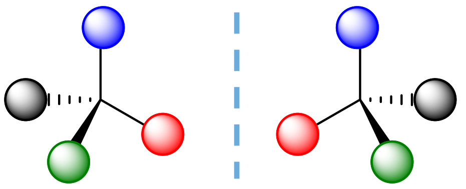
Stereochemistry



Suvarn S. Kulkarni
Department of Chemistry, IIT Bombay
suvarn@iitb.ac.in

Learning Outcomes

At the end of this module you should be able to….

- **Recognize** the elements of symmetry present in a molecule or object and **determine** if it is chiral
- **Differentiate** between various types of stereoisomers
- **Represent** 3D molecules using appropriate 2D representations

Isomers

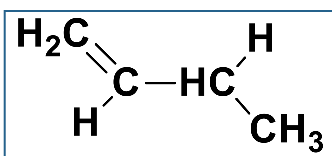
Isomers – Different molecules with the same molecular formula

Bonding connectivity

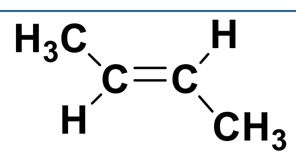
Different → **Constitutional Isomers**

Same → **Stereoisomers**

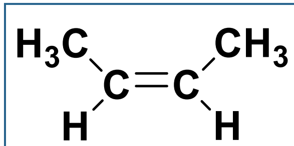
E.g., C_4H_8



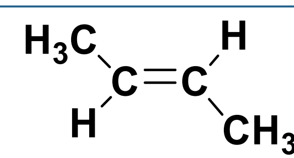
1-butene



trans-2-butene



