Symmetry, Stereochemistry and Applications

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Module No # 05
Lecture No # 22
Stereoisomerism and Local Symmetry

Welcome to the course on symmetry stereochemistry and applications. In the previous lecture we have discussed about asymmetric and dissymmetric.

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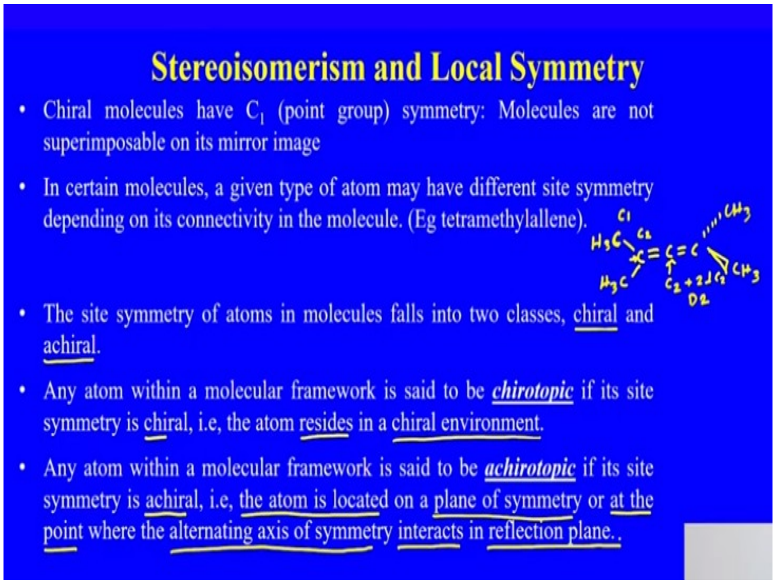

Stereoisomerism and Local Symmetry

- Chiral molecules have C_1 (point group) symmetry: Molecules are not superimposable on its mirror image
- In certain molecules, a given type of atom may have different site symmetry depending on its connectivity in the molecule. (Eg tetramethylallene).
- The site symmetry of atoms in molecules falls into two classes, chiral and achiral.
- Any atom within a molecular framework is said to be ***chirotopic*** if its site symmetry is chiral, i.e, the atom resides in a chiral environment.
- Any atom within a molecular framework is said to be ***achirotopic*** if its site symmetry is achiral, i.e, the atom is located on a plane of symmetry or at the point where the alternating axis of symmetry interacts in reflection plane..

So in this lecture we are going to discuss on the stereoisomerism and local symmetry. So what we know about chiral molecules that have C1 point group symmetry so molecules are non-super imposable on its mirror image just like the right hand and left hand cannot be super imposed. The chiral molecules having C1 symmetry so they cannot be super imposed on the mirror image. In certain molecule the given type of atom may have different side symmetry depicting on its connectivity in the molecule.

For example the tetramethylallene so if you try to draw tetrmethylallene here what we see is this. So this particular carbon has a symmetry C1, this particular carbon has a symmetry C2 and also this particular carbon has a symmetry C2 + 2 perpendicular C2's where which essentially means D2 symmetry. So, different atoms in a molecule can have different site symmetry in the molecule.

This site symmetry of atoms in molecules falls into 2 classes chiral and achiral so in a molecule a site of a carbon atom can be of 2 types can be a chiral site or an achiral site. Any atom within a molecular frame work is said to be chirotopic if it is side symmetry is chiral that is the atom resides in a chiral environment. Any atom molecular frame work is said to be achirotopic if it is site symmetry is achiral.

That is the atom is located on a plane of asymmetry or at the plane of point where the alternating axis of symmetry interact in reflection plane. So we will try to understand this in the next few slides.

