Anderson Serangoon Junior College
H3 Chemistry
Molecular Stereochemistry

Learning outcomes
Students should be able to:

(a) (i) use of stereochemical projections, including Newman projection, to represent molecules.

(ii) interpret stereochemical projections of molecules.

[knowledge of Fischer projection is not required]

(b) apply their understanding of the following types of isomerism to explain the stereochemistry of molecules, including saturated ring systems:

(i) conformational isomerism, including energy barriers to rotation and interconversion

(ii) cis–trans isomerism, including *E, Z* nomenclature

(iii) enantiomerism and diastereomerism
- *R,S* configuration
- optical activity
- optical purity as the excess of one enantiomer, including calculation of optical purity by the equation:

$$\text{optical purity} = \frac{[\alpha]_{\text{sample}}}{[\alpha]_{\text{pure enantiomer}}} \times 100\%$$

References
1. *Organic Chemistry (7th Edition)*, John McMurry, Brooks/Cole
2. *Organic Chemistry (Sixth Edition)*, Francis A. Carey, McGraw–Hill

Lesson Outline

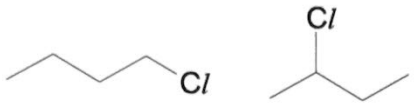
			Resources	Deadline
1	Introduction		**Lecture 1** • Mode: SLS Package **2025 H3 Chemistry Molecular Stereochemistry Section A** • Lecture notes: Pg 2 to 9 • Homework: Tutorial Q1 and Q2 for **F2F tutorial on 23 Jan**	**20 Jan**
2	Conformational isomerism			
	2.1	Conformations of ethane		
	2.2	Stability of different conformations of ethane		
	2.3	Conformations of butane		
	2.4	Conformations of cycloalkanes	**Lecture 2** • Mode: SLS Package **2025 H3 Chemistry Molecular Stereochemistry Section B** Lecture notes: Pg 10 to 16 • Homework: Tutorial Q3, Q4 and Q14 for **F2F tutorial on 23 Jan**	**22 Jan**
	2.5	Conformations of cyclohexanes		
	2.6	Conformations of mono–substituted cyclohexanes		
3	Cis–trans isomerism		**Lecture 3** • Mode: SLS Package **2025 H3 Chemistry Molecular Stereochemistry Section C** Lecture notes: Pg 17 to 29 • Homework: Tutorial Q5 to 15 for **F2F tutorial on 4 Feb**	**3 Feb**
	3.1	Cis–trans isomers		
	3.2	*E* and *Z* isomers		
	3.3	Cis–trans isomerism in a ring system		
4	Optical isomerism			
	4.1	Optical activity		
	4.2	Enantiomers		
	4.3	Optical activity of chiral molecules		
	4.4	Diastereomers		
	4.5	Meso compounds		

1. Introduction

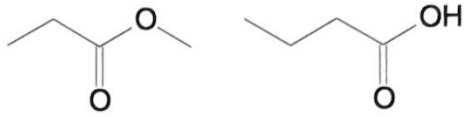
Isomers are compounds with the same molecular formula but exist in different forms due to different arrangements of atoms in their molecules. They may be either constitutional isomers or stereoisomers.

In constitutional (or structural) isomers, the atoms are *connected in different sequences.*

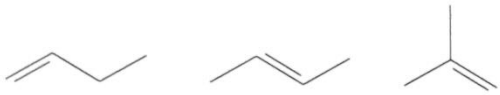
e.g.



C_4H_9Cl



$C_4H_8O_2$

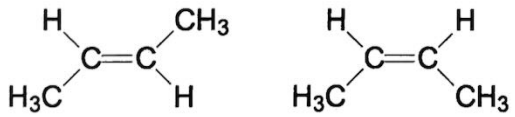


C_4H_8

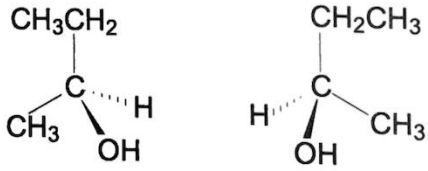
Stereoisomers have the *same constituent atoms connected together in the same sequence* but *differ in their arrangement in three–dimensional space*. Stereoisomers may be divided into two main groups:

- **Conformational isomers**
  - Isomers with different spatial arrangements of atoms in the molecules that arise from the rotations around the carbon–carbon single bond.
  - The different arrangements that can be interconverted by rotation about the C–C bond are called conformations.
- **Configurational isomers**
  - Isomers with different spatial arrangements of the atoms in the molecules that do NOT arise from the rotations about the single bonds.
  - The different arrangements that cannot be interconverted by rotation about the C–C bond are called configurations.

e.g.

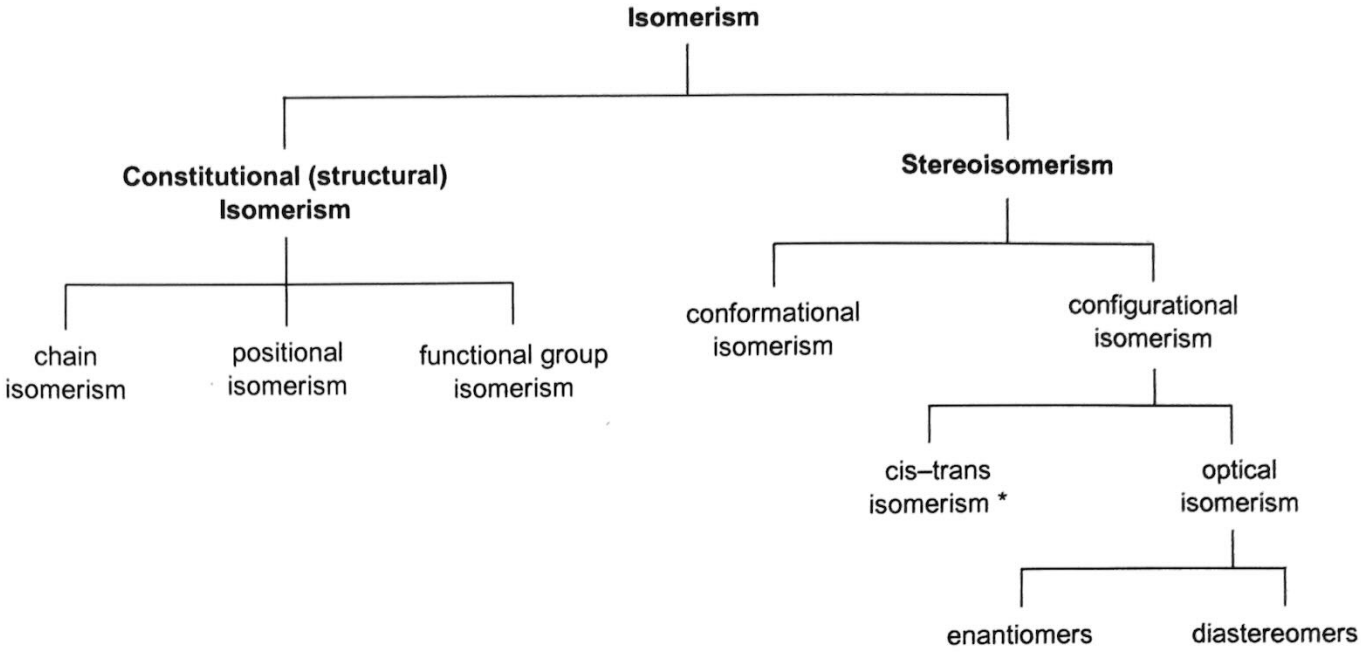


C_4H_8



$C_4H_{10}O$

Isomerism in organic compounds can be summarised as follow.



** cis–trans isomers are just another kind of diastereomers because they are non–mirror image stereoisomers.*

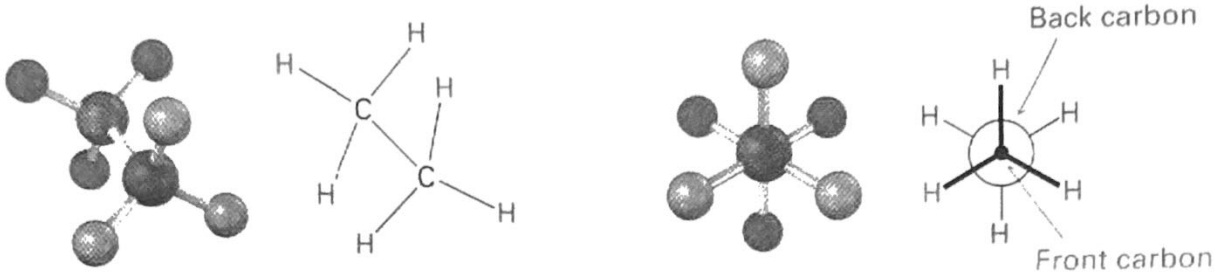
2. Conformational isomerism

Chemists represent conformational isomers in two ways.

- [Not in syllabus] **Sawhorse representations** view the carbon–carbon bond from an oblique angle and indicate spatial orientation by showing all the C–H bonds.

- **Newman projections** view the carbon–carbon bond directly end–on and represent the front carbon by a point and the back carbon by a circle. *Bonds attached to the front carbon* are represented by lines going into the center of the circle, and *bonds attached to the rear carbon* are represented by lines going to the edge of the circle.

  The advantage of Newman projections is that they are easy to draw and the relationships among substituents on the different carbon atoms are easy to see.



Sawhorse representation

Newman projection

Conformational isomers, **unlike** configurational isomers, can interconvert into one another via single bond rotation because the energy (~12 kJ mol^{-1}) required is easily available at normal temperatures.

