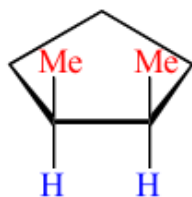
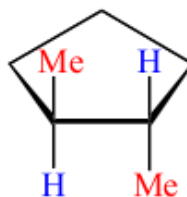


Lecture 2 by Prof. Dr. Dawood Salim Abid

A- **Diastereomers** are stereoisomers whose molecules are *not mirror images of each other*.



cis-1,2-Dimethylcyclopentane
(C₇H₁₄)



trans-1,2-Dimethylcyclopentane
(C₇H₁₄)

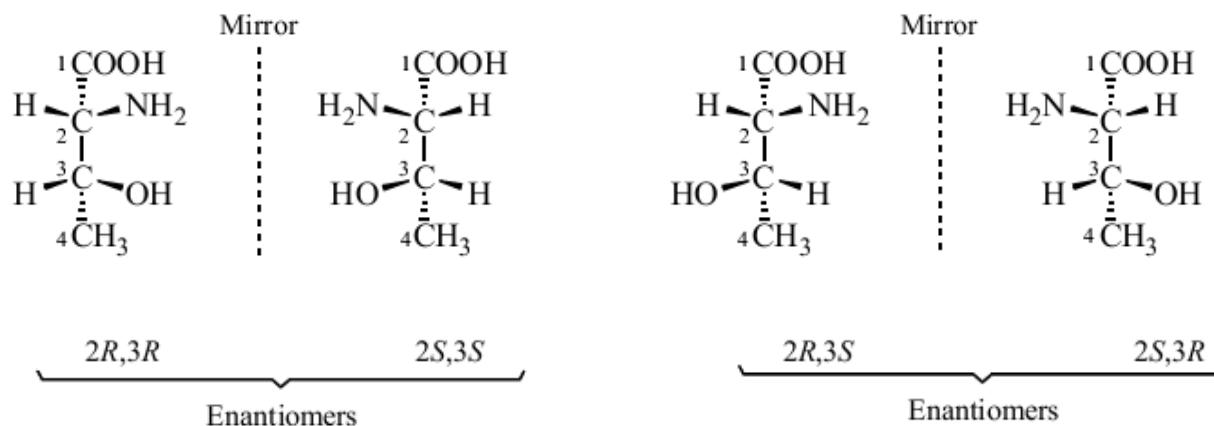
1. DIASTEREOMERS

1. Molecules have more than one stereogenic (chiral) center: **diastereomers**
2. **Diastereomers** are stereoisomers that are not mirror images of each other.

Relationships between four stereoisomeric threonines

Stereoisomer	Enantiomeric with	Diastereomeric with
2 <i>R</i> ,3 <i>R</i>	2 <i>S</i> ,3 <i>S</i>	2 <i>R</i> ,3 <i>S</i> and 2 <i>S</i> ,3 <i>R</i>
2 <i>S</i> ,3 <i>S</i>	2 <i>R</i> ,3 <i>R</i>	2 <i>R</i> ,3 <i>S</i> and 2 <i>S</i> ,3 <i>R</i>
2 <i>R</i> ,3 <i>S</i>	2 <i>S</i> ,3 <i>R</i>	2 <i>R</i> ,3 <i>R</i> and 2 <i>S</i> ,3 <i>S</i>
2 <i>S</i> ,3 <i>R</i>	2 <i>R</i> ,3 <i>S</i>	2 <i>R</i> ,3 <i>R</i> and 2 <i>S</i> ,3 <i>S</i>

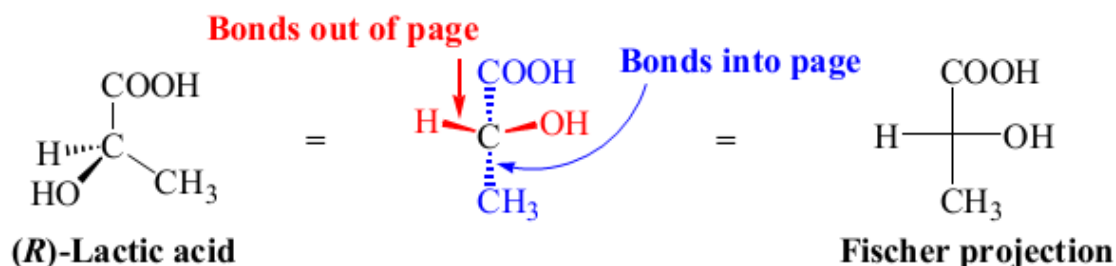
3. Enantiomers must have opposite (mirror-image) configurations at *all* stereogenic centers.



