

# Stereochemistry

Structural or constitutional isomers...

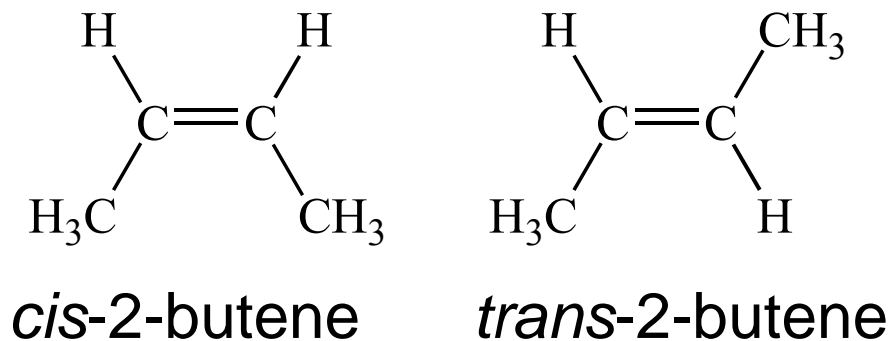
- have the same molecular formula but different connectivity (skeletal, positional, functional)

Stereoisomers...

- have the same connectivity but a different arrangement of atoms in space

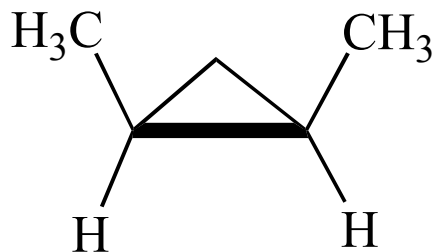
Recall:

2-butene

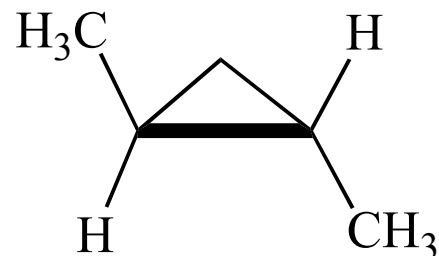


- Trans and Cis can also be used for disubstituted cycloalkanes (no bond rotation):

1,2-dimethylcyclopropane

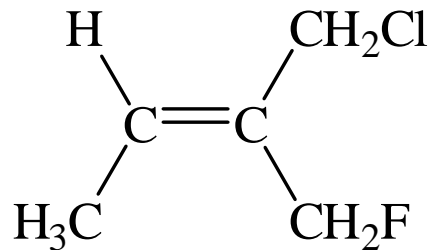
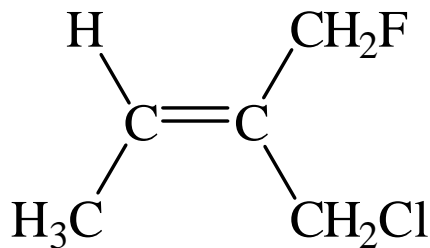


*cis*



*trans*

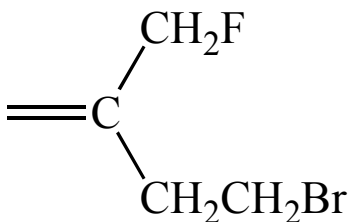
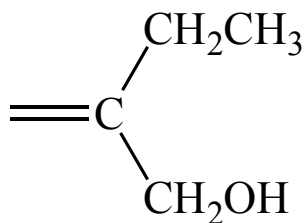
- What if there are less than 2 H atoms?
- What if more than one bonded to the alkene is the same?

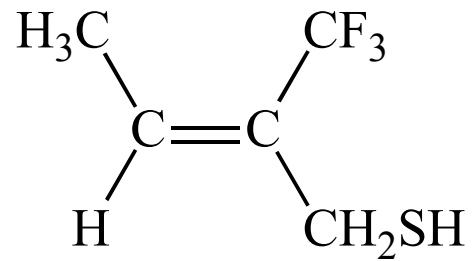
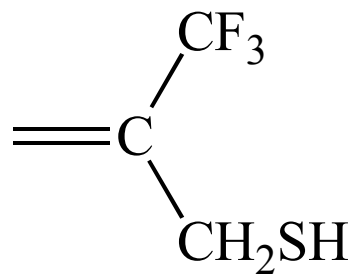
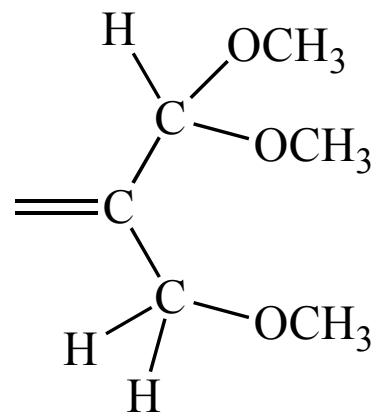


# The Cahn-Ingold-Prelog Rules for determining substituent priority:

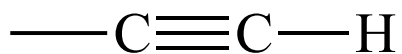
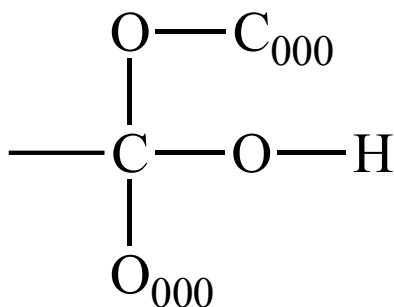
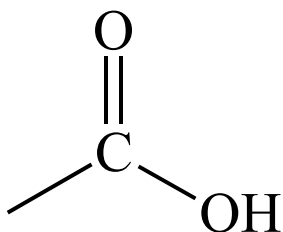
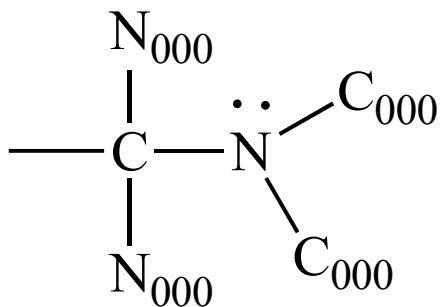
Substituents are evaluated by comparing atoms that are equidistant from the point of interest.

- 1) The higher the atomic number,  $Z$ , the higher the priority (higher atomic weight).
- 2) For atoms with the same  $Z$ , the heavier (isotope) has higher priority ( $^{13}\text{C}$  vs.  $^{12}\text{C}$ ,  $^2\text{H}$  (D) vs. H).
- 3) If the atoms attached are the same, then move out to the next shell of atoms one bond further always comparing atoms that are equidistant.
- 4) If a substituent contains  $\pi$ -bonds, interpret them as multiple  $\sigma$ -bonds between the same atoms (e.g. an aldehyde has a carbon which is bonded to 2 oxygen atoms and one hydrogen atom).

