Stereochemistry
3 -Two Chiral Centers and Cyclic Structures

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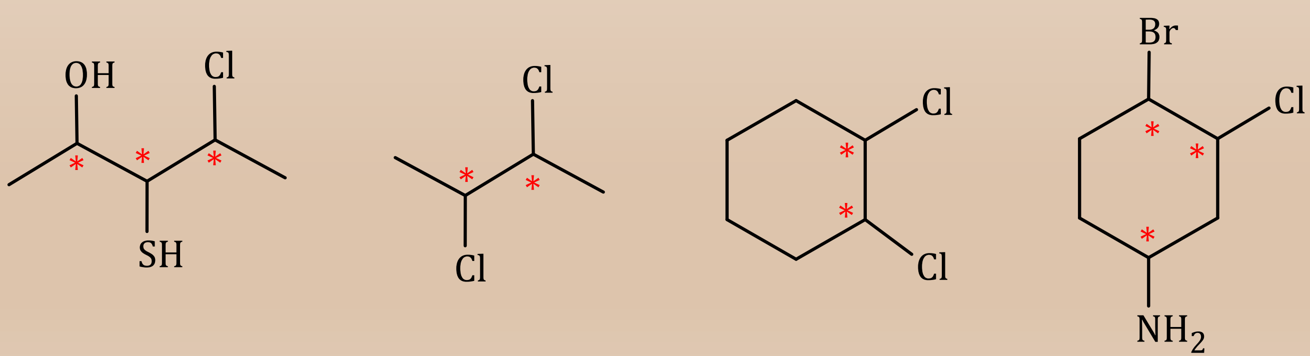
More than One Chiral Centers

Molecules can have two or more chiral centers and therefore there will be more enantiomers, determined by the number of chiral centers. Enantiomers are only the mirror images, so the other isomers are still stereoisomers but have a different relationship.

The total number of stereoisomers can be determined by the formula 2^n, where n is the number of chiral centers. A compound with 2 chiral center will have 2^2 stereoisomers and one with 4 will have 2^4, 16 stereoisomers.

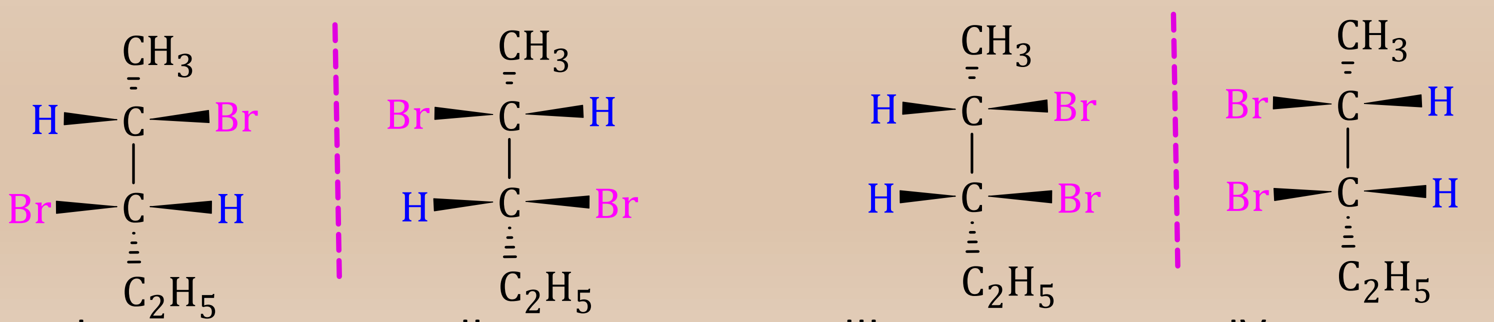
The two or more chiral centers can exist in straight chain as well as cyclic compounds. Some examples of compounds with two or more chiral centers are given below.