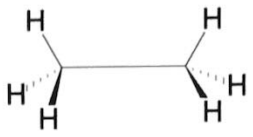
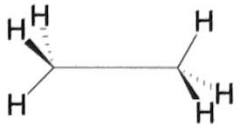
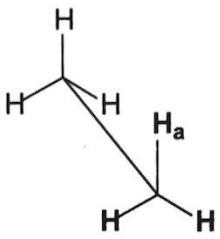
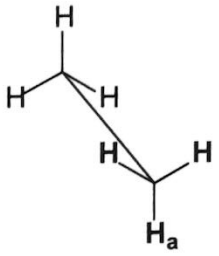
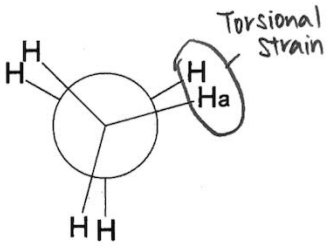
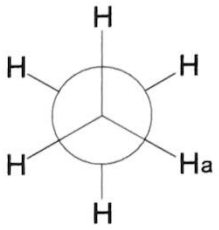
Among the conformations, **some can be more stable than the others** because of the strains present in the conformations. Because of the strains, the conformation is forced to be of higher energy state thus less stable. Typically, there are **three types of strains** in the alkanes and cycloalkanes conformations.

Eclipsing strain **Torsional strain*:**	results from the repulsion caused by electrons in between different groups when they pass by each other as the molecule is rotated about a bond.
Steric strain: 2 bulky groups close tgt	results from the repulsion caused by electrons in between different groups. Steric strain cannot be lessened by rotating the molecule around a bond.
Angle strain:	results from actual bonds angles being distorted from their ideal values (e.g. less than ideal tetrahedral angle of 109.5°).

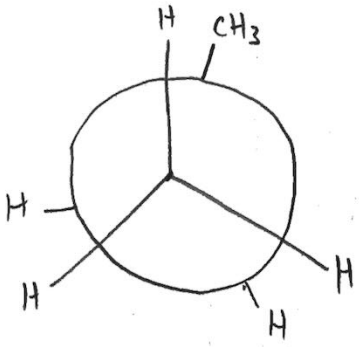
* A *torsion angle*, also known as dihedral angle, is formed by three consecutive bonds in a molecule and defined by the angle created between the two outer bonds. Conformations in which the torsion angles between adjacent bonds are other than 60° are said to have **torsional strain**.

2.1 Conformations of ethane

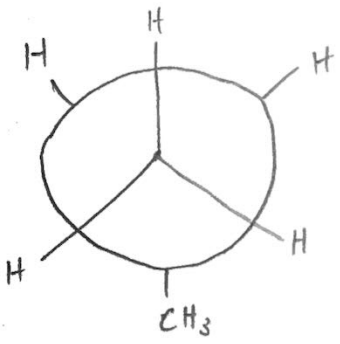
The conformations of ethane, which can be represented using **Sawhorse** and **Newman** projections, are shown below. The wedge–and–dash 3–dimensional structure, which you are more familiar with, is also included for illustration.

Conformation	Eclipsed (least stable)	Staggered (most stable)
Wedge–and–dash		
Sawhorse projection or line formula		
Newman projection		

Exercise 1: Draw Newman projections of staggered and eclipsed conformations of propane.



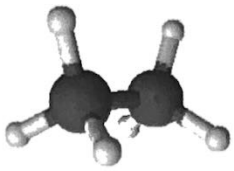
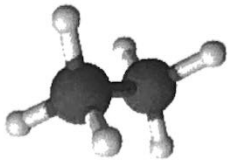
eclipsed



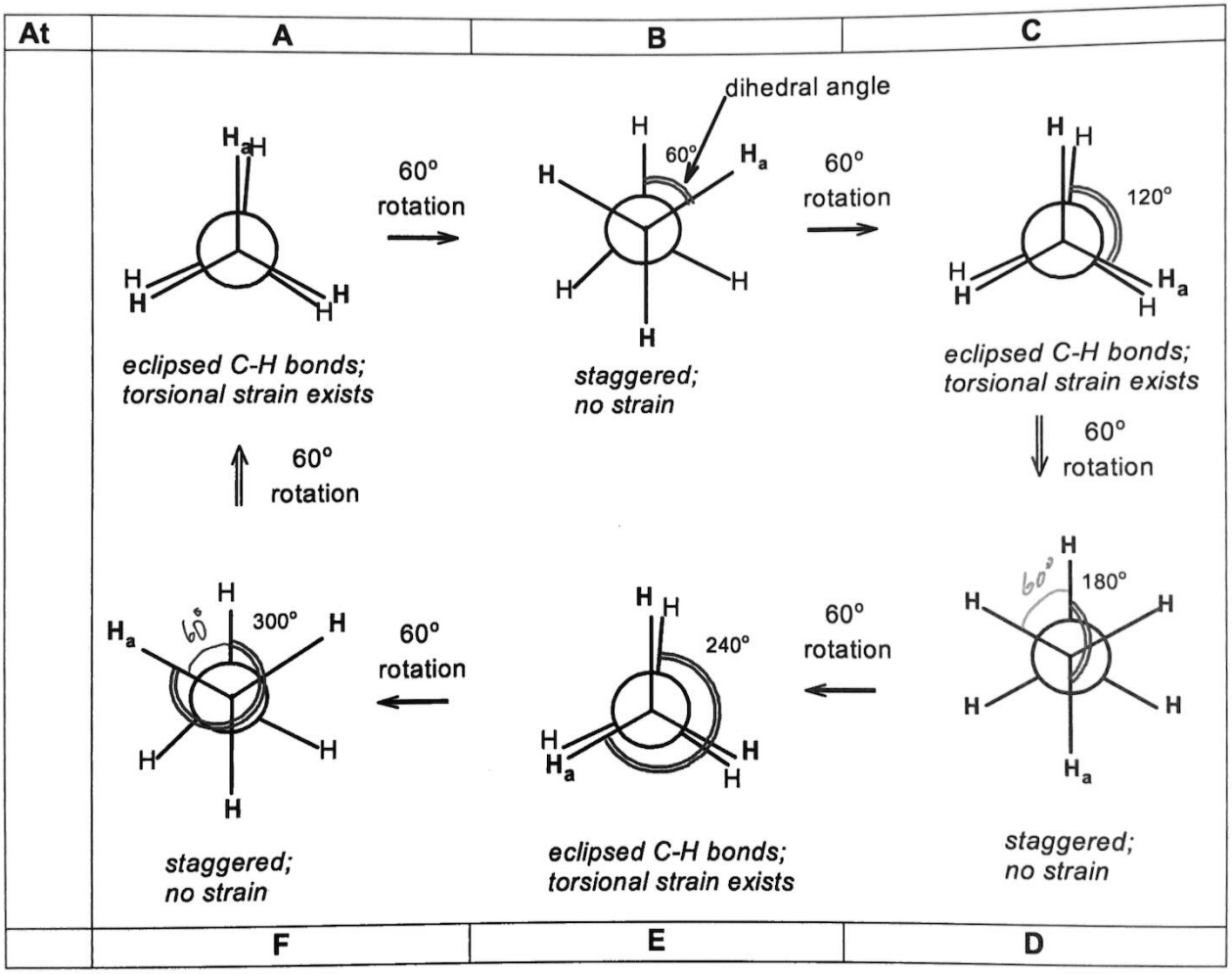
staggered

2.2 Stability of different conformations of ethane

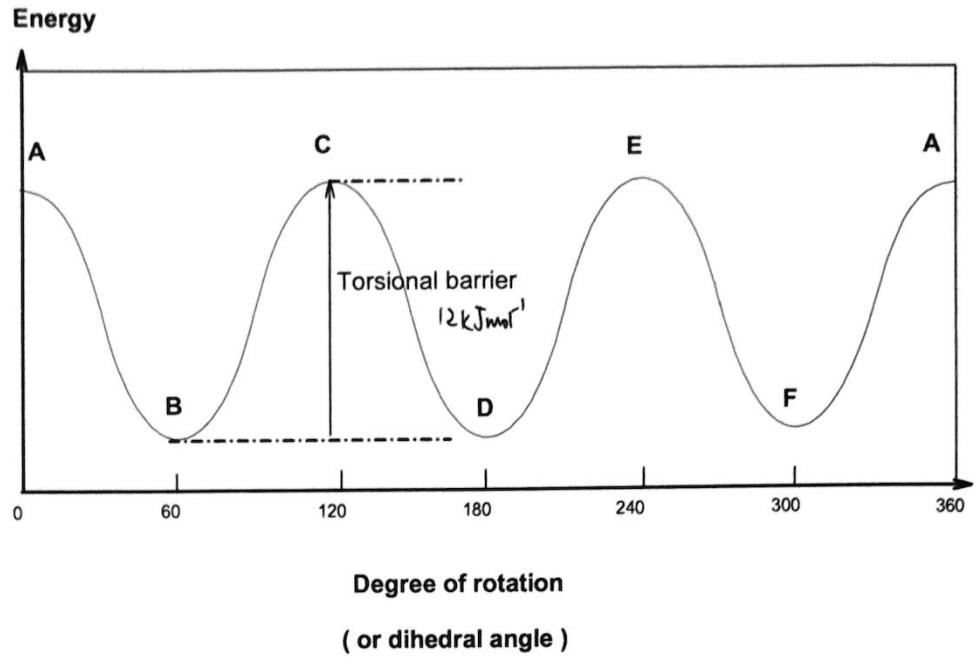
The different conformations of the ethane molecule are not of equal stability.

Conformation of ethane	Eclipsed	Staggered
3D view of conformation		
Remarks	*Least stable* conformation	*Most stable* conformation
Reasons	There is torsional strain in this conformation. This is due to repulsion caused by electrons of the eclipsed C–H bonds.	There is no torsional strain because all the hydrogen atoms are as far apart from each other as possible / there is better electron delocalisation.

The following diagram shows how **torsional strain** appears in various conformations, as C–C bond rotate (dihedral angle = 0° to 360°) in **ethane**.



