Symmetry, Stereochemistry and Applications

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Module No # 04
Lecture No # 18
Optical Activity of Organic Molecules and Isomerism

Welcome back to the course entitled symmetry, stereochemistry and applications.

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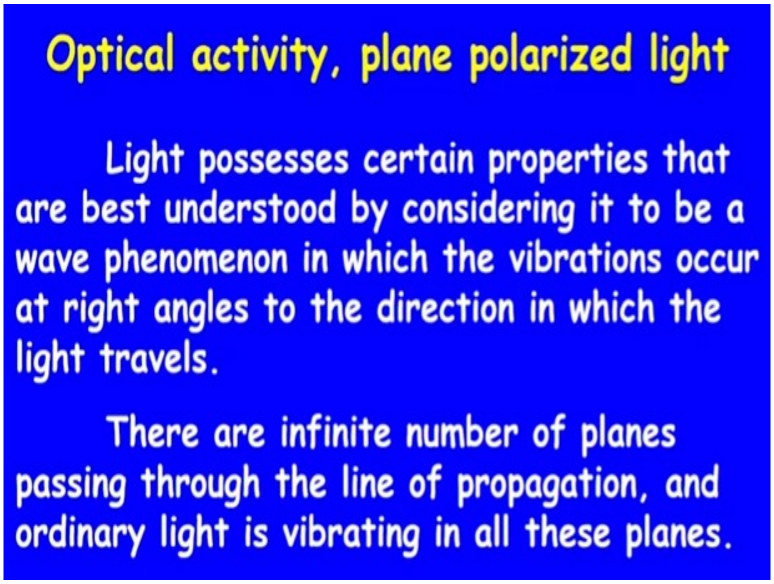

Optical activity, plane polarized light

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.

In today's lecture, we will start discussing about the optical activity of organic molecules. As you know that light possesses the properties which is best understood by considering it to be a wave phenomena in which the vibrations occur at right angles to the direction in which the light travels . So if a light is travelling in this direction towards you then the electric vectors are vibrating in the horizontal plane and the magnetic vectors are vibrating in the vertical plane.

And there are infinite number of such planes in which the electric vectors and magnetic vectors are vibrating at a perpendicular direction. So, each of this possible orientation are orientations of the electric and magnetic vibrations.

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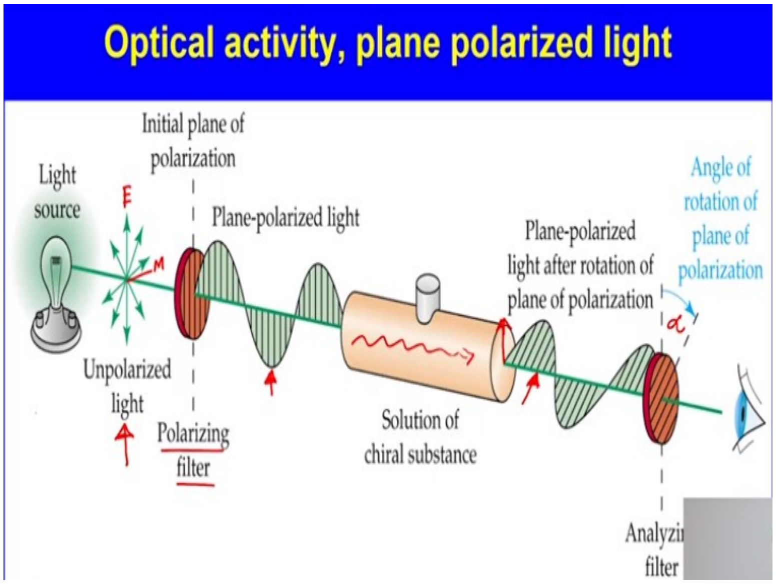

Optical activity, plane polarized light

So when we have a source of light what we have is a straight light where the electric vectors suppose these and the magnetic vectors are vibrating in perpendicular direction and those vibrations are possible in all possible directions. So when we pass this light through a polarizing filter what happens is then it only allows the one part of the light, the electric vector of the light to pass through and this gets polarized in one particular plane.