Molecules With Two Chiral Centers

Molecules with two chiral centers will have 4 stereoisomers, calculated from the formula 2^n, where n is 2. See the structures I – IV given below to understand the next few points.

- Each of the two chiral centers will have a pair of enantiomer, hence the four stereoisomers. To get III from I, we have to break the bottom C-Br and C-H bonds and exchange them because the spatial arrangement of the other groups do not change.
- There are two pairs of enantiomers (I and II) and (III and IV).
- The relationship between the non mirror image stereoisomers is called "<u>diastereomers</u>". These are stereoisomers that are not mirror images of each other. These are: I and III, I and IV or II and III or II and IV in the structures below. Diastereomers gave different physical properties and can be separated.



I II III IV

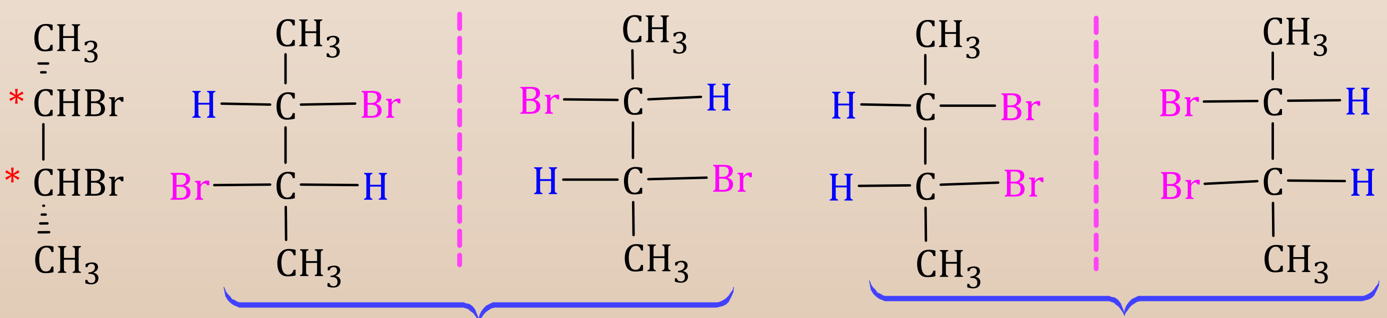
Two Chiral Centers

For two chiral centers, there are a few more points to consider.

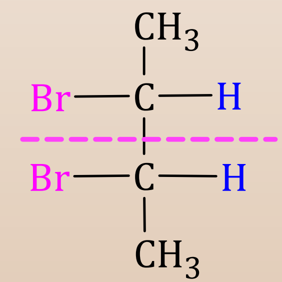
1. The previous properties of enantiomers are still valid, that their physical properties are the same except for optical rotation in equal but opposite direction.
2. Diastereomers have no optical relationship., i.e. the isomers have different optical rotations. The biggest difference between diastereomers is that they have different physical properties.
3. It is important to understand the concept of symmetry. If a molecule has internal symmetry, then the enantiomer will superimpose on each other. The pair of enantiomers will be optically inactive – it will be achiral.
4. Achiral means no optical activity. The compound can still have a chiral center.

Two Chiral Centers - Dibromobutane

Consider the following isomers given below. (I, II) and (III, IV) are the mirror images. I and II are enantiomers as they cannot be superimposed on each other. Moving one Br (not rotating) from structure I from one position to another gives III. The mirror image of III is IV. However, even though they have a chiral center, they are not optically active. They are achiral.