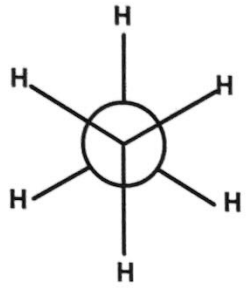
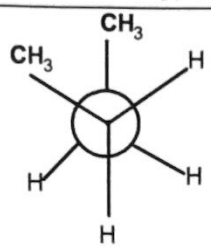
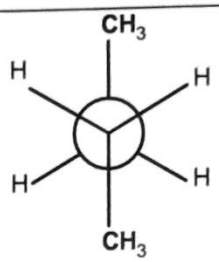
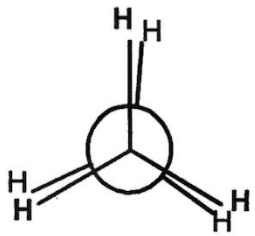
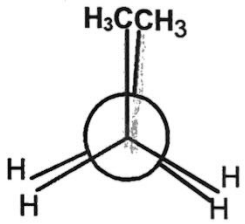
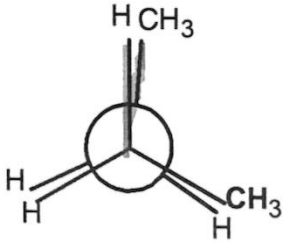
Graph of Relative Energy of conformations of ethane and dihedral angle



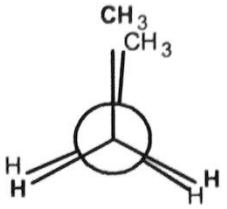
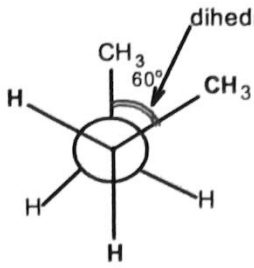
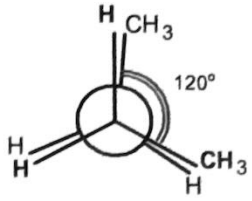
Torsional barrier is an energy barrier to the rotation from one staggered conformation to another. It was found that the three pairs of eclipsed bonds are responsible for 12 kJ mol^{-1} of torsional strain in ethane, i.e. strain, also known as energy cost, of 4 kJ mol^{-1} between each pair of bonds.

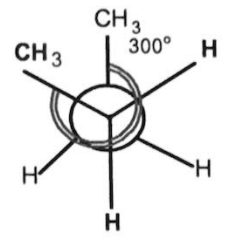
2.3 Conformations of butane

Like ethane, bigger molecules like butane has staggered and eclipsed conformations. However, they do have some differences. The following table illustrates the differences.

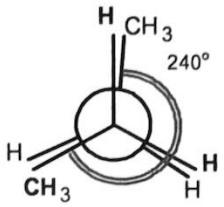
	Ethane	Butane	
Types of **staggered conformations**	One type	Two types called ***gauche*** *and* ***anti.***	
		 **gauche-staggered** **Note**: the $-CH_3$ groups are close to each other.	 **anti-staggered** **Note**: the $-CH_3$ groups are **opposite** to each other.
Types of strain present	No **torsional** strain because all the H are as far apart as possible.	No **torsional** strain BUT **Steric** strain ▪ Results from repulsion caused by electron clouds of two $-CH_3$ groups being too close together and trying to occupy the same space.	No **torsional** strain because all the groups are as far apart as possible.
Remarks			**Most stable**
Types of **eclipsed interactions**	One type	Two types respectively in	
	 C–H/C–H interactions	 C–H/C–H interactions & **C–CH_3 / C–CH_3** **also known as syn conformation**	 C–H/C–H interactions & **C–CH_3 / C–CH_3**
Types of strain present	**Torsional strain** ▪ Results from electron repulsion between eclipsed bonds	**Torsional strain &** ▪ Results from electron repulsion between eclipsed bonds. **Steric strain** ▪ Results from electron clouds of two $-CH_3$ groups being too close together and trying to occupy the same space.	**Torsional strain** - Results from repulsion between the eclipsed bonds.
Remarks		**Least stable**	

The following diagram shows how various conformations, as C–C bond rotate (dihedral angle = 0° to 360°) in **butane**.

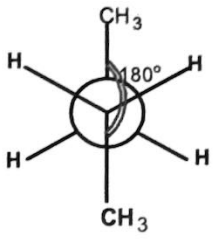
At point	A	B	C
	 eclipsed (least stable)	 **gauche**-staggered	 eclipsed
	F	E	D



gauche-staggered

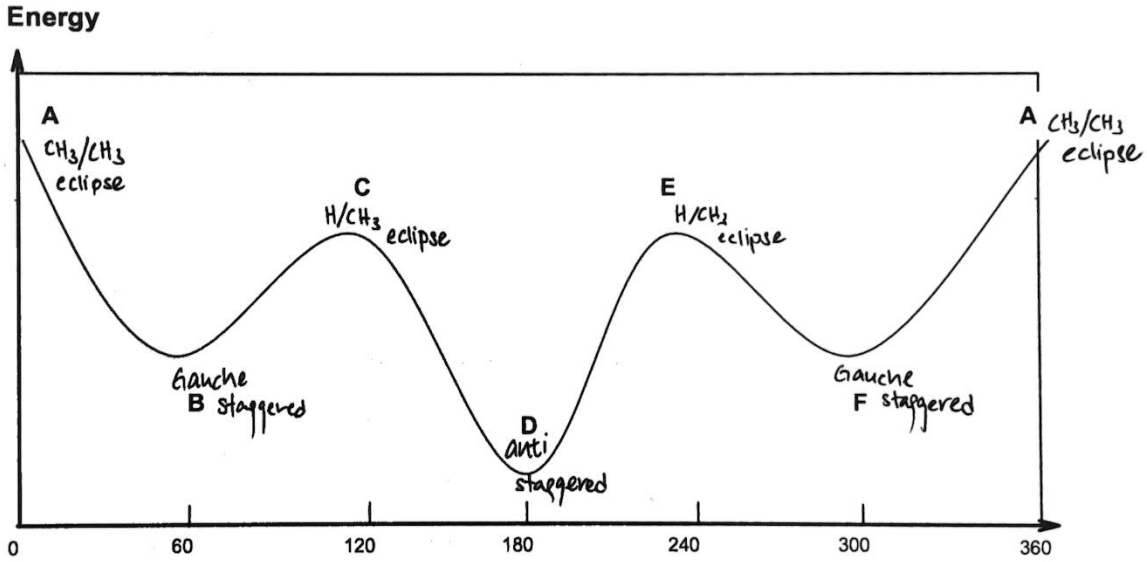


eclipsed



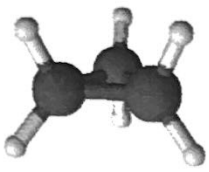
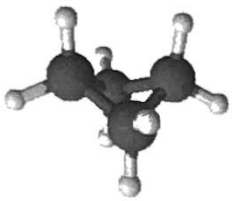
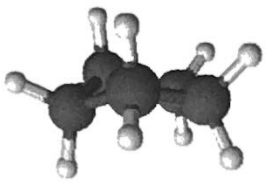
anti-staggered (most stable)

Graph of Relative Energy of conformations of butane and dihedral angle.



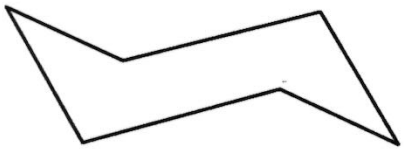
2.4 Conformations of cycloalkanes

The smallest hydrocarbon cyclic ring is cyclopropane. It is a flat ring. Unlike cyclopropane, **rings bigger than cyclopropane are puckered** ("bend" from planarity), to minimise angle strain and torsional strain.

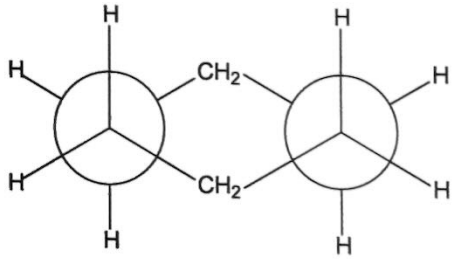
Cyclopropane	Cyclobutane	Cyclopentane	Cyclohexane
			
			
Torsional strain and angle strain present. Angle strain – strain due to compression or expansion of bond angle from the ideal tetrahedral angle (109.5°)			Virtually strain–free especially its **chair conformation** allows all C–C–C bond angle to be ~111° (closest to 109.5°)

2.5 Conformations of cyclohexane

The following information will be on the conformations of cyclohexanes.



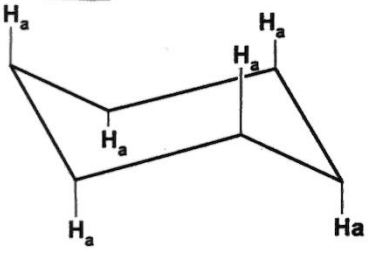
Skeletal representation



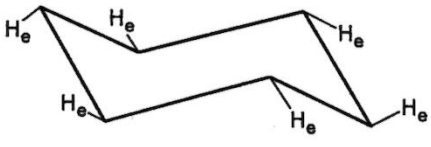
Newman projection

chair conformation of cyclohexane

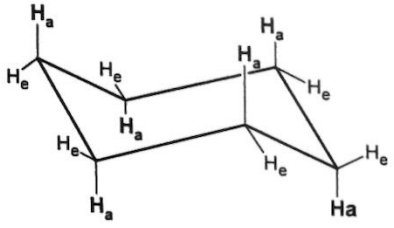
The chair conformation of cyclohexane has **six equatorial and six axial hydrogen atoms.**



