Stereochemistry
1- Introduction

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Introduction

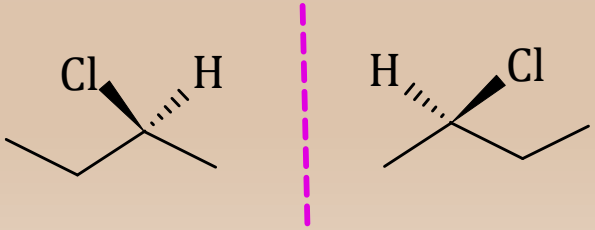
Isomerism is different structures of the same compound.

- Constitutional isomers – same molecular formula but different attachment of atoms.
- Geometric isomers – cis and trans isomers due to lack of rotation of bonds. These are in cyclic compounds and alkenes.
- Conformers – bond rotation isomers or ring flips.

The above isomers may or may not have different physical properties.

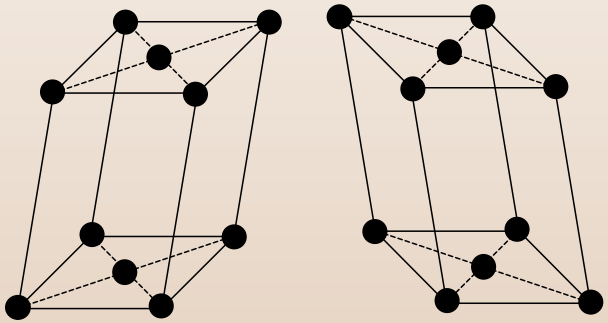
Stereoisomers have to do with left and right handedness depending on how the groups are attached on a tetrahedral atom, C.

- Any carbon that has four different groups will show chirality.
- Chirality: the mirror image of the compound will not superimpose on the original molecule. Each of these are called enantiomers.



Pasteur's Discovery of Enantiomers

Louis Pasteur discovered that sodium ammonium salts of tartaric acid crystallize into right-handed and left-handed forms, for example the crystals below are mirror images.

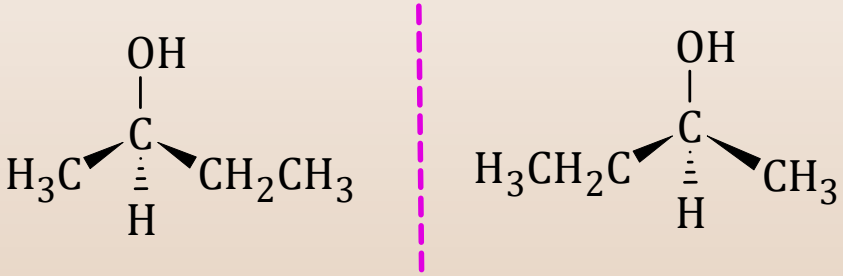


- The optical rotations of equal concentrations of these forms had opposite optical rotations.
- The solutions contain mirror image isomers, called **enantiomers** and they crystallized in mirror image shapes.
- I have covered the optical properties of enantiomers in a different power point.

Chirality and Enantiomers

A chiral carbon is one that has four different groups. Chirality is when two mirror images are non imposable on each other.

Non-superimposable mirror images are called enantiomers.



It may not seem probable that these two molecules will not superimpose on each other but watch the video in the next slide that shows a tetrahedral with four groups with this example.

Enantiomers have the same physical properties except how they rotate the plane polarized light. The rotation would be in equal and opposite direction. (Again, this is covered in another power point).

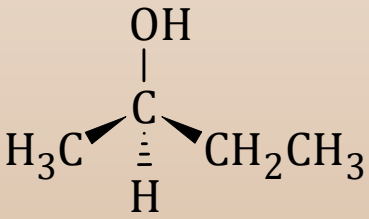
The only way one can change one enantiomer to become superimposable on another is by breaking a bond and exchanging it with another group as shown in the **video.**

Watch the video (Stereo Video 1) explaining chirality. See the link in the "Description".