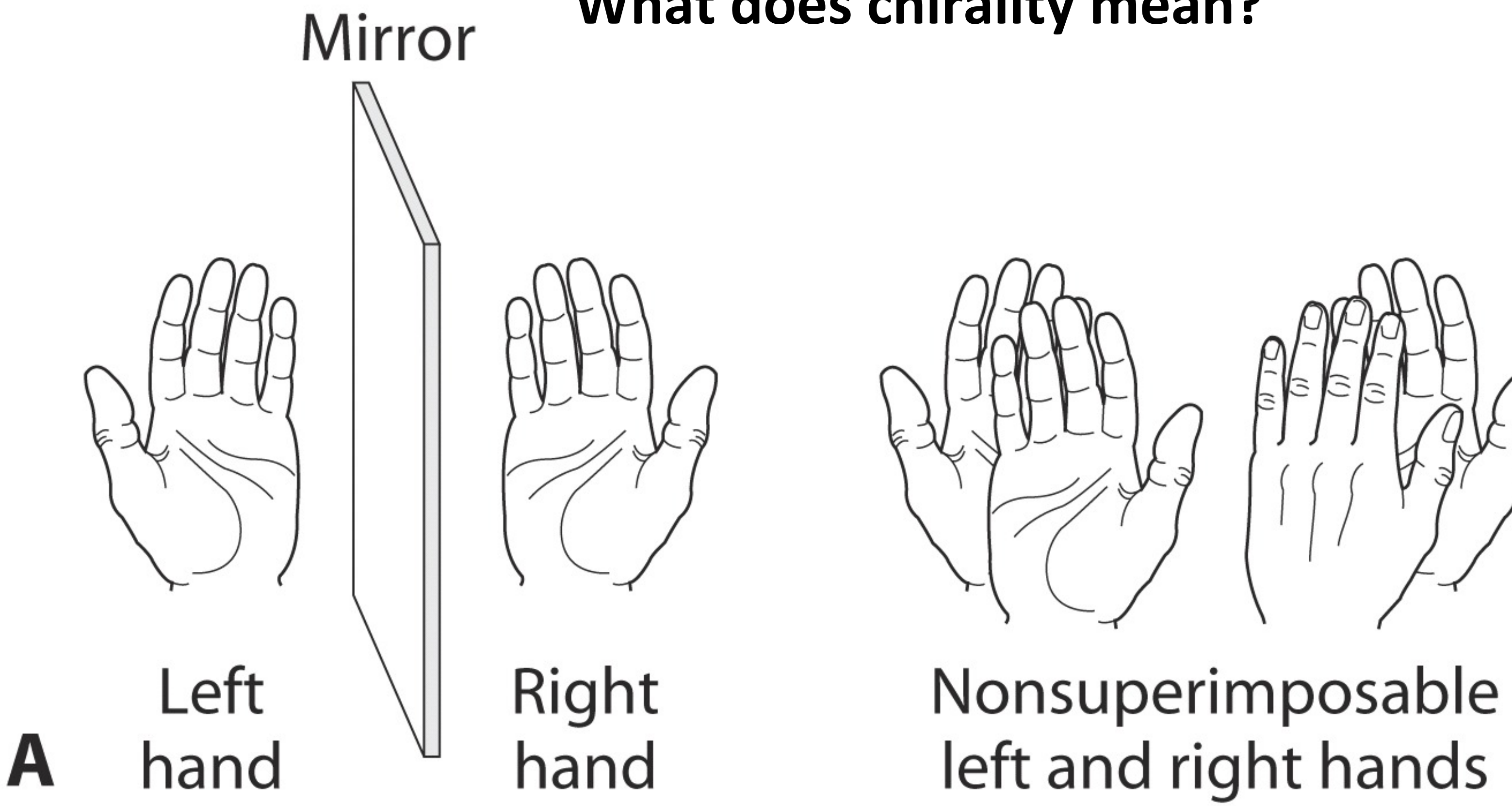
cis-2-butene



trans-2-butene

Chirality

What does chirality mean?



Object and mirror image non-superimposable ------- Chiral
Object and mirror image superimposable ------ Achiral

The word 'chiral' is derived from Greek word 'cheir' = handed

Chirality

Which of these are chiral ?

Symmetry & Chirality

Stereochemistry → Molecular Geometry → Symmetry

Molecules can be classified as chiral or achiral based on their symmetry

Symmetry Operation

Molecule / Model
Original Position

↓

Operation

↓

Molecule / Model
New Position

New Position = Original Position

Molecule possesses Element of Symmetry

corresponding to Operation

Symmetry element 1 – Axis

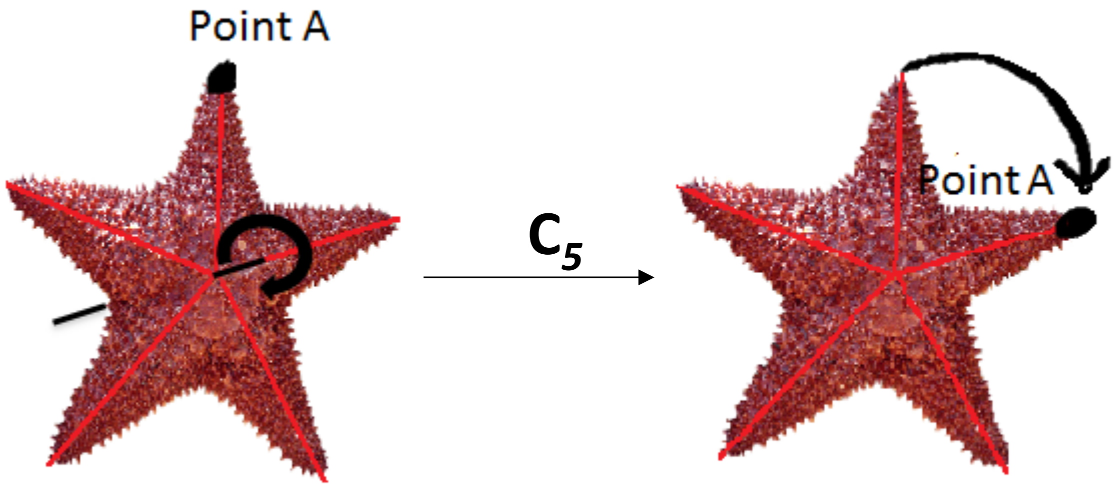
Rotate molecule around an appropriate imaginary **axis** by an angle = 360° / ***n*** .