axial positions



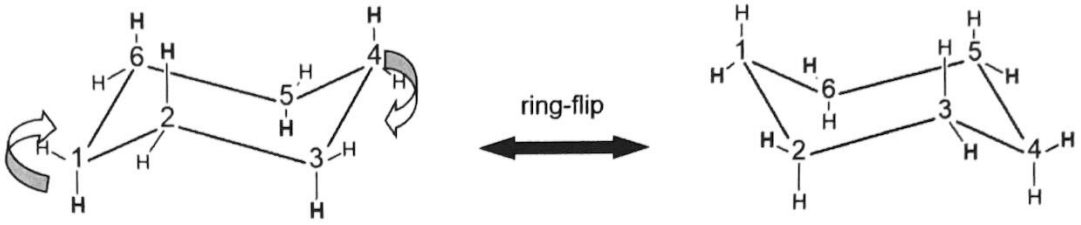
equatorial positions



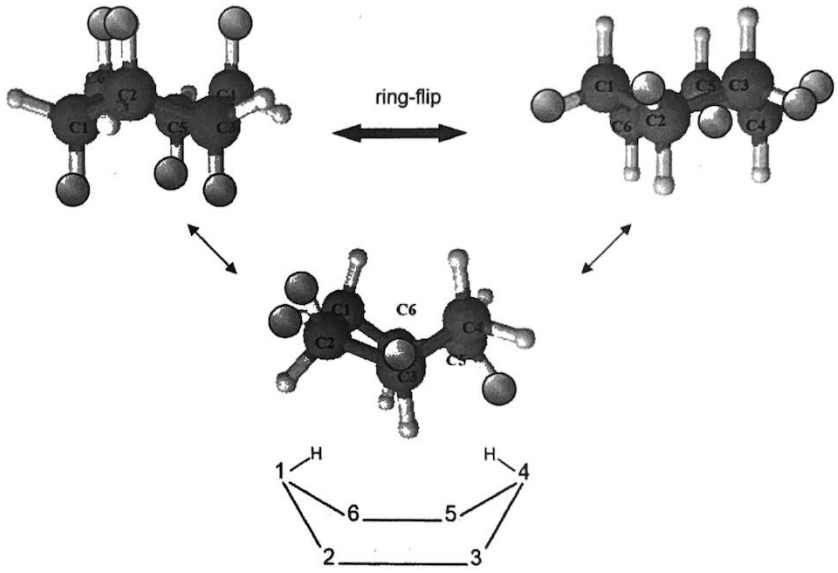
axial and equatorial positions

With C–C–C bond angles of 111°, the chair conformation is nearly free of angle strain. All its bonds are staggered, making it free of torsional strain as well. The staggered arrangement of bonds in the chair conformation is apparent in the Newman projection shown on page 10.

Cyclohexane is conformationally mobile at room temperature: there are two **possible chair conformations**. They readily interconvert, i.e. **ring–flip** from one chair conformation into another. This causes the **axial H atoms in one chair conformation becomes equatorial H** in the other chair conformation **and vice versa**.

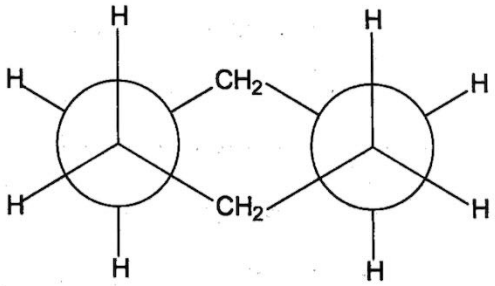


Both chair conformations are equivalent or superimposable. To interconvert from one into another, it has to adopt a "boat" conformation in the process.

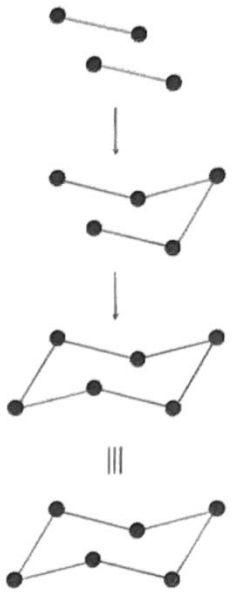


The "boat" conformation is less preferred due to torsional strain (four pairs of eclipsed C–H bonds) and steric strain between C1 and C4 hydrogens.

Thus **cyclohexane adopts the chair conformation most of the time as it is the more stable**.



Guidelines on drawing the chair conformation



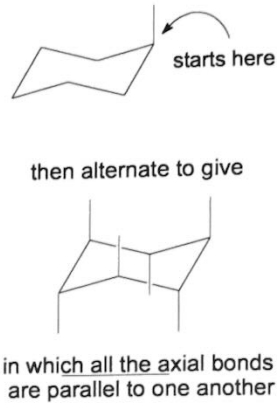
Step 1 Draw two parallel lines, slanted downward and slightly off-set from each other. This means that four of the cyclohexane carbons lie in a plane.

Step 2 Place the topmost carbon atom above and to the right of the plane of the other four, and connect the bonds.

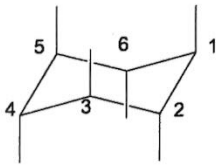
Step 3 Place the bottommost carbon atom below and to the left of the plane of the middle four, and connect the bonds. Note that the bonds to the bottommost carbon atom are parallel to the bonds to the topmost carbon.

Step 4 Draw the axial bonds before the equatorial ones, alternating their direction on adjacent carbon atoms. Always start by placing an axial bond "up" on the topmost carbon or "down" on the bottommost carbon.

(ignore the dots after you are familiar with drawing the chair conformation)



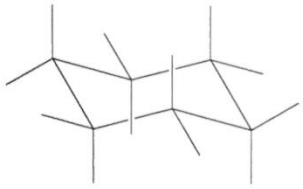
Step 5 Place the equatorial bonds so as to approximate a tetrahedral arrangement of the bonds to each carbon. The equatorial bond of each carbon should be parallel to the ring bonds of its two nearest neighbor carbons.



Place equatorial bond at C1 such that it is parallel to the bonds between C2 and C3.

Following this pattern (i.e. at C2, it will be parallel to C1 and C6) gives the complete set of equatorial bonds.

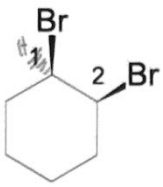
Step 6 Practise drawing cyclohexane chairs oriented in either direction.



Organic Chemistry (5th Ed), John McMurry p129

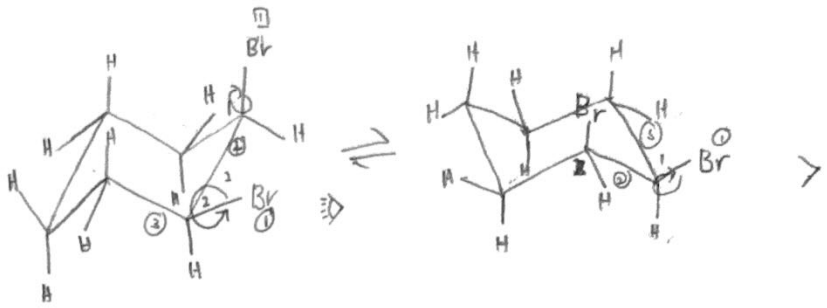
Exercise 2: Draw the chair conformation of the following molecules.

(a)



cis–1,2–dibromocyclohexane

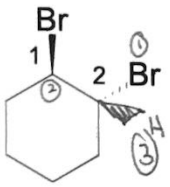
1R 2S



Where is axial/equatorial

↳ check R/S from viewpoint

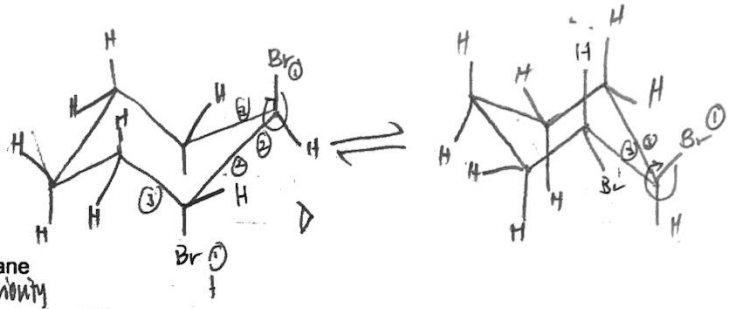
(b)



trans–1,2–dibromocyclohexane

1R 2R

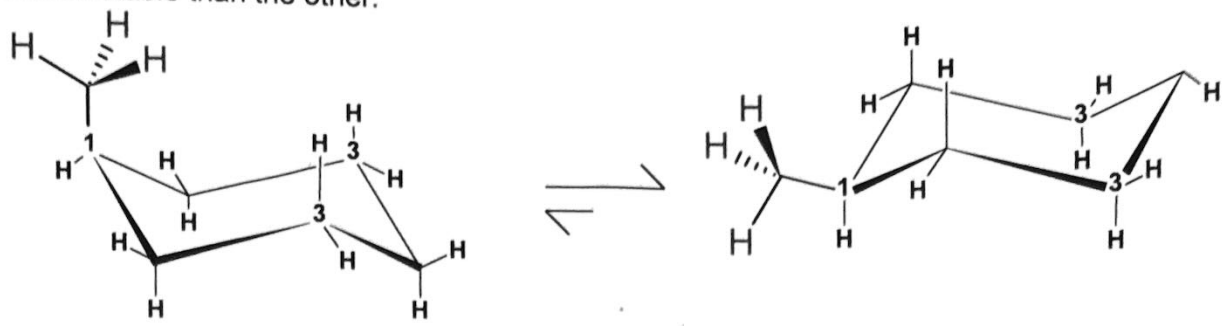
Flip direction if lower priority group is towards you.



Note: In a ring–flip, **a cis isomer remain cis**, and **trans isomer remains trans** but the equatorial and axial positions are reversed on each carbon.

2.6 Conformations of mono–substituted cyclohexanes

For mono–substituted cyclohexanes like methylcyclohexane, one of its two chair conformations is more stable than the other.



axial conformer has **1,3-diaxial steric interaction**

equitorial conformer do **not** have **1,3-diaxial steric interaction**

Because of the 1,3–diaxial steric interaction, it creates strain in the axial conformation, thus it is less stable than the equatorial conformation. Methylcyclohexane most likely to exist as equatorial conformation.

Generally, **bulky substituents** (other than H) will prefer to be in the equatorial position to acquire a more stable conformation.

Degree of 1,3–diaxial steric strain of X with H
X = F ≈ C*l* ≈ Br ≈ I < OH < CH_3 < CH_2CH_3 < $CH(CH_3)_2$ < phenyl group < $C(CH_3)_3$

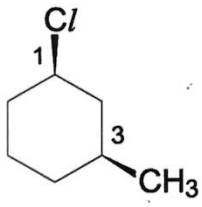
large valence orbital, but longer bond length

For more detailed explanations on the degree of 1,3-diaxial steric strain, you may refer to this website (https://www.masterorganicchemistry.com/2014/07/01/substituted-cyclohexanes-a-values/).

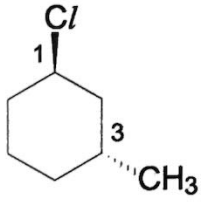
Exercise 3: Draw the two chair conformations of the compound given.