So this is called the plane polarized light and this plane polarized light, when it is passed through a solution of a chiral compound what is observed is that the plane of polarization is rotated because vibration was happening in this direction. And now the vibration is happening in the different direction and there is a specific angle between the 2 directions called alpha. And as an observer you can see this particular diversion. So based on this we can identify whether an optically active compound is rotating the light in the clockwise direction or in anticlockwise direction.

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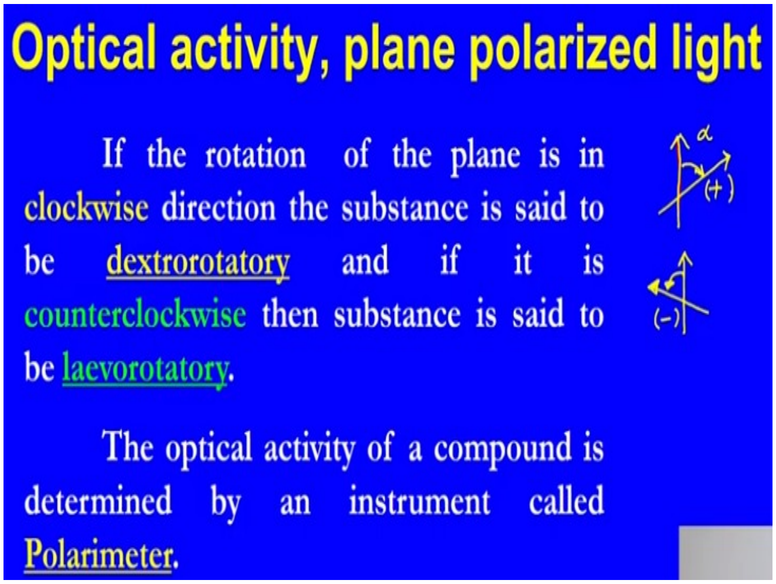

Optical activity, plane polarized light

If the rotation of the plane is in clockwise direction the substance is said to be dextrorotatory and if it is counterclockwise then substance is said to be laevorotatory.

The optical activity of a compound is determined by an instrument called Polarimeter.

A plane polarized light is a light whose vibrations take place in one possible direction or one possible plane. Ordinary light is turned into plane polarized light by passing it through a prism made of a material known as polaroid or more traditionally through a piece of calcite a crystalline form of calcium carbonate. So arranged has to constitute Nicol prism. An optical reactive substance is one rotates the plane polarized light.

If the rotation of this plane is in the clockwise direction then the substance is said to be dextrorotatory and if it is counter clockwise then the substance is said to be laevorotatory. That means if the plane of the incident radiation was in this direction and the rotated plane is in this direction it rotates in the clock wise direction by angle alpha this is called the dextrorotatary sample. And in case if the plane was in this direction before passing through the sample and then it rotates the plane in anticlockwise direction then we call it as a laevorotatory sample.

So this is termed as a plus and this is termed as a minus rotation by convention. The optical activity of a compound is determined by an instrument called polarimeter. You have seen the schematic diagram in the previous slide.