B- FISCHE PROJECTION (Emil Fischer, 1891)

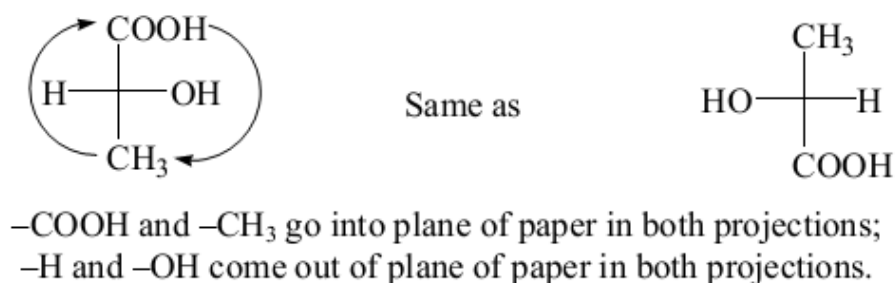
1. **Convention:** The carbon chain is drawn along the vertical line of the Fischer projection, usually with the most highly oxidized end carbon atom at the top.

- 1) **Vertical lines:** bonds going into the page.
- 2) **Horizontal lines:** bonds coming out of the page

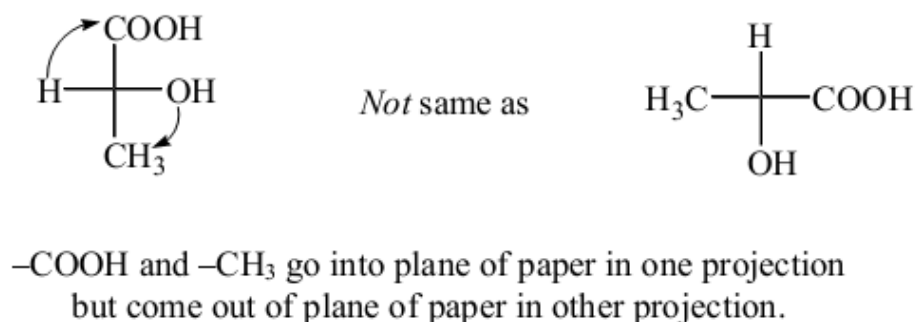


C- ALLOWED MOTIONS FOR FISCHER PROJECTION:

1. **180° rotation** (not 90° or 270°):



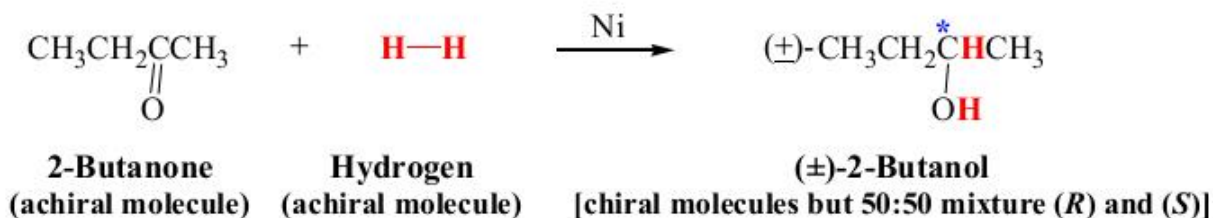
2. **90° rotation:** Rotation of a Fischer projection by 90° inverts its meaning.