↑ which is more stable

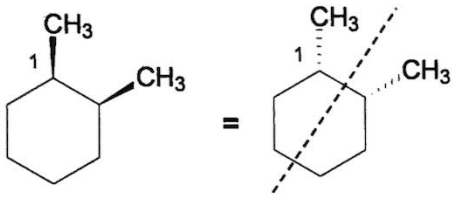
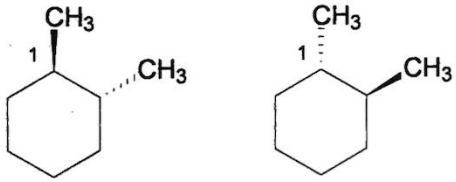
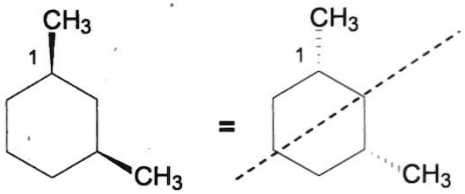
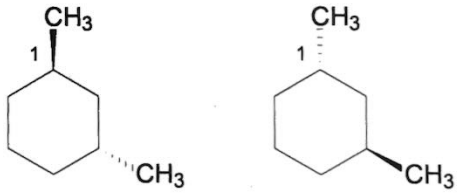
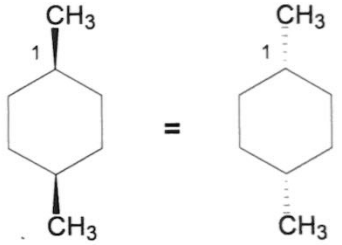
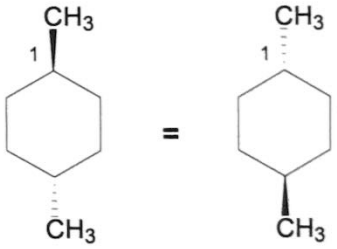
(i)



(ii)

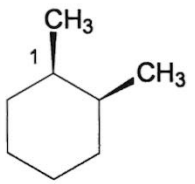


Note: the *R*, *S* configurations* do **not** change when one conformation change into the other.
** to be covered in later part.*

	1,2–dimethylcyclohexane	1,3–dimethylcyclohexane	1,4–dimethylcyclohexane
Any chiral carbons?	Yes (2)	Yes (2)	No
These two are identical molecules **Can exist as cis/trans isomers?**	cis:  (1R,2S) = (1S,2R) trans:  (1R,2R) (1S,2S)	cis:  (1R,3S) = (1S,3R) trans:  (1R,3R) (1S,3S)	cis:  = These two are identical molecules trans:  = These two are identical molecules
Can exist as optical isomers?	*Cis* isomer is a **meso** compound (Has chiral carbons and a plane of symmetry in boat conformation.); Not optically active. Trans isomer can exist as enantiomers.	Cis isomer is a meso compound; Not optically active. Trans isomer can exist as enantiomers.	No. (It has no chiral carbon and has a plane of symmetry). Not optically active.

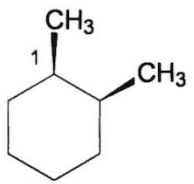
Can exist as chair conformations ?

cis

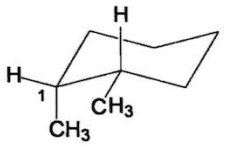


(1R,2S)

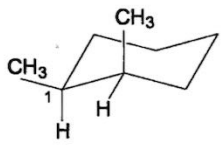
cis



(1S,2R)

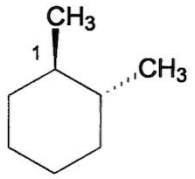


(1R,2S)



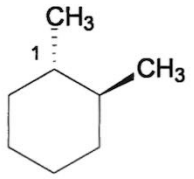
(1S,2R)

trans

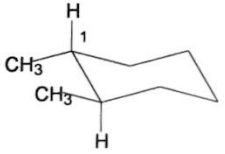


(1R,2R)

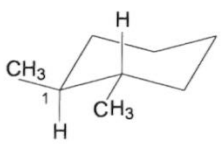
trans



(1S,2S)

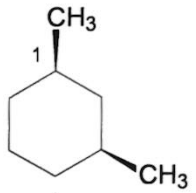


(1R,2R)



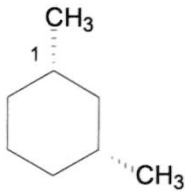
(1S,2S)

cis

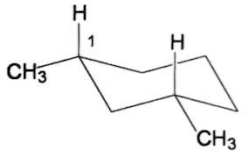


(1R,3S)

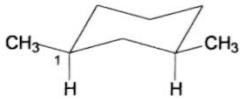
cis



(1S,3R)

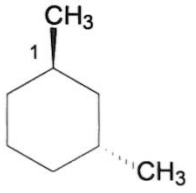


(1R,3S)



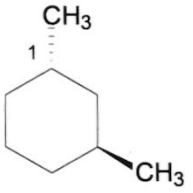
(1S,3R)

trans

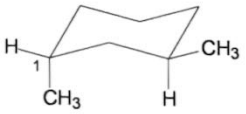


(1R,3R)

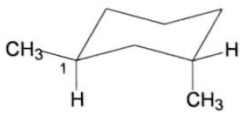
trans



(1S,3S)

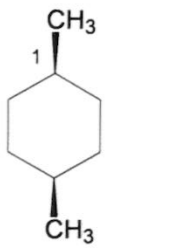


(1R,3R)



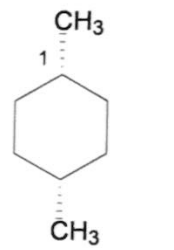
(1S,3S)

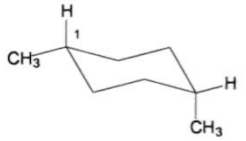
cis

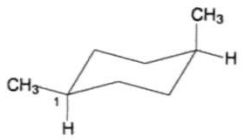


=

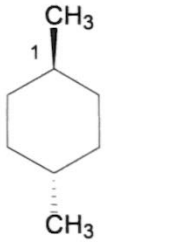
cis







trans



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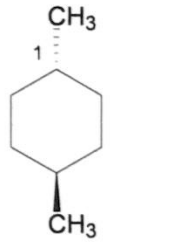
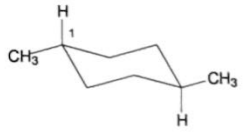
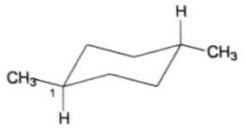
trans

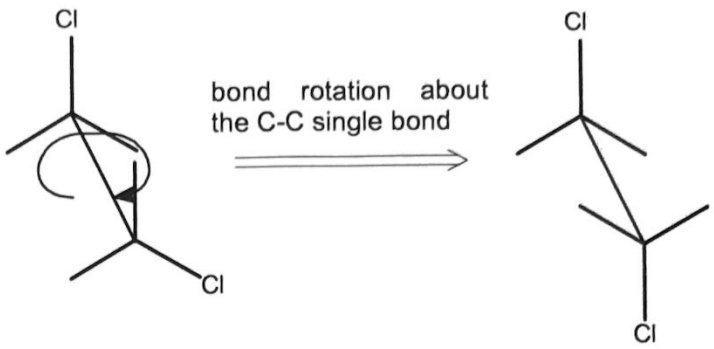






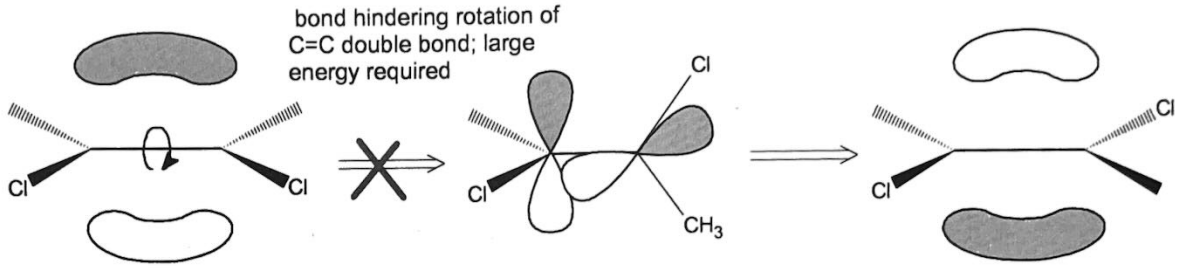
3 Cis–trans isomerism

Alkenes form a homologous series with general formula C_nH_{2n} and have similar physical properties with alkanes. However, in alkanes, the C–C single bonds can rotate freely. In alkenes, it is not possible to rotate one end of a C=C double bond relative to the other end.



1,2-dichloroethane

This is due to the π bond, which hinders the rotation. A large amount of energy is required (about 300 kJ mol^{-1}) to break the π bond and reform instead of C–C rotation (about 12 kJ mol^{-1}) which is possible at normal temperatures. Because of this hindered rotation, geometrical or *cis–trans* isomers exist.



cis–1,2–dichloroethene

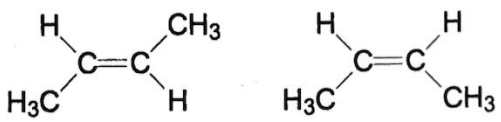
trans–1,2–dichloroethene

3.1 Cis–trans isomers

Alkenes with **two** different groups on **each** carbon atom of a C=C double bond can exhibit geometrical isomerism. E.g. Molecule **I** cannot exhibit cis–trans isomerism but molecule **II** can.

I II

For such di–substituted alkenes, they are coined '*cis*' and '*trans*' nomenclature. A *cis* structure results when two identical groups are on the "same" sides of the C=C double bond. A *trans* structure results when the two identical groups are on "opposite" sides of the C=C double bond.



trans-but-2-ene cis-but-2-ene

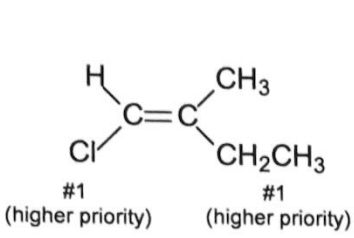
3.2 E and Z isomers

When the groups on either end of a double bond are the same or are structurally similar to each other, it is a simple matter to describe the configuration of the double bond. However, when the groups on either end of a double bond are not obvious or for tri–substituted or tetra–substituted alkenes, the '*cis*' and '*trans*' nomenclature can be ambiguous.

