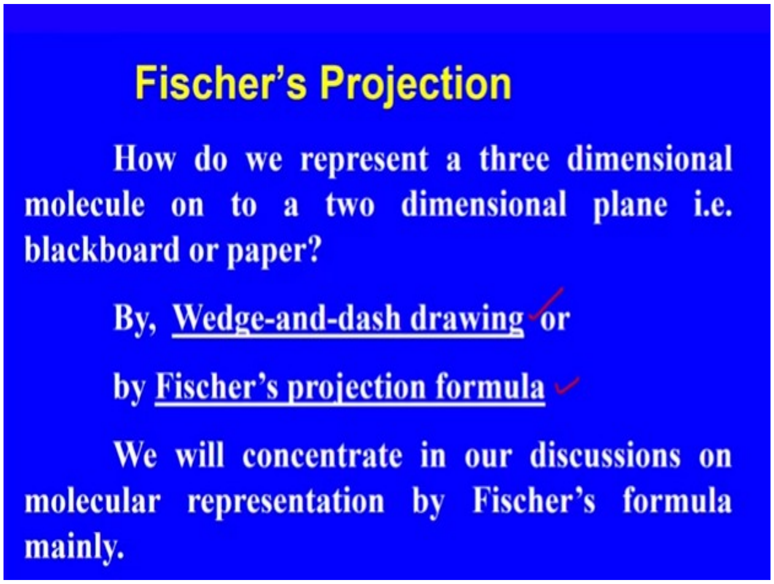

Fischer's Projection

How do we represent a three dimensional molecule on to a two dimensional plane i.e. blackboard or paper?

By, Wedge-and-dash drawing or

by Fischer's projection formula

We will concentrate in our discussions on molecular representation by Fischer's formula mainly.

So in this course now we need to learn a new method of projecting these chiral molecules, which we all know as Fischer's projection. So how do we represent a molecule, a 3 dimensional compound on a 2 dimensional plane that is on a black board or a piece of paper. We have already learned how to draw the Wedge and dash projection. We have also learnt the Newman projection and the cyclohexane chair form boat form how to draw those and all that. So now, in this lecture will try to understand how to draw a Fischer's projection, so we concentrate in our discussion on molecular representation by Fischer's formula mainly in the next part of this course.

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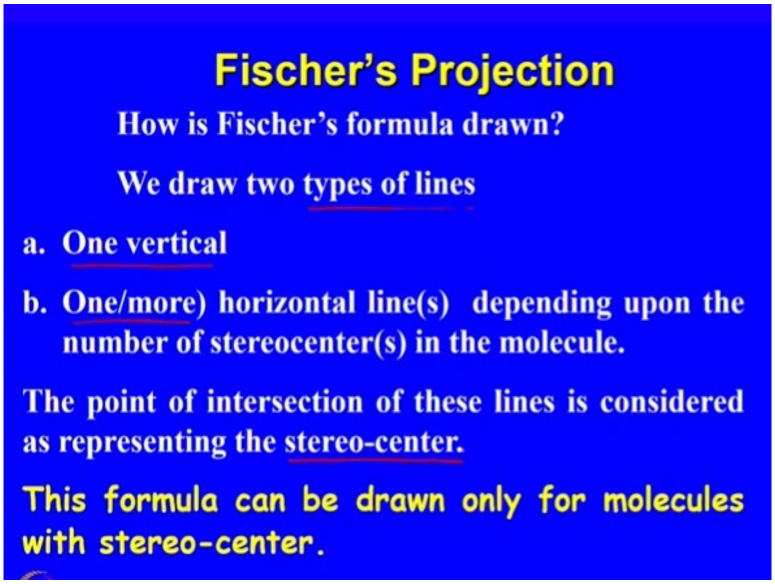

Fischer's Projection

How is Fischer's formula drawn?

We draw two types of lines

a. One vertical

b. One/more) horizontal line(s) depending upon the number of stereocenter(s) in the molecule.

The point of intersection of these lines is considered as representing the stereo-center.

This formula can be drawn only for molecules with stereo-center.

So the first question is how the Fischer's formula is drawn. We draw 2 types of lines, 1 vertical line and 1 or more horizontal lines depending upon the number of stereo centers in the molecule. The point of intersection of these lines is considered as the stereo center, this formula can be drawn only for molecules with stereo center, that is very important. We should not draw a Fischer projection for a molecule where there is no stereo center present in the molecule.

