

Stereochemistry

Stereoisomerism

Isomerism

There are three major types of isomerism:

- constitutional isomerism
 - geometrical isomerism
 - optical isomerism
- } stereoisomerism

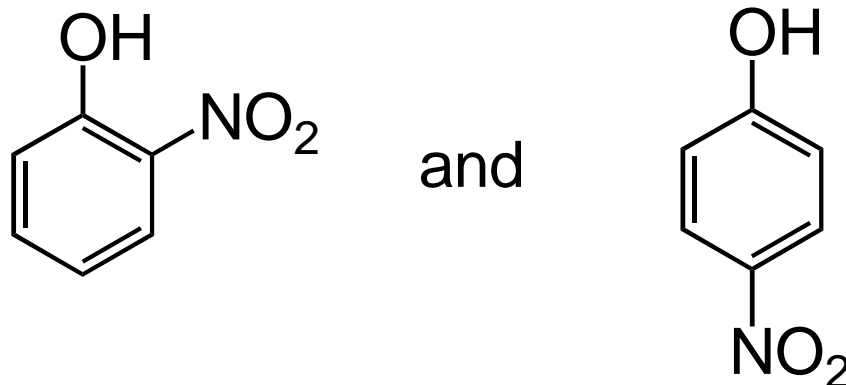
Constitutional isomers

Constitutional isomers (also known as structural isomers) have the same molecular formula but differ in the sequence in which the individual atoms are bonded (connectivity).

- skeletal isomerism



- positional isomerism



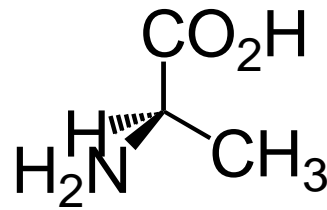
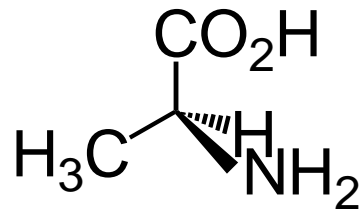
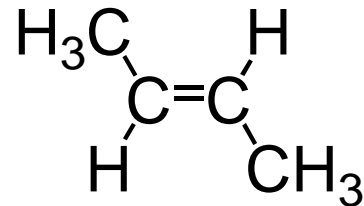
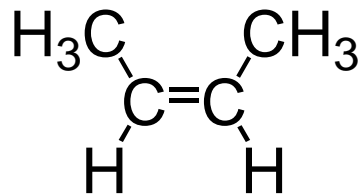
Constitutional isomers

- Functional isomers: - compounds of identical molecular formula but which have different functional groups.

e.g. $\text{C}_2\text{H}_5\text{OH}$ and CH_3OCH_3

Stereoisomerism

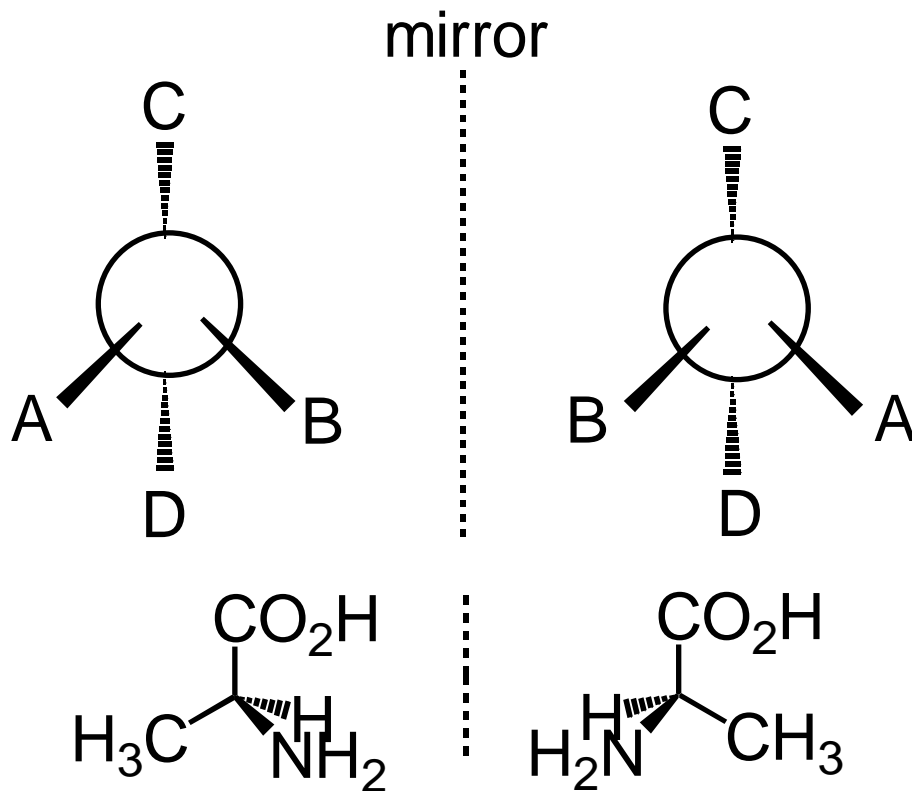
Stereoisomers have the same atomic connectivity but differ in the spatial arrangement of the constituent atoms.



alanine

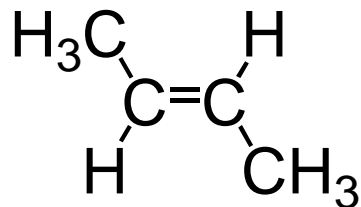
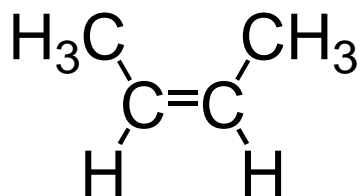
Enantiomers

Enantiomers are stereoisomers that are non-superimposable on their mirror images.



Diastereomers

Diastereomers are stereoisomers that are not mirror images of each other – they are stereoisomers that are not enantiomers.



Chirality

Molecules that can exist as enantiomers are said to be chiral; they are non-superimposable on their mirror images.

Chirality is a necessary and sufficient condition for the existence of enantiomers.

