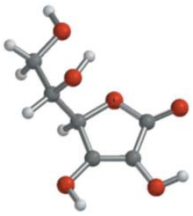
CHEM 240

PRINCIPLES OF ORGANIC CHEMISTRY I

FOR CHEMISTRY' STUDENTS, COLLEGE OF SCIENCE

PRE-REQUISITES COURSE; CHEM 107

CREDIT HOURS; 2 (2+0)



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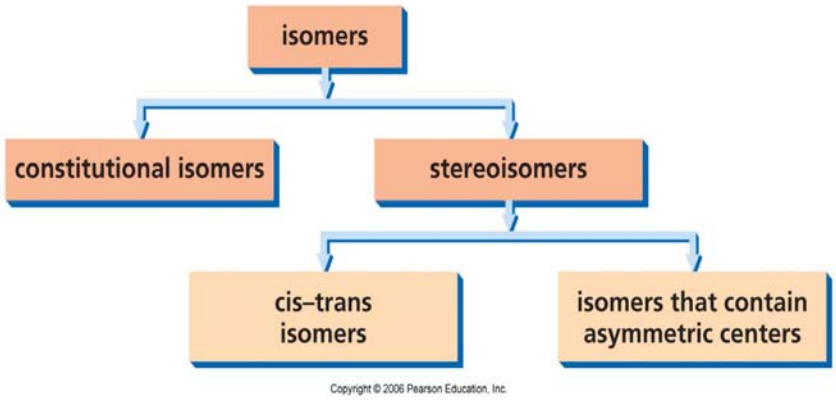
CHAPTER 3

Stereochemistry

REVIEW OF ISOMERISM

- **Stereochemistry:** The study of the three-dimensional structure of molecules

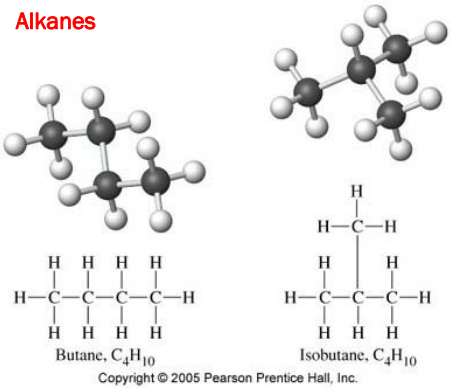


- **Isomers**: Compounds that have the same molecular formula but do not have identical structures.

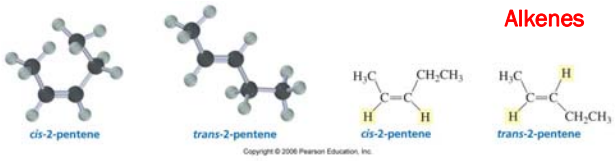
REVIEW OF ISOMERISM

- **Constitutional (Structural) Isomers:** differ in the way their atoms are connected - **Alkanes**.
- **Stereoisomers:** differ in the way their atoms are arrange in space (cannot interconvert) – **Alkenes** and **cycloalkanes**.

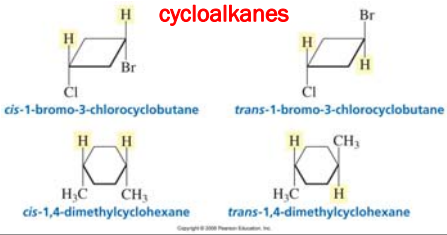
Alkanes



Alkenes

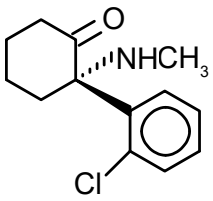


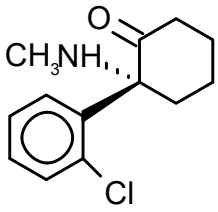
cycloalkanes



STEREOCHEMISTRY

- Stereochemistry plays an important role in determining the properties and reactions of organic compounds:
- The properties of many drugs depends on their stereochemistry:





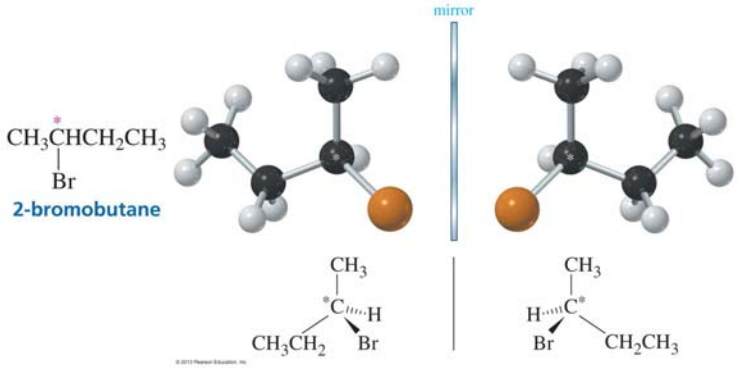
(S)-ketamine **(R)-ketamine**

anesthetic **hallucinogen**

STEREOISOMERS

- Stereoisomers: compounds with the same connectivity, different arrangement in space.
- Enantiomers: stereoisomers that are nonsuperimposible mirror images; only properties that differ are direction (+ or -) of optical rotation.

  A chiral compound and its mirror image are called enantiomers.



STEREOISOMERS

- **Stereoisomers:** compounds with the same connectivity, different arrangement in space.
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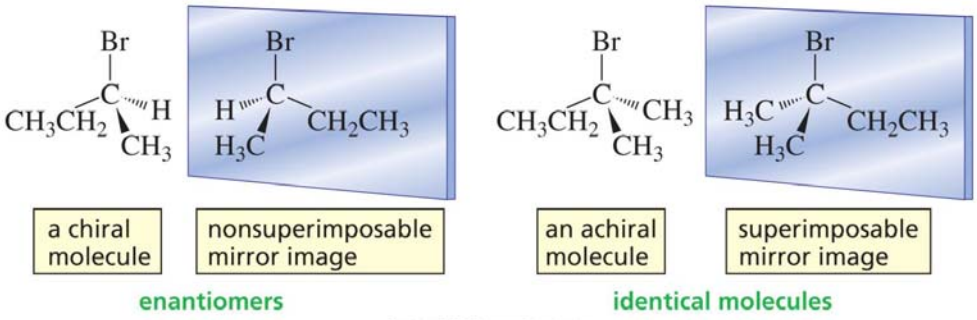
Chiral compound and its mirror image are called enantiomers.

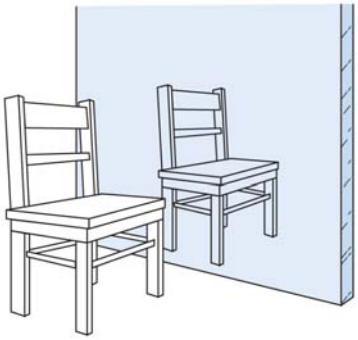


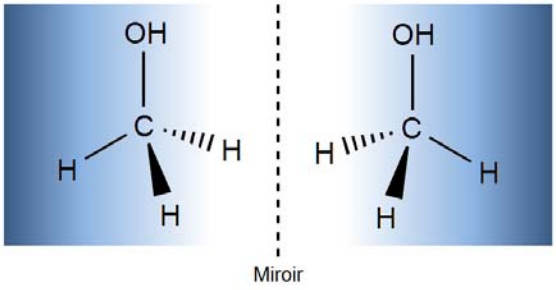
DIASTEREOMERS

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

CHIRALITY

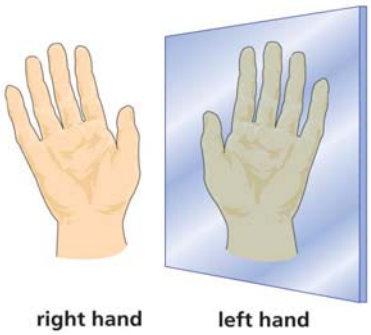
- **Achiral:** mirror images that can be superposed are achiral (not chiral).
- If a molecule (or object) has a mirror plane or an inversion center, it cannot be chiral.