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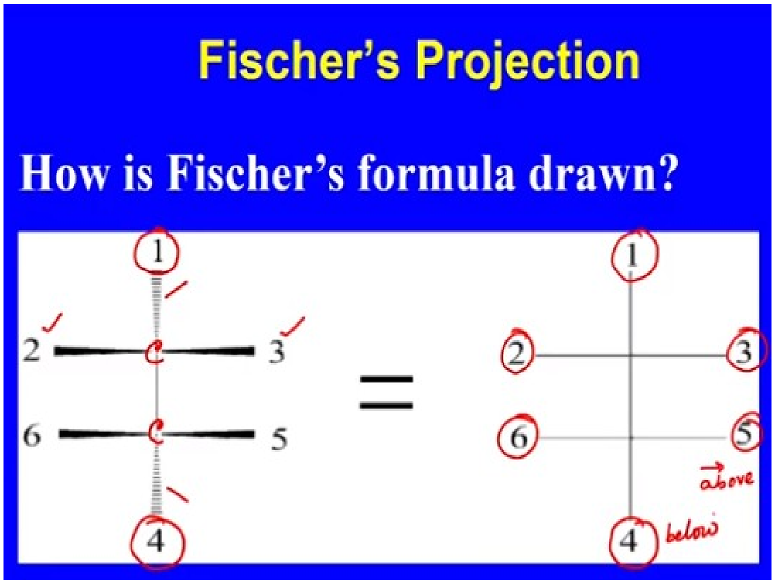

Fischer's Projection

How is Fischer's formula drawn?

So how does it work? So in case of a Fischer projection we first need to identify the different groups that are present in the molecule. We need to identify them with the numbering, so most prior groups like carboxylic acid, aldehyde or cyanide kind of functional groups should be placed at the top and given a number 1 and then from that, the chain should be drawn from top to bottom. So now the way this molecule is shown I have a model here. Suppose this group is 1 OH group, the red one and that is my most important functional group, this red is here.

So the way you see the molecule is that at that particular carbon atom on the top first carbon atom you have 2 red groups pointing towards me and on that group you have 2 atoms pointing like this 2 atoms pointing like that towards you. And this is how it is shown in this first figure on the left hand side, the groups 1 and 4 here in my case are those 2 red atoms which are pointing towards me. And these 2 groups and those 2 groups are pointing towards you.

So now the way this projection is drawn is that the C-C bond, which is in between, the C-C bond is drawn on the plane of the board and based on that C-C bond the 2 oxygen which are below the plane of the board are shown as dashed line. And the 2 other atoms which are on the right and left are shown as the bold wedges which are indicating that these 2 are above the plane of the C-C bond. So when you draw this molecule like that you simply convert it into a diagram like this.

So when we have the vertical line, the terminal atoms on the vertical line are below the plane of projection and the atoms on the horizontal line or the side atoms on the horizontal line are above the plane of projection. So these, orientation of drawing as to be kept in mind whenever we draw a Fischer projection.

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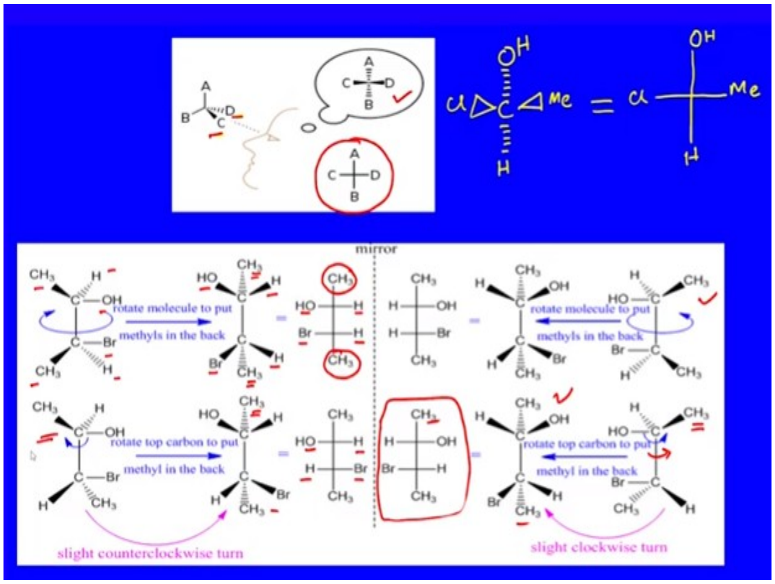

So the way we see such a molecule is to see the molecule like this we should see from 1 particular side and try to draw the molecule as we see the molecule. So from your side if you see the molecule like this what we see is from your side is that the hydrogen is on top oxygen is bottom. So we should rotate it like that so that the oxygen is up and hydrogen is down so what we do is oxygen up, carbon and hydrogen is down may be this is OH and that is hydrogen .