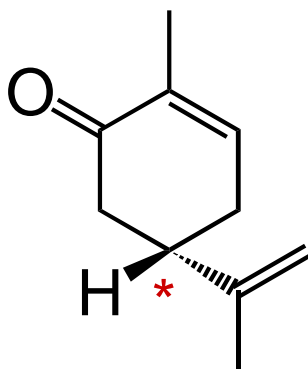
“cheir” - Greek meaning “hand”

Molecules that are superimposable on their mirror images are said to be achiral.

Try problem 5.1 on page 197 of Solomons and Fryhle.

Tetrahedral stereogenic centres

A carbon atom bonded to four different groups is called a tetrahedral stereogenic centre, asymmetric centre, or chirality centre.

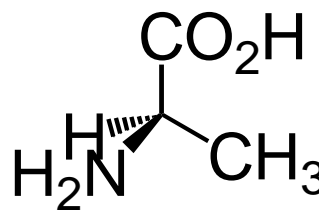
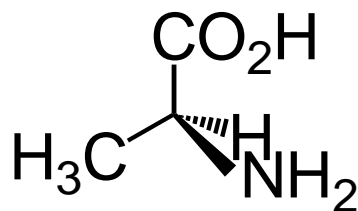
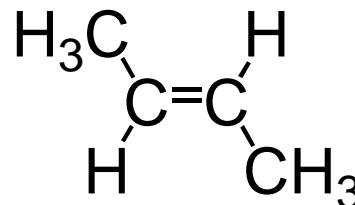
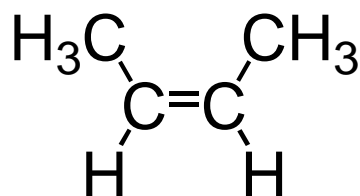


(+)-carvone

(+)-Carvone is responsible for the odour of caraway seed oil.

Stereogenic centres

A centre where a swapping of groups leads to a stereoisomer:

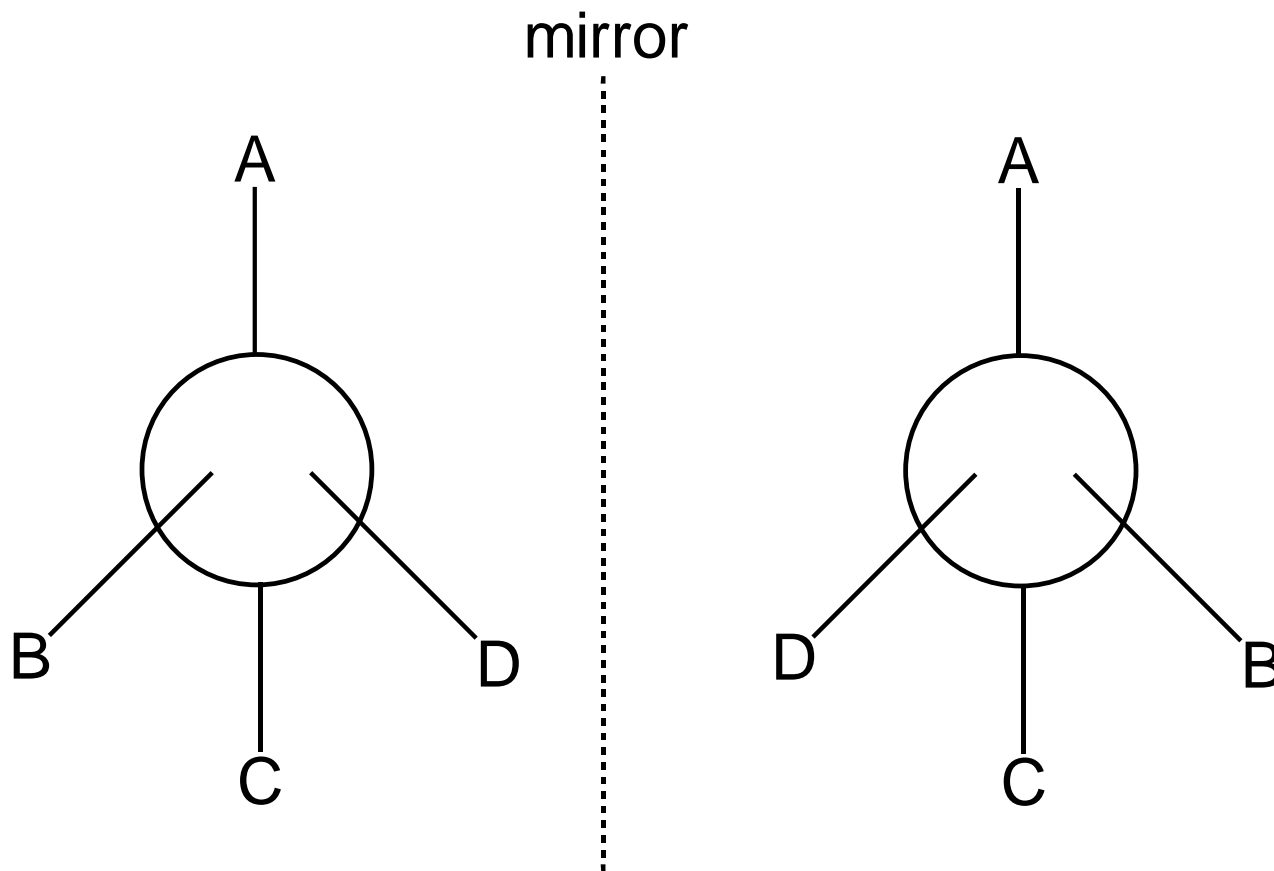


alanine

Historical origin of stereochemistry

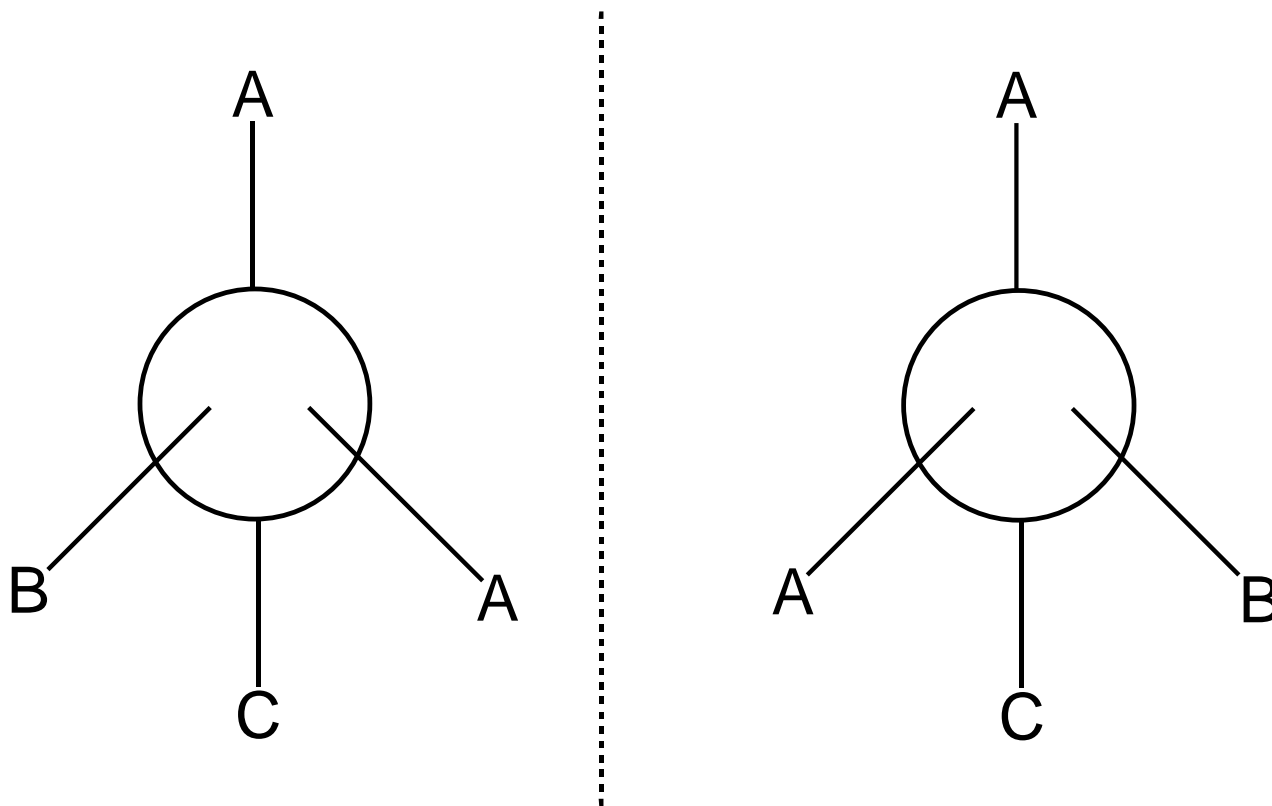
- Only one compound with the formula CH_3X is ever found.
- Only one compound with the formula CH_2XY is ever found.
- Two compounds with the formula CHXYZ are found – a pair of enantiomers.

van't Hoff and Le Bel



The two are non-superimposable, mirror images. Such isomers are called **enantiomers**.

Are these enantiomers?



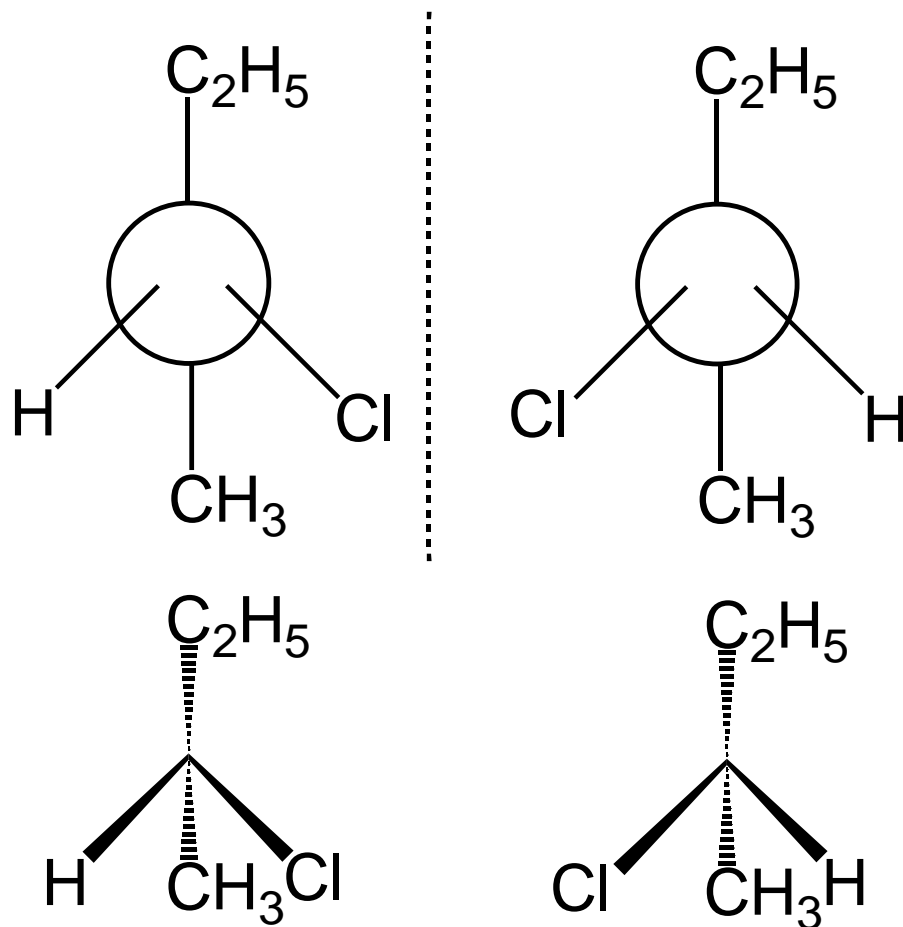
Configurations

The particular arrangement of atoms in space that is characteristic of a given molecule is called its configuration.