I II III IV

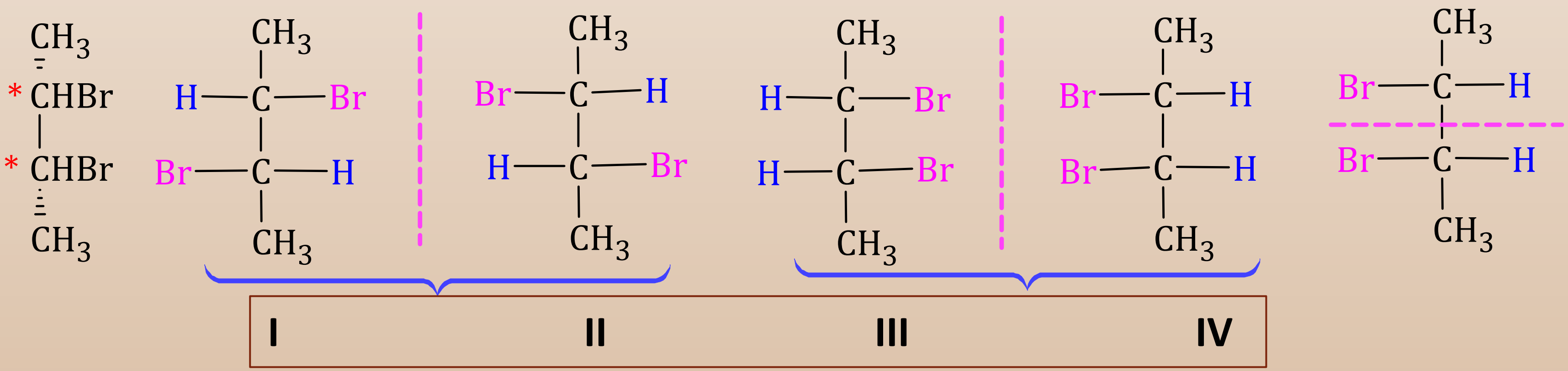


Has a plane of symmetry

The reason for achirality is that the mirror images (III and IV) are superimposable on each other. These stereoisomers are called "<u>meso</u>". Another way of looking at meso isomer is the internal plane of symmetry in molecule III (or IV).

Two Chiral Centers - Meso Compounds

Some Observations: The molecule below does not follow the 2^n rule of isomers since one pair (III and IV) is the same. There are three stereoisomers instead of the calculated 4 because the meso pair is not optically active. The meso pair will still have chiral centers and those chiral centers have the R/S configuration depending on the group priorities as usual.

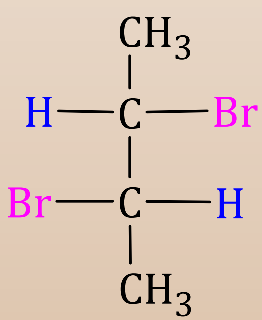


Watch the video (Stereo Video 6) to learn about diastereomers and meso. See the link in the "Description".

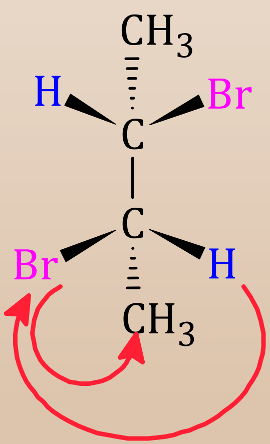
Two Chiral Centers - Naming

Naming of two chiral center follows the same guideline as for a single chiral center, assign priorities according to atomic number, keep the lowest priority group at the back and see if priority assignment is clockwise or anticlockwise.

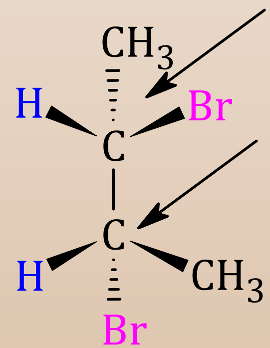
- The molecule is manipulated to assign R/S of each stereocenter separately.
- The compound below is (*2S*, *3S*)-2,3-dibromopentane. The straight bond line structure is the Fisher projection which is represented as 3D in the second structure.