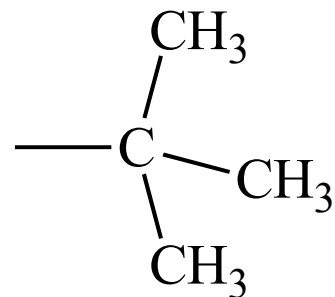




Another level of complexity with multiple bonds:

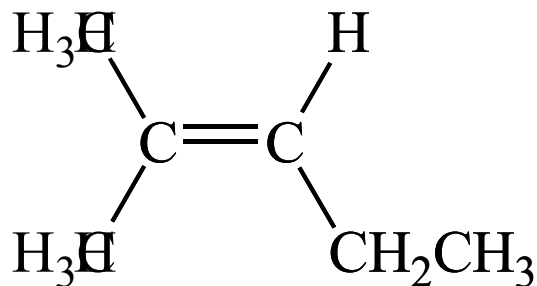
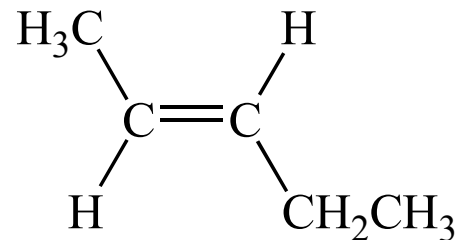
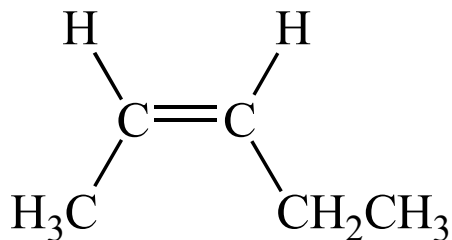


vs.



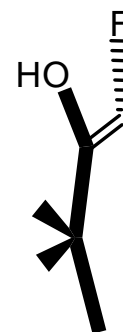
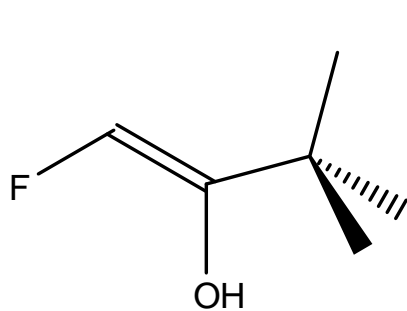
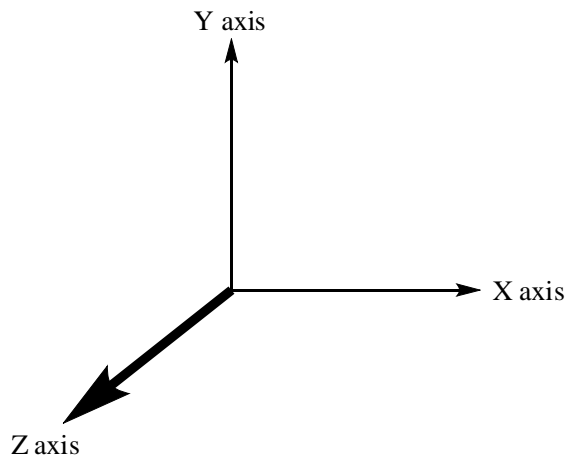
How do you know when molecules are the same?

Molecules are identical if, in *equivalent conformations*, they are **superimposable**.

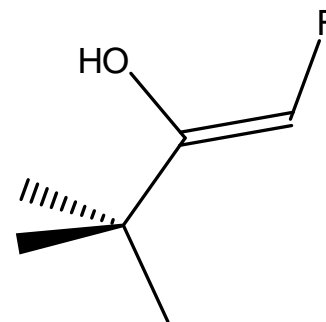


- If the connectivity of two molecules differs, then they are constitutional isomers. If the connectivity is the same but the molecules are not superimposable, then they are stereoisomers.

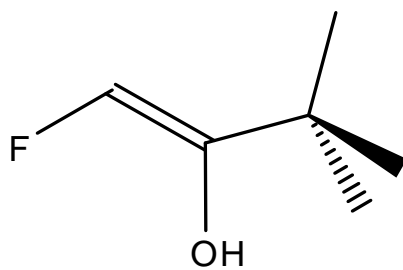
How about these two?



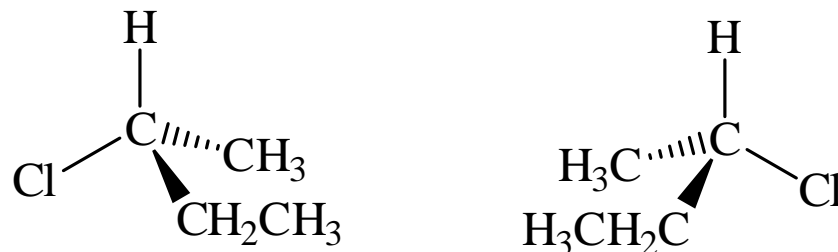
Rotate about y-axis to place most atoms in the plane of the page.



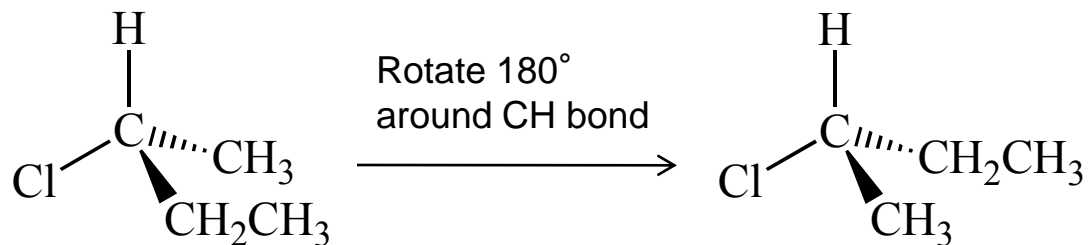
Rotate  $\sim 160^\circ$  counterclockwise about z-axis



## Stereochemistry at tetrahedral centres:



Are these molecules the same?

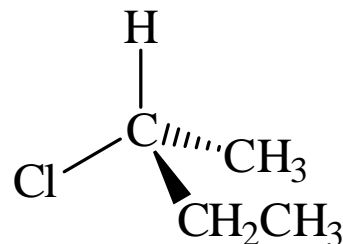
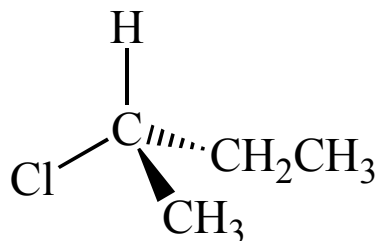


**Configuration:** the actual arrangement in space of the substituents around a given asymmetric atom that can be designated R or S. Also applies to E/Z.

