

Stereochemistry

Chiral Molecules

- Consider 2-chlorobutane

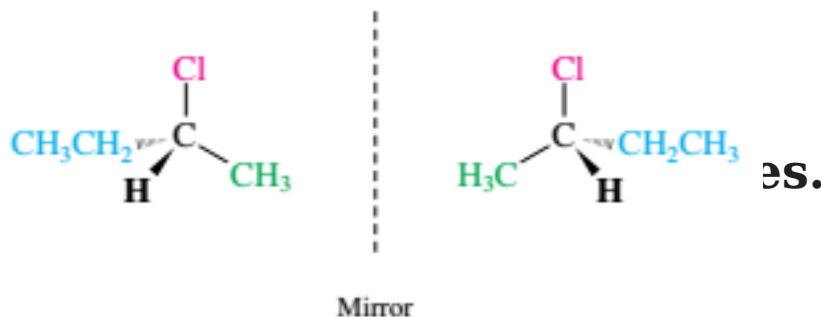


This carbon has four different groups attached to it, a **chlorine**, a **hydrogen**, a **methyl** group, and an **ethyl** group.

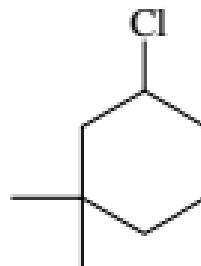
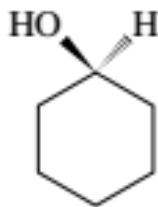
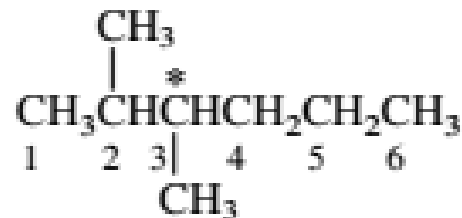
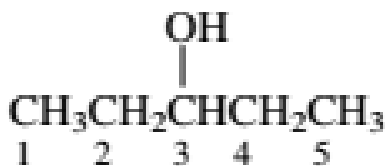
- The : examination of these two structures shows that they are not identical. Careful

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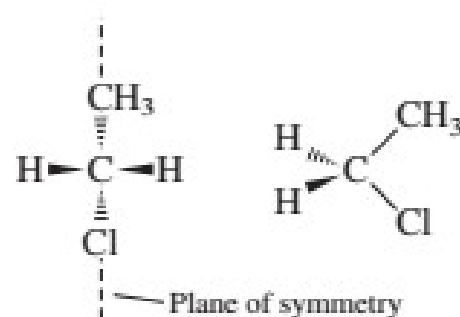
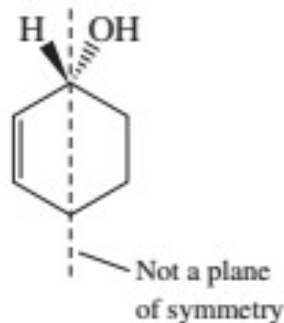
- they are **not**



- Molecules such as 2-chlorobutane are termed **chiral**.
- Chiral molecules exist as either of two stereoisomeric structures.
- These stereoisomers, a pair of nonsuperimposable mirror images, are called **enantiomers**.
- If the two molecules are superimposable in any conformation, the molecule is achiral; if they are not, it is chiral.
- **Chirality center** - a carbon attached to four different groups.
- Sometimes called *chiral carbon atom* or *asymmetric carbon atom*.
- Any molecule with one chirality center as its only stereocenter is **chiral**.

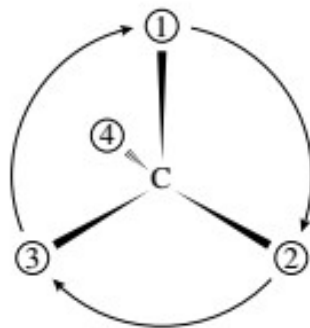


- **Plane of symmetry** or a **mirror plane**.
- An object has a plane of symmetry if an imaginary plane that passes through the center of the object divides the object so that one half is the mirror image of the other half.
- Any molecule that has a plane of symmetry :

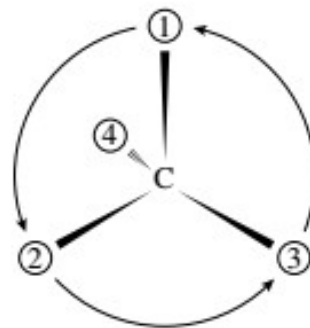


Designating Configuration of Enantiomers

- The Cahn-Ingold-Prelog sequence rules – Based on the atomic number of the atom bonded to asymmetric carbon atom
- **STEP 1**
Assign priorities from 1 through 4 to the four groups bonded to the chirality center using the Cahn-Ingold-Prelog sequence rules. The group with the highest priority receives number 1, and the lowest-priority group receives number 4.
- **STEP 2**
View the molecule so that the bond from the chirality center to group number 4 is pointed directly away from you. Now determine whether the direction of the cycle proceeding from group 1 to 2 to 3 and back to 1 is clockwise or counterclockwise. If this rotation is clockwise, the configuration is *R* (from the Latin word for right, *rectus*).
If the rotation is count