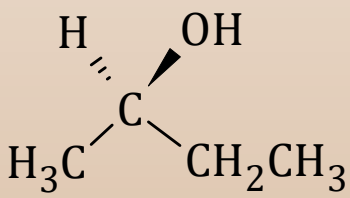
Drawing in 3D

Stereoisomers should be drawn in 3D to know which groups are attached in which orientation. It is important to be able to visualize the chiral carbon and tetrahedral nature of the chiral carbon.

- Drawing chiral molecules: draw dash (behind the plane) and wedges (coming out of paper) and plane line (in the plane) for bonds.
- Here are some representations of one compound. In structure 4 it is implied that H is at the back. Structure 5 with straight lines is called a Fisher projection.



1



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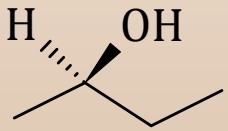

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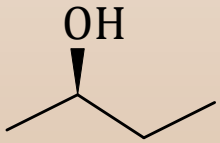

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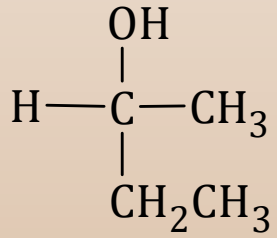


5

Watch the video (Stereo Video 2) explaining how to draw 3D molecules. See the link in the "Description".

Identifying Chiral Centers

The first task is always to identify a chiral center in a molecule. Molecules can have more than one chiral center.

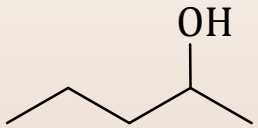
The key things to look for:

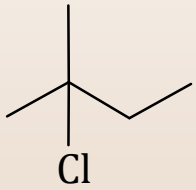
- Look for only tetrahedral (carbon or nitrogen). Why? Trigonal planar structures can be superimposed on each other as they are planar.
- No double bonds or triple bonds will have chiral centers (for now).
- Place an asterisk (*) on the chiral center.

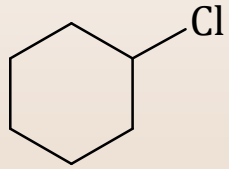
Don't be mislead by a 3D drawing which may have two of the same groups ☺.

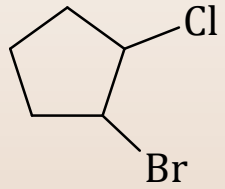
Solved Problem: Identifying chiral center

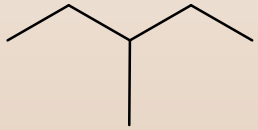
Identify the chiral centers in the following molecules.

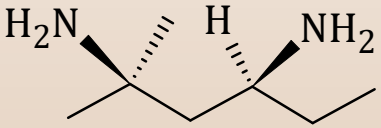
a) 

b) 

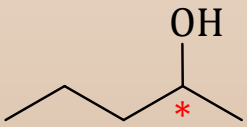
c) 

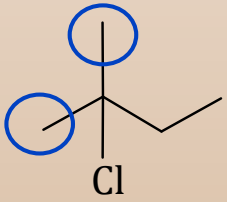
d) 

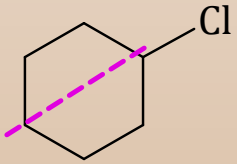
e) 

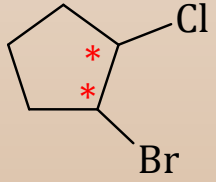
f) 

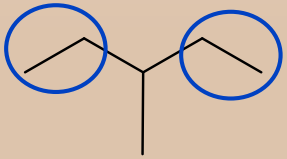
ANSWER

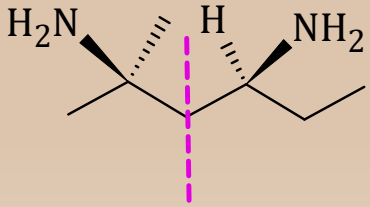
a) 

b) 

c) 