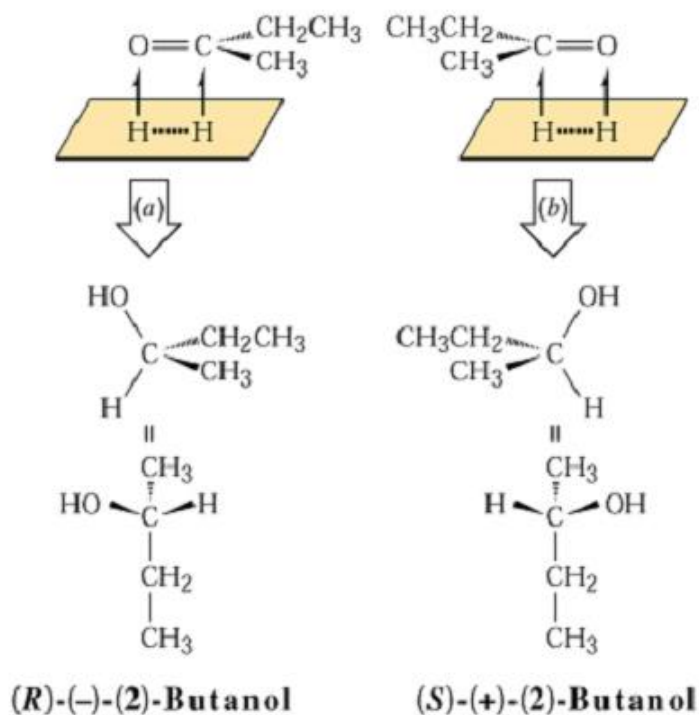
D- THE SYNTHESIS OF CHIRAL MOLECULES

RACEMIC FORMS

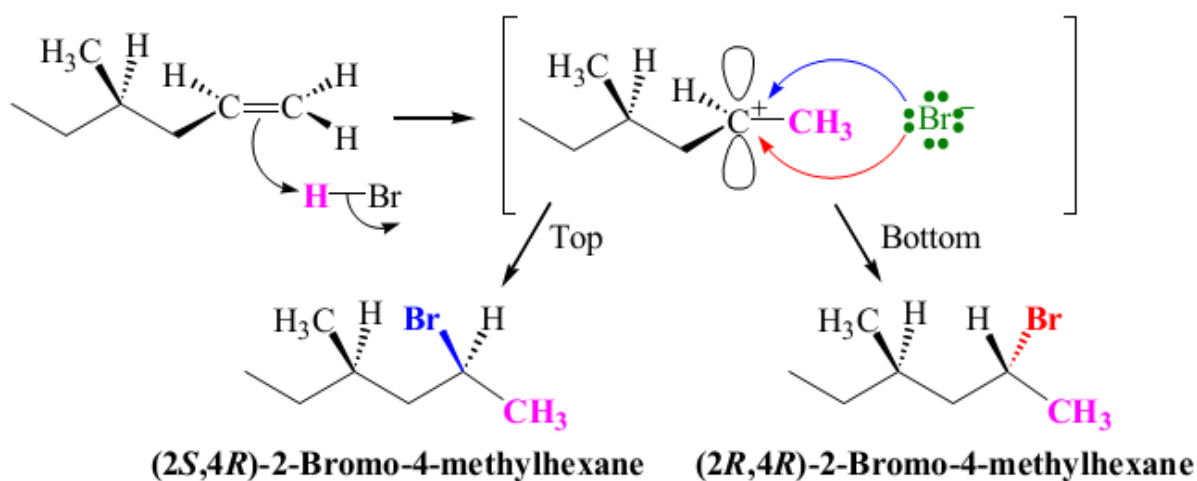
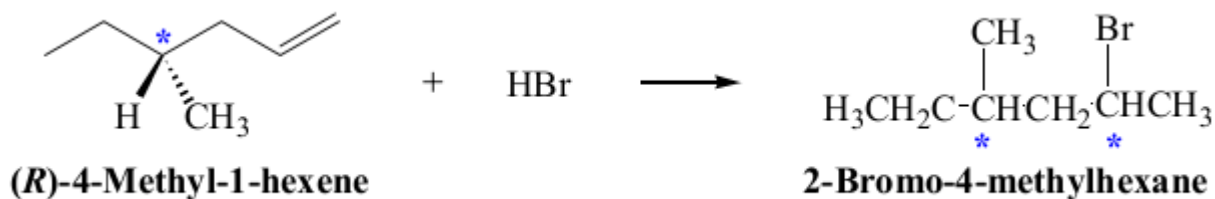
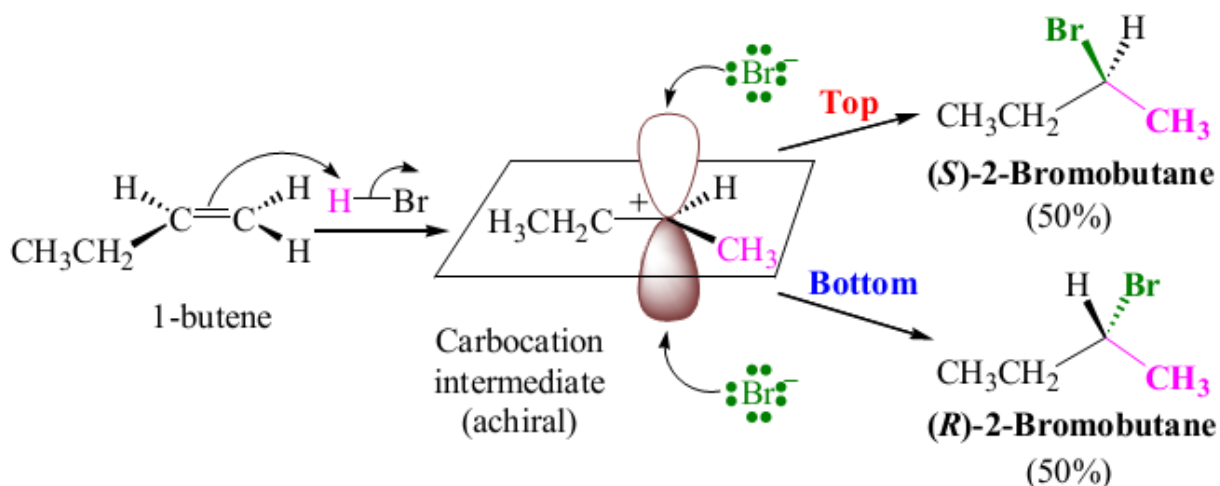
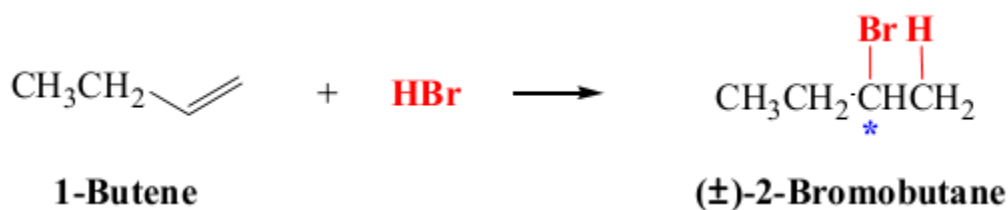
1. Optically active product(s) requires chiral reactants, reagents, and/or solvents:
 - 1) In cases that chiral products are formed from achiral reactants, racemic mixtures of products will be produced in the absence of chiral influence (reagent, catalyst, or solvent).
2. Synthesis of 2-butanol by the nickel-catalyzed hydrogenation of 2-butanone:



3. Transition state of nickel-catalyzed hydrogenation of 2-butanone:

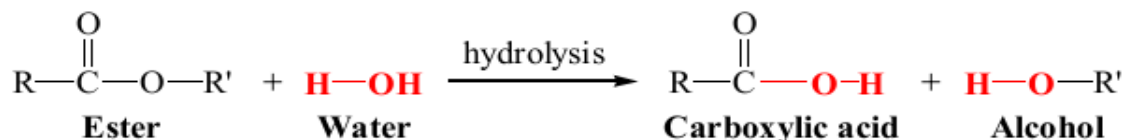


Addition of HBr to 1-butene:



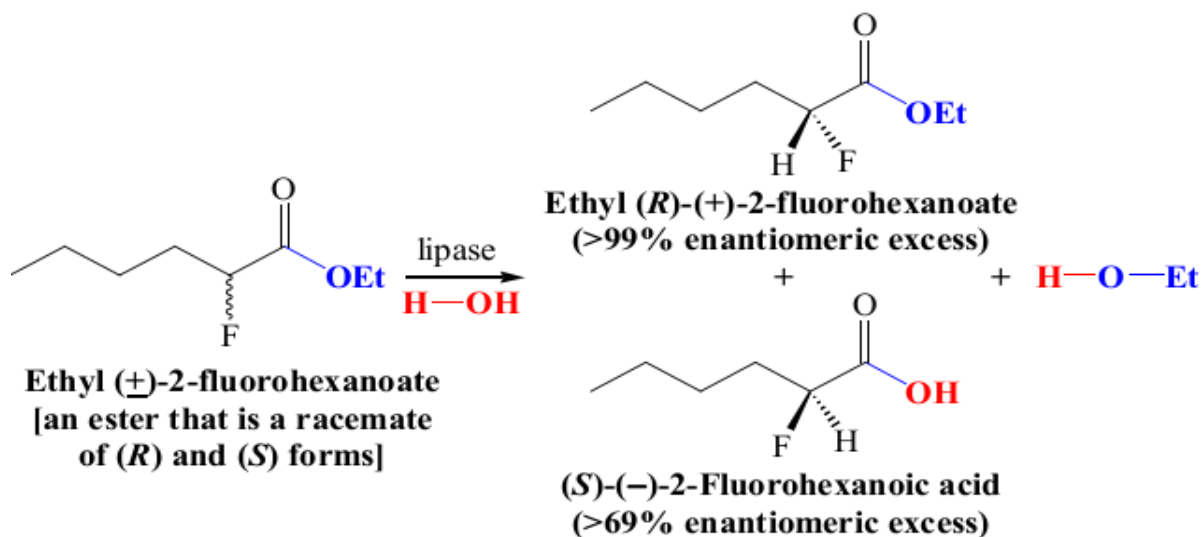
3. Enzyme-catalyzed organic reactions:

1) **Hydrolysis** of esters:



i) Hydrolysis, which means literally *cleavage (lysis) by water*, can be carried out in a variety of ways that do not involve the use of enzyme.

2) **Lipase** catalyzes **hydrolysis** of esters:



i) Use of **lipase** allows the hydrolysis to be used to prepare almost pure enantiomers.

ii) The (*R*) enantiomer of the ester does not fit the active site of the enzyme and is, therefore, unaffected.

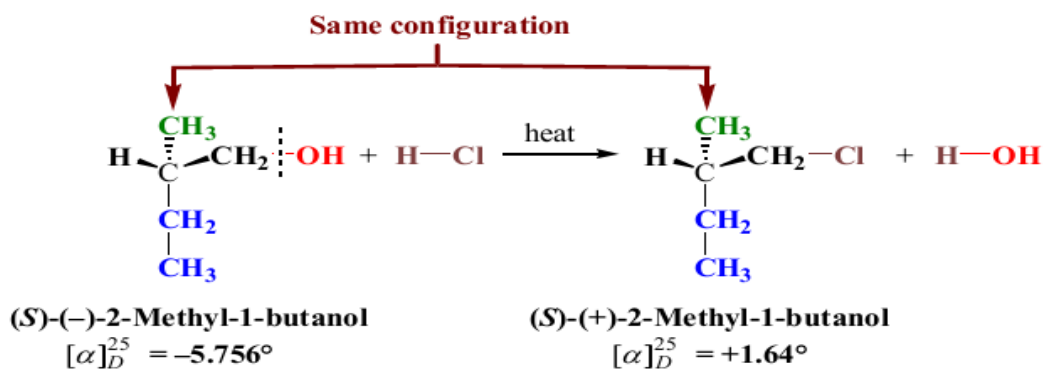
iii) Only the (*S*) enantiomer of the ester fits the active site and undergoes hydrolysis.

2) **Dehydrogenase** catalyzes **enantioselective reduction** of carbonyl groups.

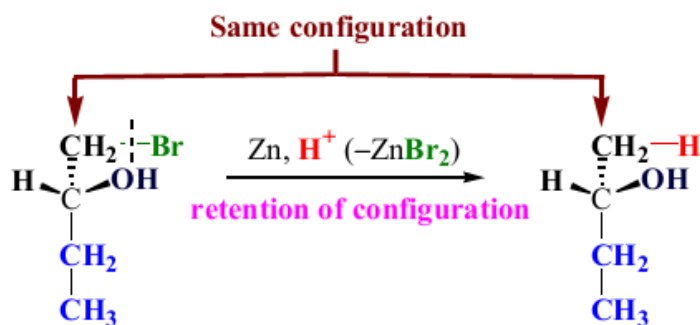
5.14 RELATING CONFIGURATIONS THROUGH REACTIONS IN WHICH NO BONDS TO THE STEREOCENTER ARE BROKEN