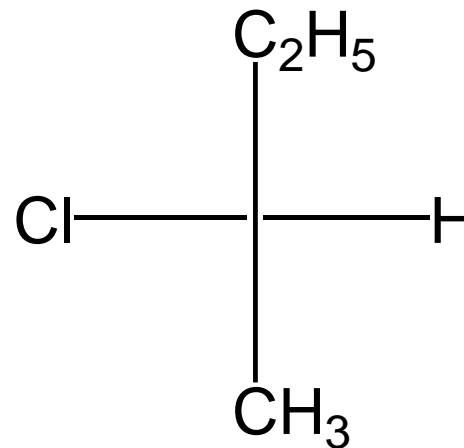
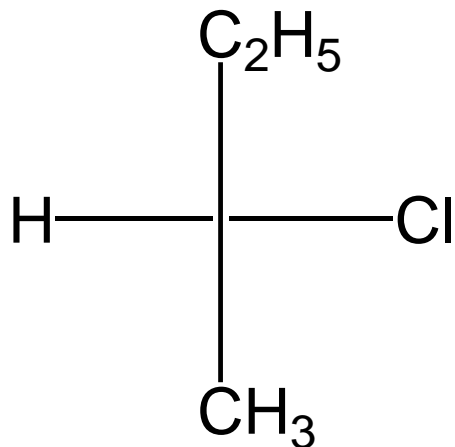
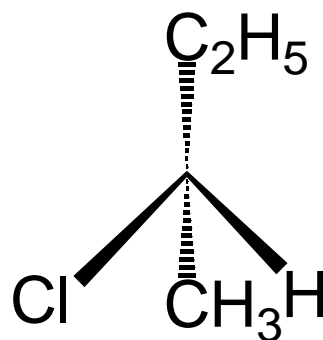
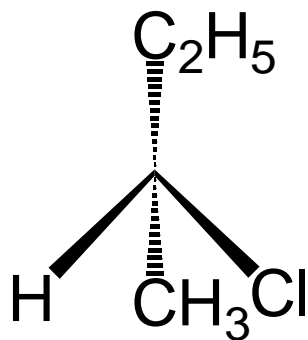
Configurations are not the same as conformations.

Conformations are interconvertible by rotation about single bond(s) whereas bonds must be broken to change one configuration into another.

How do we “draw” a chirality centre?



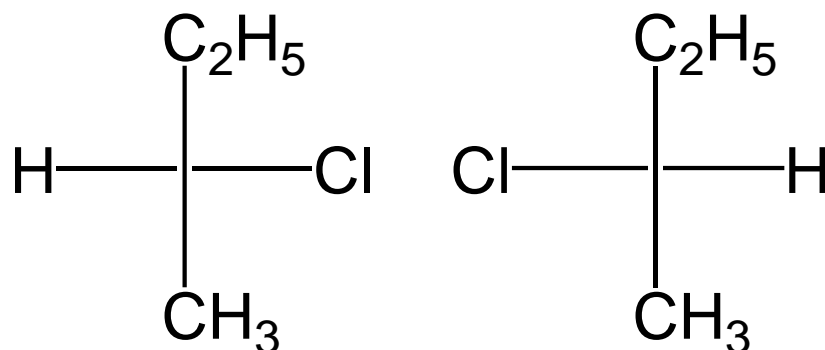
How do we “draw” a chirality centre?



Fischer structures.....

How do we “name” an enantiomer?

A problem.....How can we look at two Lewis structures and decide if they represent two identical compounds or a pair of enantiomers? How can we name them?



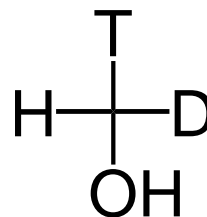
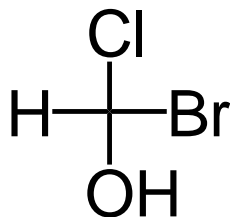
Let's take a drive through the Alps with....

R.S. Cahn, C.K. Ingold et V. Prelog, *Experientia*, 12, 81 (1956)

Cahn - Prelog - Ingold rules

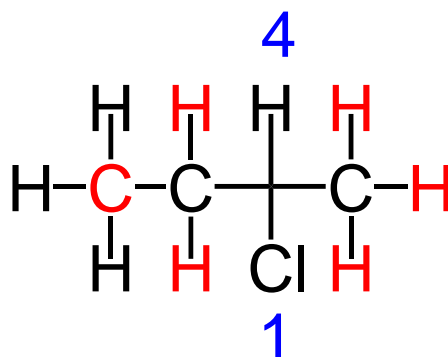
Step 1: assign a priority to the 4 atoms or groups of atoms bonded to the tetrahedral stereogenic centre:

1. If the 4 atoms are all different, priority is determined by atomic number. The atom of higher atomic number has the higher priority.



Determination of priority

2. If priority cannot be determined by (1), it is determined by a similar comparison of atoms working out from the stereocentre.

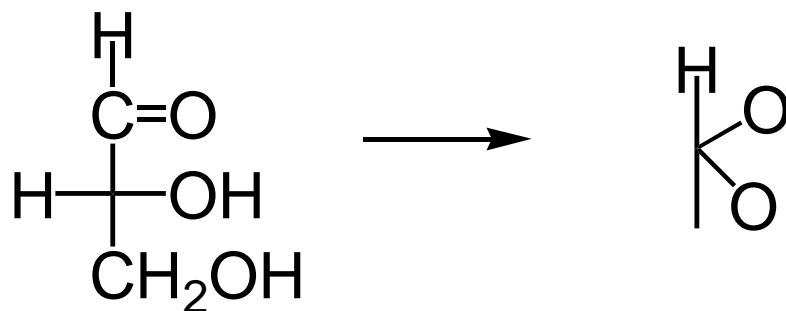


In the methyl group, the second atoms are H, H, H whereas in the ethyl group, they are C, H, H.

The priority sequence is therefore Cl, C₂H₅, CH₃, H.