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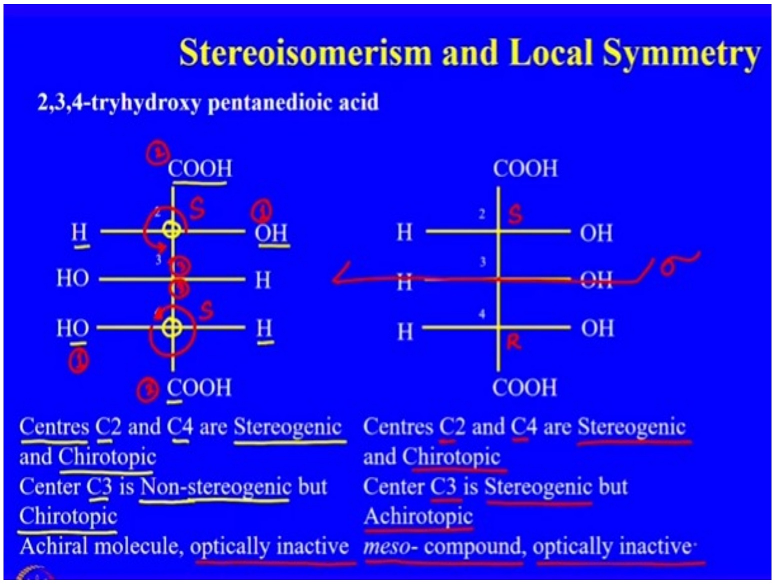

Stereoisomerism and Local Symmetry

2,3,4-tryhydroxy pentanedioic acid

Centres C2 and C4 are Stereogenic and Chirotopic
Center C3 is Non-stereogenic but Chirotopic
Achiral molecule, optically inactive

Centres C2 and C4 are Stereogenic and Chirotopic
Center C3 is Stereogenic but Achirotopic
meso- compound, optically inactive

Let us try to see what happens in case of 2, 3, 4-tryhydroxy pentanedioic acid. So what we see in this molecule that we have 3 achiral centers marked as 2, 3 and 4. And as you can see that this molecule can have different configuration at chiral centers 2, 3 and 4 depending on the orientation of the OH groups whether it is on the right hand side or left hand side of the vertical line in this Fischer projection. So what we see here is the centers C2 and C4 are stereogenic and chirotopic.

What do you mean by stereogenic center? That means at the point 2 and 4 we have 3 different groups associated with it or rather 4 different groups associated with those points. So that is the chiral center 2 and 4, have 4 different groups associated with them. So they are stereogenic centers and also they are chirotopic centers because they are in chiral environment. But in case of C3 we say that it is a non-stereogenic center but a chirotopic center what does it mean?

To understand that we need to find out the absolute configurations of the point 2 and 4 so in case of points 2 and 4 if we try to identify the priority order of those groups to identify whether it is R or S we should get the priority list done first. So this OH group is priority 1 the carboxyl acid group has a priority 2 and the group at the down as a priority 3. So when we go from 1 to 2 to 3 it is rotating in anti-clockwise direction. So it should be R but when we see the lowest priority is in the horizontal line so the actual identification of this chiral center should be S.

Similarly if we do the same for the chiral center 4 this is priority 1 this is the priority 2 and that group is priority 3. So if we do 1 to 2 to 3 what we see is it is again anti-clockwise and the lowest priority group is in the horizontal line so this center is also S. As a result this particular carbon that is C3 is a non-stereogenic because the groups above and below have the same chirality. So those 2 groups are not different but then why it is chirotopic?

Because the environment here has 4 groups which are different so it is a chirotopic center so what we see here is that, this molecule is achiral because the groups on top and the bottom are same and therefore this molecule is optically inactive. If we see the other isomer of this compound where all the 3 OH groups are on 1 side what we see the center C2 and C4 are stereogenic and chirotopic as it was before.

But center C3 is now stereogenic why? Because this carbon is absolute configuration S this carbon has now changed the position of OH. So this carbon as the configuration R but this point number 3 has a mirror plane passing through it. As a result these particular carbon C3 is not in a chiral environment therefore this center is called achirotopic center therefore this compound which has a mirror plane is called a meso compound and hence this compound is also optically inactive.

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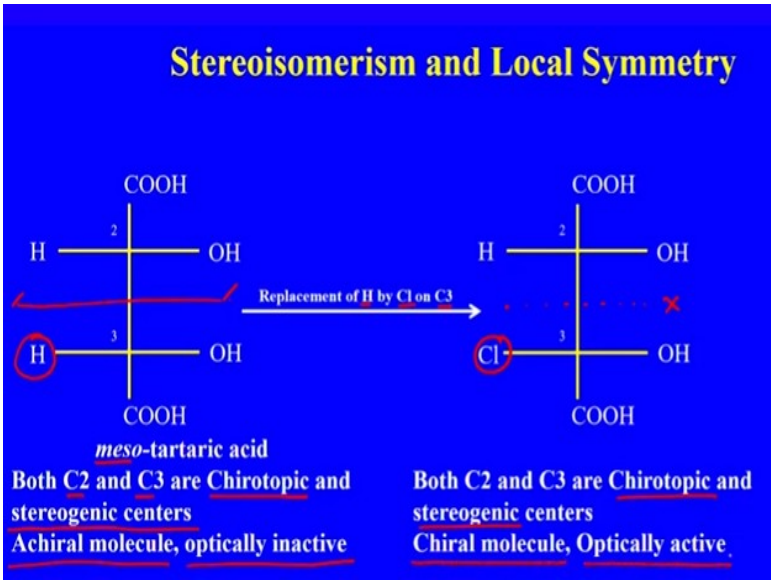