**Chiral or stereogenic centre:** Any tetrahedral atom, frequently carbon, which has 4 different substituents. Also called stereocentre

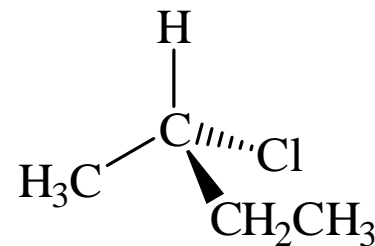
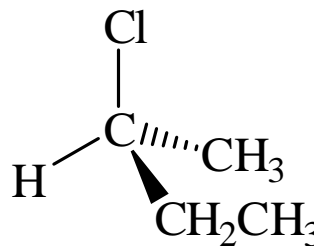
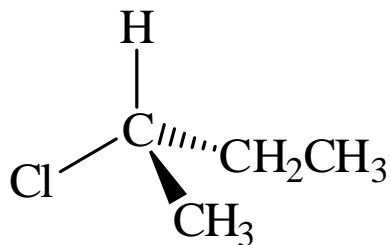
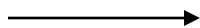
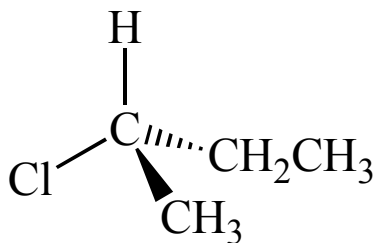


There are only 2 possible configuration for tetrahedral centres:



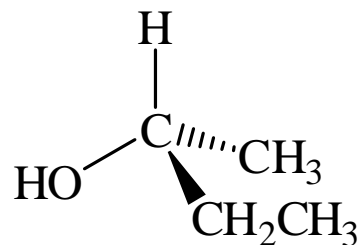
These two configurations cannot be interchanged without breaking bonds!

If you switch any two substituents, then the configuration changes:

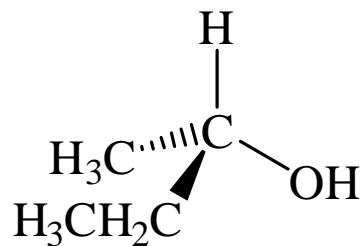


Make 2 models, convince yourself this is true...

Solutions that rotate plane-polarized light are said to be "optically active".



(-)-2-Butanol



(+)-2-Butanol

**Dextrorotatory** - rotates ppl in a clockwise direction.

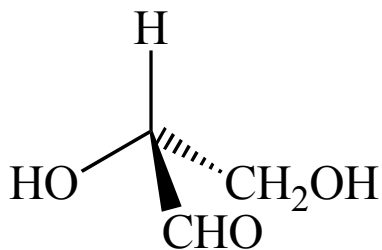
**Levorotatory** - rotates ppl in counterclockwise direction

How do we distinguish between different absolute configurations? How do we label them?

Historically...(bit still used today for certain classes of molecules)

### The D/L Convention of Fischer

Absolute configuration: The actual three-dimensional arrangement of groups around an asymmetric center.



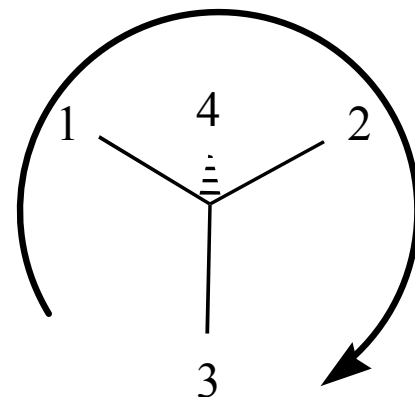
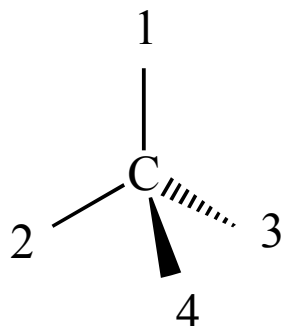
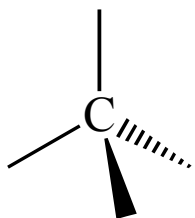
D-Glyceraldehyde

All sugars with the same absolute configuration next to the CH<sub>2</sub>OH group are "D". Those with opposite absolute configuration are "L"

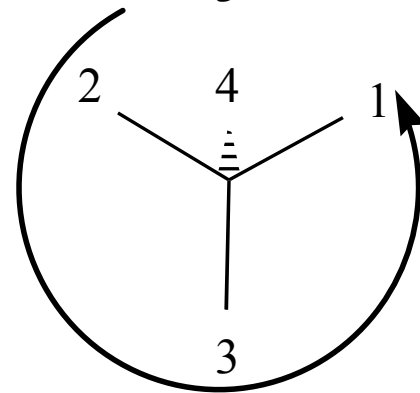
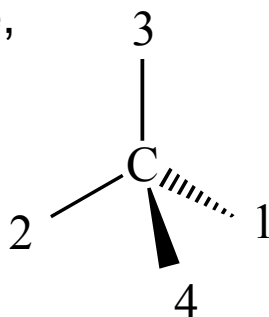
Note that this designation now has nothing to do with the direction the molecule rotates ppl.

How do we name compounds such that their absolute configuration is indicated?

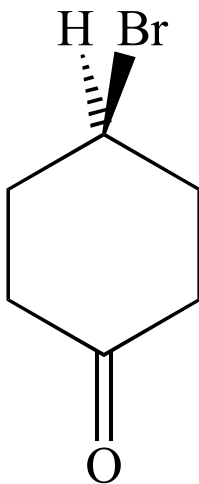
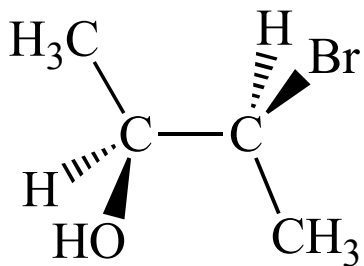
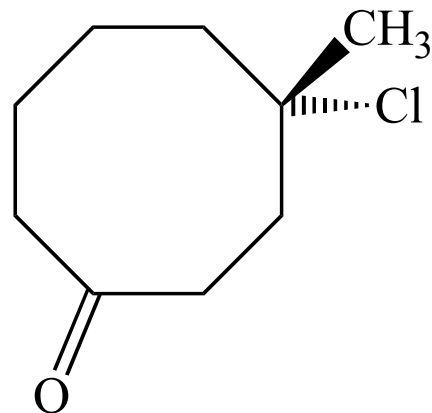
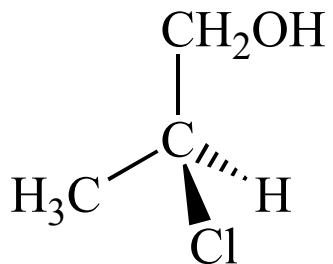
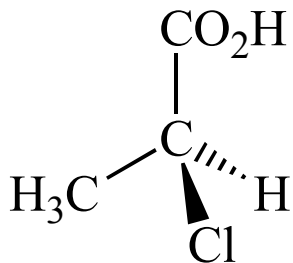
1. We assign priorities, 1 to 4 (using the rules established by Cahn, Ingold and Prelog), to the substituents of an asymmetric atom
2. Reorient the centre such that the lowest priority, 4, is positioned into the plane of the board.
3. If the remaining substituents are arrayed 1-2-3 in clockwise order, then the center has **R** configuration:



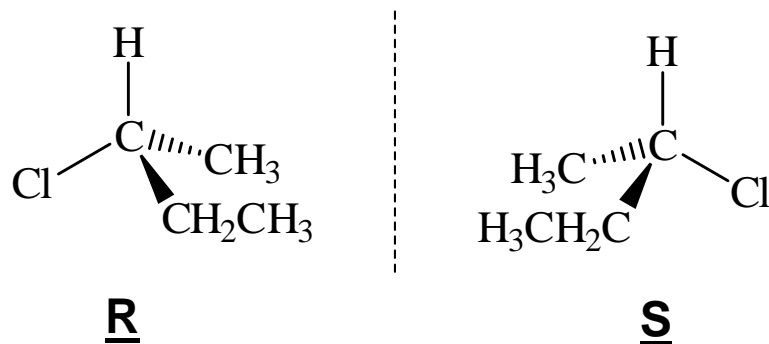
4. If the order is counterclockwise, the centre is **S**:



Try to assign these (a model kit is exceedingly helpful!):

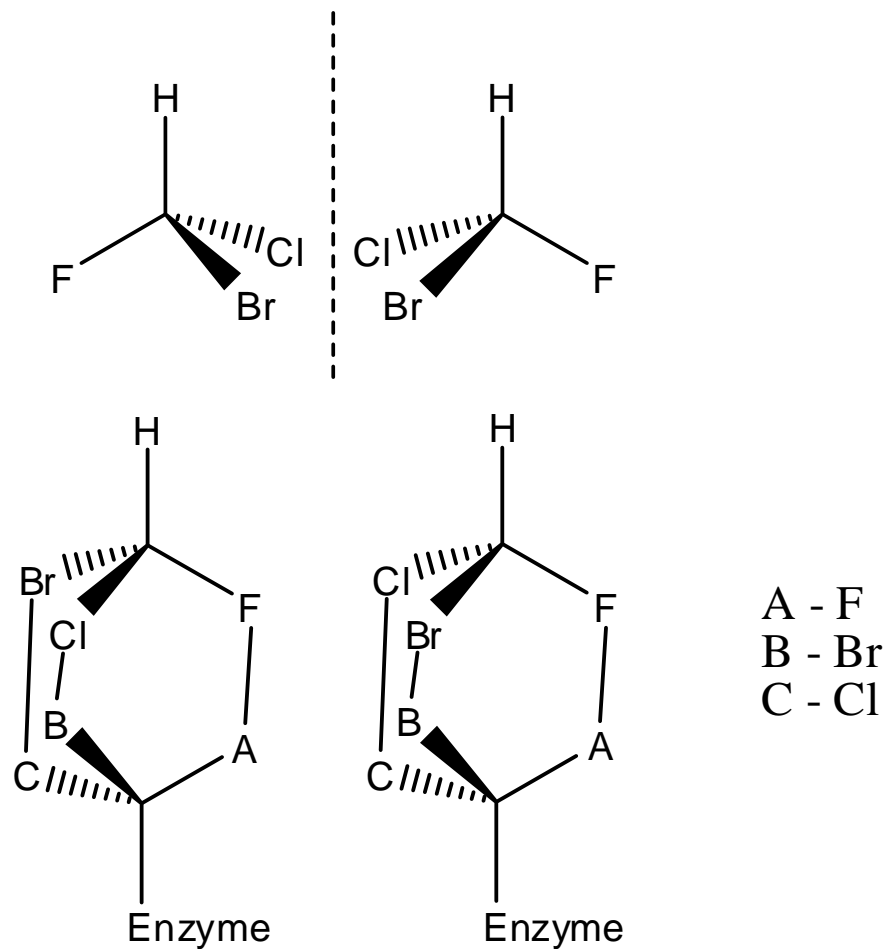


**Enantiomers**: are molecules that are non-superimposable mirror-images of one another.



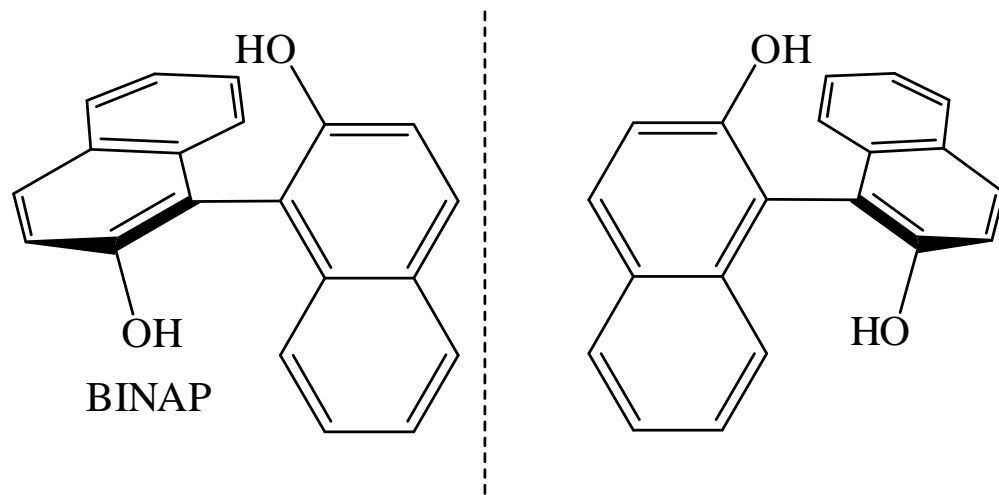
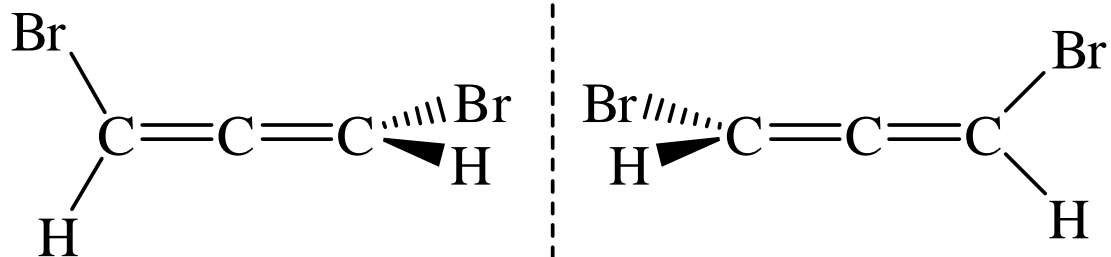
- Enantiomers have identical physical properties in all respects (thus difficult to separate from each other), except they rotate plane polarized light in opposite directions (unrelated to absolute configuration). Such molecules are said to be **optically active**.
- Thus, a 50/50 mixture of two enantiomers (a **racemic mixture**) will not rotate plane polarized light.
- A mixture of enantiomers that is optically active (i.e. not a 50/50 mixture) is said to be **scalemic**.

Why would only one enantiomer cause a certain problem/react with a given substrate?