Cahn - Prelog - Ingold rules

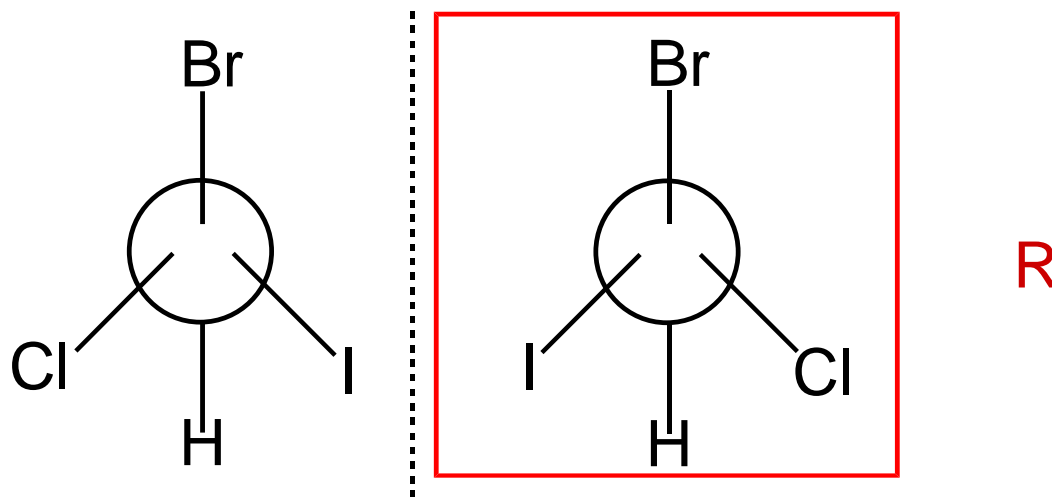
3. A double or triple bond to an atom, **A**, is considered as equivalent to two or three single bonds to **A**:



The sequence is therefore -OH, -CHO, -CH₂OH, -H.

Step 2

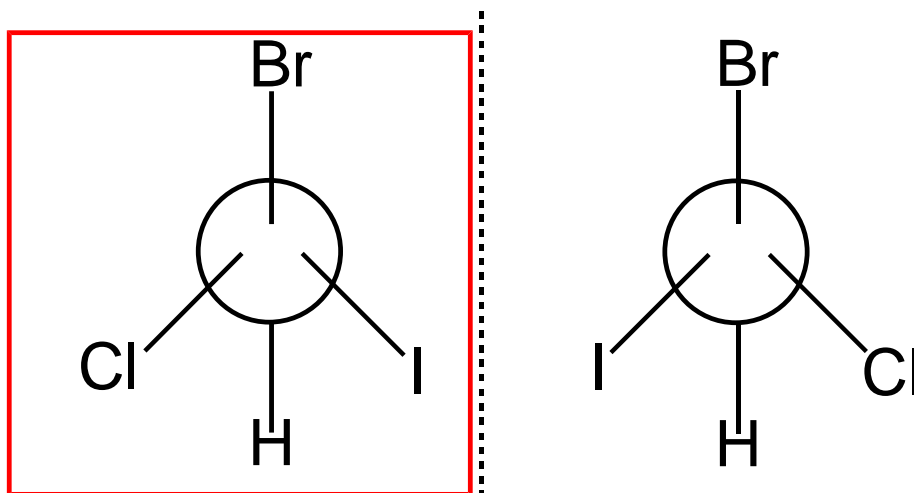
Arrange the molecule so that the group of lowest priority is pointing away from you and observe the arrangement of the remaining groups:



If, on going from the group of highest priority to that of second priority and then to the group of third priority, we go in a clockwise direction, the enantiomer is designated (R).

Step 2

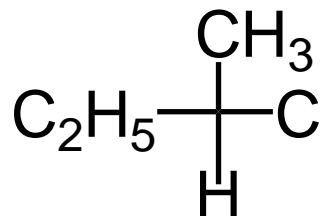
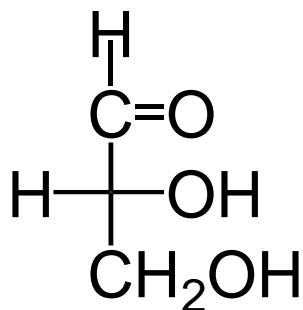
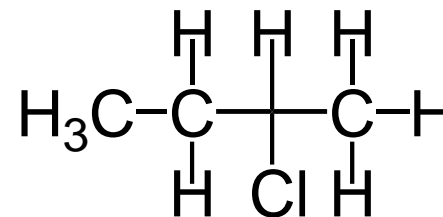
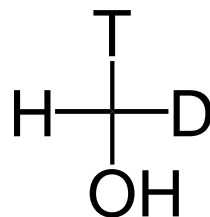
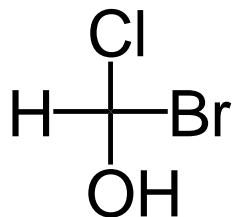
(S)



If the direction is counterclockwise, the enantiomer is designated (S).

Thus the complete name for one of the enantiomers of 2-chlorobutane is (R)-2-chlorobutane.

R or S?



Problems

Try problems 5.11 and 5.12, page 206, and 5.13 on page 208 of Solomons and Fryhle.

Properties of enantiomers

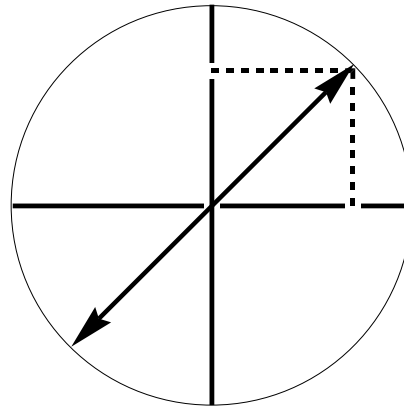
a) Physical: Enantiomers have identical physical properties with the exception that they rotate the plane of polarized light in opposite directions although $|\alpha|$ is identical.

b) Chemical: They have identical chemical properties except for their reaction with reagents which are, themselves, optically active. In this case, reaction rates differ and depend on which enantiomer of the reagent is used.

(+)-Glucose is central to the fermentation process whereas (-)-glucose doesn't react!