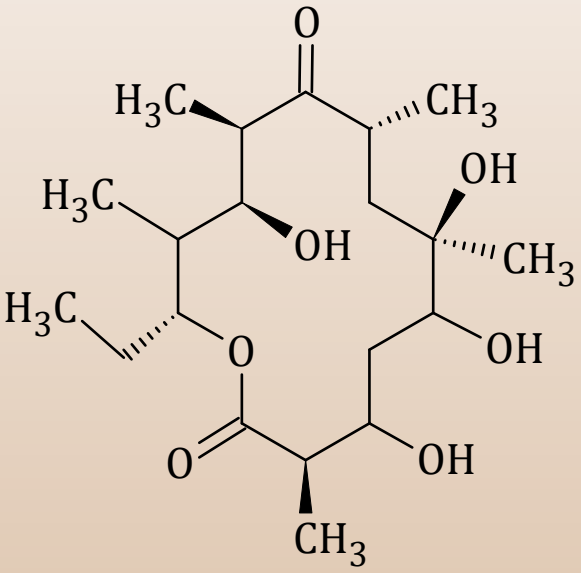
d) 

e) 

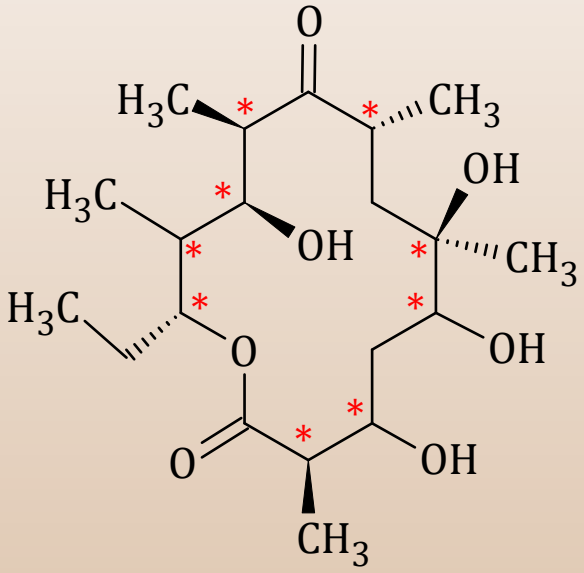
f) 

Solved Problem: Identifying chiral center

Identify the chiral centers in the following molecule.



ANSWER



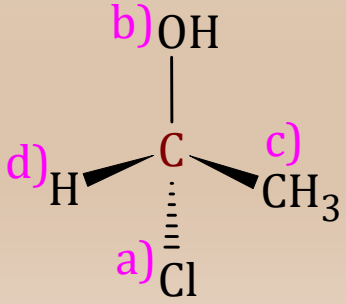
Naming Enantiomers- The *R/S* System

Enantiomers have the same names because the groups are the same. So how to distinguish one from the other? To know which enantiomer is which, the Cahn-Ingold-Prelog system of naming is used.

The four atoms attached to the chiral carbon are assigned priorities from highest (a) to lowest (d) according to their atomic numbers.

- Atoms with higher atomic number are given higher priority.
- If priority cannot be assigned based on directly attached atoms, the next set of atoms is examined.

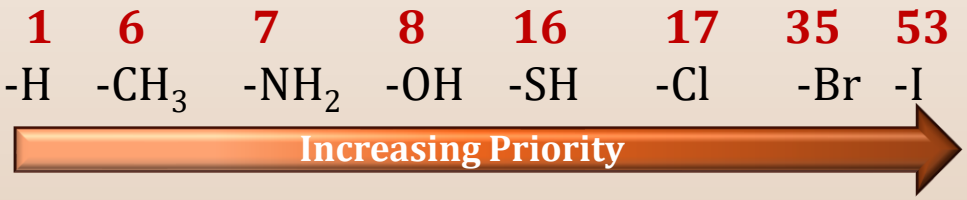
In the molecule shown below, the atoms attached to the chiral center are clear, O, C, Cl and H. Priority according to atomic number will be Cl > O > C > H. Label the groups as ***abcd***, giving ***a*** the highest and ***d*** the lowest priority.