And these 2 groups can be a methyl group and it can be a chlorine atom. Now the way we should draw this is slightly different. What we should draw is to convert this into a Fischer projection it would look like. So this is how we should try to draw the molecule, so here in this figure the observer is seeing the molecule in such a way that A and B are below the plane of projection C and D are above the plane of projection. And that is how we thought about it and then we have drawn the molecule like that.

So here in case of a few real molecules where we have drawn the molecule like this we have methyl groups, we have bromo, OH, hydrogen and hydrogen and it is obvious that the connectivities of this carbon and connectivity of these carbon and that groups are different. So those are chiral centers both of them are chiral centers. So now if you rotated this molecule in such a way about this bond that the 2 hydrogens are on one side and the methyl groups are below the plane of the board both the methyl groups.

We see this molecule like that, we have rotated the entire molecule about the C-C bond so now by rotating we see that this methyl is below the plane, that methyl is below the plane, so those 2 groups have fallen in the vertical line and the hydrogens which are on the right is here in the horizontal line. The bromine and OH which are on the left side are also on the horizontal line indicating that those 4 atoms are pointed upwards from the plane of projection.

So now if we draw the mirror image of this particular molecule we can draw it like that and when we go back to the other side try to understand that what happens if you draw it in this way with the Wedge and Dash formula, we end up getting a different molecule so these 2 mirror images are not super imposable on one another and therefore these two are 2 different enantiomers. Similarly here what we see is that this molecule will rotate in such a way that just the rotate the top carbon to put the methyl group to the back we get this condition.

And then while you draw the Fischer projection, the 2 methyl groups on up and top and bottom are below the plane of projection the O and H here and hydrogen and bromine are pointing upwards from the plane of projection. Similarly the corresponding mirror image would look like this and that mirror image corresponds to this molecule because this methyl and that methyl are below the plane. And then again you just rotate the molecule about its top C-C bond axis you will get this molecule which is different from that starting point. So these 2 compounds are again non super imposable mirror image relations.

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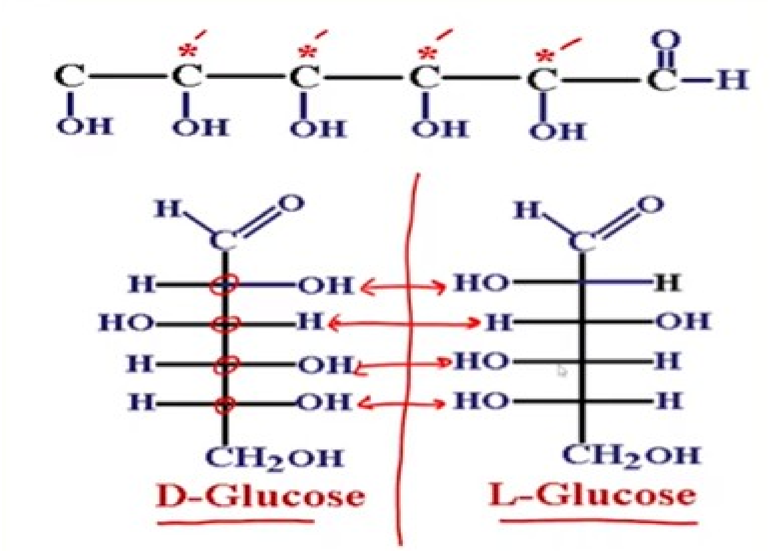

So now when we talk about Glucose we see that this molecule has 4 chiral which are marked as stars. So the way we try to draw this in a Fischer projection is shown here and there are 2 different combinations of glucose which are D and L. And what we see is that, this 2 are basically mirror image of one another. This OH and OH are mirror, hydrogen and hydrogen are mirror and OH and OH are mirror. So when you invert every chiral center the chirality of every center you get the other version.