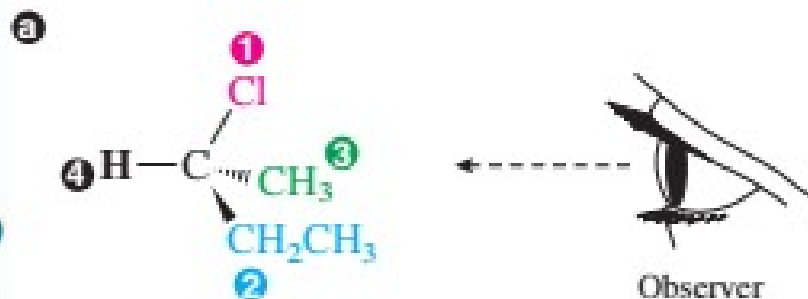


Clockwise rotation, so *R*



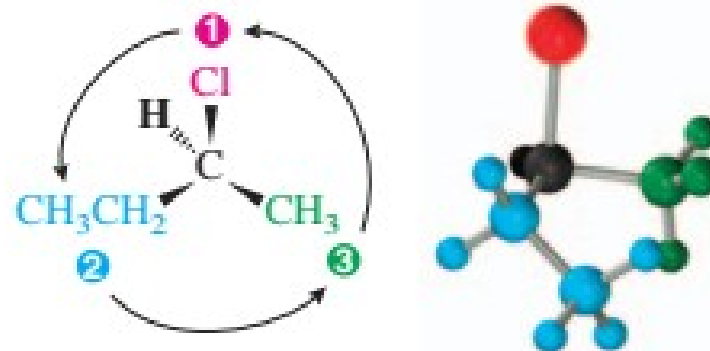
Counterclockwise rotation, so *S*

from the Latin



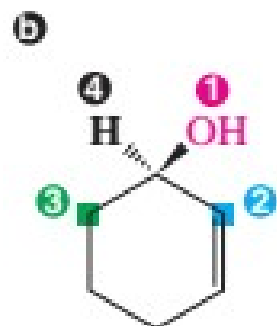
(S)-2-Chlorobutane

The group priorities are **chlorine = 1**, **ethyl = 2**, **methyl = 3**, and **hydrogen = 4**. Viewing from the right side, so that the bond from the carbon to the hydrogen is pointed away from the observer, $1 \rightarrow 2 \rightarrow 3 \rightarrow 1$ is counterclockwise, so the configuration is S. This is easier to see if the structure is rotated.



(S)-2-Chlorobutane

In this view, the structure has been rotated so that the bond from the carbon to the hydrogen is pointing directly away from you as you view the page. Now it is easier to see that the direction of $1 \rightarrow 2 \rightarrow 3 \rightarrow 1$ is counterclockwise.

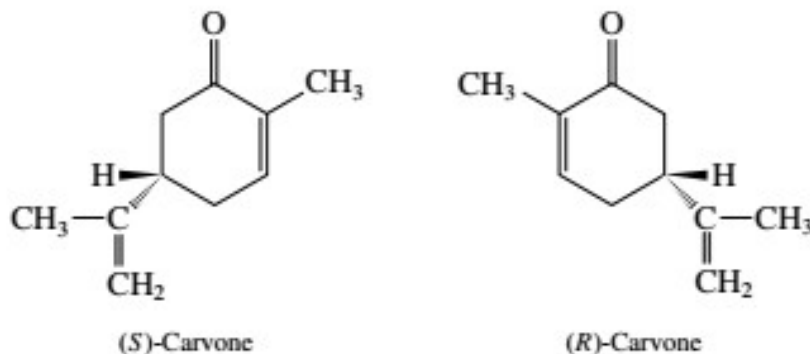


(R)-2-Cyclohexenol

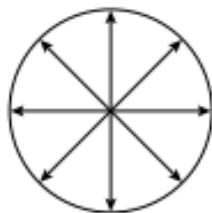
The chirality center is the ring carbon bonded to the OH. The highest-priority group is the **OH**, and the lowest-priority group is the H. Because the **ring carbon on the right** of the chirality center is doubly bonded to another carbon, it has higher priority than the **other carbon**. The lowest-priority group, the hydrogen, is almost pointed directly away from you so the clockwise direction of rotation of $1 \rightarrow 2 \rightarrow 3 \rightarrow 1$ can be easily seen.

Properties of Enantiomers

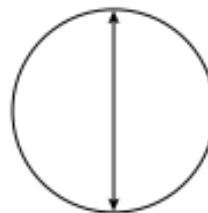
- Enantiomeric molecules are different when they are in a chiral environment.
- Most commonly, the chiral environment is the presence of one enantiomer of another chiral compound. Otherwise, their properties are identical.
- (*R*)- and (*S*)- carvone have identical melting points, boiling points, solubilities in ethanol, and heats of combustion. However, they have different solubilities in one enantiomer of a chiral solvent, and they have different odors
- *enantiomers have different rates of reaction with one enantiomer of a chiral reagent*



- The most common method used to detect the presence of chiral molecules in a sample employs the interaction of plane-polarized light with the sample.
- When plane-polarized light is passed through a sample containing one enantiomer of a chiral compound, the plane of polarization of the light is rotated. (Samples that rotate plane-polarized light are said to be **optically active**.)



Regular light waves consist of electromagnetic fields that oscillate in all directions perpendicular to the direction of travel of the wave. If we could see these fields while viewing the light beam coming directly at us, the oscillations would occur along the arrows.



When a regular light beam is passed through a polarizer (polarized sunglasses will work), all of the light waves, except those whose electromagnetic fields oscillate in a single direction, are filtered out. The result is a beam of **plane-polarized light**. The oscillations all occur in a single plane as shown.