Stereoisomerism and Local Symmetry

meso-tartaric acid

Both C2 and C3 are Chirotopic and stereogenic centers

Achiral molecule, optically inactive

Both C2 and C3 are Chirotopic and stereogenic centers

Chiral molecule, Optically active

Now let us try to see with another example of mesotartaric acid, so in this case what we have? We have 2 carbon centers, C2 and C3 both C2 and C3 are chirotopic and stereogenic centers because in both the cases you have different substitutions present at this carbon C2 and C3. And this molecule has a mirror plane that is present therefore this molecule is called the meso compound or mesotartaric acid therefore this compound is an achiral compound and therefore optically inactive.

Now what we are trying to do is we are trying to replace H by chlorine on C3 so this hydrogen is now replaced by chlorine on C3. So what has happened here is that both C2 and C3 are as before chirotopic and stereogenic and the mirror plane which was present before is now absent. Therefore this molecule is converted to a chiral molecule and therefore it is optically active.

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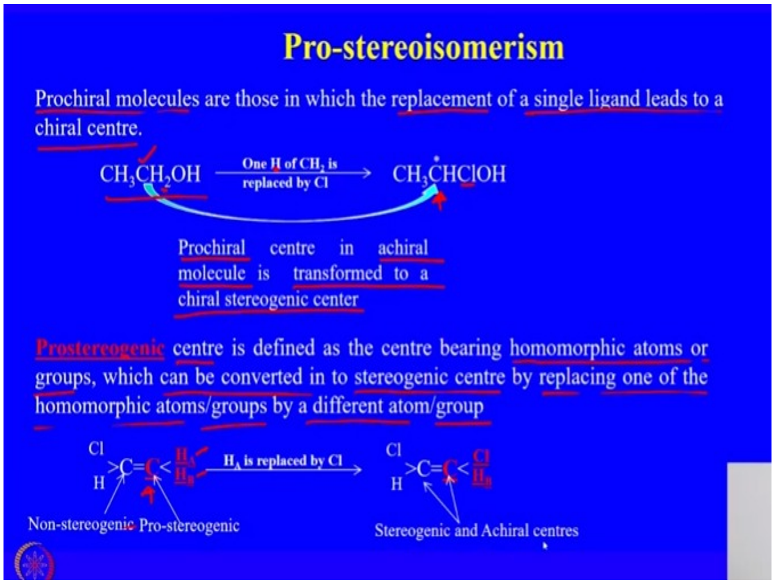

Pro-stereoisomerism

Prochiral molecules are those in which the replacement of a single ligand leads to a chiral centre.

$CH_3\overset{}{C}H_2OH \xrightarrow[\text{replaced by Cl}]{\text{One H of } CH_2 \text{ is}} CH_3\overset{*}{C}HClOH$

Prochiral centre in achiral molecule is transformed to a chiral stereogenic center

Prostereogenic centre is defined as the centre bearing homomorphic atoms or groups, which can be converted in to stereogenic centre by replacing one of the homomorphic atoms/groups by a different atom/group

$\mathrm{(Cl)(H)}>C=C<\mathrm{(H_A)(H_B)} \xrightarrow{H_A \text{ is replaced by Cl}} \mathrm{(Cl)(H)}>C=C<\mathrm{(Cl)(H_B)}$

Non-stereogenic Pro-stereogenic

Stereogenic and Achiral centres

Now let us try to understand the new term called pro-stereoisomerism. Prochiral molecules are those in which these replacement of a single ligand leads to a chiral center. That means you have a molecule where you select one particular atom and replace it with something else. Then you generate a new chiral center and the compound becomes a chiral molecule then that particular carbon center is called a prochiral center and a molecule is called the prochiral molecule.