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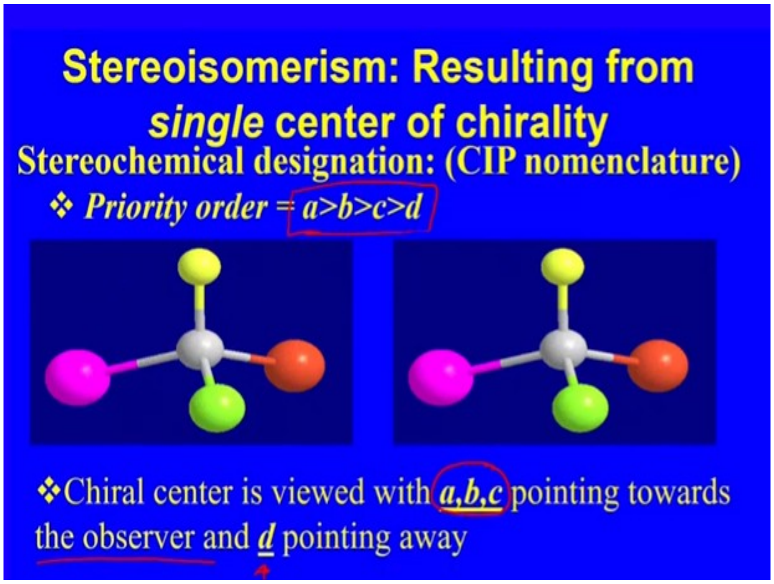

Stereoisomerism: Resulting from *single* center of chirality

Stereochemical designation: (CIP nomenclature)

- *Priority order = a>b>c>d*

- Chiral center is viewed with *a,b,c* pointing towards the observer and *d* pointing away

So when we see that the 4 atoms that are connected to one center gives rise to 2 different isomers or 2 different compounds then we must identify those isomers using some nomenclature. So the stereoisomerism resulting from single center of chirality, we have to have a stereo-chemical designation. So when we trying to designate, again if you remember our rules of IUPAC nomenclature, we have to prioritize groups and based on the group priority we had to give them numbers. And then based on those numbers we used to identify a molecule and write the IUPAC name of the compound.

So in this case we need to prioritize those groups which are bonded to the carbon center and put them in a given priority order. And then the chiral center is observed viewing with a, b and c which are high prior groups pointing towards the observer and the lowest prior group d pointing away from the observer. So what does it mean? It means that suppose if I have this molecule and I need to prioritize these groups may be this is a, that is b and that is c and which we will look at the molecule like this.

The hydrogen has the lowest priority so you should look from the direction opposite to that particular hydrogen atom and look at the molecule and try to identify whether 1 to 2 to 3 it is clockwise or 1 to 2 to 3 is anticlockwise and based on that we will identify those centers as R and S.

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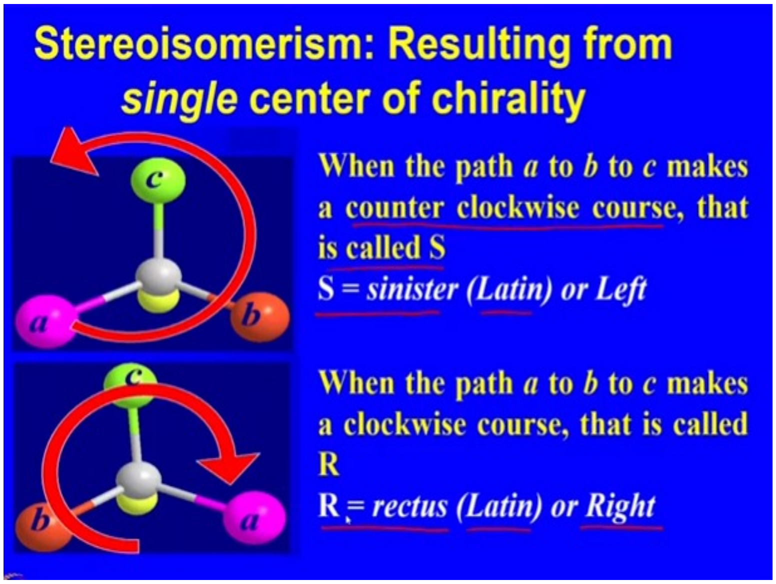

Stereoisomerism: Resulting from *single* center of chirality

When the path *a* to *b* to *c* makes a counter clockwise course, that is called S

S = *sinister (Latin) or Left*

When the path *a* to *b* to *c* makes a clockwise course, that is called R

R = *rectus (Latin) or Right*

So when you see that, when the path a to b to c makes a counter clockwise course, that is called S. So in this particular case it is the opposite, in this particular case if I say that the red is 1 and blue is 2 and this violet is 3, 1 to 2 to 3 is anticlockwise. So this particular compound should be termed as the S isomer or sinister isomer in Latin which means left, so 1 to 2 to 3 here is anticlockwise direction. Remember that you are viewing from the direction opposite to the fourth group.