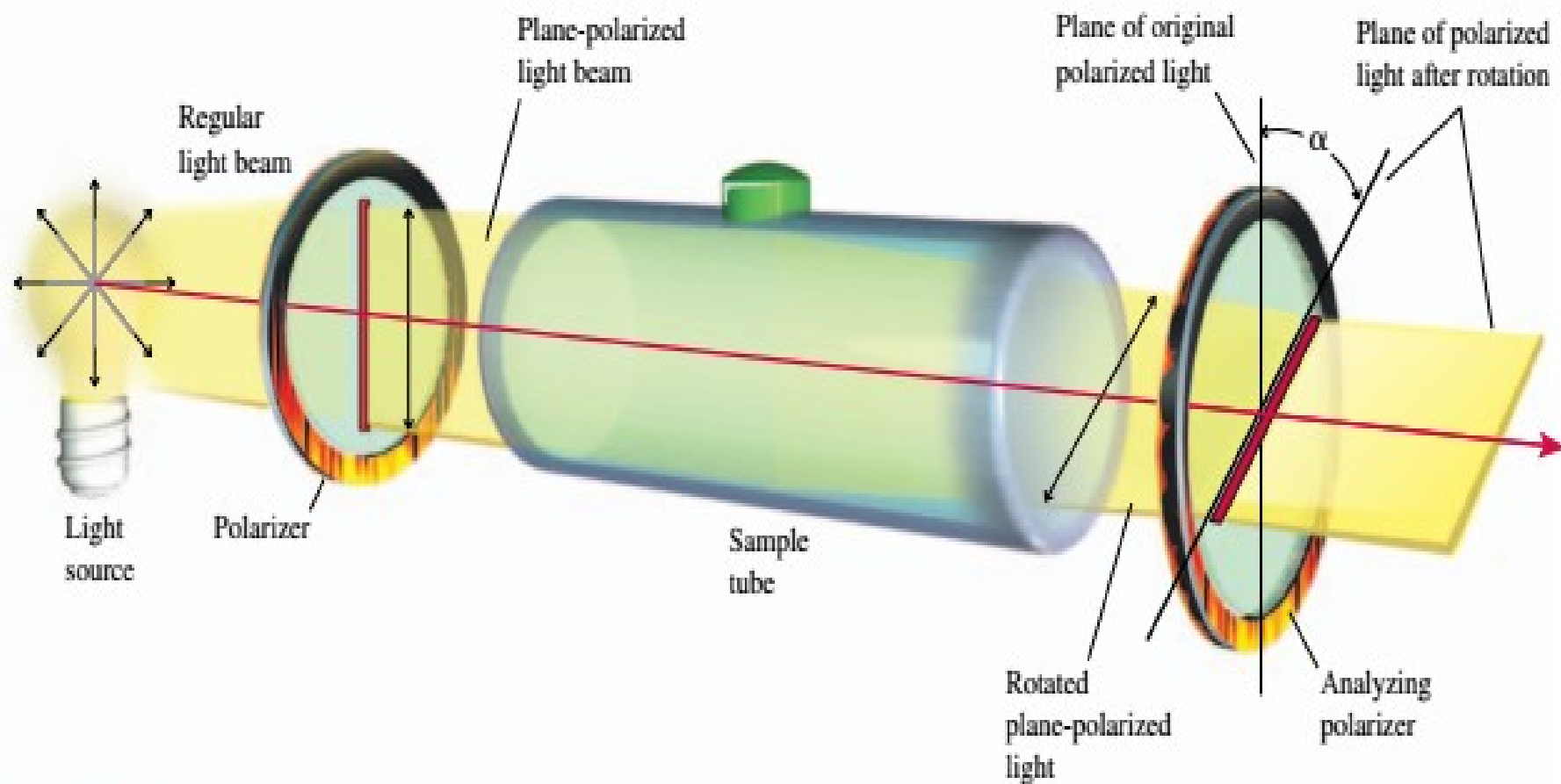


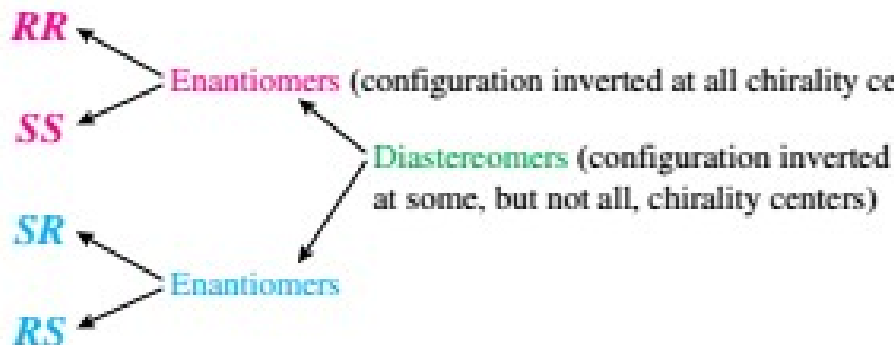
Figure 7.4

SCHEMATIC DIAGRAM OF A POLARIMETER.

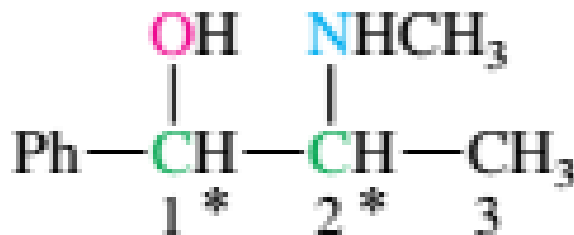
- Enantiomers rotate plane-polarized light by identical magnitudes but in opposite directions.
- The enantiomer that rotates the light clockwise is called **dextrorotatory**, (*d*) or (+), while the one that rotates light counterclockwise is called **levorotatory**, (*l*) or (-).
- A common way to encounter a chiral compound is as an equal mixture of enantiomers, called a **racemic mixture** or a **racemate**.
- A racemic mixture, often designated as *d,l* or ($\pm$), does not rotate plane-polarized light because the rotation due to one enantiomer is canceled by that of the other.