1. Retention of configuration:

- 1) If a reaction takes place **with no bond to the stereocenter is broken**, the product will have the **same configuration** of groups around the stereocenter as the reactant
 - 2) The reaction proceeds with **retention of configuration**.
2. (*S*)-(-)-2-Methyl-1-butanol is heated with concentrated HCl:

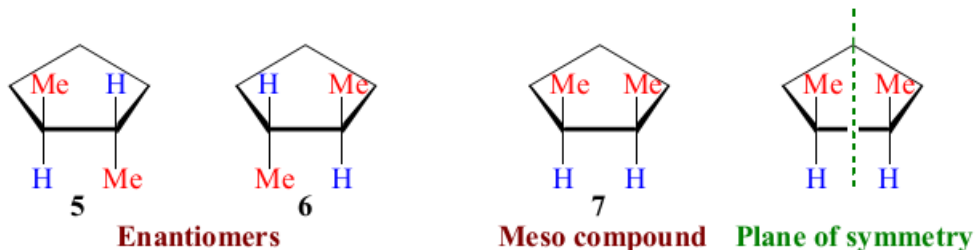


- 1) The product of the reaction must have the **same configuration** of groups around the stereocenter that the reactant had \Rightarrow comparable or identical groups in the two compounds occupy the same relative positions in space around the stereocenter.
 - 2) While the (*R*-*S*) designation **does not change** [both reactant and product are (*S*)] the direction of optical rotation **does change** [the reactant is (-) and the product is (+)].
3. (*R*)-1-Bromo-2-butanol is reacted with Zn/H⁺:



E- STEREOISOMERISM OF CYCLIC COMPOUNDS

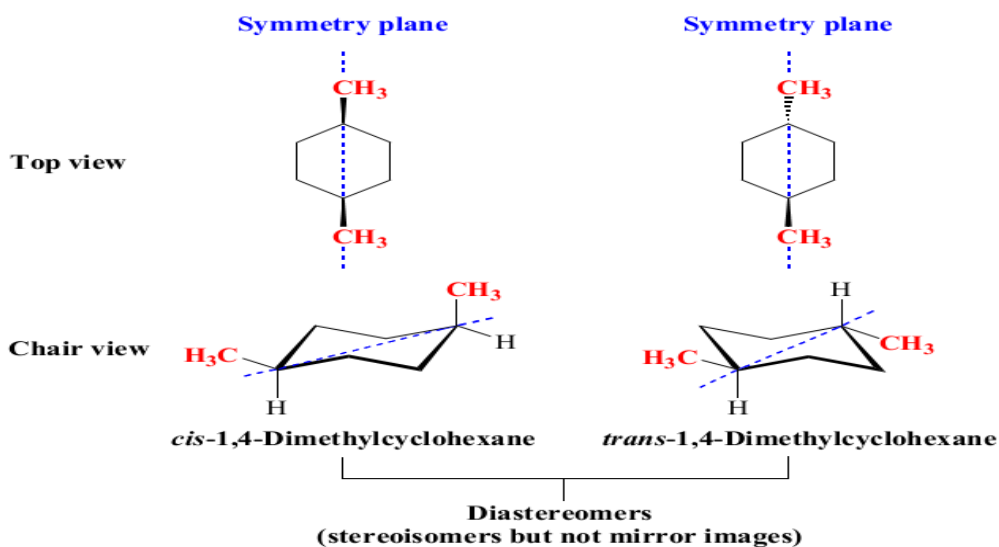
1. 1,2-Dimethylcyclopentane has two stereocenters and exists in three stereomeric forms **5**, **6**, and **7**.



- 1) The *trans* compound exists as a pair of enantiomers **5** and **6**.
- 2) *cis*-1,2-Dimethylcyclopentane has a plane of symmetry that is perpendicular to the plane of the ring and is a meso compound.