If I take the second molecule in the same orientation what you can see is that 1 to 2 to 3 is now clockwise rotation 1 to 2 to 3 being in clockwise rotation we call it as rectus Latin which is essentially means right. So clockwise rotation from priority 1 to 2 to 3 makes it R and anticlockwise rotation makes this nomenclature as S. So we identify stereoisomers by writing R or S with the chiral center.

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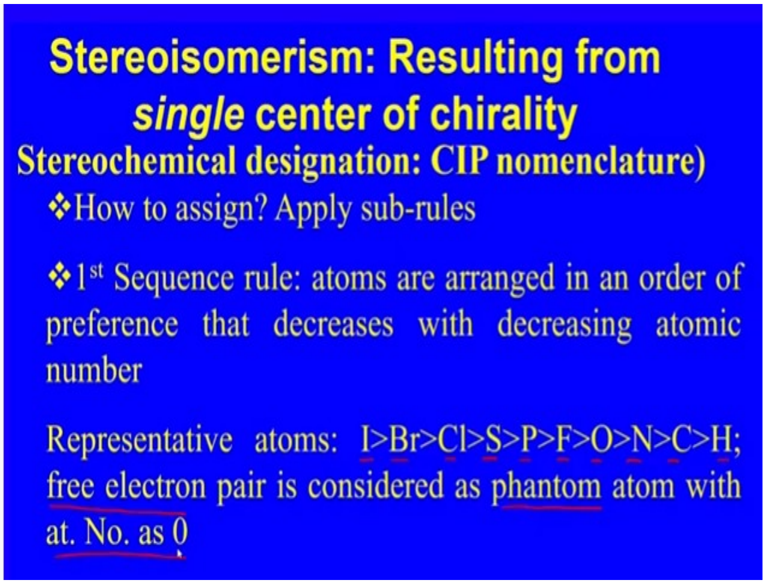

Stereoisomerism: Resulting from *single* center of chirality

Stereochemical designation: CIP nomenclature)

- ❖How to assign? Apply sub-rules
- ❖1st Sequence rule: atoms are arranged in an order of preference that decreases with decreasing atomic number

Representative atoms: I>Br>Cl>S>P>F>O>N>C>H; free electron pair is considered as phantom atom with at. No. as 0

So when we have multiple chiral centers we would follow the rule to identify those chiral centers in terms of their priority and then we apply various sub rules. So the first rule is first sequence rule, atoms are arranged in a order of preference that decreases with decreasing atomic number. So if you have different groups connected to a central atom then the group with highest atomic number gets priority over the atoms which are having lower atomic number.

So in this the order is iodine, bromine, chlorine. Sulfur, phosphorous fluorine oxygen nitrogen carbon hydrogen like that which are in general present in various organic molecules. A free electron pair is considered as phantom atom with atomic number as 0 and is given the lowest priority.

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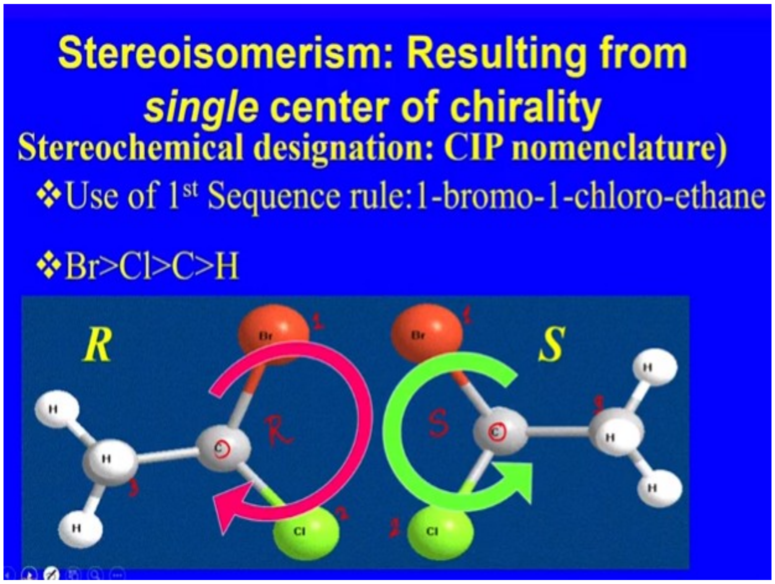