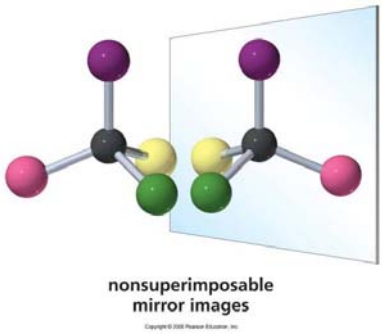




CHIRALITY

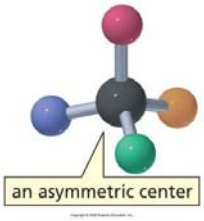
- **Chiral:** Nonsuperimposable on its mirror image (*if its mirror image is different from the original object*).





ASYMMETRIC CARBONS

- **Asymmetric center:** sp^3 carbon with four different groups attached.



$CH_3CH_2CH_2\overset{*}{C}HCH_2CH_2CH_2CH_3$ (OH)
4-octanol

$CH_3\overset{*}{C}HCH_2CH_3$ (Br)
2-bromobutane

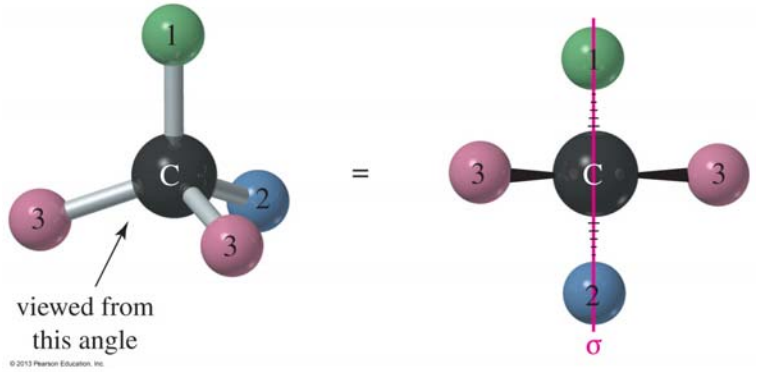
$CH_3CH\overset{*}{C}H_2CHCH_2CH_3$ (CH_3 on the first CH; CH_3 on the second CH)
2,4-dimethylhexane

- The most common feature that leads to chirality in organic compounds is the presence of an asymmetric (or chiral) carbon atom.

In general:

- no asymmetric C → usually achiral
- 1 asymmetric C → always chiral
- > 2 asymmetric C → may or may not be chiral

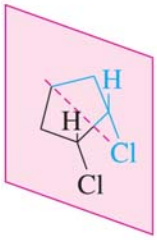
INTERNAL PLANE OF SYMMETRY

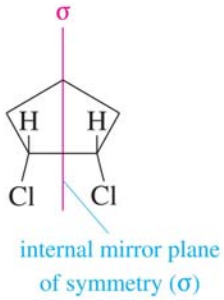


A molecule that has a plane of symmetry is ***achiral***.

INTERNAL PLANE OF SYMMETRY

Cis Cyclic Compounds





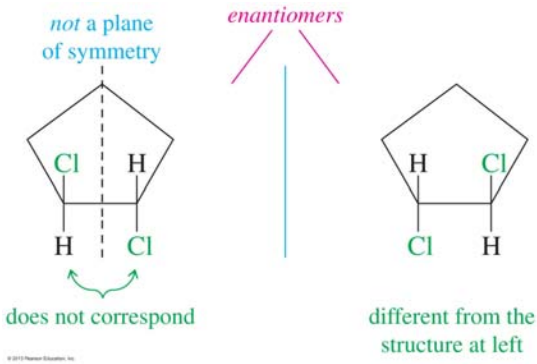
- Contains an internal mirror plane of symmetry
- Both structures can be superimposed (they are identical to their mirror images).
- Any molecule that has an internal mirror plane of symmetry is achiral even if it contains asymmetric carbon atoms.