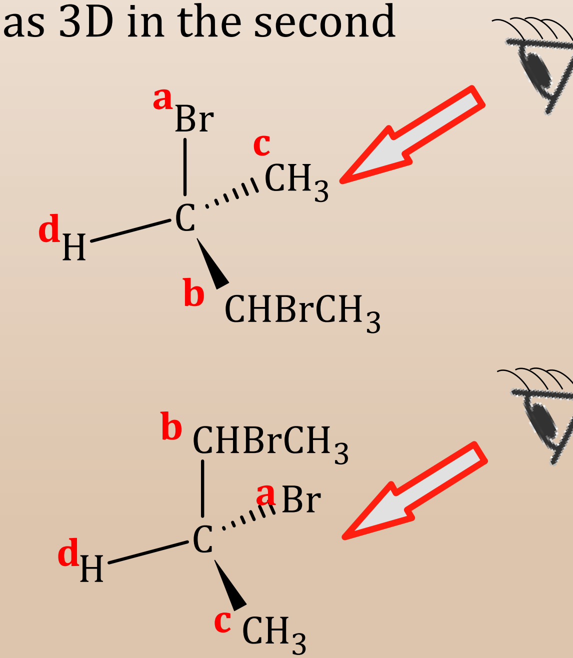


Fisher projection



3D projection



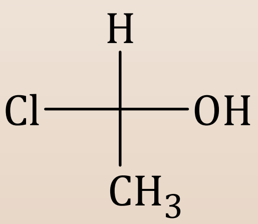


Watch the video (Stereo Video 8) to learn R/S configuration for two chiral centers. See the link in the "Description".

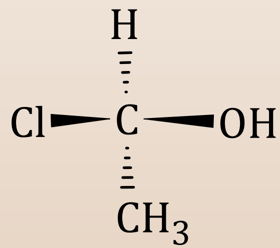
Fisher Projections

A 2-dimensional representation of chiral molecules.

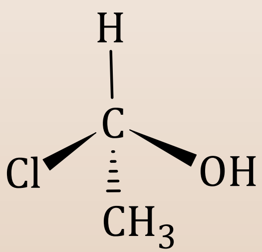
- Vertical lines represent bonds that project behind the plane of the paper
- Horizontal lines represent bonds that project out of the plane of the paper



Fisher Projection

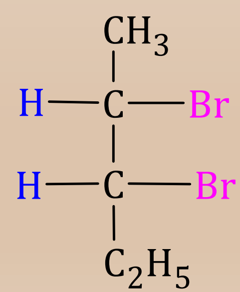


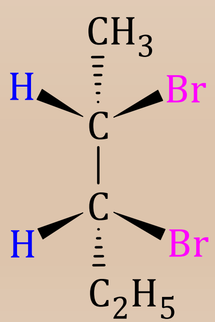
Conversion to 3D representation



Tilt the molecule towards yourself to see another tetrahedral view for easier R/S configuration determination.

Fisher to 3D representation for 2 chiral centers is as follows: the bond between th two chiral centers is in the plane, while the two horizontal atoms are coming out of the plane and top and bottom are behind the plane.





Two Chiral Centers – Cyclic Compounds

In cyclic compounds with two chiral centers, we have to take into account three things:

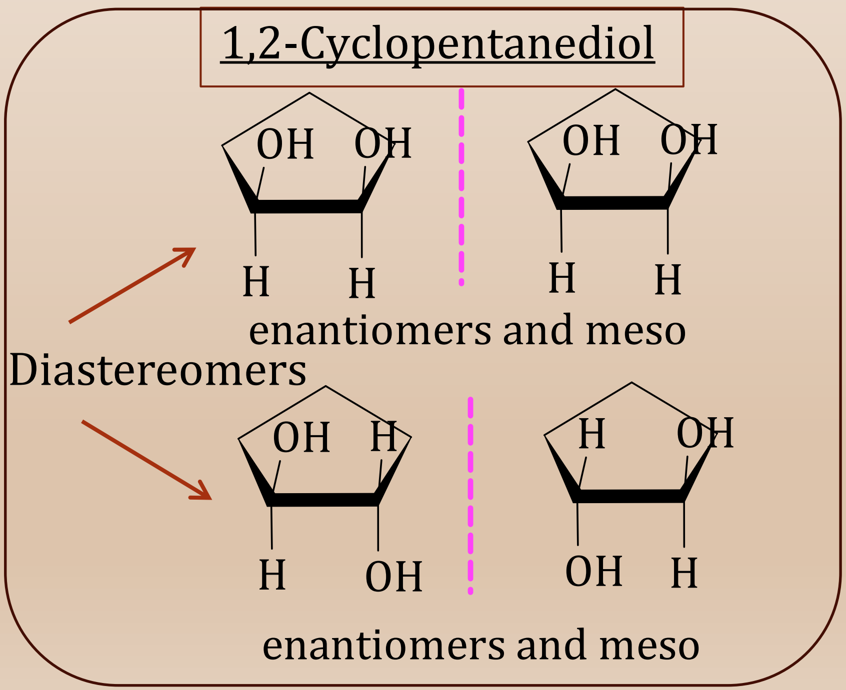
1) The groups on the stereocenter: If the groups on those chiral center are identical then there are chances that the molecule can have internal symmetry and can be meso (no optical activity). If the groups are different, then there is no chance of internal symmetry.
2) Size of the ring: A five membered ring is more planar than a six membered ring and has a better chance of superimposition of enantiomers.
3) Cis and trans isomers. The geometric location of these groups can also affect the plane of symmetry in the ring which then may be a meso or not.

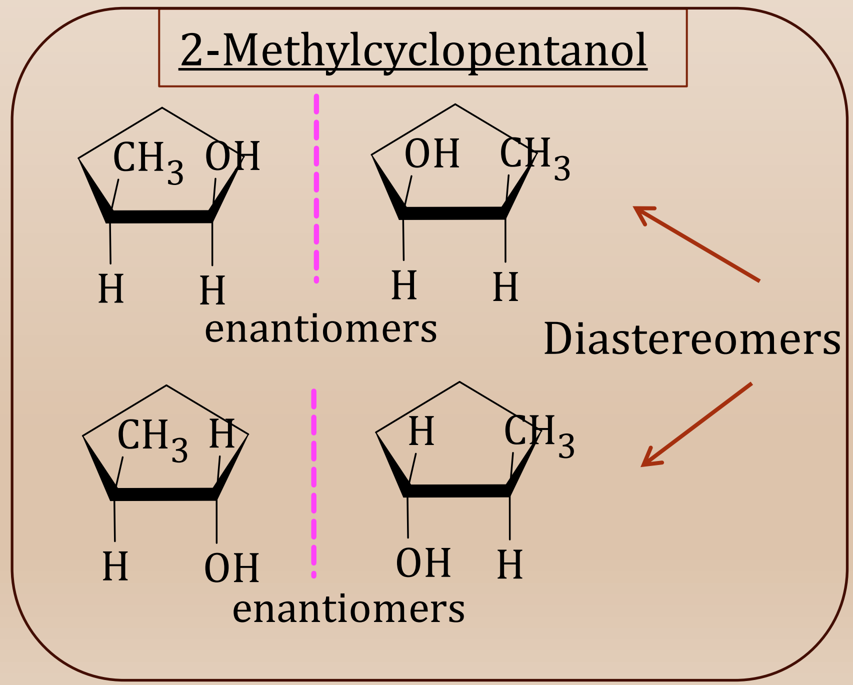
See the examples on the next few slides for 5 and 6 member rings with two chiral centers.

Two Chiral Centers – 5 Membered Ring

If the groups on the chiral center are identical then the molecule can have internal symmetry and can be meso (no optical activity).
See example below for 1, 2-cyclopentanediol.

If the groups are different, then there is no possibility of internal symmetry and enantiomers will have optical activity.
See example below for 2-methylcyclopentanol.