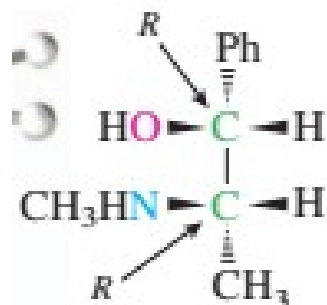
Multiple asymmetric centers

- Let's consider the simplest possibility: a molecule with two chirality centers.
- Each chirality center can have either the *R* or the *S* absolute configuration.
- There are four possible combinations: *RR*, *SS*, *RS*, and *SR*.
- The mirror image of a chiral molecule, that is, its enantiomer, has the opposite configuration (inverted configuration) at all chirality centers.
- Therefore, the *RR* and the *SS* stereoisomers are enantiomers, as are the *RS* and *SR* stereoisomers.
- The *RR* and the *RS* stereoisomers are not mirror images. Such non-mirror-image stereoisomers are called diastereomers. They have the opposite configuration at some, but not all, chirality centers.

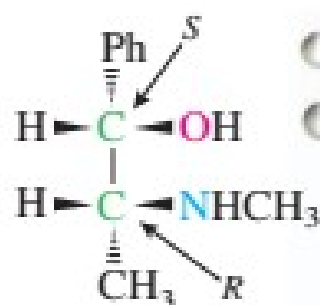


- Diastereomers, on the other hand, are not mirror images and have different properties in all environments. They have different physical properties and different chemical properties.
- A molecule with a number of chirality centers equal to n has a maximum of 2^n stereoisomers:
- maximum number of stereoisomers = 2^n (n = number of chirality centers)
- Consider 2-(methylamino)-1-phenyl-1-propanol:

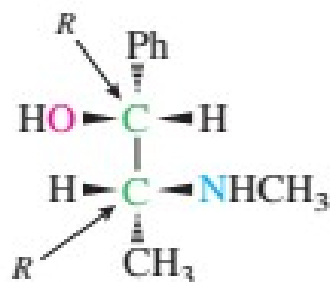




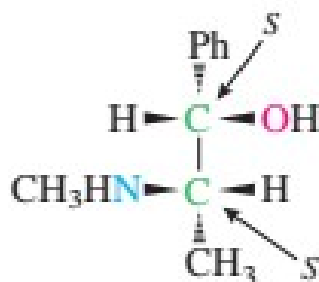
(1*R*,2*S*)-Stereoisomer
 (-)-ephedrine
 mp: 40°C
 [α]_D: -6.3



(1*S*,2*R*)-Stereoisomer
 (+)-ephedrine
 mp: 40°C
 [α]_D: +6.3

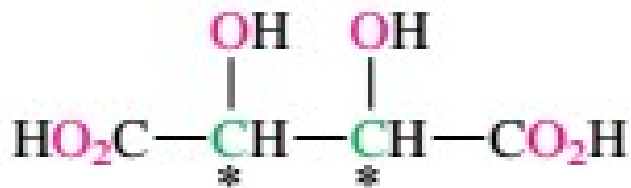


(1*R*,2*R*)-Stereoisomer
 (-)-pseudoephedrine
 mp: 118°C
 [α]_D: -52



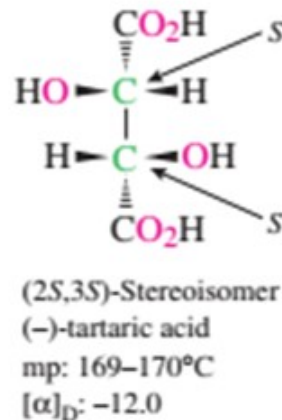
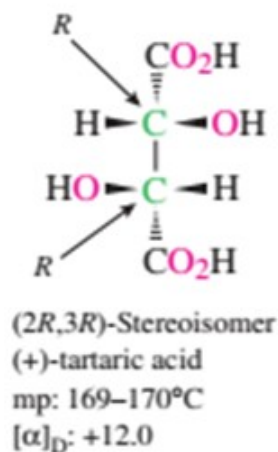
(1*S*,2*S*)-Stereoisomer
 (+)-pseudoephedrine
 mp: 118°C
 [α]_D: +52

- Sometimes there are fewer stereoisomers than predicted by the preceding rule.
- This occurs when identical chirality centers are symmetrically placed in a compound.
- As an example consider the case of tartaric acid

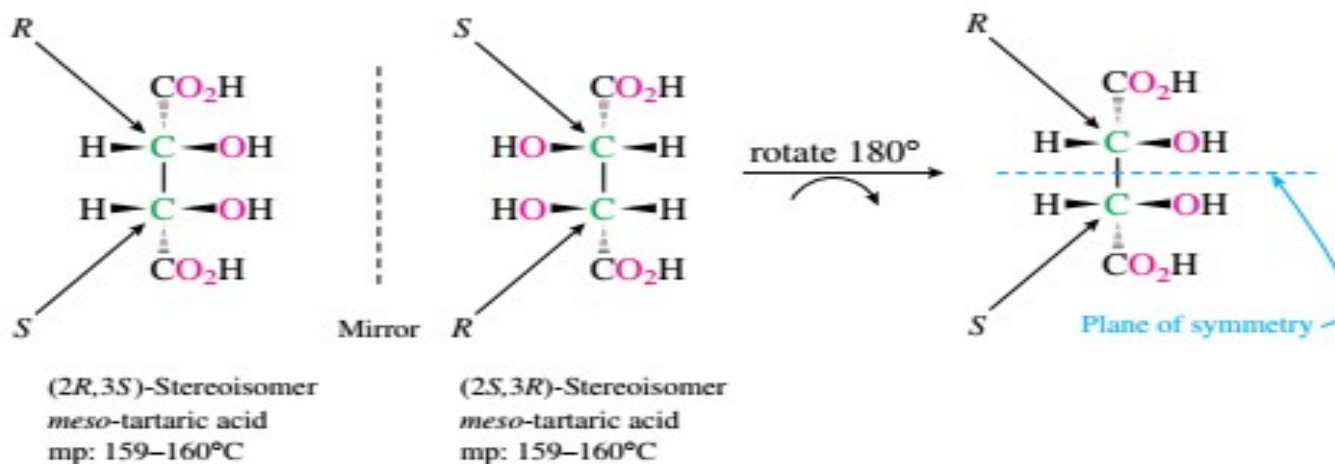


Tartaric acid

- There are two chirality centers, so the formula predicts a total of four stereoisomers. However, each of the chirality centers has identical groups attached to the carbon, so fewer than four stereoisomers actually exist.
- The (2*R*,3*R*)-isomer and the mirror image of this, the (2*S*,3*S*)- stereoisomer are nonsuperimposable —enantiomers