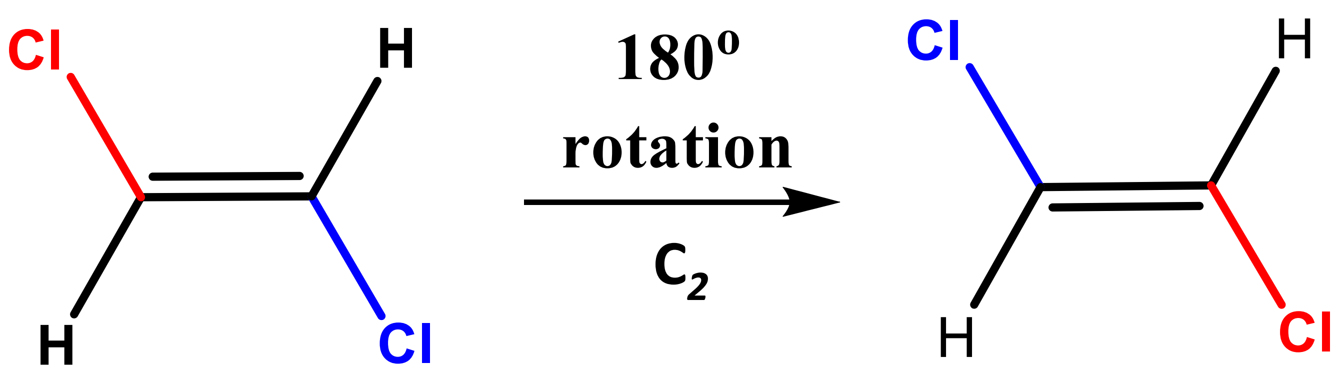
New position = original one

Element of symmetry – C_n

Operation

ROTATION





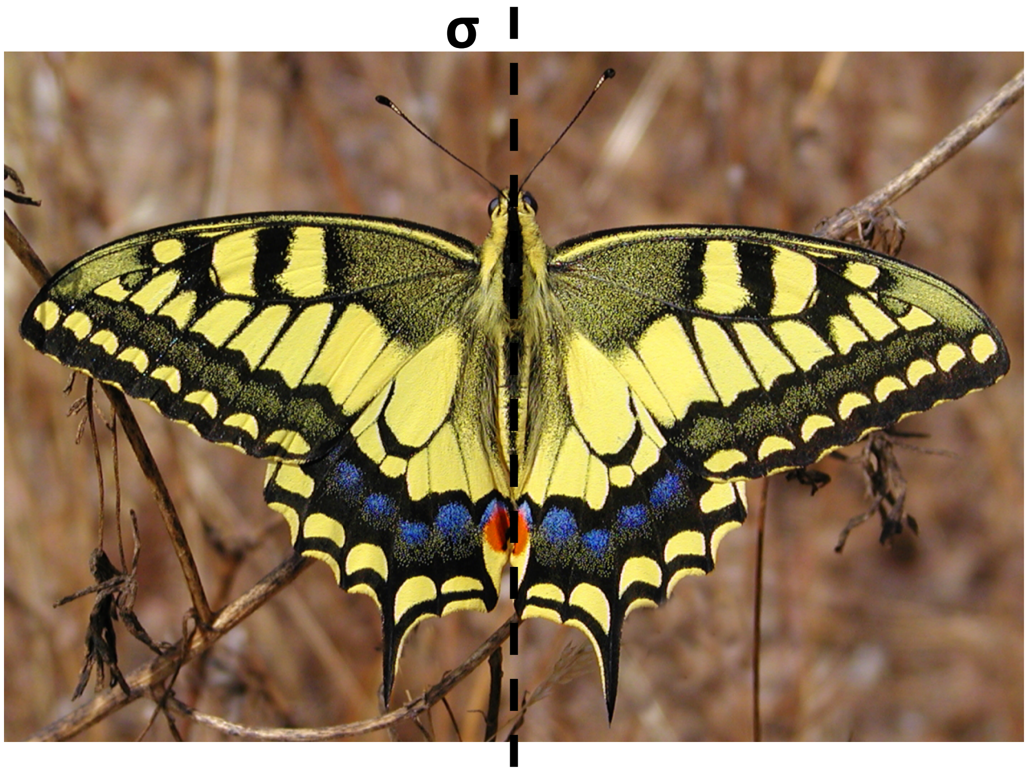
Element 2 – Plane of Symmetry

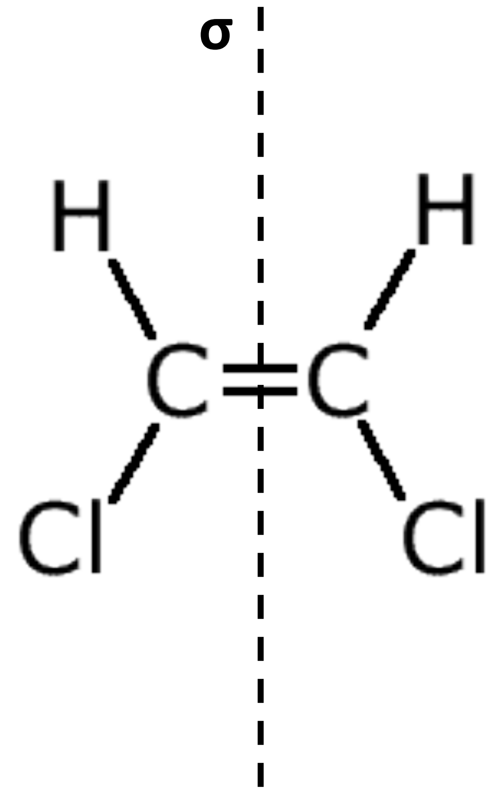
A **mirror plane** in the molecule such that reflected molecule = original