Cis-1,2-dichlorocyclopentane is a meso compound:

- an achiral compound that contains chiral centers
- often contains an internal mirror plane of symmetry

INTERNAL PLANE OF SYMMETRY

Trans Cyclic Compounds

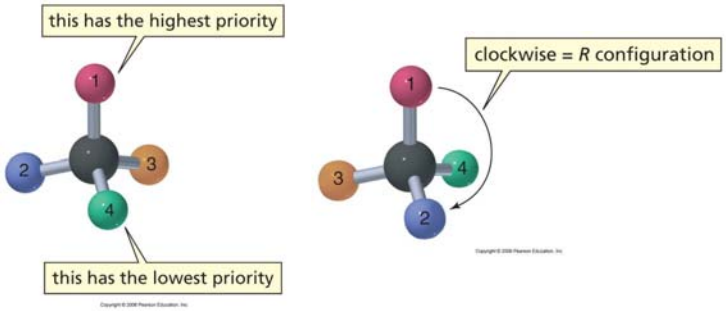


Trans-1,2-dichlorocyclohexane does not have a plane of symmetry so the images are nonsuperimposable and the molecule will have two enantiomers.

CHIRAL VS. ACHIRAL

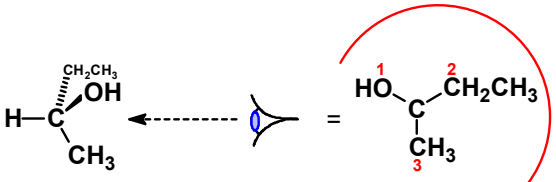
- To determine if a compound is chiral:
  - 0 asymmetric carbons: → Usually achiral
  - 1 asymmetric carbon: → Always chiral
  - 2 asymmetric carbons: → Chiral or achiral
    - Does the compound have an internal plane of symmetry?
      - Yes: → achiral
      - No:
        - If mirror image is non-superimposable, then it's chiral.
        - If mirror image is superimposable, then it's achiral.

NAMING ENANTIOMERS: THE *R*,*S* SYSTEM



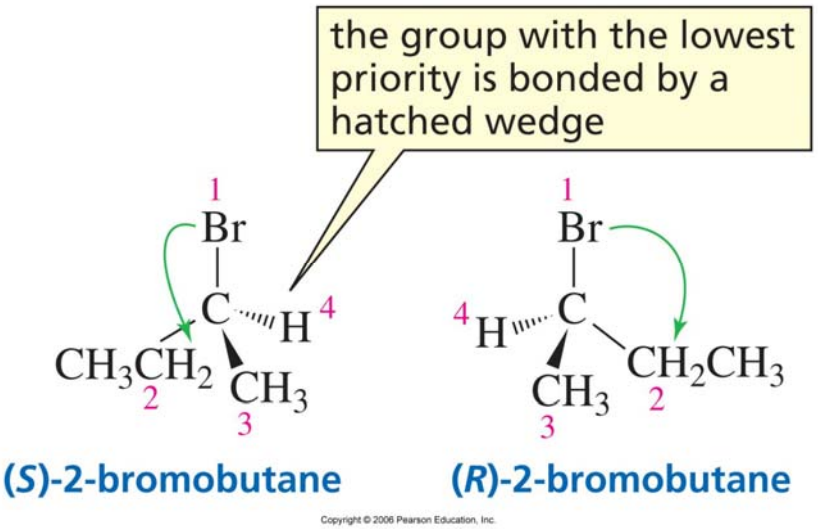
R* and *S

Assign priorities to the remaining groups based on atomic numbers.
Clockwise (highest to lowest priority) ⇒ *R*
Counterclockwise ⇒ *S*