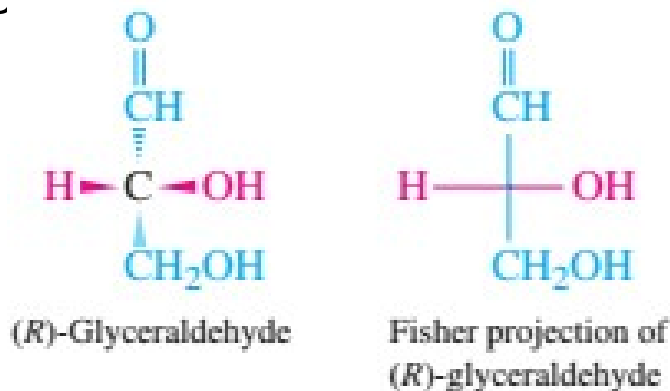


- A diastereomer of these compounds is constructed by interchanging the H and OH on one of the chirality centers
- Careful examination of these mirror images shows that they are, in fact, identical. If the (2*S*,3*R*)-stereoisomer is rotated 180° in the plane of the paper, the structure on the right is produced and it is identical to the (2*R*,3*S*)-stereoisomer on the left
- Because the compound is superimposable on its mirror image, it is not chiral and does not rotate plane polarized light.
- Another way to determine that this compound is not chiral is to note that it has a plane of symmetry that bisects the C-2±C-3 bond.
- Compounds such as this one, which contain chirality centers but are not

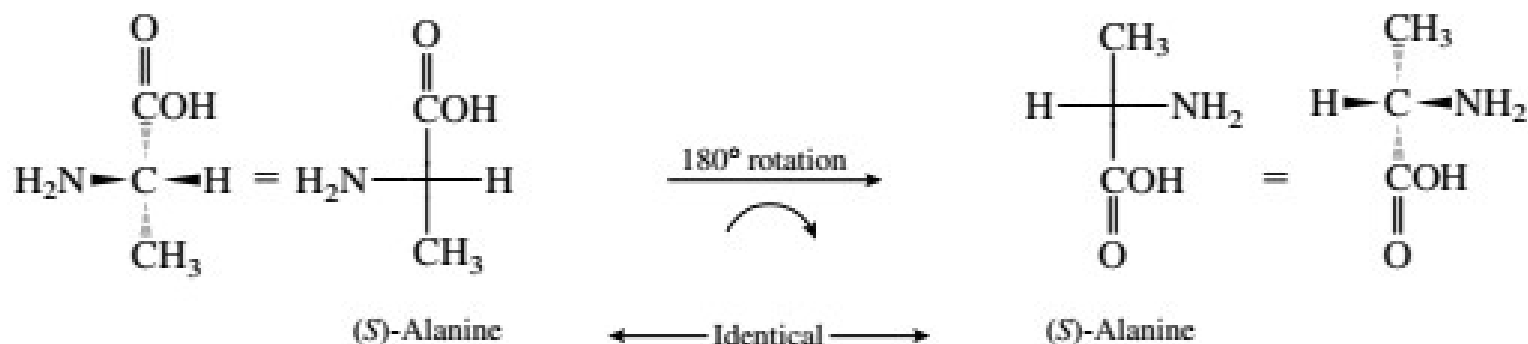


Fischer projection

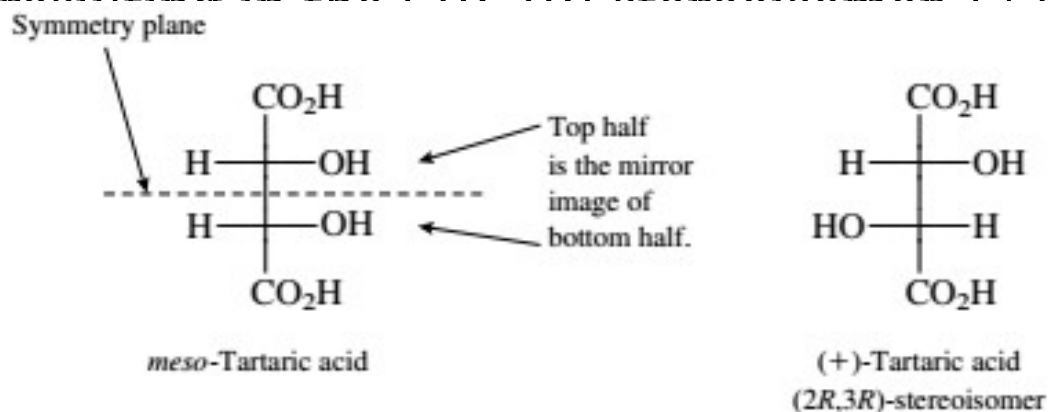
- Representation of chiral molecules
- the molecule is first arranged with the horizontal bonds to its chirality center projecting above the plane of the page and the vertical bonds projecting behind the page.
- the bonds are “projected” into the plane of the page, resulting in a cross with the chirality center at its center