Stereoisomerism: Resulting from *single* center of chirality

Stereochemical designation: CIP nomenclature)

- ❖Use of 1st Sequence rule:1-bromo-1-chloro-ethane
- ❖Br>Cl>C>H

So now use a first sequence rule 1 bromo 1 chloro ethane, bromo chloro carbon and hydrogen and then we draw the molecule like this. There are 2 different isomers that are drawn here. Now we see the molecule in such a way that the hydrogen on this carbon is behind the carbon and on this it is behind this carbon. And then we try to see the priority of those groups, so bromine gets number 1, chlorine is number 2 and this carbon gets number 3.

So 1 to 2 to 3 is a clockwise rotation so we write it as R and in the other case the bromine 1, chlorine is 2, and methyl group is 3. So 1 to 2 to 3 is a rotation in anticlockwise direction so this is the S isomers of 1 bromo 1 chloro ethane.

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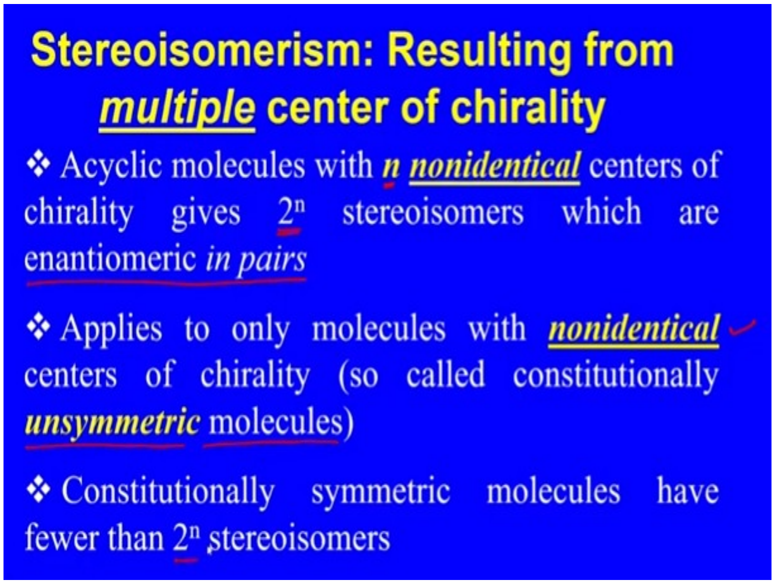

Stereoisomerism: Resulting from *multiple* center of chirality

- ❖ Acyclic molecules with *n* ***nonidentical*** centers of chirality gives 2^n stereoisomers which are enantiomeric *in pairs*
- ❖ Applies to only molecules with ***nonidentical*** centers of chirality (so called constitutionally ***unsymmetric*** molecules)
- ❖ Constitutionally symmetric molecules have fewer than 2^n stereoisomers

Now in most of the cases we see compound which has multiple stereo centers or multiple chiral centers. So in those cases we have to have the priority on those chiral centers as well. Acyclic molecules; with n number of non-identical stereo centers of chirality gives 2 to the power n stereo isomers which are enantiomeric in pairs. We will discuss about this in the few minutes. It applies to only molecules with non-identical chiral centers so called the unsymmetric molecules. Consequently, the symmetric molecules have fewer than 2 to the power n stereo isomers.