σ plane or plane of symmetry

Operation

REFLECTION





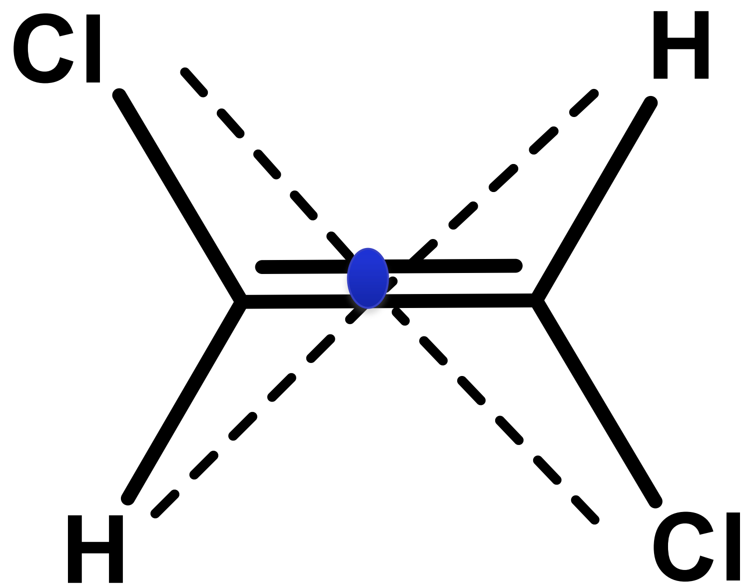
Cis-1,2-dichloroethane

Element 3- Inversion Centre

A **point** within a molecule such that if an atom is joined to it and the line is extrapolated to an equal distance beyond it, an equivalent atom is obtained is the inversion centre, ***i***