(*R*)-2-butanol

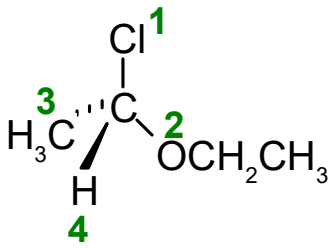
NAMING ENANTIOMERS: THE *R,S* SYSTEM

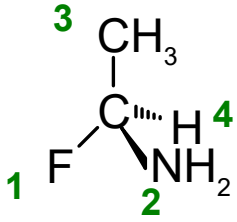


(R) AND (S) NOMENCLATURE

- Assign a numerical priority to each group bonded to the asymmetric carbon:
  - group 1 = highest priority
  - group 4 = lowest priority
- Rules for assigning priorities:
  - Compare the first atom in each group (i.e. the atom directly bonded to the asymmetric carbon)
    - Atoms with higher atomic numbers have higher priority

(R) AND (S) NOMENCLATURE



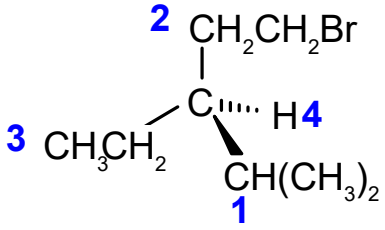


Example priorities:

I > Br > Cl > S > F > O > N > ^{13}C > ^{12}C > ^{3}H > ^{2}H > ^{1}H

(R) AND (S) NOMENCLATURE

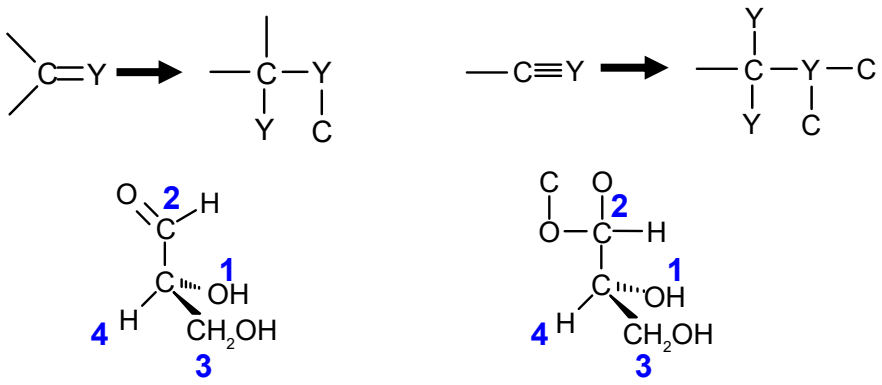
- In case of ties, use the next atoms along the chain as tiebreakers.



$CH(CH_3)_2$ > CH_2CH_2Br > CH_3CH_2

(R) AND (S) NOMENCLATURE

- Treat double and triple bonds as if both atoms in the bond were duplicated or triplicated:

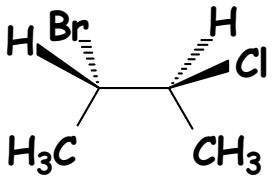


(R) AND (S) NOMENCLATURE

- Using a 3-D drawing or model, put the 4th priority group in back.
- Look at the molecule along the bond between the asymmetric carbon and the 4th priority group.
- Draw an arrow from the 1st priority group to the 2nd group to the 3rd group.
  - + Clockwise arrow → (R) configuration
  - + Counterclockwise arrow → (S) configuration

(R) AND (S) NOMENCLATURE

- When naming compounds containing multiple chiral atoms, you must give the configuration around each chiral atom:
  - position number and configuration of each chiral atom in numerical order, separated by commas, all in ( ) at the start of the compound name



(2S, 3S)-2-bromo-3-chlorobutane

PROPERTIES OF ENANTIOMERS

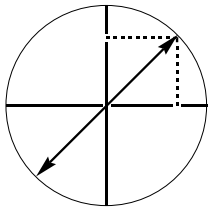
a) Physical: Enantiomers have identical physical properties with the exception that they rotate the plane of polarized light in opposite directions although $|\alpha|$ is identical.