Assigning Priority – 1 – Different Atoms

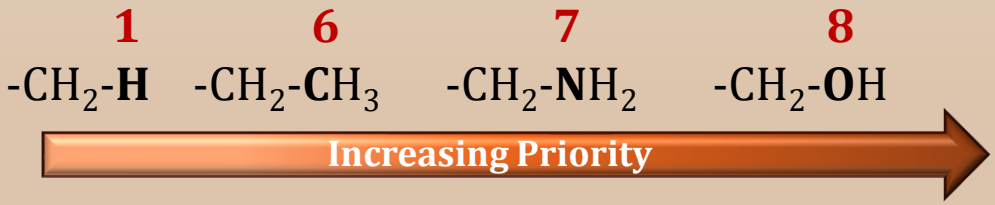
Here are more details on how to assign priority to the groups.

1. Look at the atom (*not the group*) directly attached to the carbon and arrange according to atomic number (*given in red below*).



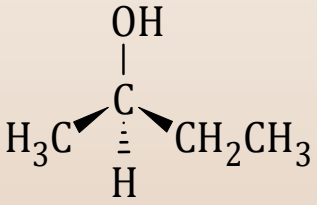
2. If priority cannot be assigned per the atoms bonded to the chiral center, look to the next set of atoms; priority is assigned at the first point of difference.

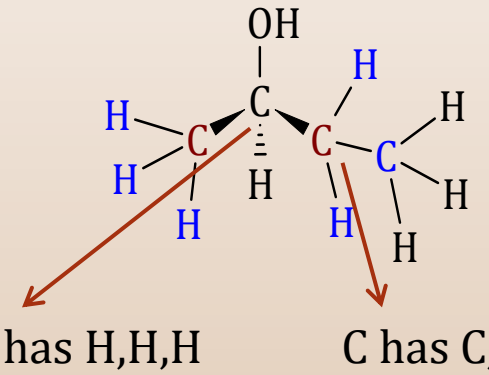
   For CH_3, CH_2CH_3, CH_2NH_2 and CH_2OH, follow the guideline below.

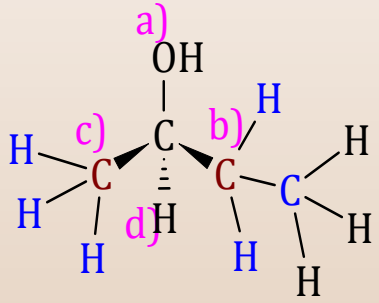


Assigning Priority – 2 - Carbons

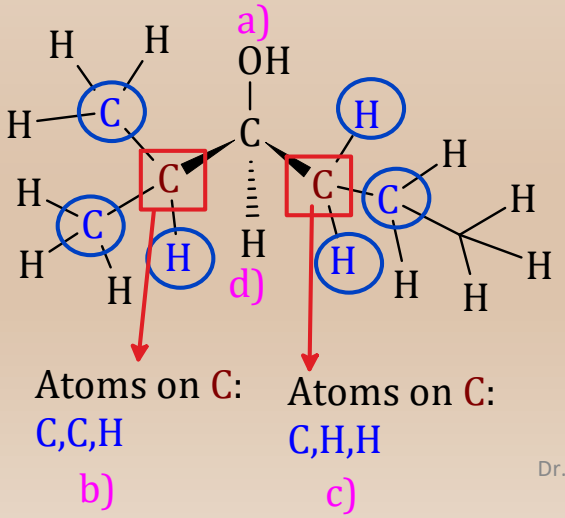
In cases where there are two of the same atoms, then look at the next atom and what is attached to it. In the cases below we are looking at carbon attachments.







Write attached atoms in descending order of priority. The first point of difference is where you stop.