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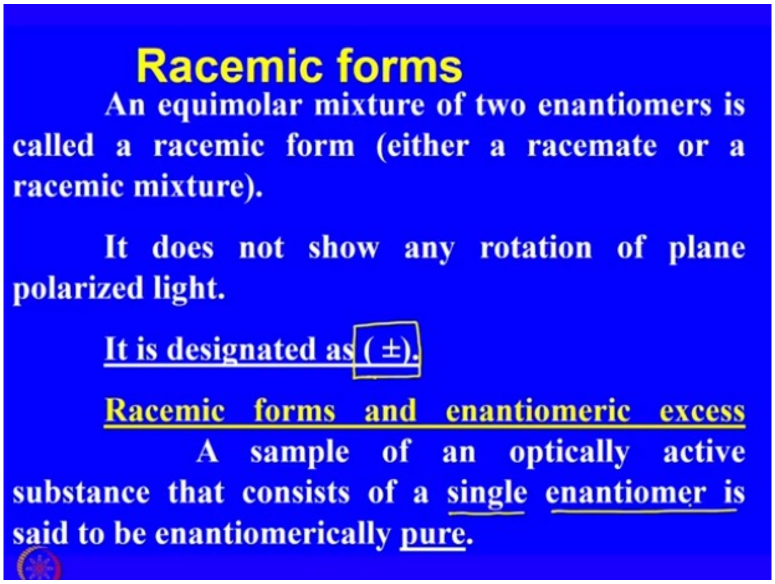

Racemic forms

An equimolar mixture of two enantiomers is called a racemic form (either a racemate or a racemic mixture).

It does not show any rotation of plane polarized light.

It is designated as $\boxed{(\pm)}$.

Racemic forms and enantiomeric excess

A sample of an optically active substance that consists of a single enantiomer is said to be enantiomerically pure.

So when we have an optically active compound, an equivalent mixture of 2 enantiomers is called a racemic form or either a racemate or a racemic mixture which essentially means that you have both the enantiomers present in one is to one ratio giving rise to 0 optical rotation. So it does not show any optical rotation of the plane polarized light and that is why it is designed as a plus minus compound. Similarly racemic forms and enantimeric excess we need to understand.

A sample of an optically active substance that contains a single pure enantiomers is said to be enatiomerically pure. And optical activity of that particular compound identifies the specific rotation of that particular substance.

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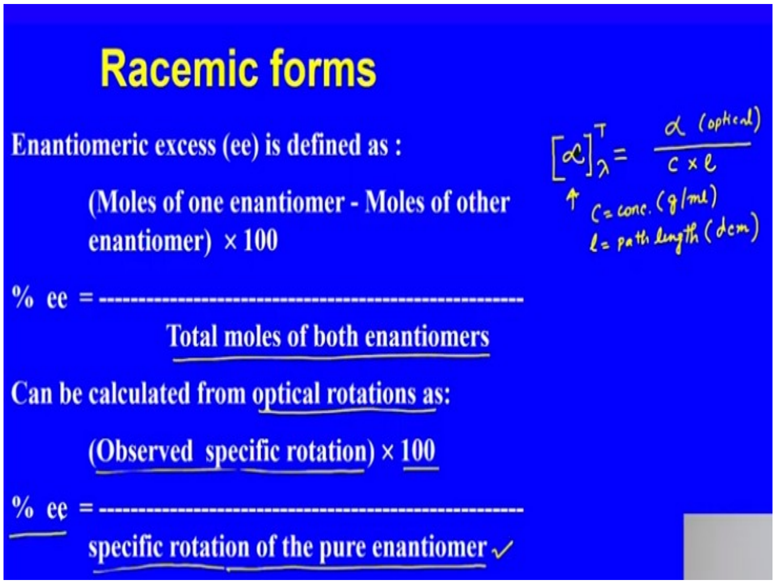

Racemic forms

Enantiomeric excess (ee) is defined as :

$$\% \text{ ee} = \frac{(\text{Moles of one enantiomer - Moles of other enantiomer}) \times 100}{\text{Total moles of both enantiomers}}$$

Can be calculated from optical rotations as:

$$\% \text{ ee} = \frac{(\text{Observed specific rotation}) \times 100}{\text{specific rotation of the pure enantiomer}} \checkmark$$

$$[\alpha]_\lambda^T = \frac{\alpha \text{ (optical)}}{c \times l}$$

↑

c = conc. (g/ml)

l = path length (dcm)

So when we calculate enantiomeric excess it is defined as the moles of one enantiomer minus moles of the other enantiomer multiplied by 100 divided the total number of both the enantiomers that is present. So that can be calculated from the optical rotation as observed specific rotation divided the specific rotation of the pure enantiomer multiplied by 100. So here I have introduced a term called specific rotation, which is written in square bracket with the sign alpha and T and lambda are the 2 constants temperature is mentioned as T normally 25 degree centigrade and the lambda is the wavelength of the light that is used.