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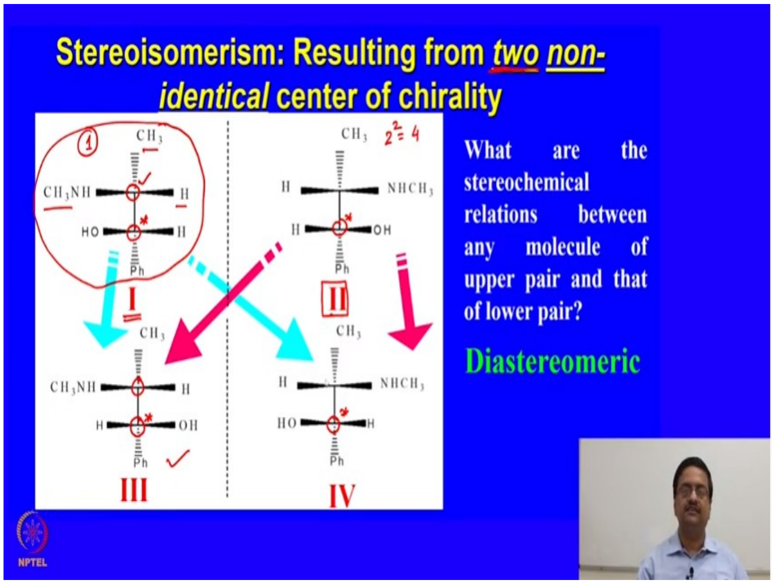

Stereoisomerism: Resulting from *two non-identical* center of chirality

What are the stereochemical relations between any molecule of upper pair and that of lower pair?

Diastereomeric

Let us see with one example so we have in this case 2 non-identical centers of chirality. So what we have here are the chiral centers at this and this points. And these 2 chiral centers are not identical in the sense that the substituents are different in these 2 centers. So therefore it should have 2 to the power 2 that means 4 isomers and those 4 isomers should be enantiomeric pairs. So the way first we can draw this molecule as shown here as number 1.

And the corresponding mirror image is drawn here as number 2 so this 1 and 2 are mirror images of one another. So a pair of enantiomer, and now if we look at the lower molecule in blue they are called diastereomers because their case they are not mirror image of one another. What we see here is that if you place this particular molecule next to this molecule 3, the difference is there only in 1 chiral center which is this one, the other chiral center as the same chirality.

Similarly here the difference arises in this chiral center and not on the other one. So these molecules are called diasteromers.

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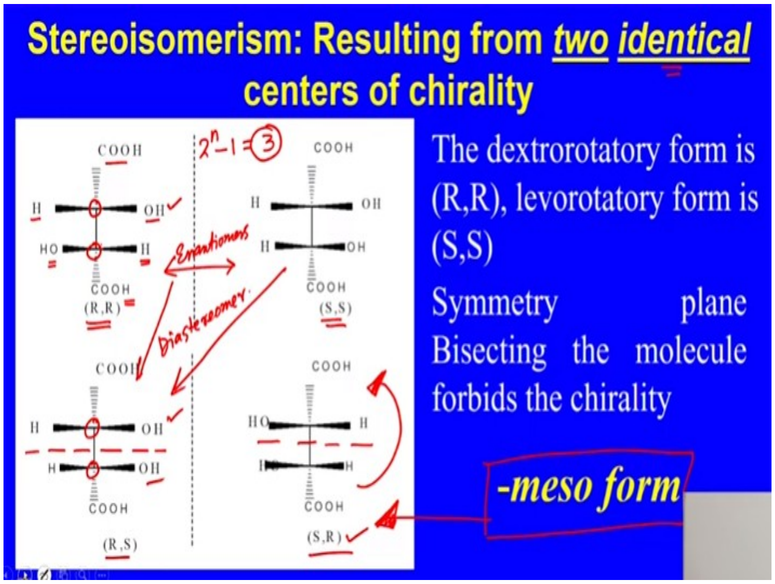

Stereoisomerism: Resulting from *two identical* centers of chirality

The dextrorotatory form is (R,R), levorotatory form is (S,S)

Symmetry plane Bisecting the molecule forbids the chirality

-meso form

Now if we have a different molecule where we have 2 identical centers of chirality when we say identical centers of chirality it means that the groups associated with the each of those chiral centers are same. So what we have here is that carboxyl acid with OH and hydrogen associated with this carbon center. And here this as carboxylic acid, hydrogen and OH associated with the second chiral center. So both the chiral centers have same set of groups. So we said that 2 identical centers of chirality and what we have here is R, R and S, S because these are the 2 centers designated as R, R and S, S.

Whereas the other possibility we are keeping this groups here same we change the second one and make it this one. The corresponding mirror image of R, S becomes S, R but what we see here is that there is a mirror plane in these 2 molecules. So these 2 molecules are not different they are the same molecule because you can rotate this molecule above 180 degree in plane like that and super impose on the other molecule. So they give rise to the same molecule, so these particular pair of isomer is called the meso compounds and it forbids the chirality of this molecule.