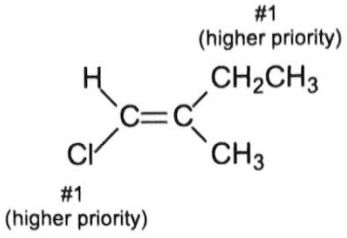
For such alkenes, the system of *E*/*Z* nomenclature, in which a set of sequence rules to establish an order of precedence of atoms and groups, is used.

- *E* (derived from German word, *entgegen*), meaning *opposite*
- *Z* (derived from German word: *zusammen*), meaning together on the *same* side

If atoms/ groups of atoms of higher priority are on the "same" side of the >C=C< double bond, it is a *Z* isomer. If they are on "opposite" sides of the >C=C< double bond, it is an *E* isomer.



Z isomer



E isomer

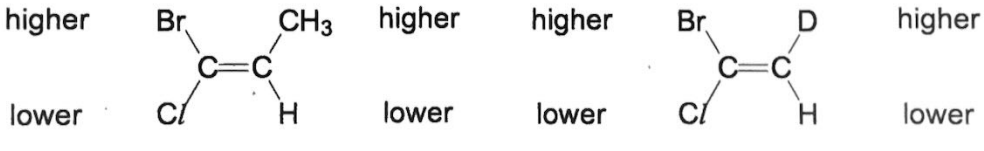
To determine which atom or groups of atoms are of higher priority, the Cahn–Ingold–Prelog (CIP) priority rules are described in Table 3.2.

Table 3.2: Cahn–Ingold–Prelog priority rules

1. Higher atomic number takes precedence over lower. Bromine (atomic number 35) outranks chlorine (atomic number 17). Methyl (C, atomic number 6) outranks hydrogen (atomic number 1).

   In case of **isotopes**, the higher the **atomic mass**, the higher the priority.
   D (i.e. ^{2}H) outranks ^{1}H; ^{37}Cl outranks ^{35}Cl

   e.g.

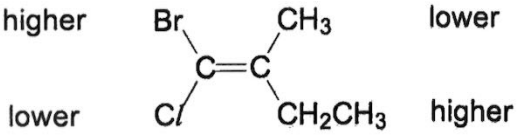
   

2. When two atoms directly attached to the double bond are identical, compare the atoms attached with these two on the basis of their atomic numbers. Precedence is determined at the first point of difference.

   Ethyl [–C(**C**,H,H)] outranks methyl [–C(**H**,H,H)].

   Similarly, *tert*–butyl [–C(CH_3)$_3$] [–C(C,C,**C**)] outranks isopropyl [–CH(CH_3)$_2$] [–C(C,C,**H**)], and isopropyl outranks ethyl.

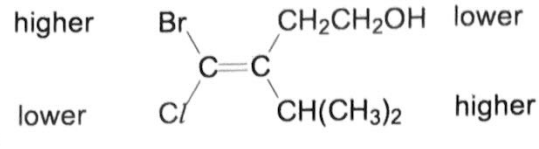
   e.g.

3. Work outward from the point of attachment, comparing all the atoms attached to a particular atom before proceeding further along the chain.

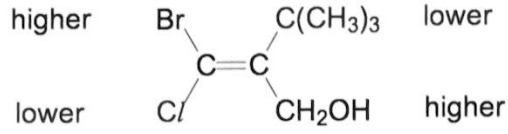
   $-CH(CH_3)_2$ [–C(C,**C**,H)] outranks $-CH_2CH_2OH$ [–C(C,**H**,H)].

   e.g.



4. When working outward from the point of attachment, always evaluate substituent atoms one by one, never as a group. Because oxygen has a higher atomic number than carbon, $-CH_2OH$ [–C(**O**,H,H)] outranks $-C(CH_3)_3$ [–C(**C**,C,C)].

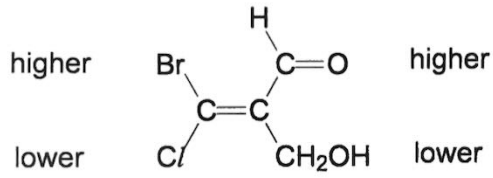
   e.g.



5. An atom that is multiply bonded to another atom is considered to be replicated as a substituent on that atom.

   –CHO is treated as if it is [–C(O,O,H)]. The group –CH=O [–C(O,**O**,H)] outranks $-CH_2OH$ [–C(O,**H**,H)]

   e.g.



Exercise 4: Use the CIP system to deduce which substituent group is of a higher priority.

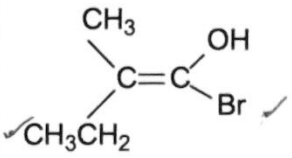
		Higher priority
(a)	$-CH_2CH_3$, $-CH_2OH$	$-CH_2OH$
(b)	$-CH_3$, –COOH	–COOH
(c)	–Br, –CHO	–Br
(d)	–CHO, –COOH	–COOH

Exercise 5: Use CIP system and assign priority to the substituents groups, starting from the highest priority to the lowest.

		Highest → Lowest
(a)	$-CH_2CH_3$,$-CH_2OH$, –Br, $-CH_2CH_2OH$	$-Br \rightarrow -CH_2OH \rightarrow -CH_2CH_2OH \rightarrow CH_2CH_3$
(b)	$-CH_2OH$, $-CO_2CH_3$,–COOH, –OH	$-OH \rightarrow -CO_2CH_3 \rightarrow -COOH \rightarrow -CH_2OH$
(c)	–CN, $-NH_2$,$-CH_2NH_2$, $-CH_2NHCH_3$	$-NH_2 \rightarrow -CN \rightarrow -CH_2NHCH_3 \rightarrow -CH_2NH_2$
(d)	$-CH_2Br$, –Cl, –Br, $-CH_2Cl$	$-Br \rightarrow -Cl \rightarrow -CH_2Br \rightarrow -CH_2Cl$

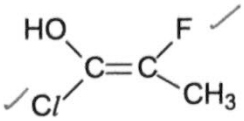
Having assigned the priority, we can now practice assigning the *E* and *Z* configuration.

Exercise 6: Assign *E/Z* configuration to the following molecules **and** the examples in Table 3.2.



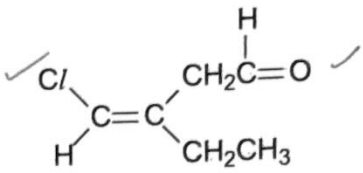
(A)

Z



(B)

E

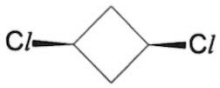


(C)

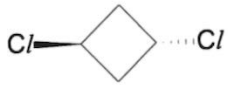
E

3.3 Cis–trans isomerism in a ring system

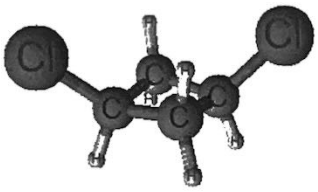
Cis–trans isomerism also occurs in rings systems like cycloalkanes. This is because the rotation around a single bond is prevented by the linkage in the ring.

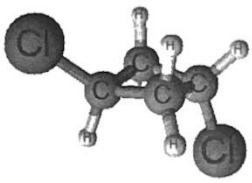


cis-1,3-dichlorocyclobutane



trans-1,3-dichlorocyclobutane



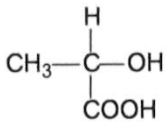


3D view of cis–1,3–dichlorocyclobutane & trans–1,3–dichlorocyclobutane

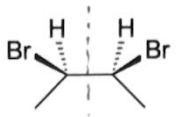
4. Optical isomerism

Optical isomerism arises from the inherent asymmetry of the molecules. If the molecule has **no plane** or centre **of symmetry**, it is said to be **chiral** and **can exhibit optical activity**. Conversely, all achiral substances are optically inactive.

Exercise 7: Which molecules are chiral?

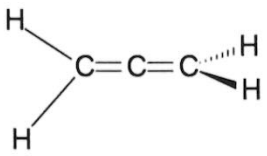


(A)
chiral



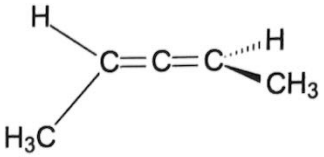
(B)
achiral

For your information:



(B)

achiral
(has a plane of symmetry)



(C)

chiral
(has no plane of symmetry)

Hands–on activity

(a) Make a model and draw a three–dimensional structure for 2–bromobutane.

(b) Draw and make a model of the mirror image of your original structure and determine whether the mirror image is the same compound or its enantiomer.

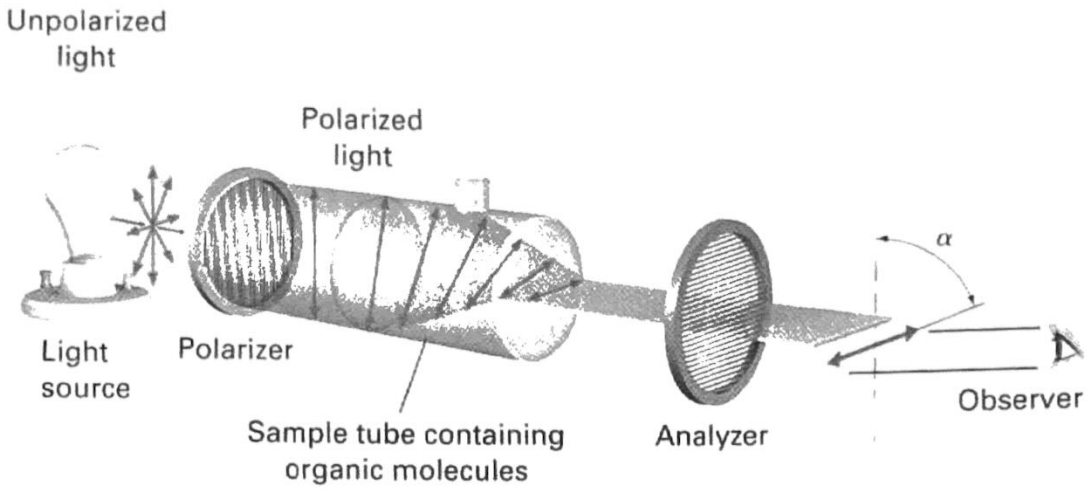
(c) Exchange the positions of any two groups of one of the models and determine
(i) whether the mirror image is the same compound or its enantiomer.
(ii) the stereochemical consequence of this action.