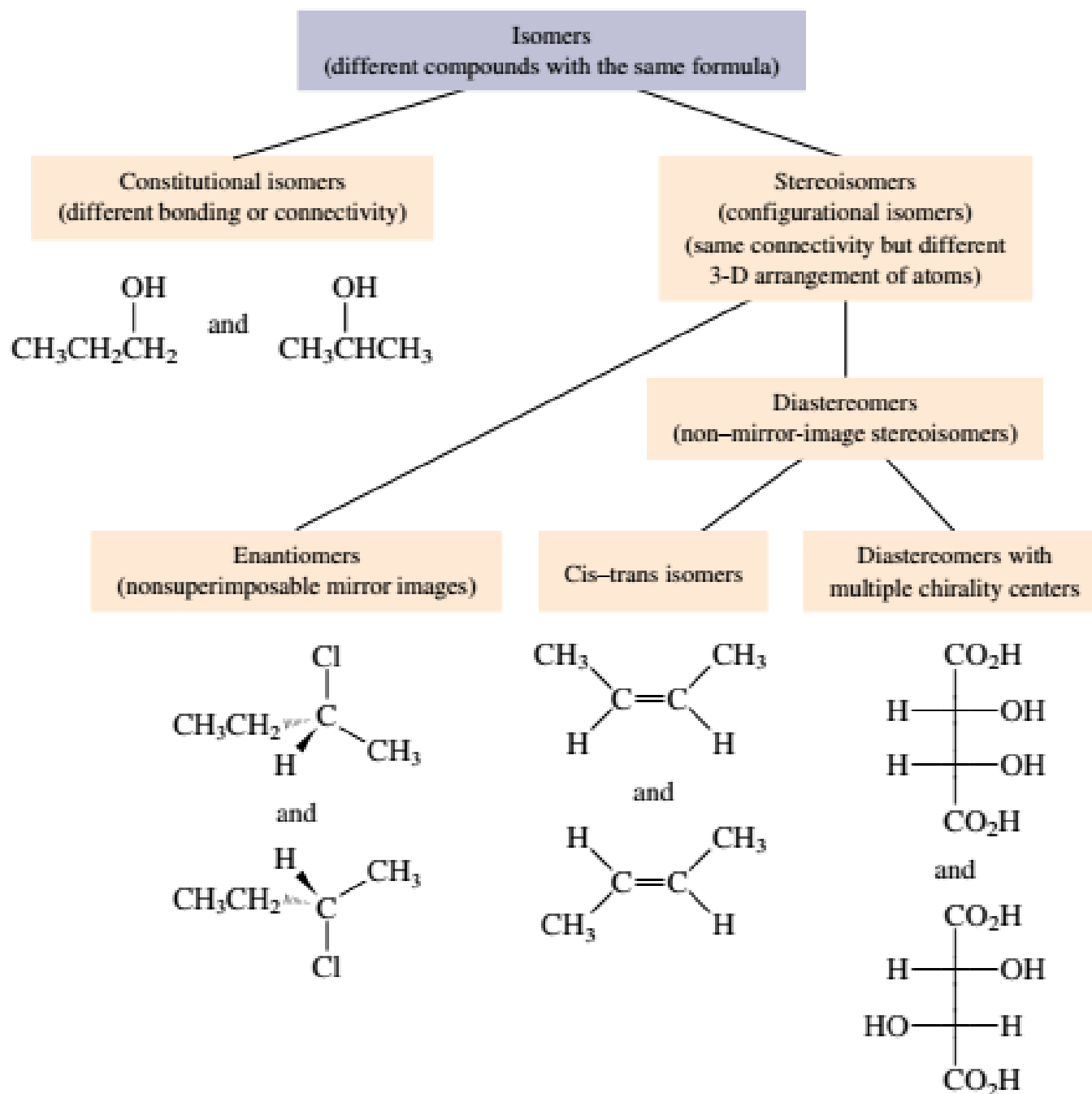


- Because they are two-dimensional representations of three-dimensional objects, extreme care must be used in manipulating Fischer projections to avoid changing the configuration.
- Structures may not be “lifted” out of the plane of the paper.
- A 180° rotation *in the plane* is permitted, but 90° and 270° rotations are not allowed.



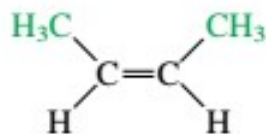
- Fischer projections are especially useful in the case of compounds with more than one chirality center.
- For example, it is easy to see the plane of symmetry in *meso* tartaric acid.
- As was the case with regular structures, interchanging any two groups in a Fischer projection results in inversion of configuration at the chirality center.
- Thus, interchanging the H and OH on the lower chirality center of *meso*-tartaric acid inverts the configuration at that chirality center, resulting in the $(2R,3R)$ stereoisomer, (+)-tartaric acid.
- It is also possible to have a plane of symmetry in a molecule that has two chirality centers.





Cis-Trans Isomers

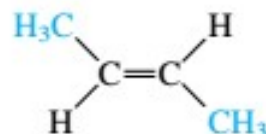
- Consider 2-butene $\text{CH}_3\text{CH}=\text{CHCH}_3$.
- There are two ways to draw the structure: Cis and Trans form
- One has the two methyl groups on the same side of a line that runs through the doubly bonded carbons (on the same side of the double bond) – cis , and the other has the two methyl groups on opposite sides of this line (on opposite sides of the double bond) – trans:
- These structures have the same bonds, so they are not constitutional isomers. However, they have a different arrangement of these bonds in three dimensions—they are stereoisomers.
- Stereoisomers like these, that differ in the placement of groups on one side or the other of the double bond, are called **cis-trans isomers**.