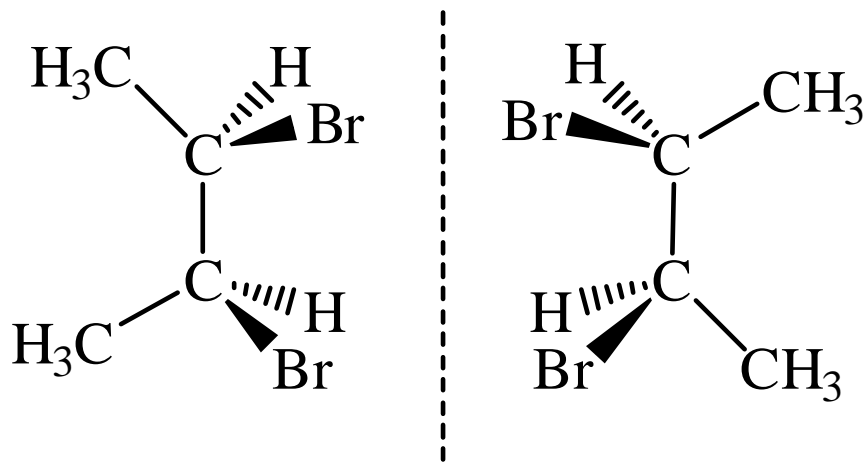
- An object is **chiral** if it is nonsuperimposable on its mirror image.
  - **Achiral**: an object (molecule) which is superimposable upon its mirror image.
- If a molecule has a plane of symmetry it is not chiral.

Can a molecule without any chiral centres be chiral?



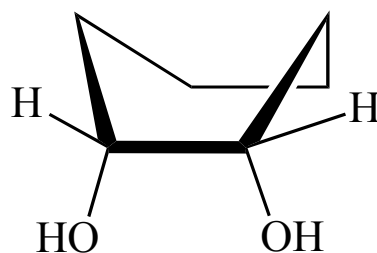
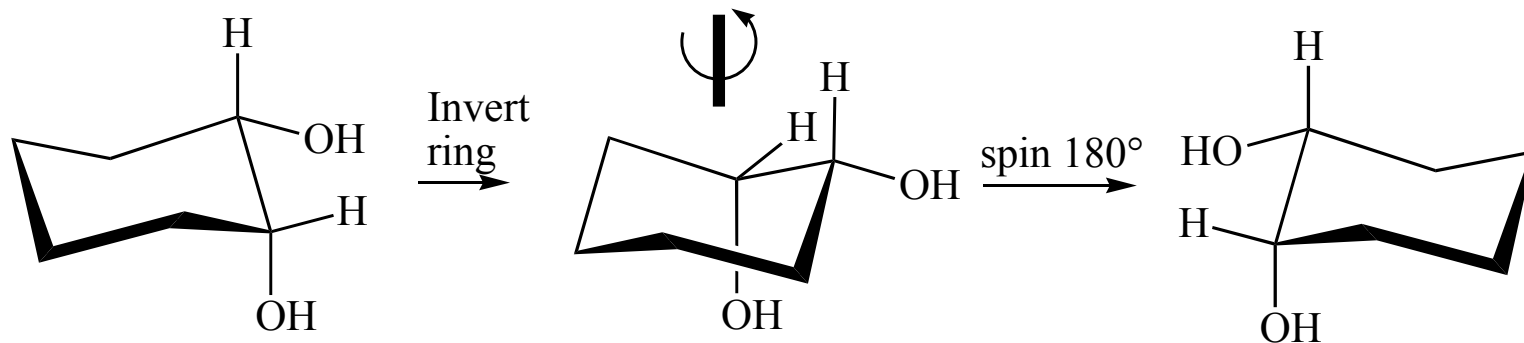


Can a molecule with centres be achiral?

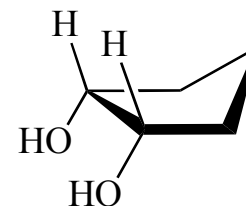
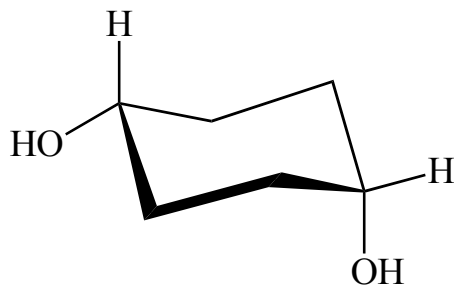


- Only if there is an even number of chiral centres.

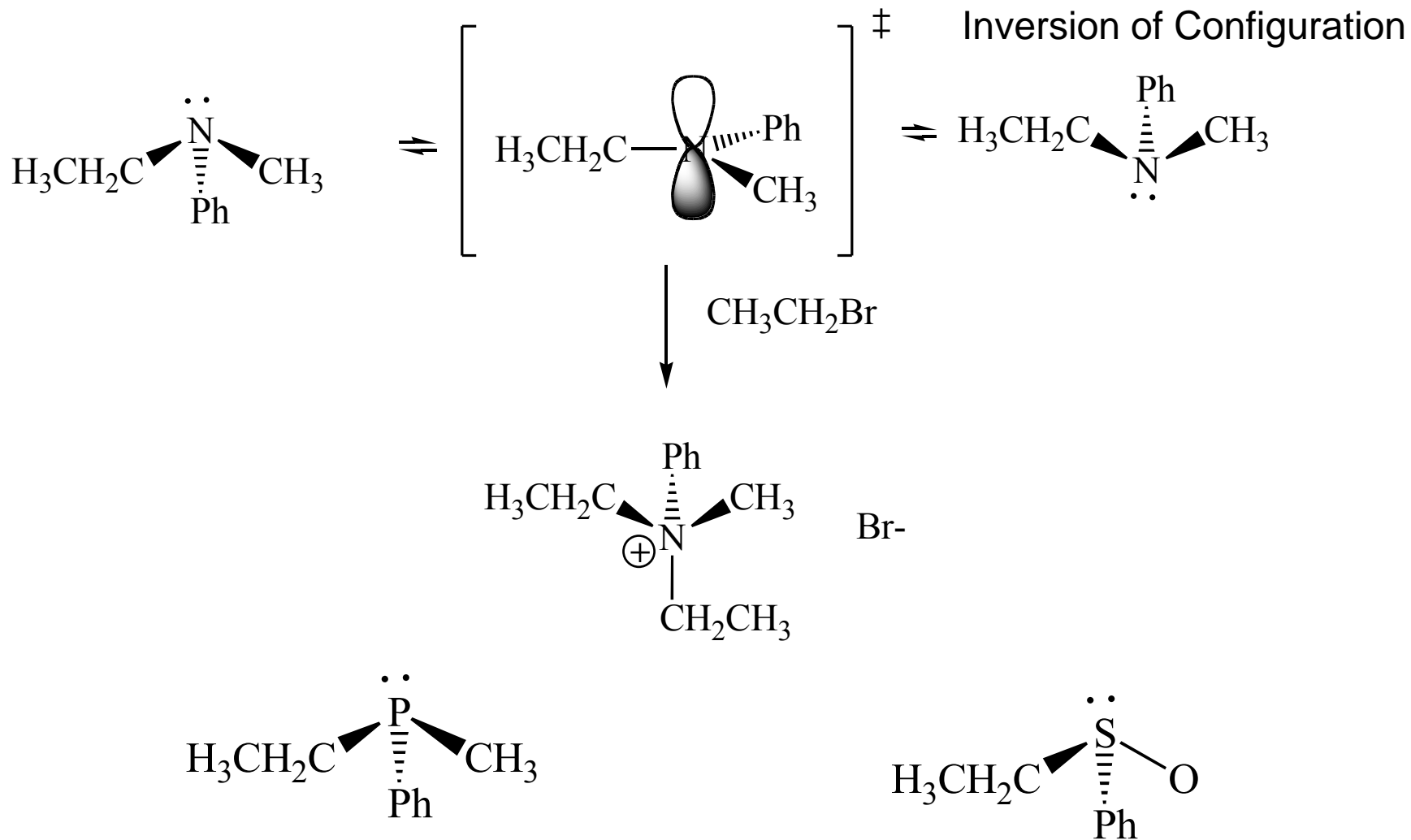
**Meso** compounds have chiral centres, but are achiral (they have an internal plane of symmetry)