So here instead of having 2 to the power n we have 2 to the power n - 1 that is 3 different isomers where these 2 are enantiomers and here the relationship is diastereomer where diastereomers means they are not mirror image of one another.

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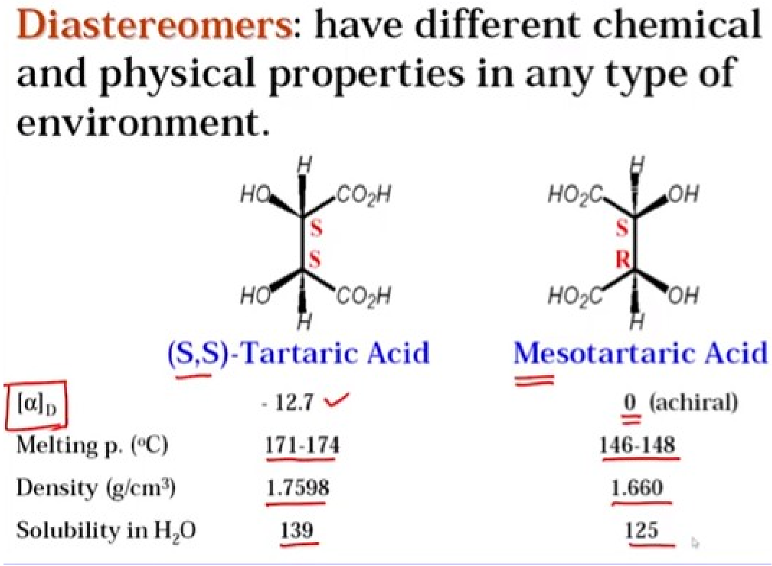

Diastereomers: have different chemical and physical properties in any type of environment.

	(S,S)-Tartaric Acid	Mesotartaric Acid
$[\alpha]_D$	- 12.7 ✓	0 (achiral)
Melting p. (°C)	171-174	146-148
Density (g/cm^3)	1.7598	1.660
Solubility in H_2O	139	125

So when we talk about the diastereomers we should know what is the difference between the diastereomeric pairs? Diastereomers have different chemical and physical properties in any type of environment so when we talk about S, S tartaric acid and the mesotartaric acid, the optical rotation about which we will discuss in the next lecture, the compound S, S has a specific rotation which means it is chiral whereas the mesotartaric acid does not have any optical rotation or specific rotation.

Therefore it is achiral, they have different melting point an all, their densities are different and their solubility in water in grams per liter is also different and these differences are because of there being 2 different set of compound and being diastereomers of the same compound.

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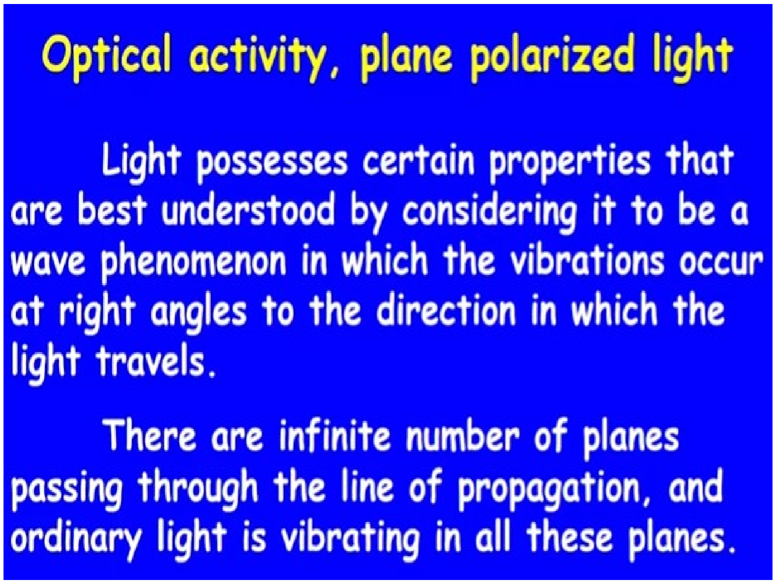

Optical activity, plane polarized light

Light possesses certain properties that are best understood by considering it to be a wave phenomenon in which the vibrations occur at right angles to the direction in which the light travels.

There are infinite number of planes passing through the line of propagation, and ordinary light is vibrating in all these planes.

So in the next lecture we will discuss about the optical activity and plane of polarized light and how the optical activity is used to identity various chiral compounds. So in the next lecture we will start from here thank you.