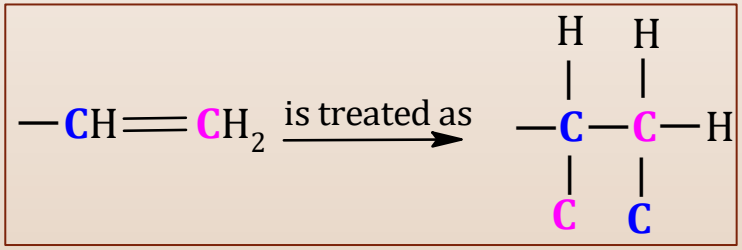


Here is one more example of a propyl group vs isopropyl group.

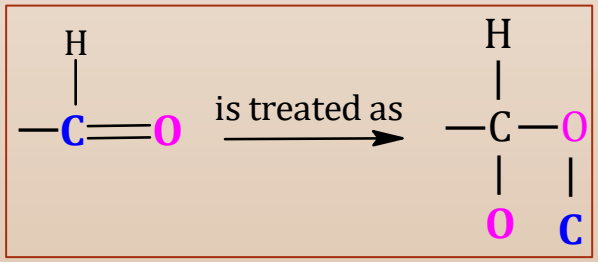
The isopropyl group gets higher priority because the first different C is attached to CCH while in propyl group it is CHH.

Assigning Priority – 3 – Multiple Bonds

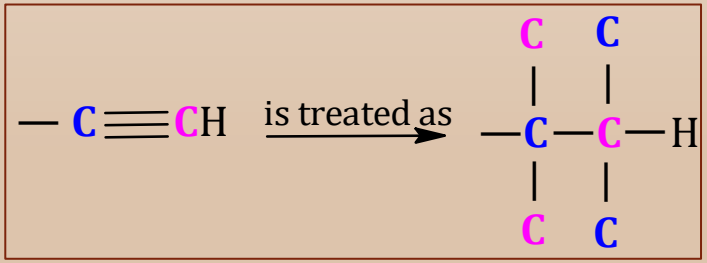
When there are multiple bonds: double and triple, they are manipulated to make them single bonds. Follow the color on the atom to understand this.



In case of a double bond, the carbons are attached to both the carbons to make them single bonds.



When carbon is attached to oxygen, a carbon and oxygen is attached to the opposite side.



Solved Problem: Determining priorities

Determine the priorities of the groups below.

ANSWER

a) Cl, Br, H

b) OH, NH_2, SH

c) C≡N, C≡C, N≡C

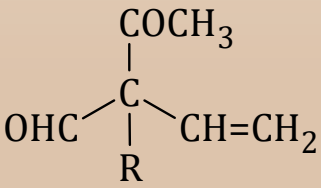
d) CHO, $COCH_3$, $CH=CH_2$

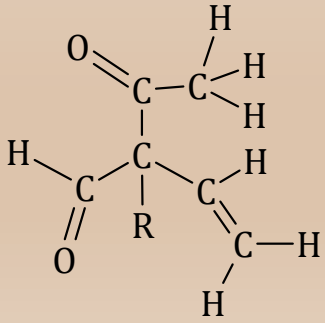
a) Br > Cl > H

b) SH > OH > NH_2

c) N≡C > C≡N > C≡C

d) $COCH_3$> CHO > $CH=CH_2$

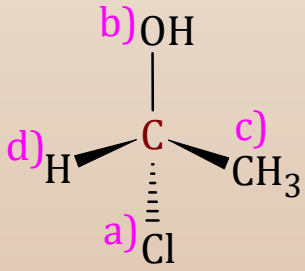




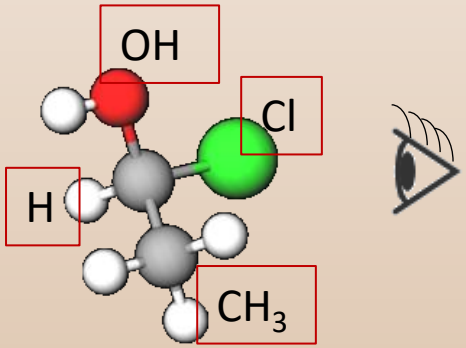
Naming Enantiomers- The *R,S* System, contd..