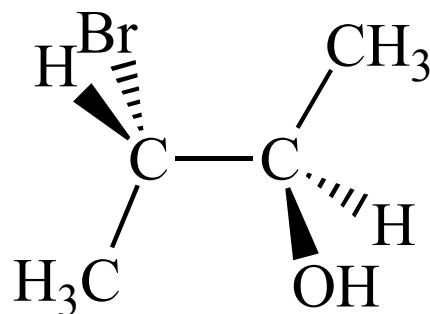
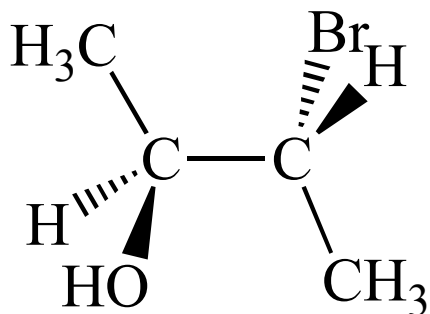
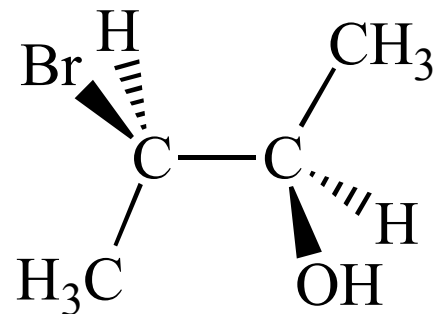
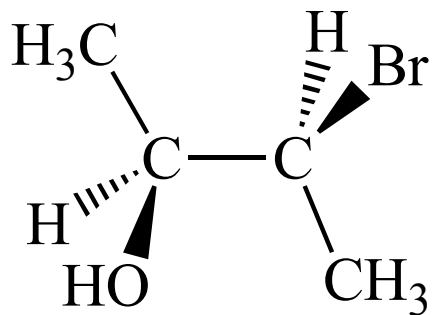
If there exists any (accessible) conformation in which a molecule is achiral, then it is achiral, period.



Atoms other than carbon?



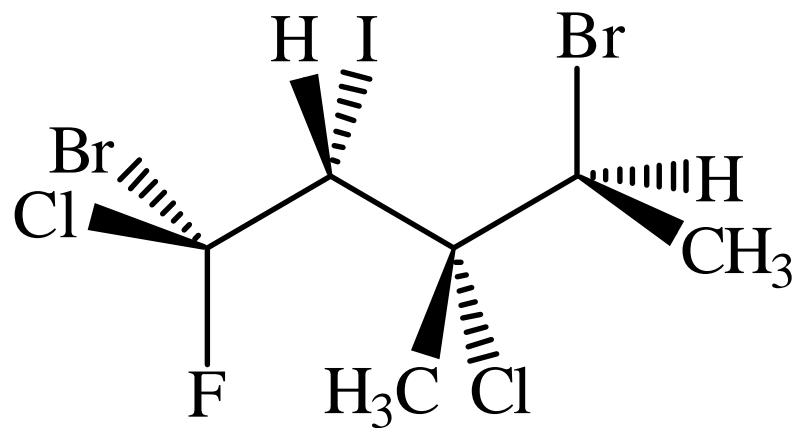
## Molecules with two chiral centers...



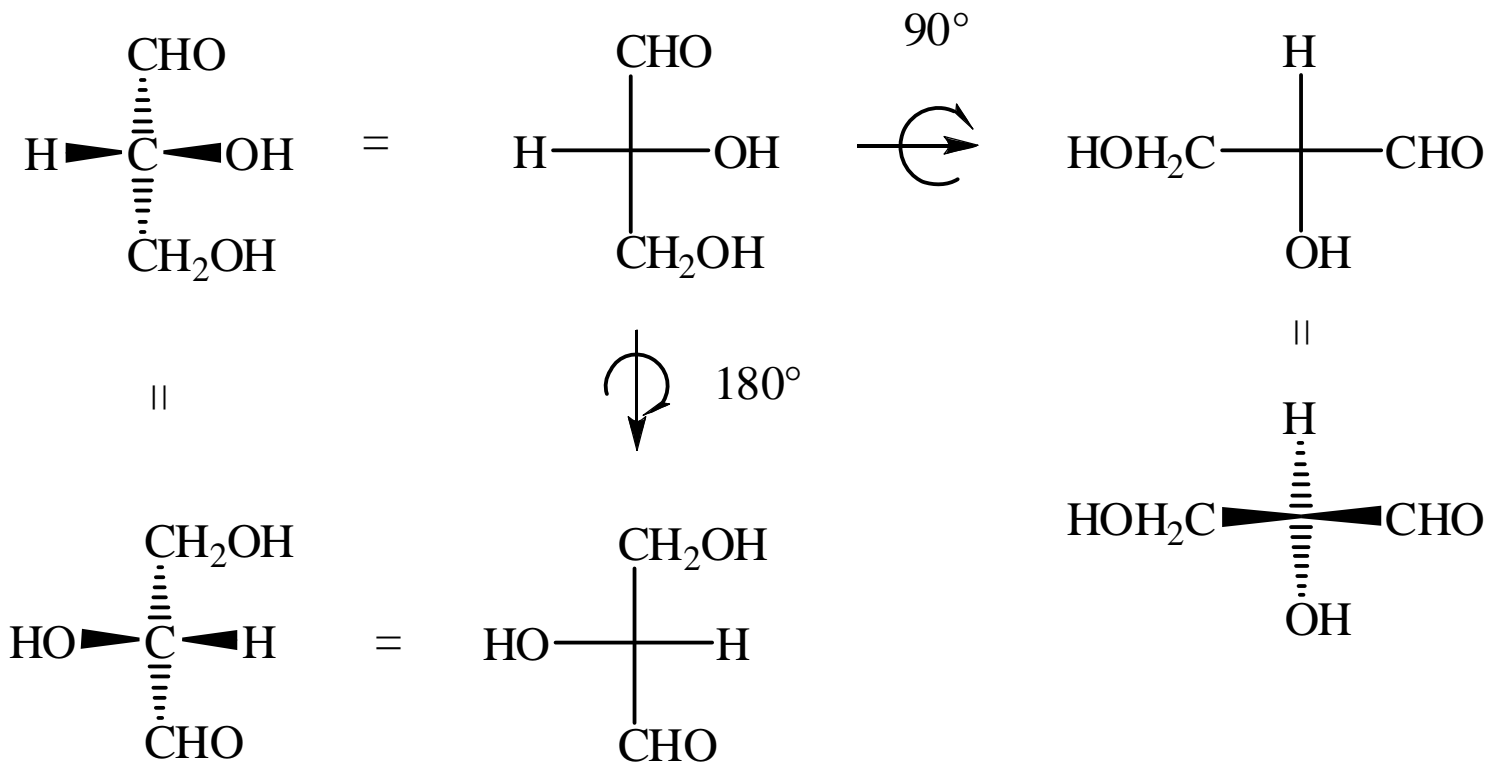
**Diastereomers**: non-superimposable, non-mirror images

- Diastereomers have different physical properties and can easily be separated from one another.
- A molecule can have a maximum of  $2^n$  possible stereoisomers ( $n$  = number of chiral centres).