So let us see these with a very simple example of ethanol so in case of ethanol if we replaced 1, hydrogen of the CH2 group here by chlorine we get this particular molecule which is 2 chloro ethanol. And what we see is the second carbon here or rather the carbon number 1 with which the Cl and the OH are connected is a chiral center and these, becomes a chiral compound. So by doing this a prochiral center which is this one in achiral molecule which is ethanol is transformed to a chiral stereogenic center by a single replacement.

So then we call ethanol as a prochiral molecule and C1 of ethanol is a pro chiral center, so pro stereogenic center is defined as the center bearing homomorphic atoms are groups which can be converted into stereogenic center. By; replacing one of the homomoprhic atoms; or groups by a different atom or group. So we will understand this by the following example. So in this particular compound what we see is? It is simple chloroethene so the carbon which is marked as red is a pro stereogenic center and those hydrogens are called the homomoprhic atoms.

The other carbon in white color is a non-stereogenic center the other carbon is a non-stereogenic center. So when we try to replace Ha by chlorine we get this molecule. So what we see is now that both the centers are stereogenic and achiral centers.

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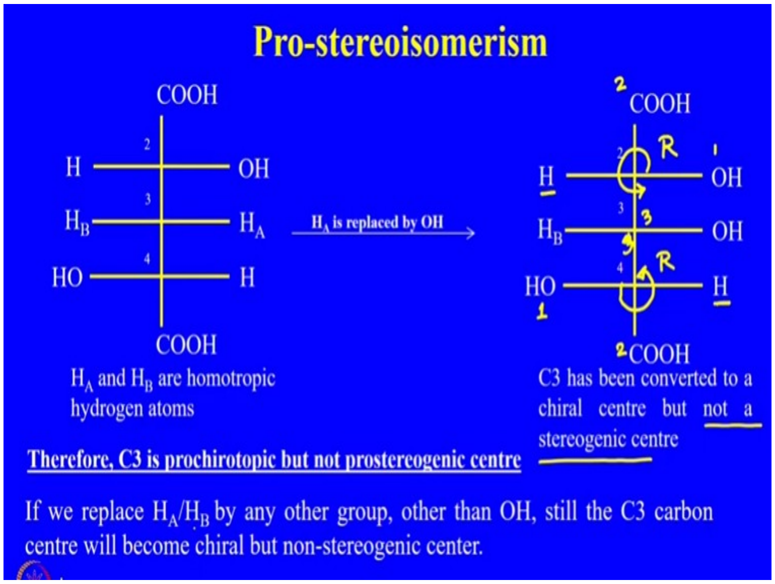

Pro-stereoisomerism

H_A and H_B are homotropic hydrogen atoms

C3 has been converted to a chiral centre but not a stereogenic centre

Therefore, C3 is prochirotopic but not prostereogenic centre

If we replace H_A/H_B by any other group, other than OH, still the C3 carbon centre will become chiral but non-stereogenic center.

So let us try to take one more example to understand pro stereoisomerism. So in this example if you can see there are 2 hydrogen atoms Ha and Hb located on the carbon center 3 this 2 hydrogens are homotopic hydrogens because these replacement of these 2 by another group will mean that it will result into the same compound. So if we replace Ha by OH we would get this particular compound.

So now what we see here that C3 has been converted to a chiral center but not a stereogenic center how? Let us try to identify the absolute configurations of the carbon centers 2 and 3. So when we try to find out the absolute configuration of 2 and 3 we need to identify the priority order of the groups connected to carbon number 2. So this group OH is 1 this CO2H gets priority 2 and the group here gets priority 3.

So 1 to 2 to 3 anticlockwise so it should be S but the lowest locant, the lowest priority group in the horizontal line. So the absolute configuration of that center should be R on the other hand, for the chiral center 4 this OH group is 1 carboxylic acid is 2 and that group on the up is 3. So again if we go from 1 to 2, 2 to 3 it is anticlockwise so should be S but this lowest priority group is in the horizontal line so this group should be R.

So what we see here is that two groups at 2 and 4 have same absolute configuration so this center 3 is not a stereogenic center but center 3.But it has been converted to a chiral center by replacement of 1, hydrogen by OH group. So therefore C 3 is pro chirotopic but not pro stereogenic center and if we replace Ha or Hb by any other group say chlorine, bromine whatever other than OH.

Still that C3 carbon center will become chiral but non-stereogenic center. So we will continue this lecture from here in the next class thank you