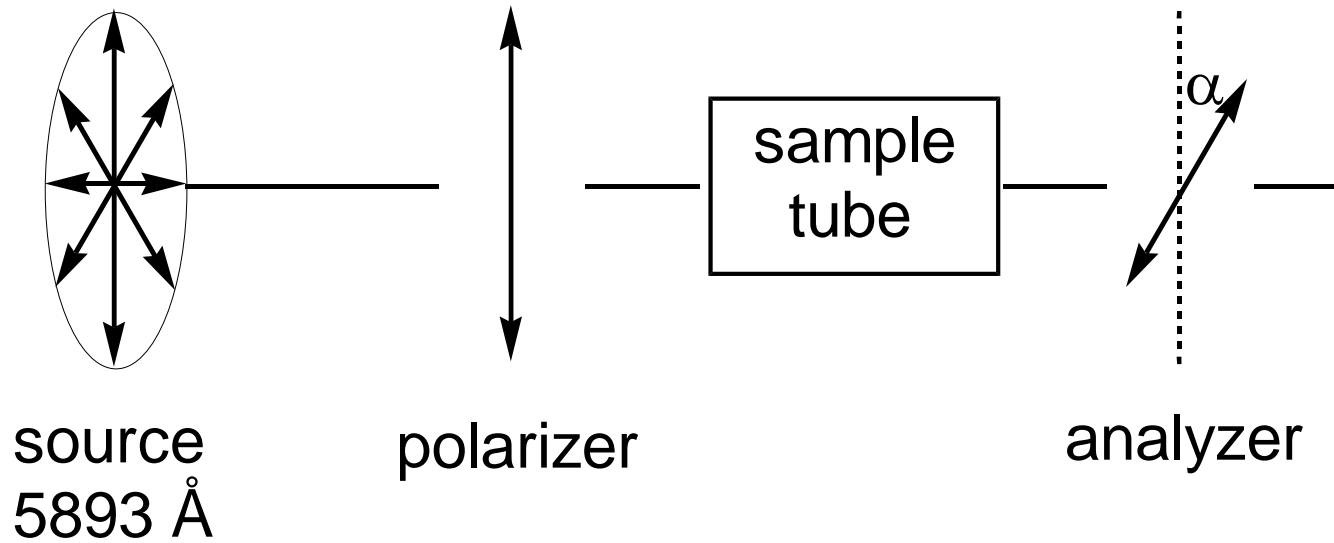
Plane-polarized light

Ordinary light is a moving wave whose vibrations take place in all directions perpendicular to the direction in which the light is travelling. One can envisage each vibration as the vector of two vibrations which are mutually at right angles.



One of these components can be eliminated by passing ordinary light through a polarizer - Polaroid filter. The resulting light is said to be polarized - all its vibrations are parallel to a single plane.

Polarimeter



Optical activity

An optically active compound is one which rotates the plane of polarization.

If from the vantage point of the observer the rotation is in the clockwise direction, the sample is said to be dextrorotatory. The angle of rotation, α , is considered to be positive (+).

If the rotation is in the counterclockwise direction, the sample is said to be levorotatory and the angle, α , is then negative (-).

There is no correlation between (+)/(-) and (R)/(S). Thus (R)-2-chlorobutane is the levorotatory enantiomer.

Specific rotation

α is proportional to the concentration of the sample and the length of the sample tube:

$$[\alpha]_{\lambda}^t = \frac{\alpha}{l \times c}$$

α - angle of rotation measured in degrees

t - temperature

λ - wavelength of light

l - length of sample cell

c - concentration in grams of substance contained in 1 mL of solution

Racemic mixtures

An equimolar mixture of two enantiomers.

Prefix the name with \pm .

Reactions performed using an achiral reagent can form products have a tetrahedral stereogenic centre. However the product will be a racemic mixture.

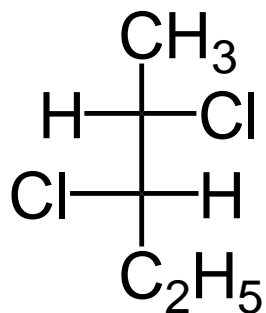
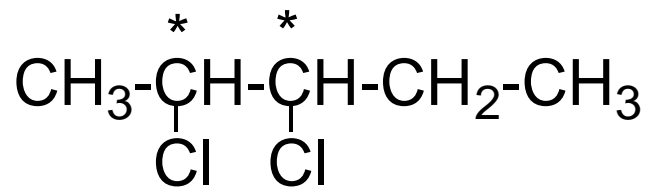
If the reagent is chiral, one can often produce a single enantiomer of the product molecule.

Molecules with more than one stereogenic centre

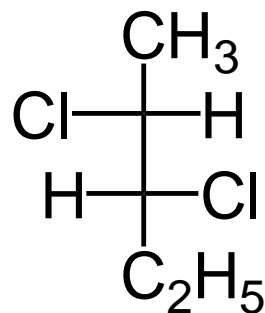


How many stereoisomers exist for this compound?

2,3-dichloropentane

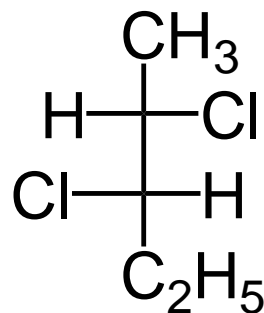


(2S,3S)

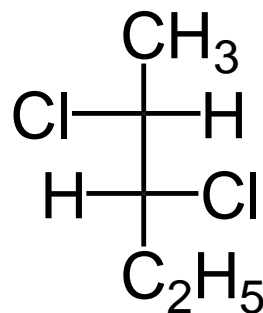


(2R,3R)

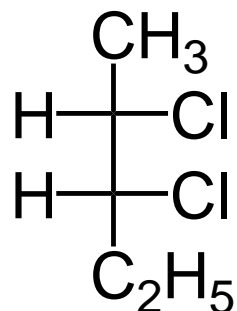
2,3-dichloropentane



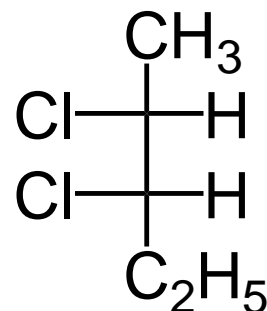
(2S,3S)



(2R,3R)



(2S,3R)



(2R,3S)

How many stereoisomers exist?

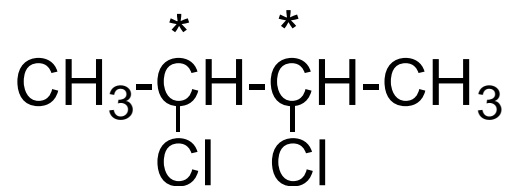
The **maximum** number of stereoisomers that can exist is equal to

$$2^n$$

where n is the number of tetrahedral stereogenic carbons in the molecule.

2,3-dichlorobutane

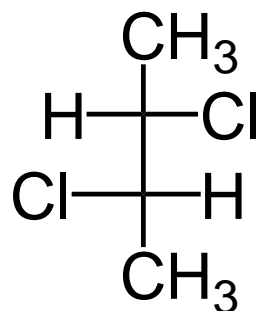
Look at 2,3-dichlorobutane. Are there four different isomeric forms?