cis-2-Butene

0.33
4°C
–139°C

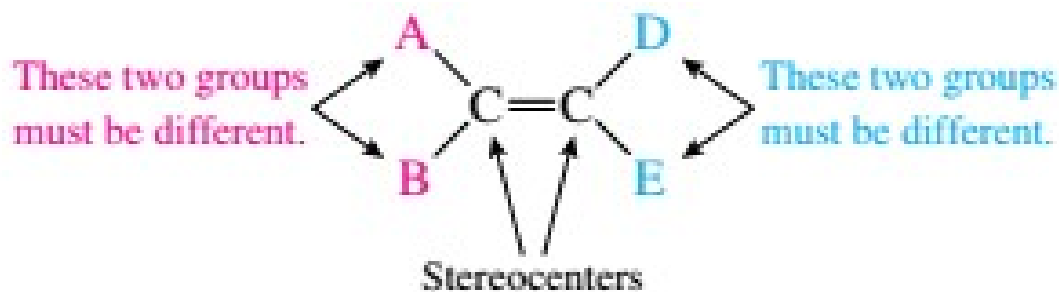
Dipole moment (Debyes)
Boiling point
Melting point

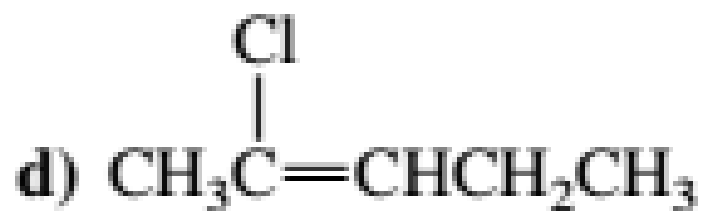
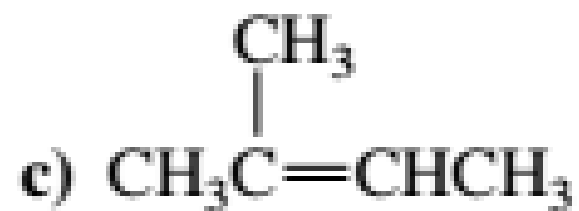


trans-2-Butene

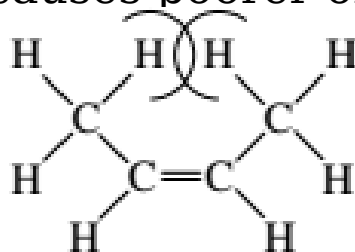
0
1°C
–106°C

- For an alkene to exhibit cis-trans isomerism, the two groups on one end of the double bond must be different and the two groups on the other end of the double bond must be different.
- That is, in terms of the following structure, A must be different from B, and D must be different from E. When this is the case, both of the carbons of the double bond are said to be stereocenters.
- A **stereocenter** or **stereogenic atom** is defined as an atom at which the interchange of two groups produ





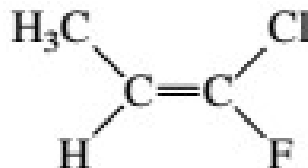
- Cis isomers are slightly stable than trans isomers
 - This is due to increase in energy due to strain in the molecules.
 - **Strain** is any factor that destabilizes a molecule by forcing it to deviate from its optimum bonding geometry.
 - Different atoms cannot occupy the same region of space. If atoms that are not bonded approach each other too closely (inside their van der Waals radii), they repel each other.
 - A molecule whose structure forces nonbonded atoms too close together will distort its bond lengths and/or bond angles to partially relieve this repulsive force. This causes poorer orbital overlap, resulting in weaker destabil
- is type of **ain.**



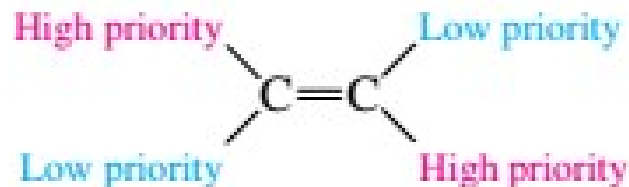
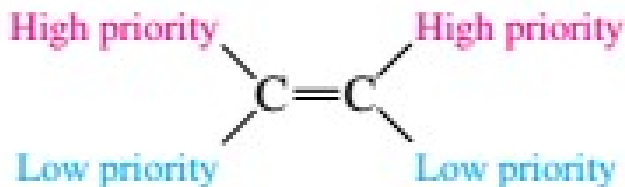
The planar geometry of the double bond causes a hydrogen on each of the methyl groups to be forced too close together, resulting in some steric strain.

Designating Configuration

- The three-dimensional arrangement of groups about a stereocenter in a molecule is termed its **configuration**.
- is the following isomer of 1-chloro-1-fluoro-1-propene the *cis*- or the *trans*-stereoisomer?



- If the high-priority groups are on the *same side* of the double bond, the configuration is designated **Z** (from the first letter of the German word *zusammen*, which means “together”), and if the high-priority groups are on *opposite sides*, the configuration is designated as **E** (from the German word *entgegen*, which means “opposite”)



- **RULE 1**

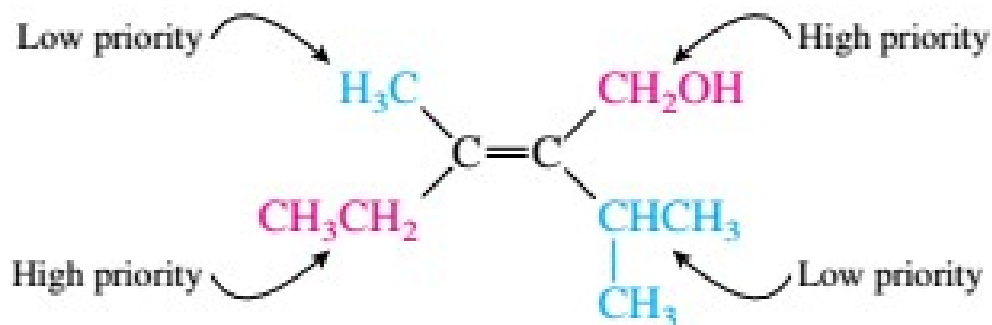
Of the two atoms attached to one carbon of the double bond, the one with the higher atomic number has the higher priority

- In 1-chloro-1-fluoro-1-propene the methyl group has a higher priority than the hydrogen. On the right carbon, Cl has a higher priority than F.
- Because the high-priority groups, the CH₃ and the Cl, are on the same side of the double bond, the configuration of this stereoisomer is Z.
- The compound is named (Z)-1- chloro-1-fluoro-1-propene.