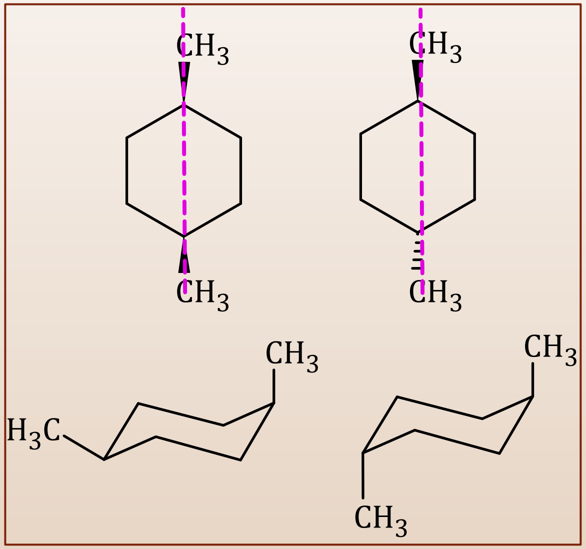




Two Chiral Centers – 6 Membered Ring

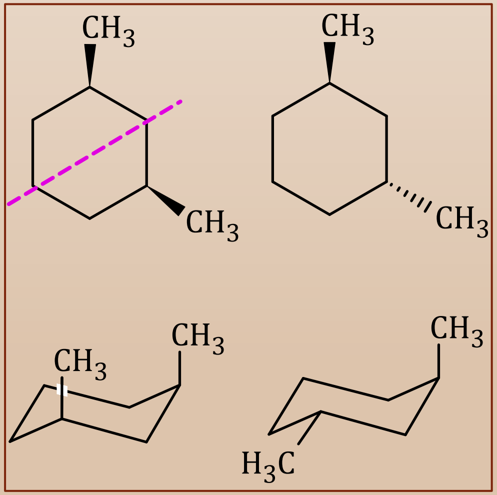
1,4-dimethylcyclohexane (shown on the right)

- Neither of the two isomers is optically active.
- Both have a plane of symmetry.