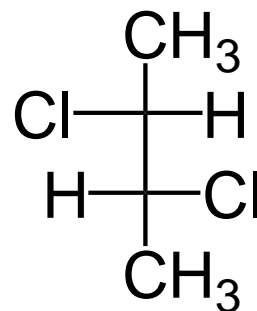
There are two tetrahedral stereogenic carbons..... 2^n ?

2,3-dichlorobutane

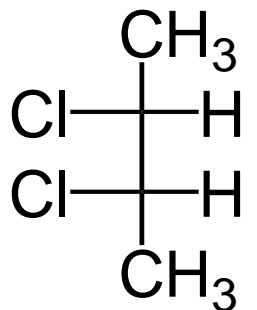
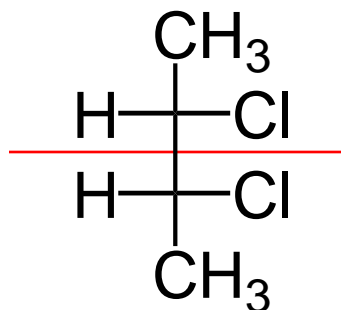
(2S,3S)



(2R,3R)

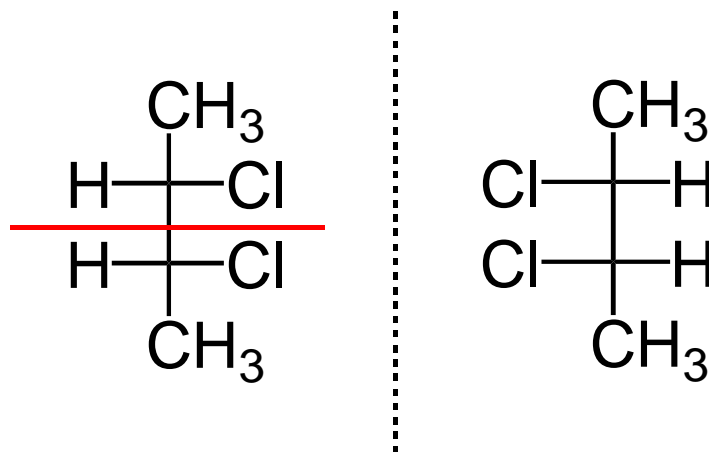


(2S,3R)?



meso compounds

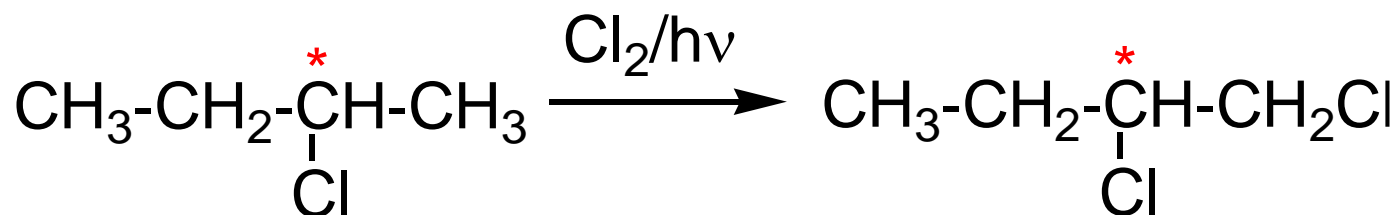
A meso compound is one which is superimposable on its mirror image even though it contains stereogenic centres. The molecule is achiral.



Problems

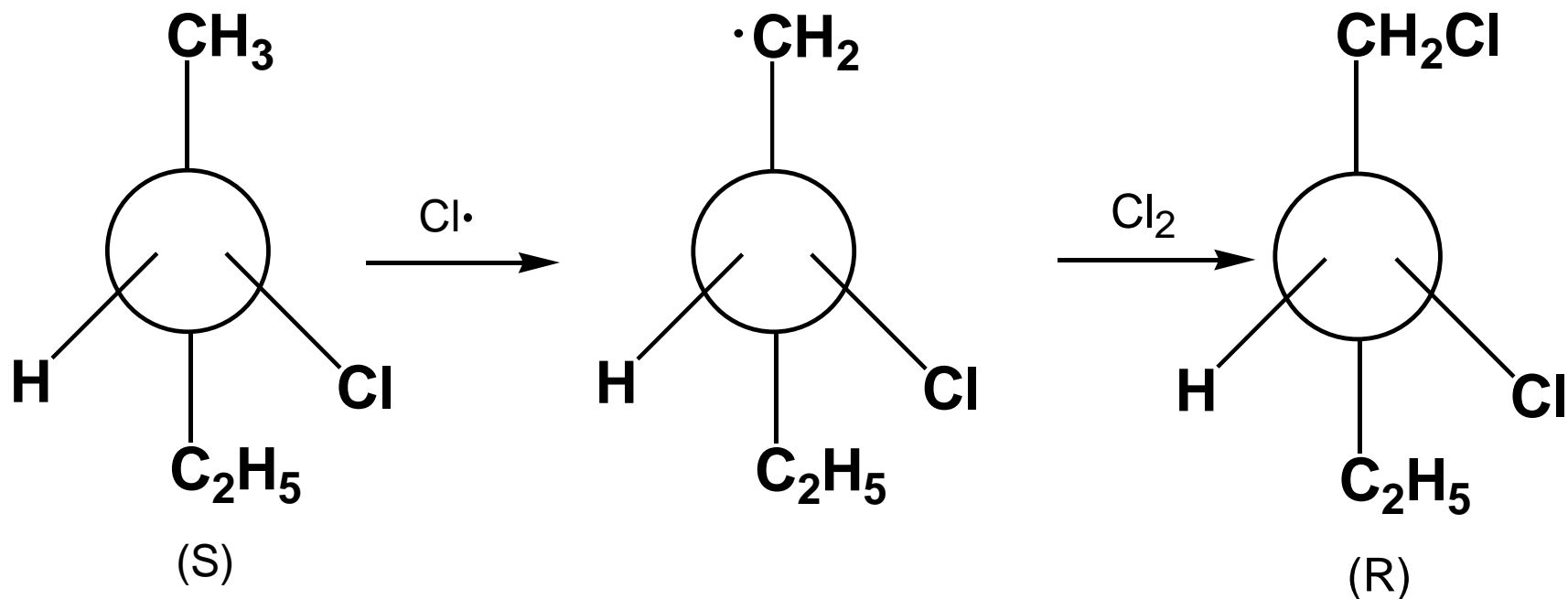
Try problems 5.18 – 5.23 on pages 221 - 223 of Solomons and Fryhle.