After assigning priorities, make sure that **the lowest priority group is at the back.**

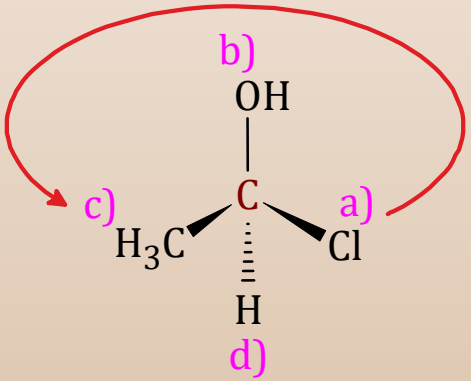
- If the groups descend in priority (a,b then c) in clockwise direction the enantiomer is *R.*
- If the groups descend in priority in counterclockwise direction the enantiomer is *S.*



Original molecule



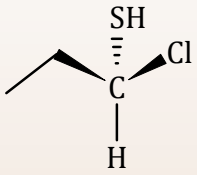
Rotate the molecule so the H, lowest priority group is at the back. You cannot just switch Cl and H! Rotate the tetrahedral to get H at the back.

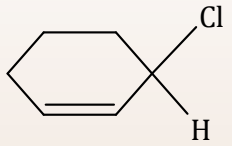


Go from the highest priority to lowest priority group.

Watch the video (Stereo Video 3) to learn R/S system. See the link in the "Description".

Solved Problem: Determining R/S

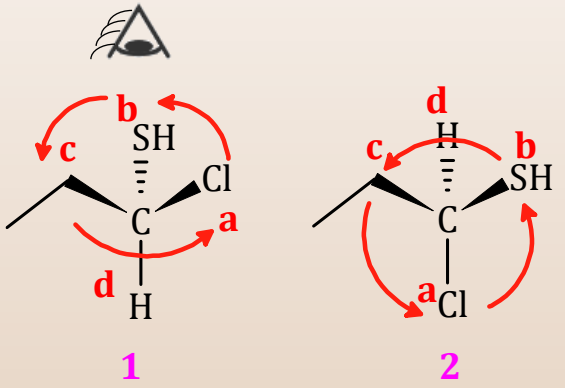
Assign R/S configuration for the following two structures. a) 

b) 

ANSWER

a) Assigning Priority: Cl > S > C > H. View from top, groups go anticlockwise, so S.

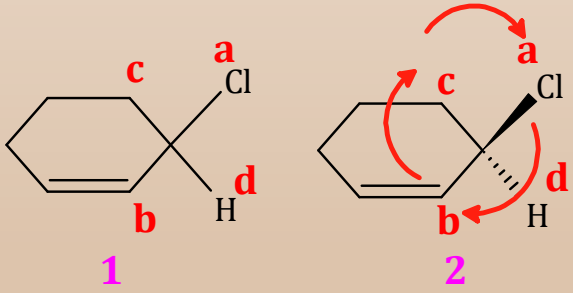
Or you can hold group C as is and rotate H to the back as shown in structure 2. Now all groups are front facing.



Watch the video (Stereo Video 4) to see R/S of this molecule. See the link in the "Description".

b) Assigning Priority: Cl > = C > -C > H. Double bonds have higher priority than single bonds.

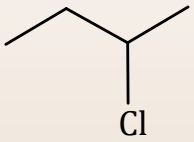
As drawn, the ring is seen in the plane, the Cl going up is coming out of plane and H is going down. See structure 2 to understand the 3D and use it to determine R/S. Groups are going clockwise, so R.

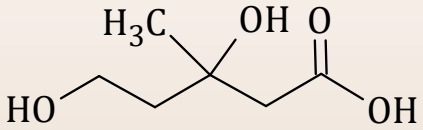


Watch the video (Stereo Video 5) to see R/S of this molecule. See the link in the "Description".