In general we use sodium vapor lamp so sodium d line wavelength is used for this measurement. This is nothing but equal to alpha that is the optical rotation that is observed divided by C into l where c is the concentration of the solution and l is the path length of the polarimeter tube. This concentration c is measured in grams per ml unit and this path length is measured in decimeter unit. So this specific rotation is first measured for the pure enantiomer and specific rotation of a mixture of 2 different enantiomers is measured accurately using a known concentration of the solution. And then one can calculate this percentage enantiomeric axis.

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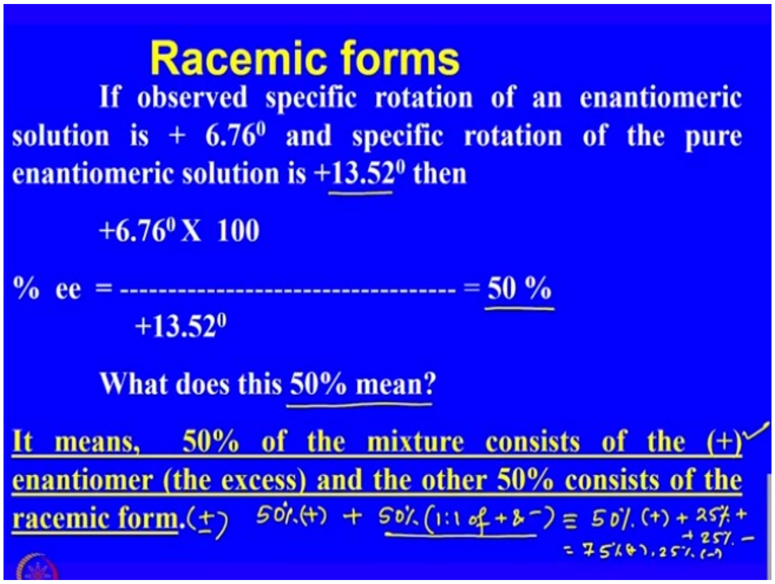

Racemic forms

If observed specific rotation of an enantiomeric solution is + 6.76^0 and specific rotation of the pure enantiomeric solution is $\underline{+13.52^0}$ then

$$\% \text{ ee} = \frac{+6.76^0 \text{ X } 100}{+13.52^0} = \underline{50\ \%}$$

What does this $\underline{50\% \text{ mean?}}$

It means, 50% of the mixture consists of the (+) ✓ enantiomer (the excess) and the other 50% consists of the racemic form.(±) 50%(+) + 50%(1:1 of + & −) ≡ 50%(+) + 25% + + 25% − = 75%(+), 25%(−)

So let us see with one example if the observed specific rotation of an enantiomeric solution is 6.76 degree and the specific rotation of the pure enantiomeric solution is 13.52 degree then, what is the enantiomeric excess percentage? So use the previous formula that we have seen in the previous slide 6.76 degree divided by 13.52 degree into 100 which gives you 50%. Now the question is, what do we mean by this 50% enantiomeric excess. It means 50% of the mixture consists of plus enantiomers that is the excess and the other 50% consists a racemic form which is essentially plus minus.

So what does it mean? I have 50% of plus in excess plus 50% is a mixture of rather 1 is to 1 mixture of plus and minus which essentially means 50% of plus, plus from this part 25% plus and 25% of minus. So overall this is 75% of the plus isomer and 25% of the minus isomer so this is how we should interpret the enantiomeric excess value that is sometimes written in the label of a compound which we may buy from a shop.