4.1 Optical activity

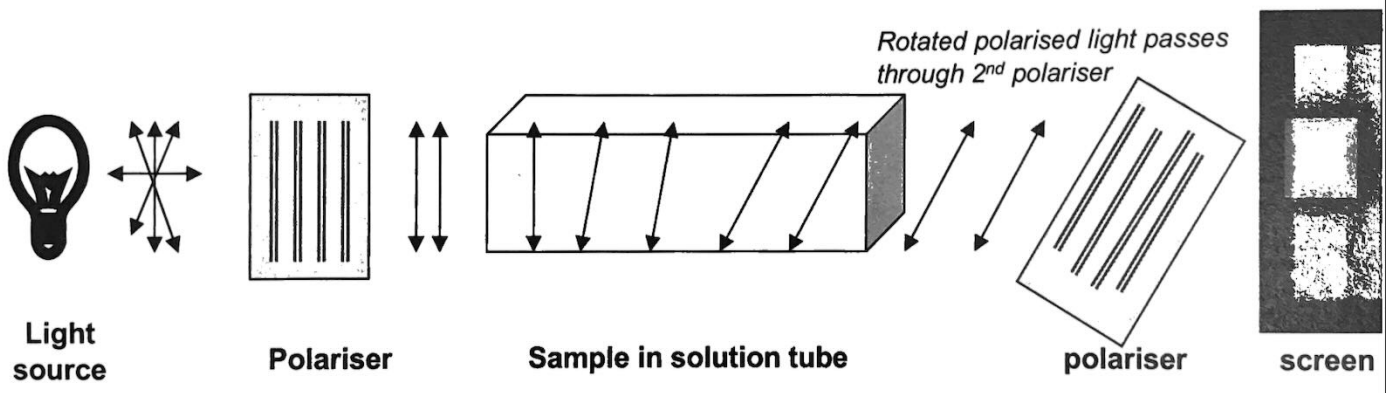
Optical activity is the **ability of a chiral substance to rotate the plane of plane–polarised light** and is measured with an instrument called a polarimeter (shown in figure below).

In the polarimeter, a beam of unpolarised light is transformed to plane–polarised light by passing it through a polarising filter (which removes all waves except those in the same plane as the filter). The plane–polarised light now passes through a sample tube containing the analysed substance (either in liquid phase or as a solution in a suitable solvent – usually water, ethanol or chloroform). The sample is optically active if it rotates the plane–polarised light. The direction and magnitude of rotation are measured using a second polarising filter (the "analyser") and cited as α, the observed rotation

To be optically active, the sample must contain a chiral substance and one enantiomer must be present in excess of the other.



Schematic representation of how the polarimeter works



By rotating the 2nd polarising filter until light can be seen on screen, we can tell can tell in which direction and to what extent the sample has rotated the plane–polarised light.

4.2 Enantiomers

Optical isomerism **most** commonly occurs when a carbon atom has four different groups of atoms attached to it. These types of carbon centres are called **chiral** / stereogenic **centres**. Two possible arrangements of these groups give rise to two molecules that are mirror images of each other. These two mirror images are called ***enantiomers***.

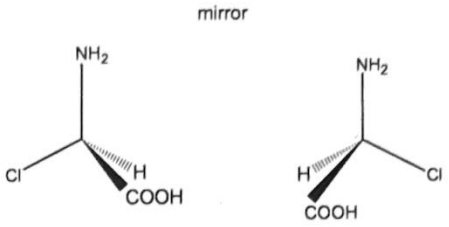


Figure (a): optical isomers also known as enantiomers are mirror images of each other

Enantiomers are a **pair** of stereoisomers that have non–superimposable mirror images of each other. Both rotate the plane of polarised light in **different directions**. Rotation of the light in clockwise is taken as positive (+), and rotation in the anticlockwise sense is taken as a negative (–). Older terms for (+) and (–) rotations are *dextrorotary* and *laevorotary* (*dextro* and *laevo* meaning right and left respectively in Latin) and the symbols *d* and *l* are used to distinguished between enantiomeric forms of a substance.
E.g. (+)–butan–2–ol [or *d*–butan–2–ol]; (–)–butan–2–ol [or *l*–butan–2–ol].

Enantiomers have:

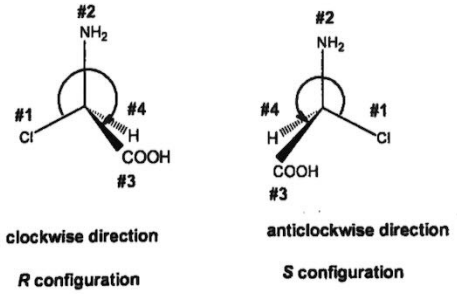
- identical physical properties like melting points, solubility in solvents **except optical activity**, and
- identical chemical reactivity **except with chiral reagents**

A 50:50 mixture of (+) and (–) isomers will have no effect on the plane of polarised light and it is called a **racemic mixture** or **racemate**.

To differentiate one enantiomer from another, the actual configuration of the isomer has to be described using the CIP sequence rules. The above molecules in Figure (a) are used as an illustration. Note that neither the sign nor the magnitude of rotation by itself can tell us the configuration of a substance

1 Assign priority to the four groups of atoms attached to the chiral centre. The higher the atomic number, the higher the priority.

2 Visualise the molecule with the atom/group of atoms with the lowest priority behind the chiral centre.

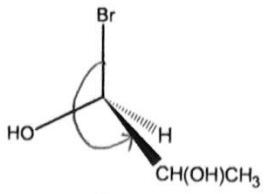


R(ight)

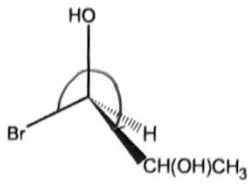
3 Follow the direction from the highest priority (#1) to second lowest (#3). If it is a clockwise direction, it is assigned a ***R* configuration**. If it is an anticlockwise direction, it has a ***S* configuration**.

Exercise 8: Assign R/S configuration to the molecules and determine whether they are *enantiomers* or identical molecules.

(a)



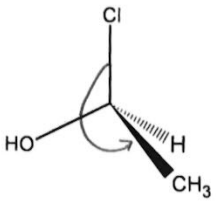
S



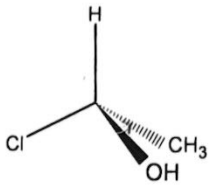
R

Enantiomers

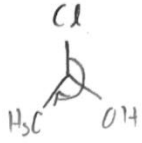
(b)



S

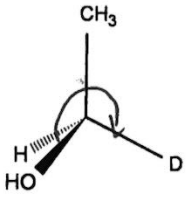


R

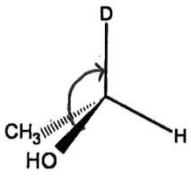


Enantiomers

(c)

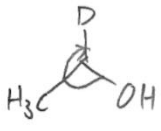


R



R

Note: D = ^{2}H



Identical

Note:
Any substance that is non–superimposable with its mirror image is chiral. While a chiral centre focusses on chirality on a certain point in a molecule, there can be also chiral molecules that lack such centres. Such molecules can be viewed as helical, and could have propeller or screw–shaped structures (e.g. right handed or left handed DNA, helicene).

helicene

4.3 Optical activity of chiral molecules

The observed rotation of an optically pure substance depends on how many molecules the light beam encounters. The greater the number of molecules encountered by the plane–polarised light, the greater the degree of rotation. Consequently, the magnitude of the angle through which an enantiomer rotates plane–polarised light depends on:

- wavelength of the light (in most cases a sodium lamp is used)
- length of the cell (l) through which the light passes
- concentration (c) of the optically active species in the solution through which the light passes
- the specific rotation ($[\alpha]$) of the species, which reflects its relative ability to rotate plane–polarised light. This value can be used as a guide for the enantiomeric purity of a sample, i.e. how much of each enantiomer the substance contains.

An equation to express the relationships between the quantities is:

$$[\alpha]_D^{20} = \frac{\text{observed rotation (degrees)}}{\text{path length, } l \text{ (dm)} \times \text{concentration (g/cm}^3\text{)}} = \frac{\alpha}{l \times c}$$

where 20 refers to 20 °C, and D refers to wavelength of 589 nm (D line of a sodium lamp). Units of l is in dm and c is in g cm^{-3}.

Worked example:
A 1.20 g sample of cocaine, $[\alpha]_D^{20} = -16°$, was dissolved in 7.50 ml of chloroform and placed in a sample tube having a pathlength of 5.00 cm. What was the observed rotation?

$$[\alpha]_D^{20} = \frac{\alpha}{l \times c}$$

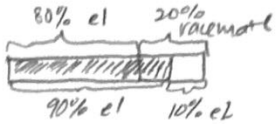
$$\alpha = l \times c \times [\alpha]_D^{20} = 0.5 \text{ dm} \times \frac{1.20}{7.50} \times -16 = -1.3°$$

A racemic mixture/racemate must show zero optical rotation because an equal amount of (+) and (–) forms are present. The (+) rotation from one enantiomer exactly cancels the (–) rotation from the other enantiomer.

Specific rotation, [α], provides a way to assess the **optical purity** of a sample.
For example, if [α] for (S)–2–bromobutane is +23.1°, it indicates that the pure sample of the S isomer rotates polarised light 23.1° in a clockwise manner. Thus if a particular sample of 2–bromobutane shows a [α] of +23.1°, it is a pure sample.

Optical purity of a mixture of enantiomers could be described in the following equation:

$$\text{Optical purity} = \frac{[\alpha]_{\text{sample}}}{[\alpha]_{\text{pure enantiomer}}} \times 100\%$$



If optical purity is 80%, this means that enantiomer 1 is in excess of 80% over the other. The mixture contains 90% of enantiomer 1 and 10% of enantiomer 2, as 10% of enantiomer 1 can be paired with 10% of enantiomer 2 to form 20% racemate.