Solved Problem: Writing structures with R/S

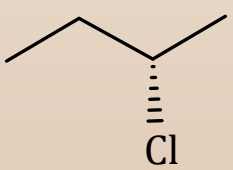
Draw the structures for the following compounds using the proper stereochemistry assigned,

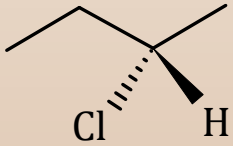
a) (*S*)-2-Chlorobutane, 

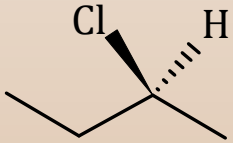
b) (*R*)-Mevalonic acid. 

ANSWER

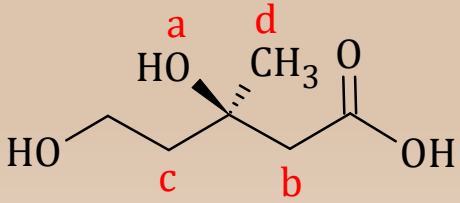
a) (*S*)-2-Chlorobutane – first identify the chiral center. It is the carbon with Cl. The decreasing order of priority is: Cl, CH_2CH_3, CH_3 and H. In the two structures shown the first is not as clear. The 2nd and 3rd are better as we can clearly see the tetrahedral nature of carbon.





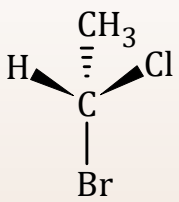


b) (*R*)-Mevalonic acid - first identify the chiral center. It is the carbon with CH_3 and OH. Assign priorities to all groups OH> CH_2COOH> CH_2CH_2OH> CH_3 and arrange them in R configuration. CH_3 is lowest priority and should be going to the back.

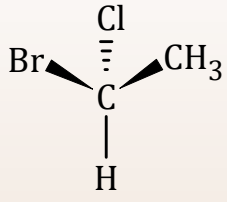


Solved Problem: Relationship of molecules

Are the following molecules same or enantiomers?



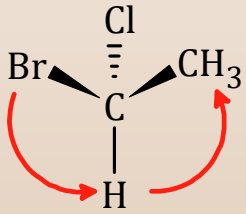
A



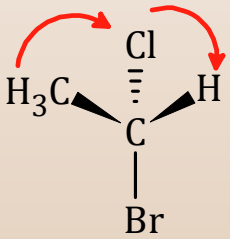
B

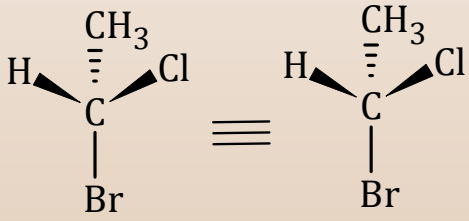
ANSWER

Manipulate B by rotating the groups to see if it will become superimposable with A



B

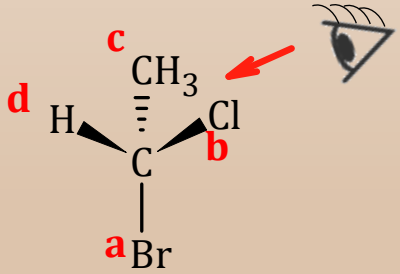


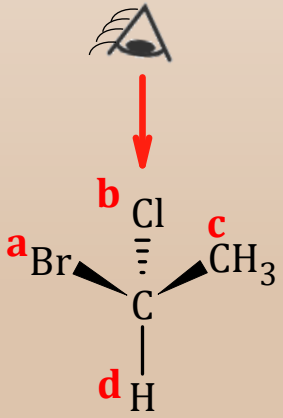


A

The other best way to determine relationship, without rotating, is to determine their configurations – R/S. Look from where the eye is shown to keep the smallest priority group at the back.

Both are R.





Watch the video (Stereo Video 6) to see how you can use models to answer this question. See the link in the "Description".

Key Words/Concepts

- Stereoisomers
- Chiral Center
- Chirality
- Enantiomer
- Plane polarized light
- Dextrorotatory (d)
- Laevorotatory (l)