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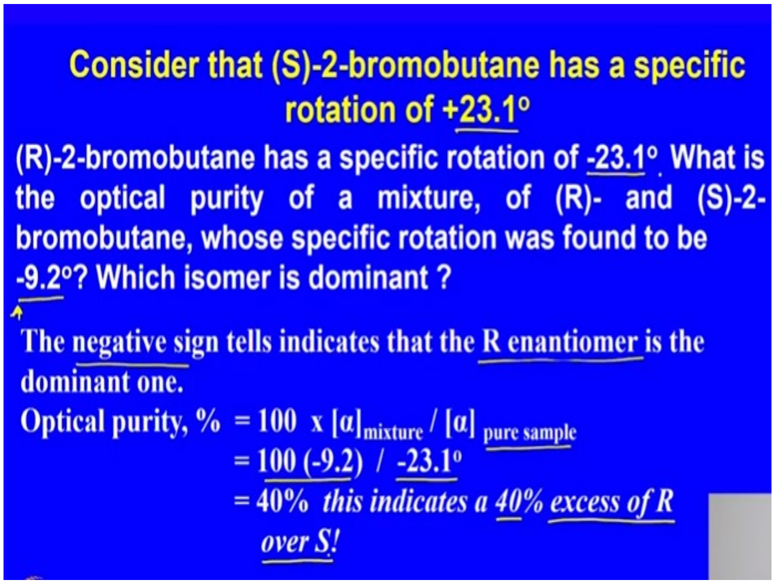

Consider that (S)-2-bromobutane has a specific rotation of +23.1°

(R)-2-bromobutane has a specific rotation of -23.1°. What is the optical purity of a mixture, of (R)- and (S)-2-bromobutane, whose specific rotation was found to be -9.2°? Which isomer is dominant ?

The negative sign tells indicates that the R enantiomer is the dominant one.

Optical purity, % $= 100 \times [\alpha]_{mixture} / [\alpha]_{pure\ sample}$

$= 100\ (-9.2)\ /\ -23.1^\circ$

$= 40\%$ *this indicates a 40% excess of R over S!*

Consider the second case, consider that the S 2 bromo butane has a specific rotation of +23.1 degree. And therefore R will have -23.1 degree it is obvious and that is the optical activity of a mixture of R and S 2 bromo ethane whose specific rotation was found to be -9.2. So we want to know what is the concentration ratio of this R and S. So what we see that the negative sign here tells you that the R enantiomer is in excess or is dominant one because R has negative optical rotation. That means it is rotating the plane in the anticlockwise direction.

So then we can calculate the optical purity as specific rotation of the mixture by specific rotation of pure sample. So we can identify it as 100 into -9.2 divided by -23.1. Therefore the calculation shows that this indicates a 40% excess of R over S. Hope you can follow this.

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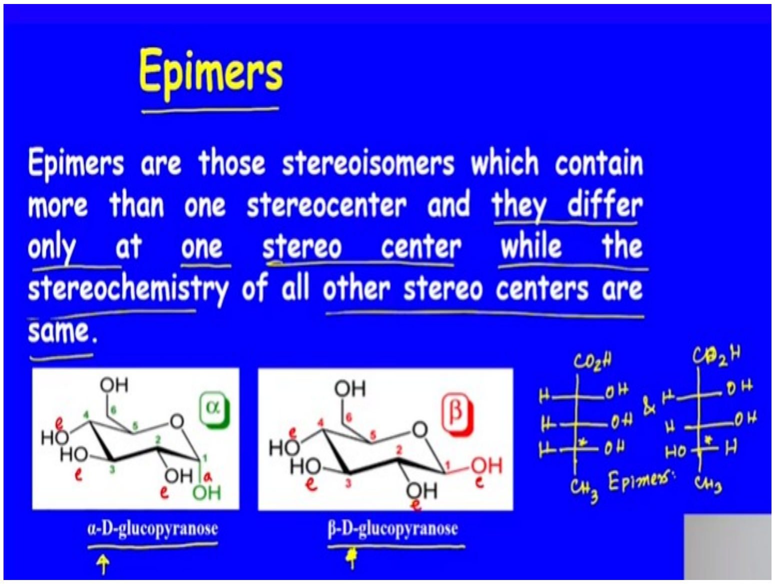

Epimers

Epimers are those stereoisomers which contain more than one stereocenter and they differ only at one stereo center while the stereochemistry of all other stereo centers are same.