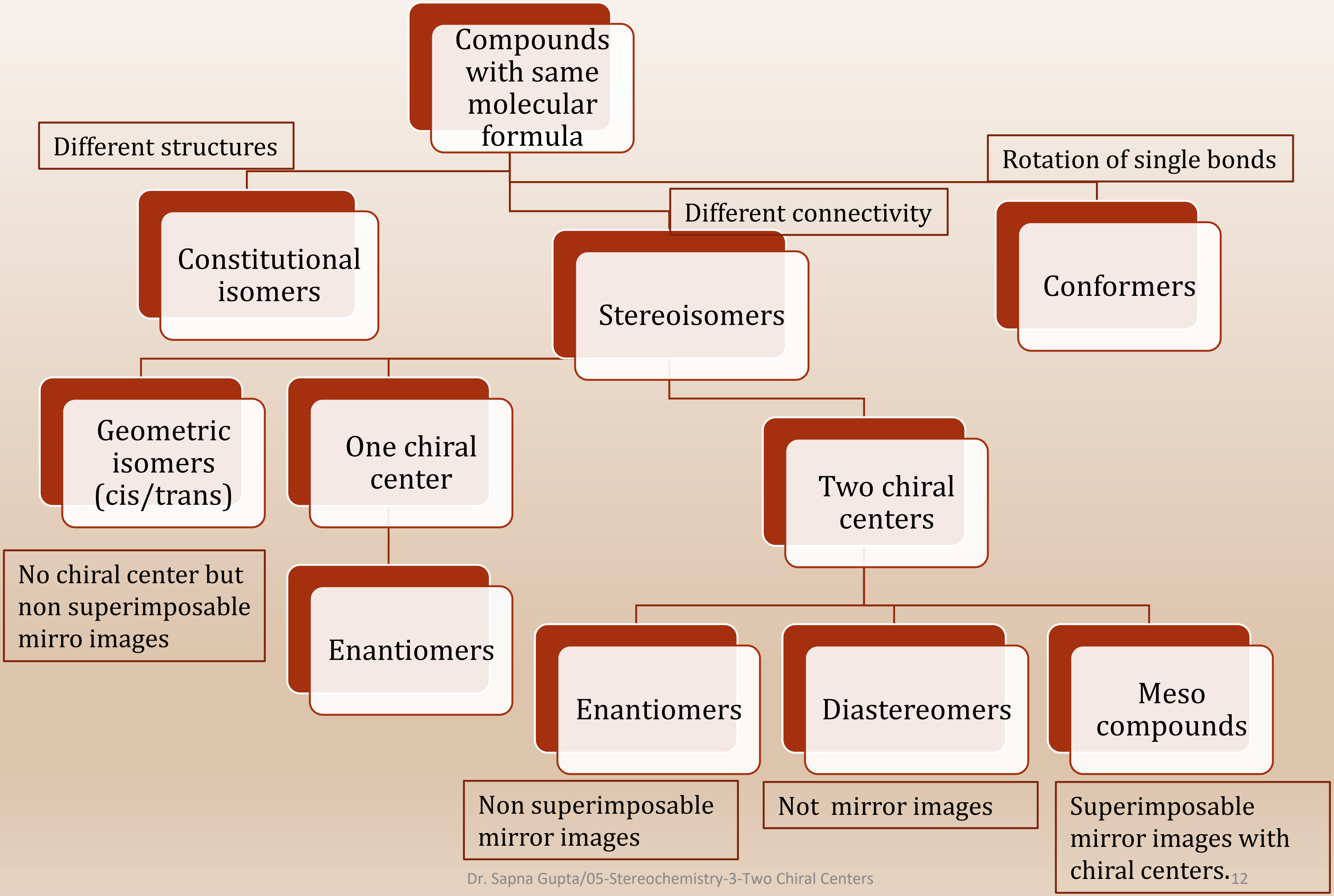
1,3-dimethylcyclohexane (shown on the right)

- The trans and cis compounds have two stereo centers each.
- The **cis** compound has a plane of symmetry and is meso
- The **trans** compound exists as a pair of enantiomers