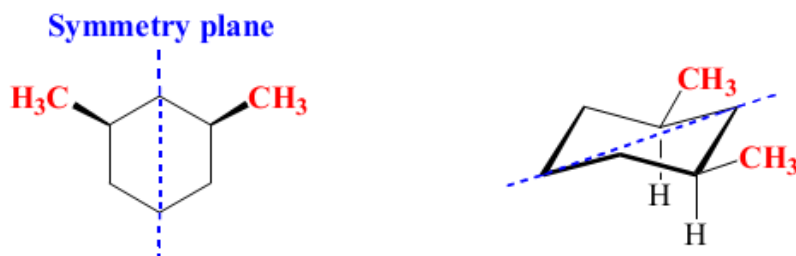
F- CYCLOHEXANE DERIVATIVES

1. **1,4-Dimethylcyclohexanes:** two *isolable stereoisomers*
 - 1) Both *cis*- and *trans*-1,4-dimethylcyclohexanes **have a symmetry plane** \Rightarrow **have no stereogenic centers** \Rightarrow **Neither *cis* nor *trans* form is chiral** \Rightarrow neither is optically active.
 - 2) The *cis* and *trans* forms are diastereomers.



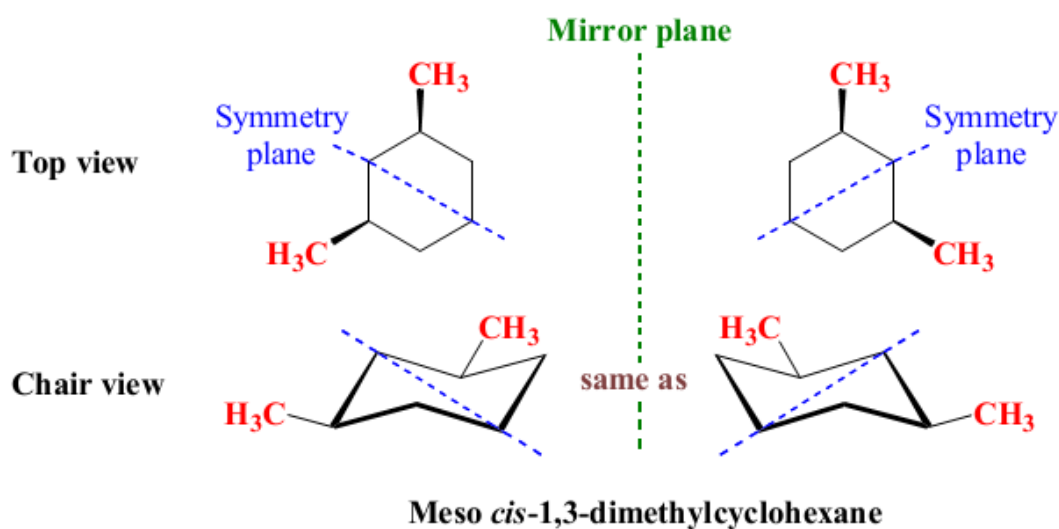
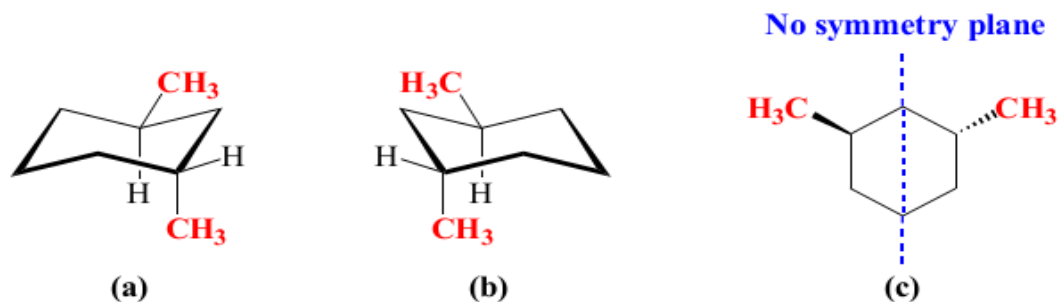
2. **1,3-Dimethylcyclohexanes:** three *isolable stereoisomers*