α-D-glucopyranose

β-D-glucopyranose

So now we move to in next part of this course where we will try to understand other different possible isomerisms. So in that we need to learn what are epimers? Epimers are those compounds which contain more than 1 stereo center and those compounds differ only at one stereo center while the stereo chemistry of all other stereo centers, are the same. Which means if you have a compound and they have multiple stereo centers except one all stereo centers have this same R or S designation and there is a difference about only one stereo center. So those compounds are called the epimers.

So here we have an example where we have alpha D glucopyranose and beta D glucopyranose, see note this term D which we will discuss in one of the future lectures for the time being you take it as a designation of the chiral center which is designated here. So now in this case you see the chiral centers 1, 2, 3, 4, 5 all of them except one as the same stereo arrangement like this, is in the equatorial plane. This is equatorial, this is also equatorial, this is equatorial, this one is also equatorial, this OH is equatorial, this OH is also equatorial.

But when we look at the OH group at carbon number 1 here it is in the axial position and here it is in the equatorial position. So these 2 isomers are termed as alpha and beta forms of D gluopyranose. So these are called the epimers. Similarly if I try to draw another molecule like this and this molecule where we have 3 chiral centers but the chirality of this point is different in these 2 compounds. So these are also called the epimers, hope you can understand which compounds are called the epimers.

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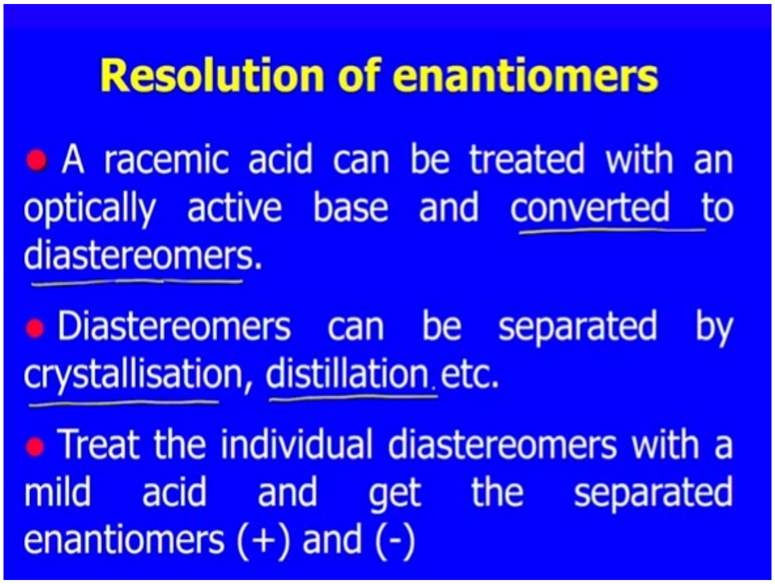

Resolution of enantiomers

- A racemic acid can be treated with an optically active base and converted to diastereomers.
- Diastereomers can be separated by crystallisation, distillation etc.
- Treat the individual diastereomers with a mild acid and get the separated enantiomers (+) and (-)

So when we have a set of different enantiomers in a solution we call it as a racemic mixture. And sometimes we may need to isolate the 2 enantiomers from a given racemic mixture. So a racemic acid can be treated with an optically active base to convert it into diastereomers. We have discussed about diastereomers a bit and we will come back to these once again in the coming lectures. Diastereomers can then be separated by crystallization and distillation methods and sometimes by their solubility as well.