Draw all possible stereoisomers and indicate which are enantiomers and which are diastereomers:



**Fischer Projections:** a shorthand notation for showing absolute configurations. In no way do these diagrams attempt to show the actual shape of molecules.

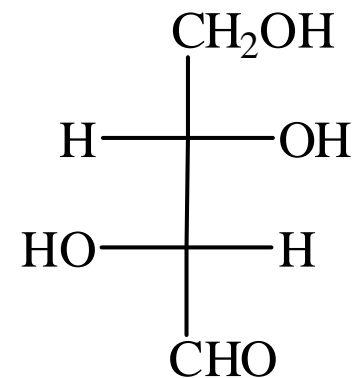
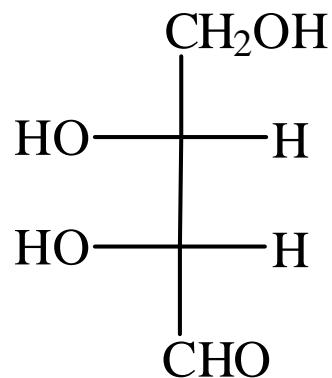
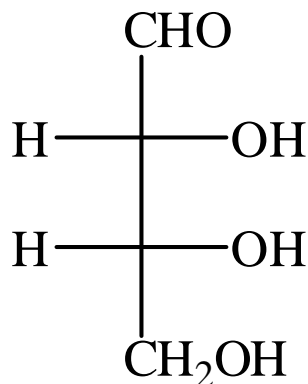
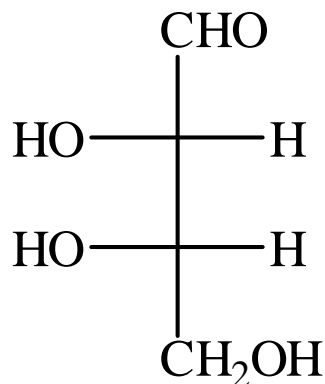


A 90° or 270° rotation of a Fischer projection generates...

A 180° rotation of a Fischer projection generates...

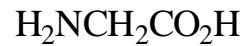
Use models to convince yourself this is true!

Fischer projections were developed to aid in drawing molecules (sugars) with many chiral centers. It is easy to spot enantiomers and superimposable molecules when drawn as these projections.



Amino acids are chiral and have the same absolute configuration.

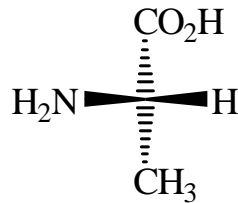
Amino acids



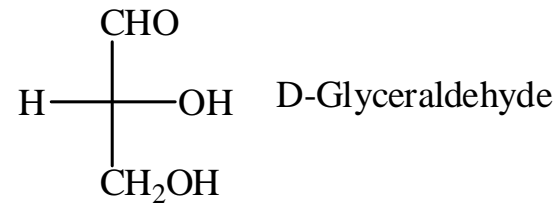
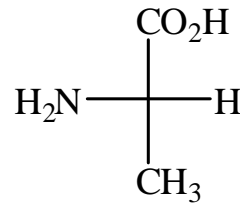
Glycine