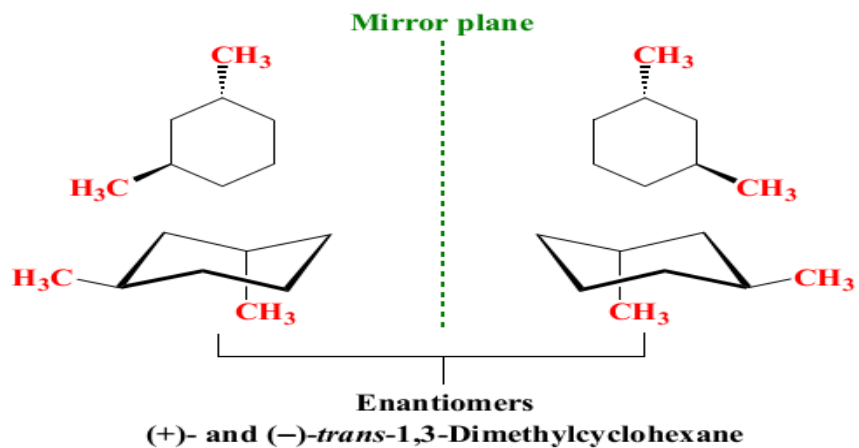
- 1,3-Dimethylcyclohexane has two stereocenters \Rightarrow 4 stereoisomers are possible.
- cis*-1,3-Dimethylcyclohexane has a plane of symmetry and is achiral.



3) *trans*-1,3-Dimethylcyclohexane does not have a plane of symmetry and exists as a pair of enantiomers.

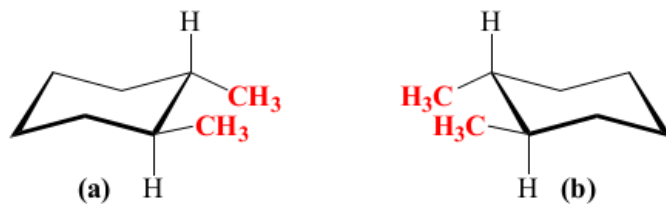
- They are not superposable on each other.
- They are noninterconvertible by a ring-flip.



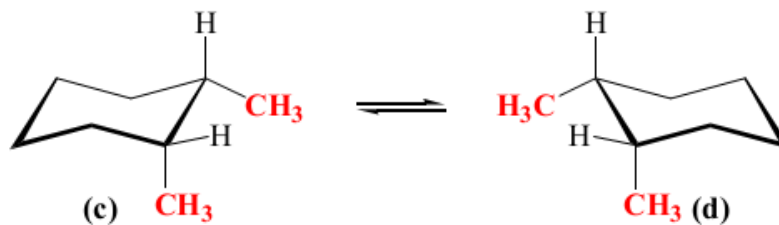


3. **1,2-Dimethylcyclohexanes:** three *isolable stereoisomers*

- 1) 1,2-Dimethylcyclohexane has two stereocenters \Rightarrow 4 stereoisomers are possible.
- 2) *trans*-1,2-Dimethylcyclohexane has no plane of symmetry \Rightarrow exists as a pair of enantiomers.

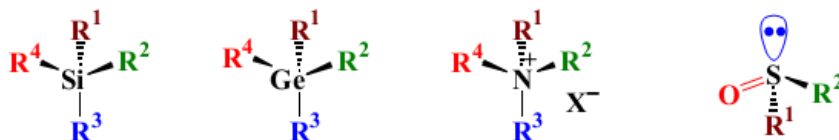


3) *cis*-1,2-Dimethylcyclohexane:



5.16 COMPOUNDS WITH STEREOCENTERS OTHER THAN CARBON

- Stereocenter:** any tetrahedral atom with four different groups attached to it.
 - Silicon and germanium compounds with four different groups are **chiral** and the enantiomers can, in principle, be separated.



- Sulfoxides where one of the four groups is a nonbonding electron pair are **chiral**.
- Amines where one of the four groups is a nonbonding electron pair are **achiral** due to **nitrogen inversion**.

5.17 CHIRAL MOLECULES THAT DO NOT POSSESS A TETRAHEDRAL ATOM WITH FOUR DIFFERENT GROUPS

- Allenes:**

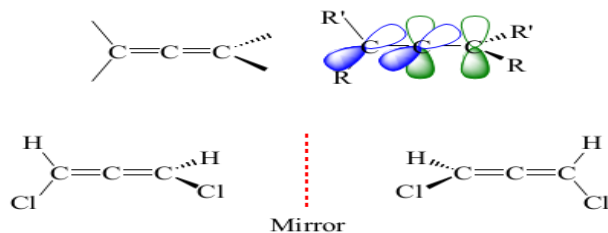


Figure 5.22 Enantiomeric forms of 1,3-dichloroallene. These two molecules are nonsuperposable mirror images of each other and are therefore chiral. They do not possess a tetrahedral atom with four different groups, however.