So then we treat the individual diastereomers with a mild acid and get the separated enantiomers out as a plus and minus forms. Now let us try to understand the isomerism in allenes and biphenyl systems.

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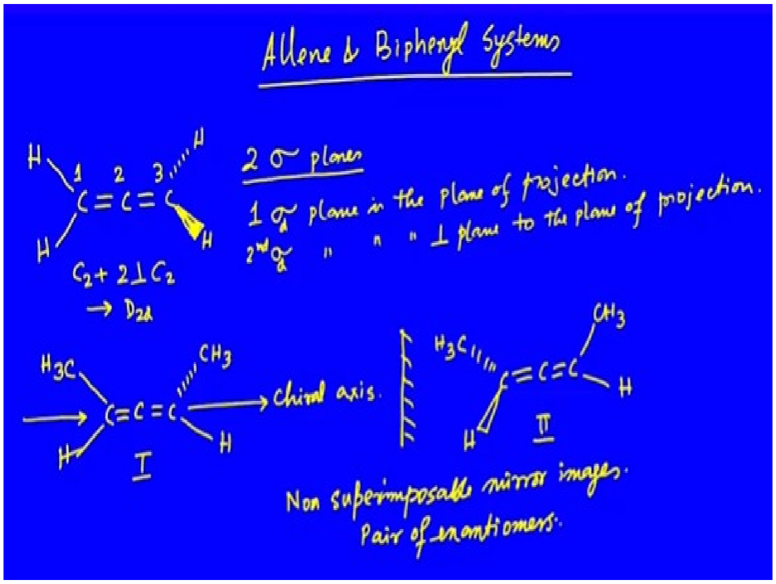

Allene & Biphenyl Systems

2 σ planes

1 σ_d plane in the plane of projection.

2nd σ_d " " " ⊥ plane to the plane of projection.

$C_2 + 2 \perp C_2 \rightarrow D_{2d}$

Non superimposable mirror images.

Pair of enantiomers.

What we know about allene? Allenes are those compounds which contain C double bond C in a row like this. And the 2 hydrogens on the other carbon are above and below the plane of projection. So this contains 2 sigma planes, one sigma plane is the plane of projection and the second sigma plane is the perpendicular plane to the plane of projection. So this compound has, as you know a C2 plus 2 perpendicular C 2's so it gives you the point group D2 and then we have in the past seen that this molecule has the diagonal planes rather sigma D's this sigma's are actually sigma D's.

So we determine the point group as D2d but then when we substitute these hydrogens 2 of the hydrogen numbers on carbon number 1 and 3 by some group. What we see that it gives rise to a chiral axis so suppose if we substitute one of the hydrogens on first carbon by methyl group and the other hydrogen on carbon number 3 by a methyl group. So these gives rise to a chiral axis which is the axis containing the 3 carbon atoms. So when we try to draw the mirror image of this molecule what we see is this one.

What we now clearly see that these 2 molecules that is molecule suppose say 1 and 2 they are non-super imposable mirror image. So they are pair of enantiomers which means we should be able to designate them by the nomenclature of R and S. So let us try to see how those R, S can be done in the next slide.