Relating configurations - chlorination of 2-chlorobutane



Consider the formation of one of the products, 1,2-dichlorobutane.

Chlorination of 2-chlorobutane



A reaction which does not involve breaking a bond to a stereogenic centre, proceeds with **retention** of configuration about this centre.

Racemic mixtures

An equimolar mixture of two enantiomers.

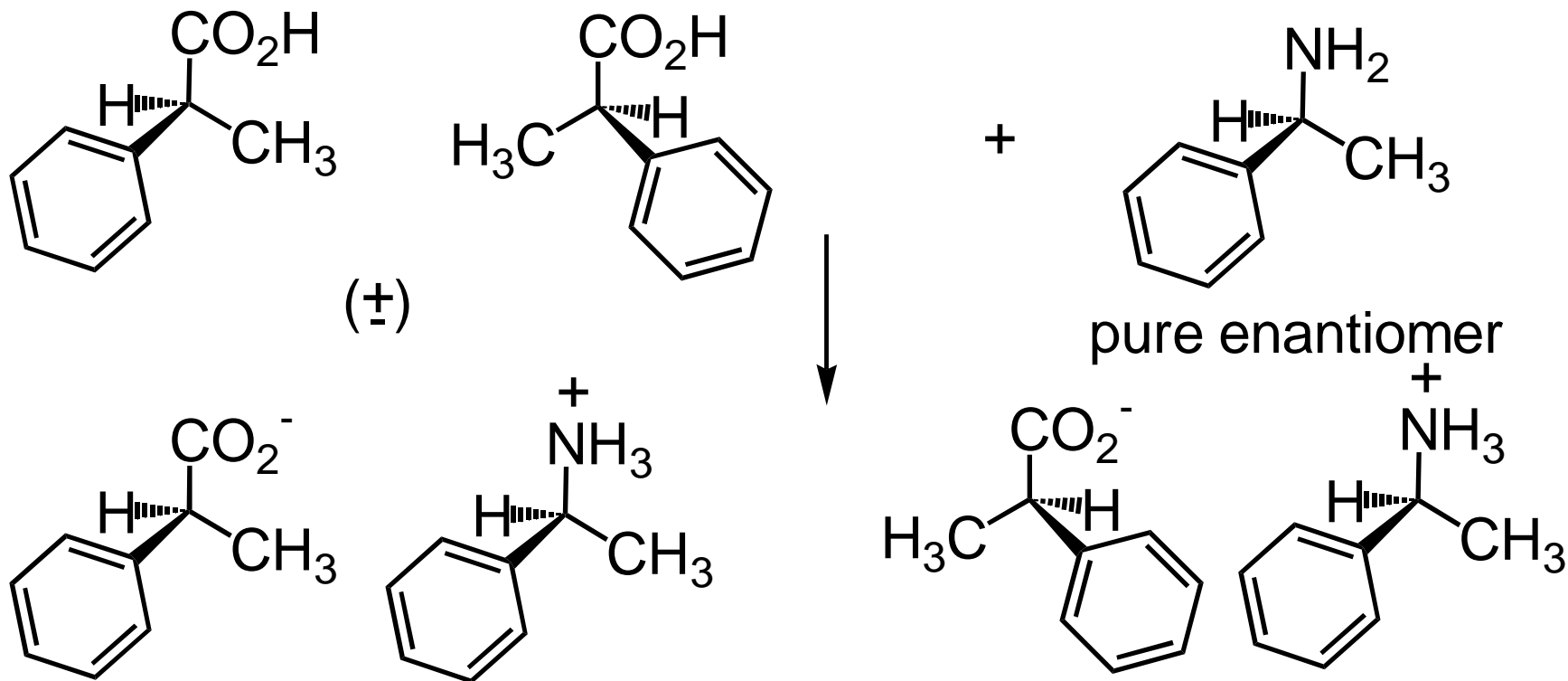
Prefix the name with \pm .

A problem.....How can we separate a pair of enantiomers?

The racemic mixture must be converted into a pair of diastereomers.

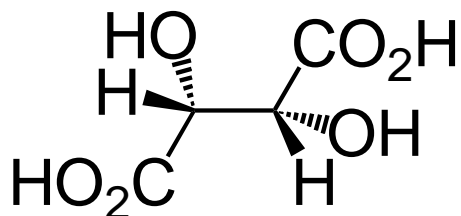
Resolution of enantiomers

To do this, we react a racemic mixture with an optically pure compound:

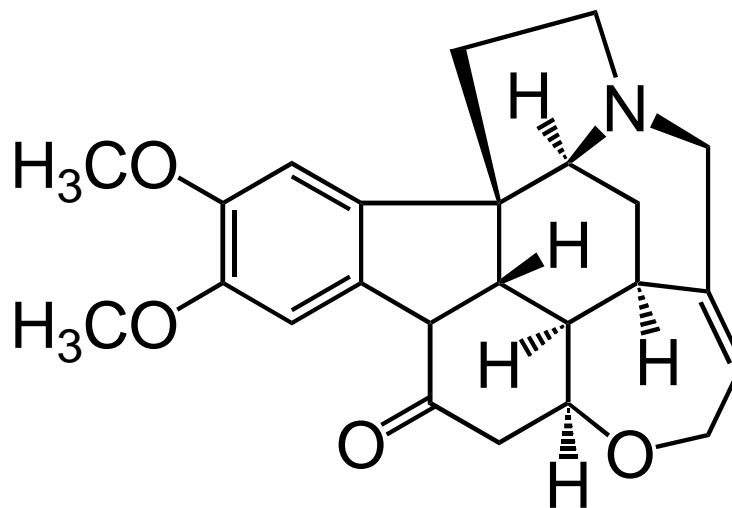


This mixture consists of salts that are **diastereomers**. They can be separated by conventional means.

Optically active natural products



(+)-tartaric acid



(-)-brucine