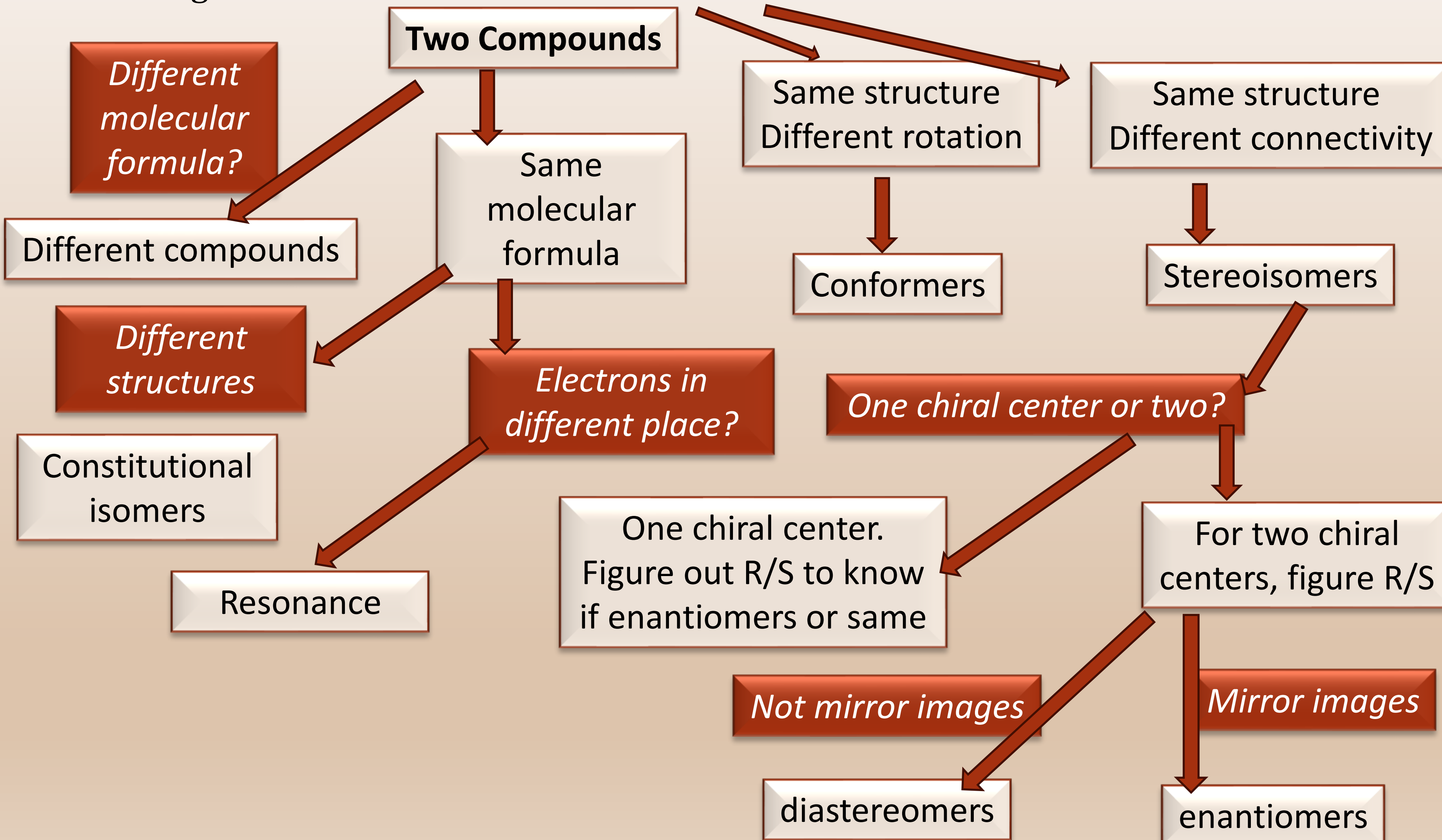
Watch the video (Stereo Video 9) to see stereochemistry in cyclic compounds. See the link in the "Description".

Review of all Isomers



Determining Stereochemistry

Use this guideline to determine all the isomers.



Key Words/Concepts

- Stereoisomers: Isomers that have different 3D spatial arrangement.
- Chiral Center: A tetrahedral atom that has four different groups on it.
- Chirality: The ability of a stereoisomer to show optical activity.
- Enantiomers: Nonsuperimposable mirror images of the same compound.
- Plane polarized light: Light that is only in one plane of direction.
- Dextrorotatory (d): A compound that rotates plane polarized light in the right (positive) direction.
- Laevorotatory (l): A compound that rotates plane polarized light in the left (negative) direction.
- Diastereomers: Non superimposable images of the same compound.
- Meso compounds: Compounds with two or more chiral center that whose mirror images superimpose on each other.
- Configurations (R and S): Cahn Ingold Prelog system of nomenclature where groups are assigned priorities according to atomic numbers. When those priorities go from highest to lowest in clockwise direction, the configuration is R and when anticlockwise, the configuration is S.
- Racemic mixture: Equal mixture of R and S enantiomers.
- Enantiomeric excess: The ratio of the two enantiomers where one enantiomer is more than the other.
- Absolute configuration: Determining the R and S configuration.

Key Words/Concepts

- Stereoisomers
- Chiral Center
- Chirality
- Enantiomer
- Plane polarized light
- Dextrorotatory (d)
- Laevorotatory (l)
- Diastereomers
- Meso compounds
- Cahn Ingold and Prelog nomenclature
- Configurations (R and S)
- Racemic mixtures
- Fisher projections
- Enantiomeric excess
- Absolute configuration