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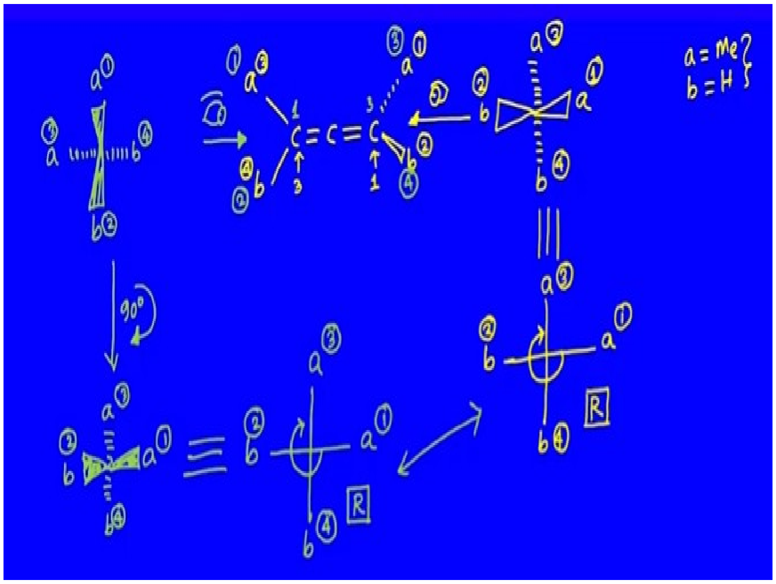

Now suppose we take the molecule like this, with 2 groups having substitutions A and B and on that also I have A and B. Remember A is methyl and B is hydrogen for my simple understanding I am converting it into A and B. So now this molecule has to be converted into the Wedge projection first to make it Fischer projection. Suppose I am looking at this molecule from this side, so what do I see? I see that the molecule as this A and B pointing upwards with respect to the front carbon and it is on the right and left hand side of other observer.

So, on the right hand side of the observer you have the group A on the left hand side of the observer you have group B. When you look at this carbon from the right hand side this A and B will appear above and below but both are pointing away or behind the carbon on which it is connected. So we draw those 2 carbons as the points which are below. Now the question is how we determine the priority? So the priority is determined based on the front carbon first and then the back carbon.

And on the front carbon methyl is higher priority over hydrogen so the priority here is 1 and 2 and on the back carbon the priorities are 3 and 4. I have the priority identified here as 1, 2, 3 and 4, now if you look at this Wedge projection it is depicting the method of Fischer projection in which you should draw a Fischer projection. So we can straight away convert it into a Fischer projection. In Fischer projection the bonds which are in the vertical line are below the plane of projection and the bonds which are in the horizontal line are above plane of projection.

Therefore we can straight away draw the projection like this with the priorities identified. So what we see here we should go from 1 to 2 to 3 it is clockwise rotation that is right. So this is the R isomer of the compound. Now let us try to see what happens if we look at this molecule from the left hand side. I have taken a different color for your easy understanding. So when we are looking at this molecule from the left hand side my first carbon turns out to be this and third carbon turns out to be that whereas in case of the previous figure we have taken that as 1 and that as 3.

So now when we are looking at this molecule from the left hand side what we have is A and B which are pointing towards me like this. So these 2 groups which; are in front of me pointing towards me above the plane of projection. So those 2 groups should come like that and the 2 groups which are on the back carbon are pointing like this and on the right I have B on the left I have A, sorry on the right I have B and on the left you have A.

Now what about the priority? Once again now the priority will be on the first carbon so the groups on the first carbon will get the priority, higher priority 1 and 2. And the groups on the back carbons will get priority 3 and 4. So this 1 and 2 comes here and 3 and 4 comes in the horizontal line. Now you see here this particular projection is not in the way a Fischer projection should be drawn. So what we should draw is we should rotate the molecule in plane by 90 degree and come to this projection where I have group A.

Where I have group A number 3 at the top group B at the bottom which is 4 and the group which was A at the top comes to the right hand side as number 1. And the group at the bottom which was number 2 comes to the left as 2 so now this orientation where vertical line contains bonds which are below the plane of projection and the horizontal line contains the bonds which are above the plane of projection. So it can be converted into a Fischer position like this.

Now you see the priorities are again as it was before. So now again 1 to 2 to 3 is clockwise rotation and this clockwise rotation means the right hand side rotation. So this isomer is the R isomer. So what we can see that a particular molecule looked at from either side turns out to be the same absolute configuration. Therefore this molecule is the R isomer 1, 3 dimethyl allene so if we take the molecule which is the other enantiomer we will try to find out what would be the S isomer in the following class.