Optical purity is equivalent to enantiomeric excess (e.e.), which is defined as the excess of one enantiomer over the other, expressed as a percentage of the whole:

% e.e. = % enantiomer 1 – % enantiomer 2

Unlike optical purity, e.e. describes the composition of a chiral substance without relating to a physical measurement.

Worked example:
The [α] for (S)–2–bromobutane is +23.1° and (R)–2–bromobutane is –23.1°.

If the specific rotation of a sample of 2–bromobutane is –9.2, what is the enantiomeric excess of R enantiomer?

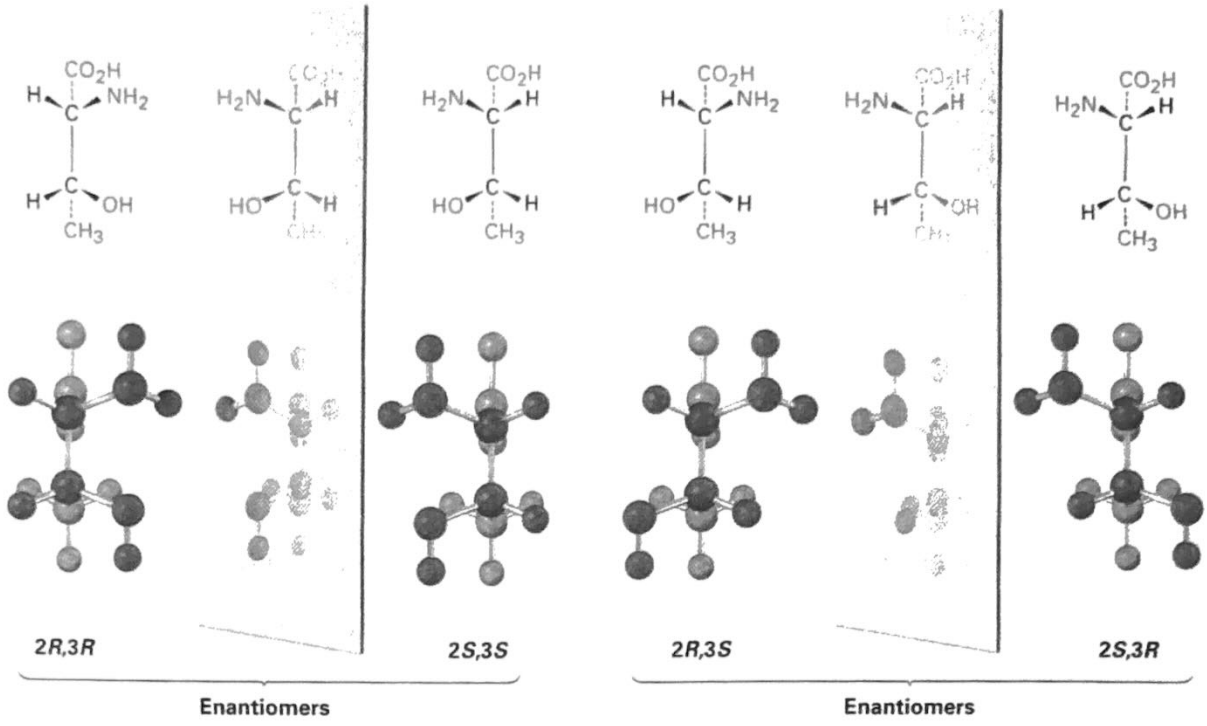
Enantiomeric excess of R enantiomer = $\frac{9.2}{23.1} \times 100\% = 40\%$

This implies that the remaining 60% of the sample is racemic (30% R, 30% S)
Thus, the sample contains 70% (R)–2–bromobutane and 30% (S)–2–bromobutane.

4.4 Diastereomers

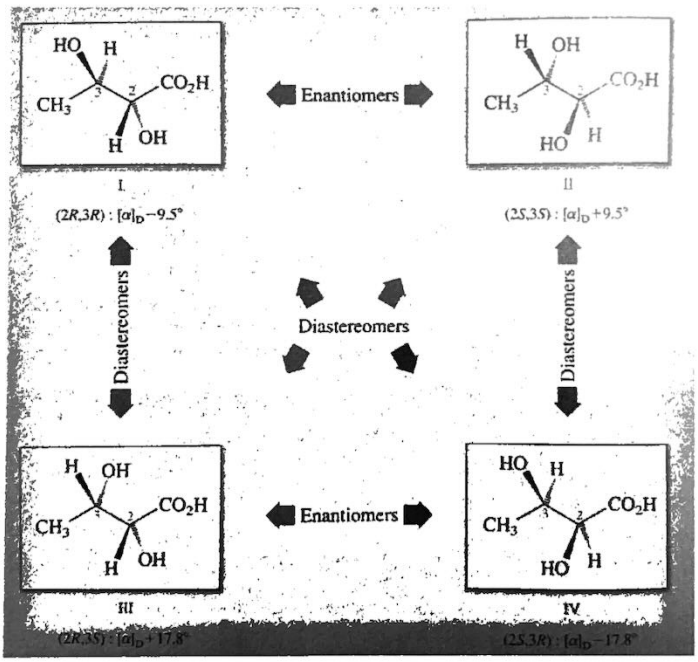
Diastereomers are stereoisomers that are not mirror images. They are non–superimposable, non–mirror image isomers. Enantiomers have opposite configurations at all chirality centers, but diastereomers have opposite configurations at some (one or more) chirality centers but the same configuration at others.

Organic Chemistry (5th Ed), John McMurry, p321&323



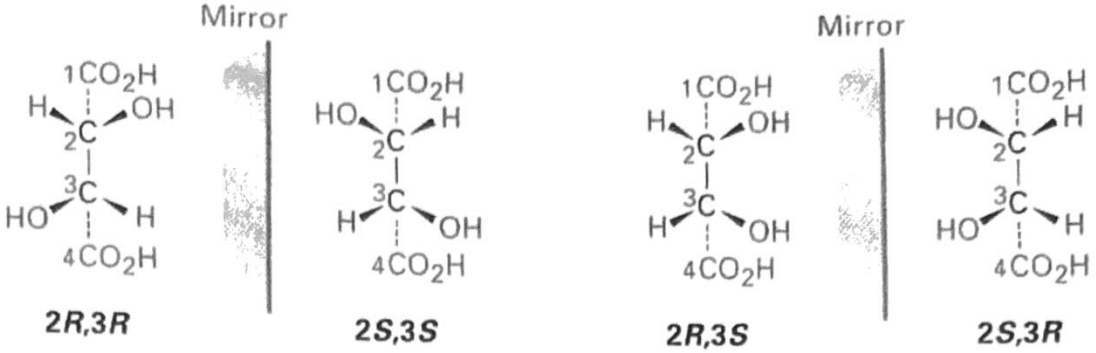
The table below shows the relationships among the four stereoisomers of threonine.

Stereoisomer	Enantiomer	Diastereomer
2R,3R	2S,3S	2R,3S and 2S,3R
2S,3S	2R,3R	2R,3S and 2S,3R
2R,3S	2S,3R	2R,3R and 2S,3S
2S,3R	2R,3S	2R,3R and 2S,3S

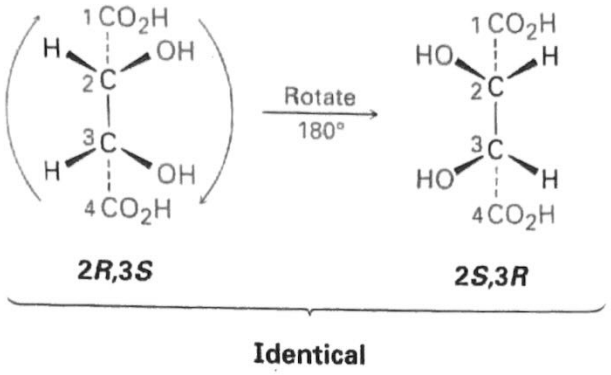


4.5 Meso compounds

Using the example of tartaric acid, the four stereoisomers can be drawn as follows:

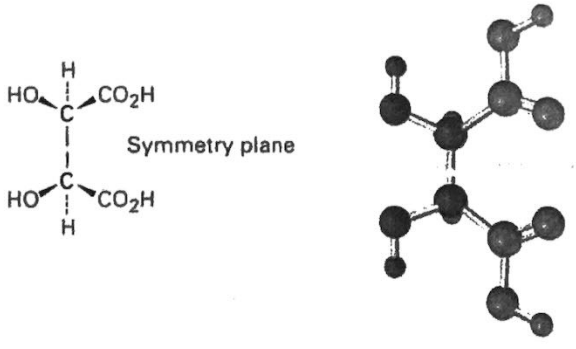


The mirror image of 2R,3R and 2S,3S structures are not identical and therefore represents a pair of enantiomers. However, the 2R,3S and 2S,3R structures are identical, as can be seen by rotating one structure 180°.



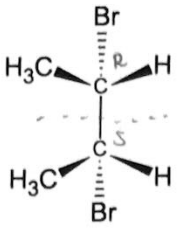
The 2R,3S and 2S,3R structures are identical because the molecule has a plane of symmetry and is therefore achiral (not chiral). The symmetry plane cuts through the C2–C3 bond, making one half of the molecule a mirror image of the other half (image below). Because of the plane of symmetry, the molecule is achiral, though it has two chirality centers.

Compounds that are achiral, yet contain chirality centers, are called meso compounds. Thus, tartaric acid exists in three stereoisomeric forms: two enantiomers and one meso form.



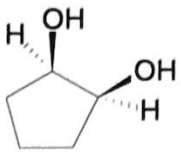
Exercise 9: Which of these structures represent meso compounds?

(a)



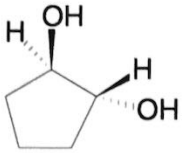
Meso

(c)



Meso

(b)



Not meso

Enantiomer : Non-superimposable mirror-image

Diastereomer : Non-superimposable NON-mirror images

Meso : contains chiral centres but is achiral ∵ of plane of symmetry