- **RULE 2**

If the two atoms attached to the carbon are the same, compare the atoms attached to them in order of decreasing priority.

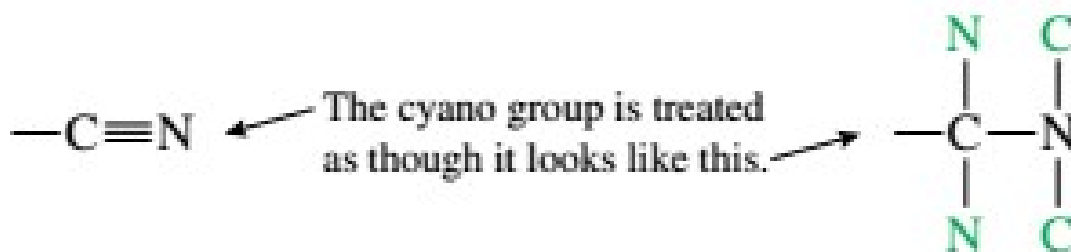
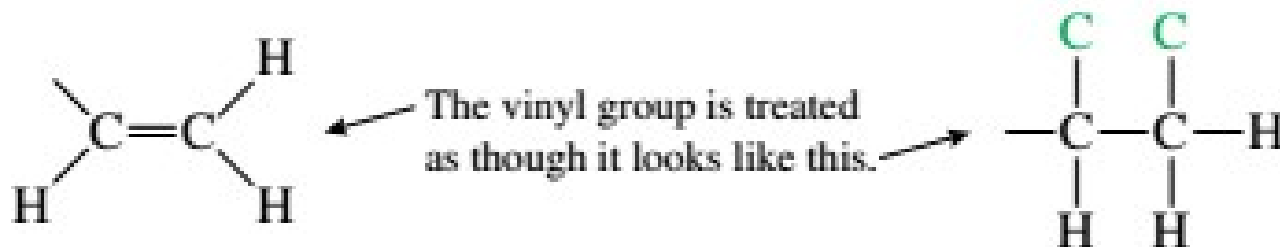
- The decision is made at the first point

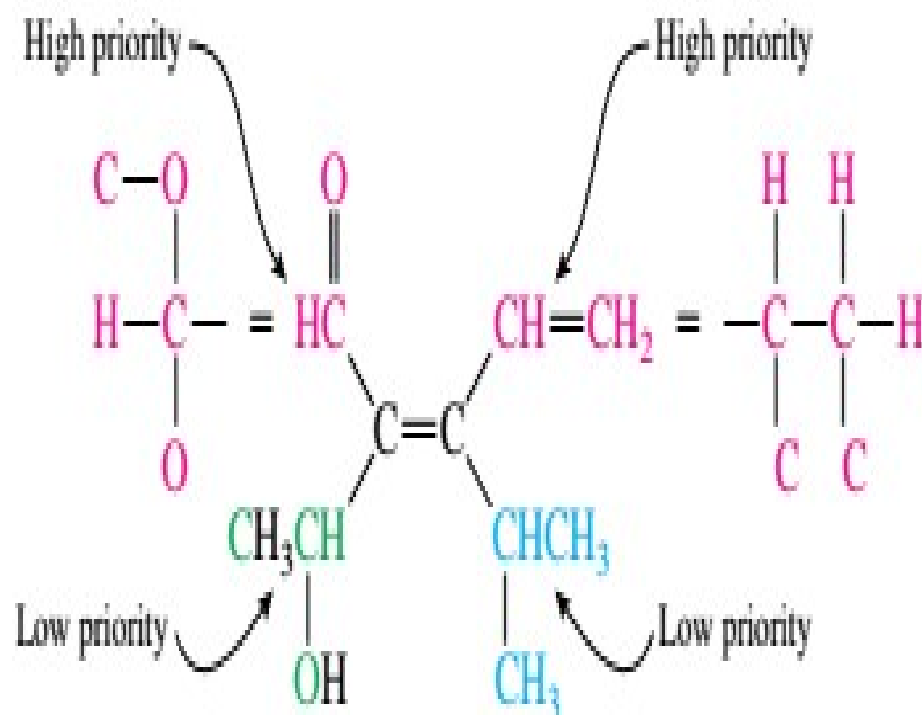


(E)-2-Isopropyl-3-methyl-2-penten-1-ol

- **RULE 3**

Double and triple bonds that are part of the groups attached to the double bond are treated as though they are constructed from two or three single





On this side of the double bond, the **upper (aldehyde) group** has higher priority. Its **carbon** is bonded to **O**, **O**, and **H**, whereas the **carbon of the bottom group** is bonded to **O**, **C**, and **H**.

On this side of the double bond, the **upper (vinyl) group** has higher priority. Its **carbon** is bonded to **C**, **C**, and **H**, but so is the **bottom carbon**. The **next carbon out** on the vinyl group is bonded to **C**, **H**, and **H**, whereas the next **carbon on the lower group** is bonded to **H**, **H**, and **H**.

- On the left side the upper carbon has higher priority because it is bonded to two C's and one H, whereas the lower carbon is bonded to one C and two H's. On the right side the oxygen of the upper group is attached directly to the carbon-carbon double bond and has a higher priority than the carbon of the lower group. The higher-priority groups are on the same side, so this is the (Z)-isomer.