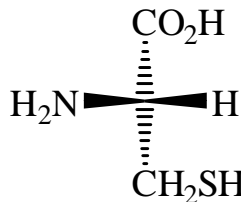
Alanine



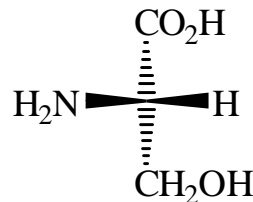
L-Alanine



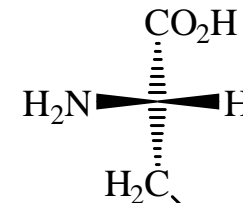
D-Glyceraldehyde



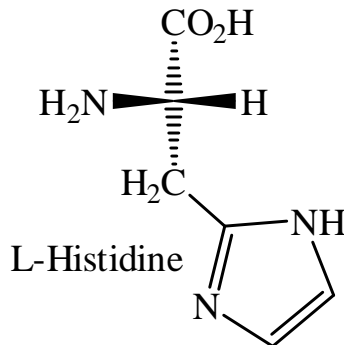
L-cysteine



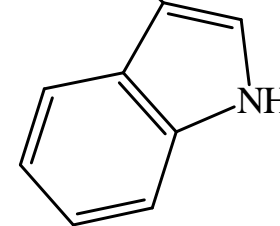
L-Serine



L-tryptophan

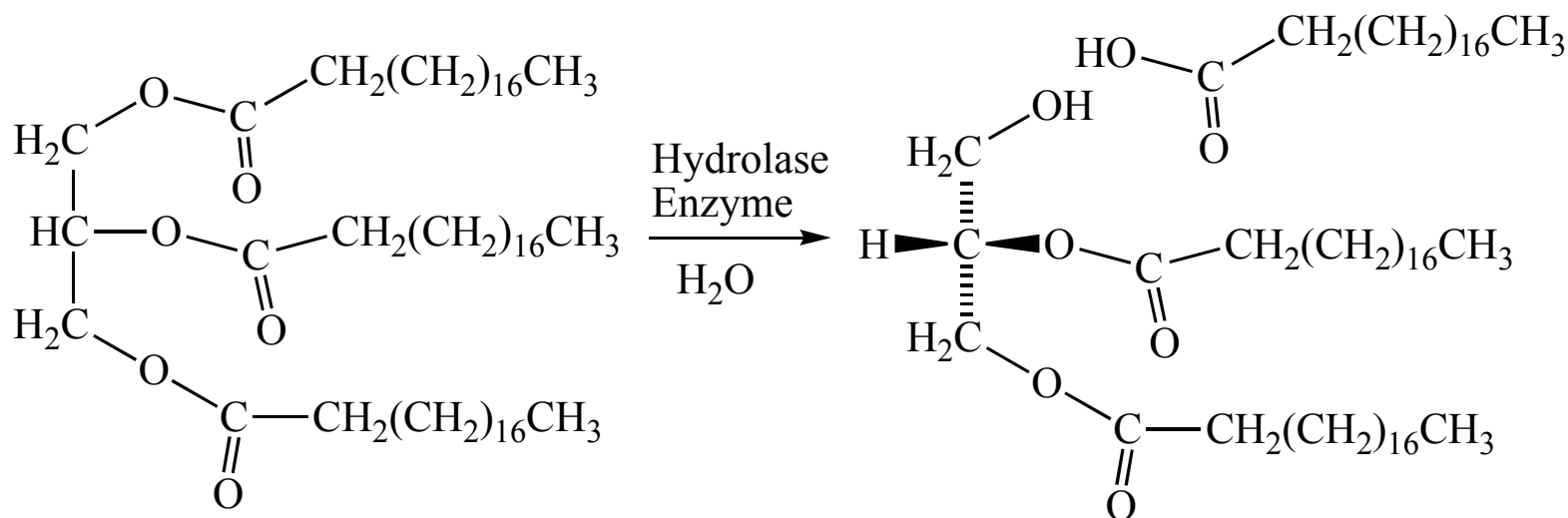
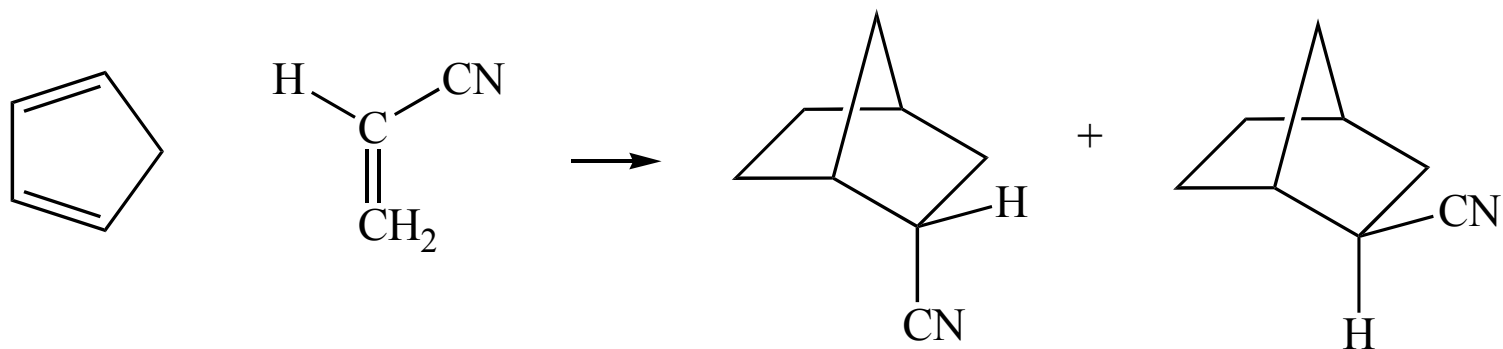


L-Histidine



These are called L-amino acids not because they all rotate plane-polarized light in a levorotatory fashion (they don't) but because of their structural relationship to D-glyceraldehyde.



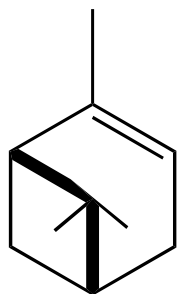


Tristearyl glycerol, a triglyceride

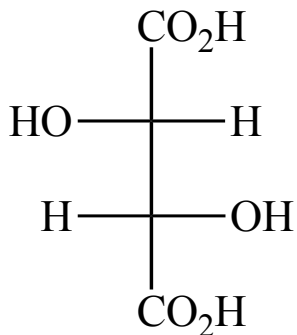
A diglyceride.

You cannot make one enantiomer of a product preferentially starting only with achiral molecules. In other words, you must use optically active material (catalyst, reactant, solvent etc.) in order to prepare something that is optically active.

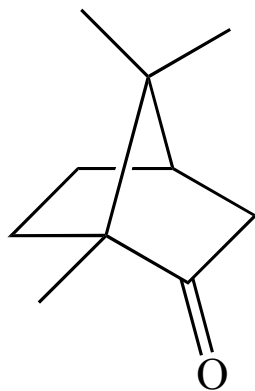
The chiral pool...



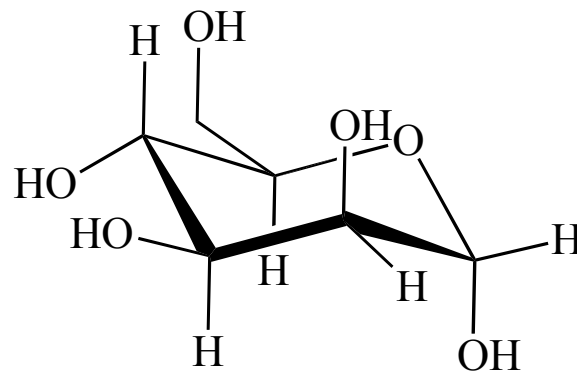
R-+-Pinene



D-Tartaric acid

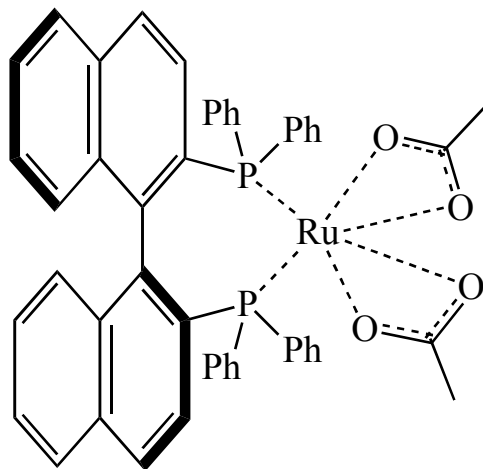


R-+-Camphor

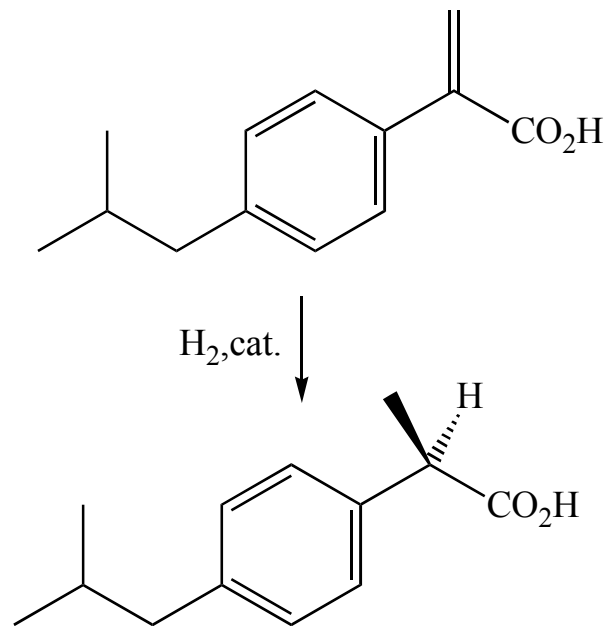


D-Mannose

## Asymmetric Catalysis



S-BINAP



## Stereochemistree

So, you've got two molecules and you want to know their relationship...