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!

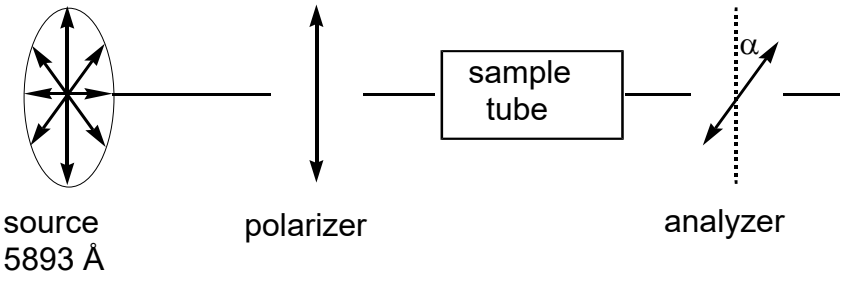
PLANE-POLARIZED LIGHT

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 ±.

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.

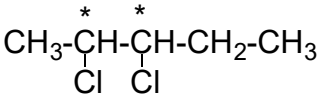
MOLECULES WITH MORE THAN ONE STEREOGENIC CENTRE

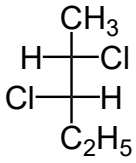
$CH_3CHClCHClCH_2CH_3$

How many stereoisomers exist for this compound?

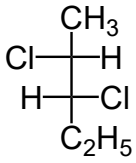
MOLECULES WITH MORE THAN ONE STEREOGENIC CENTRE

2,3-DICHLOROPENTANE

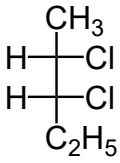




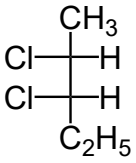
(2S,3S)



(2R,3R)



(2S,3R)



(2R,3S)

HOW MANY STEREOISOMERS EXIST?

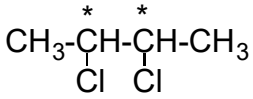
The **maximum** number of stereoisomers that can exist is equal to

2^n

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

2,3-DICHLOROPENTANE

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

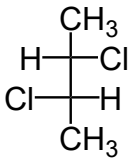


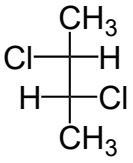
There are two tetrahedral stereogenic carbons.....2^n?

HOW MANY STEREOISOMERS EXIST?

2,3-DICHLOROBUTANE

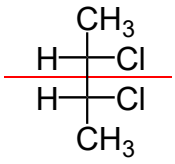
(2S,3S)

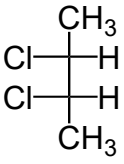




(2R,3R)

(2S,3R)?

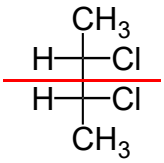


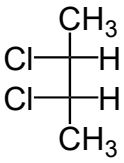


MESO COMPOUNDS

A meso compound is one which is superimposable on its mirror image even though it contains stereogenic centers.

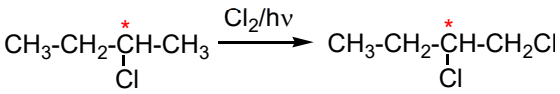
The molecule is achiral.



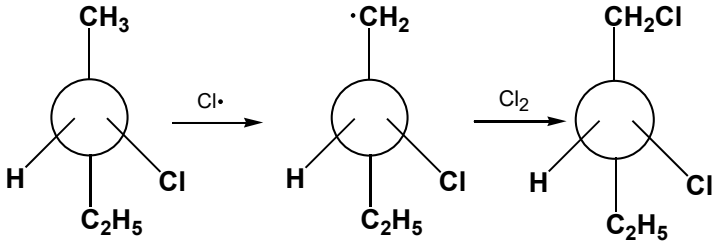


RELATING CONFIGURATIONS -CHLORINATION OF 2-CHLOROBUTANE

CHLORINATION OF 2-CHLOROBUTANE



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



(S) (R)

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