Operation

INVERSION



Element 4 - Alternating Axis

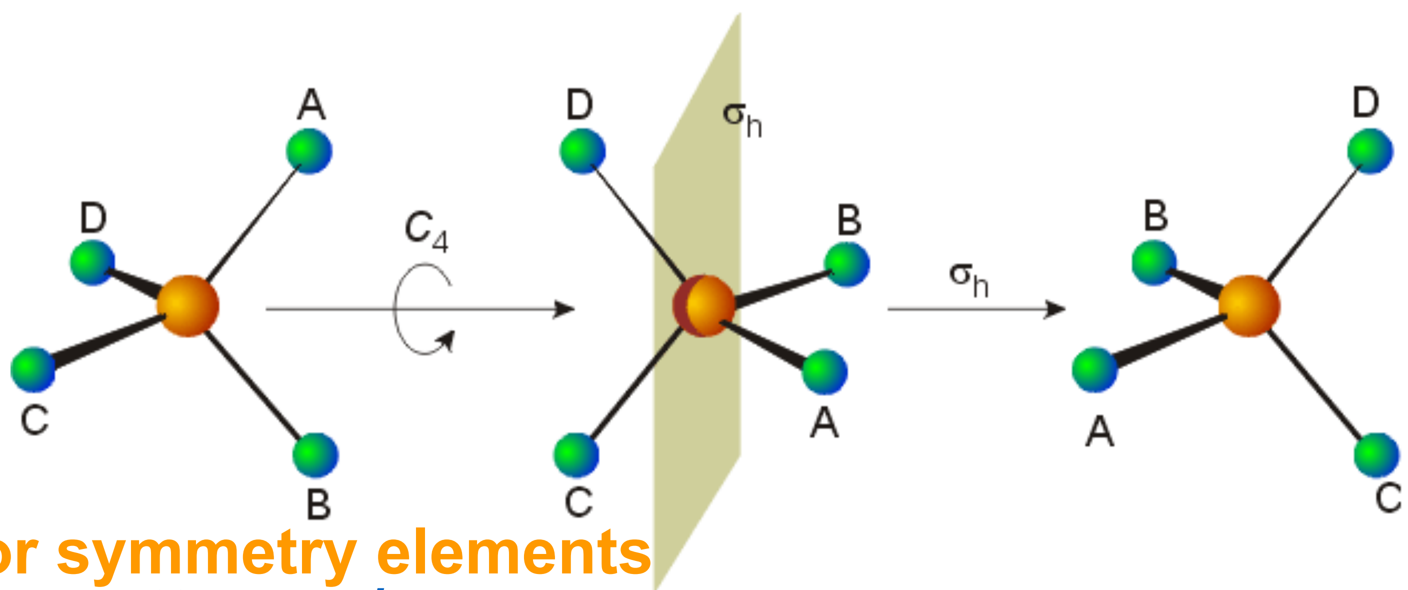
Operation

ROTATION

REFLECTION

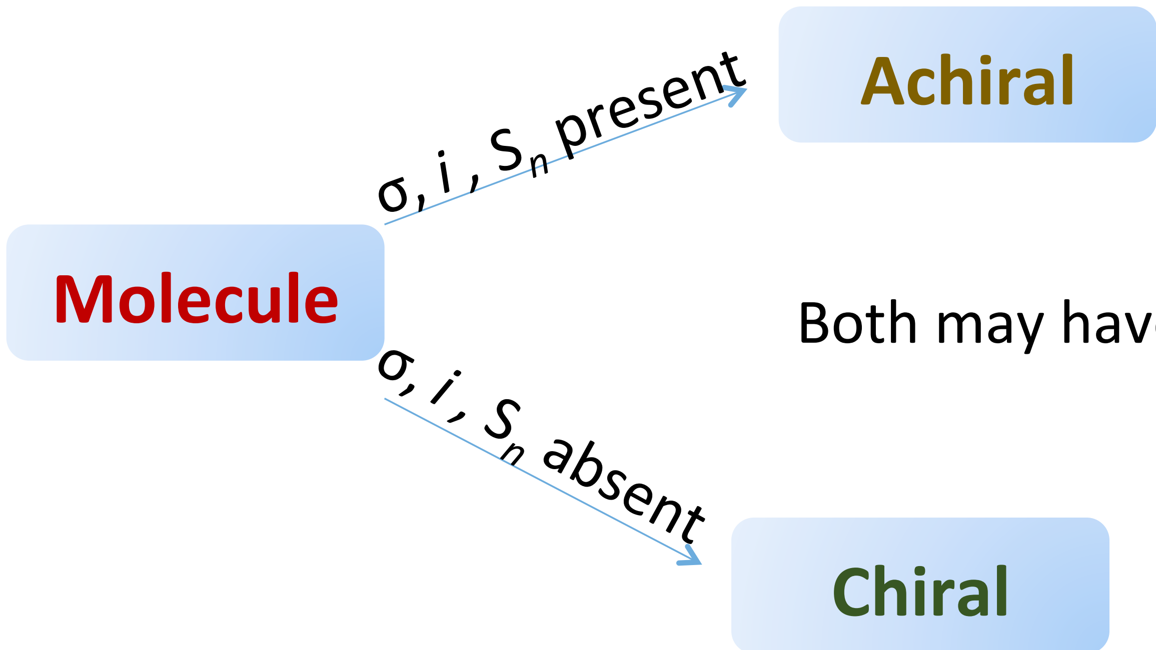
If rotation around a **C_n axis** followed by **reflection** in a **plane perpendicular** to the axis gives same molecule, it possesses $\mathbf{S_n}$, alternating axis of symmetry

Order of the two operations can be reversed to give the same result



Visit for symmetry elements
http://symotter.org/

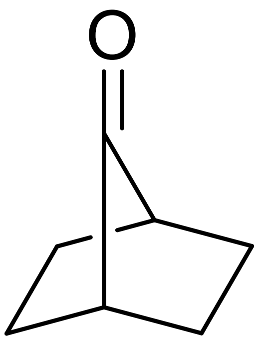
Chirality and Symmetry



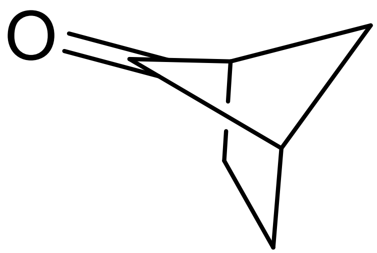
Both may have one or more Cn

Remember - Presence of a stereocenter (chiral center) i.e. C with four different substituents is neither necessary nor sufficient requirement for molecular chirality

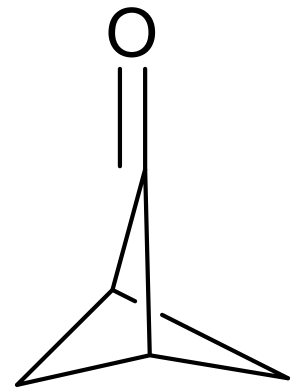
Chiral



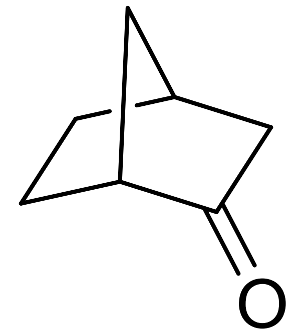
A



B



C



D

Chiral

Stereoisomers - Classification

Relationship based on symmetry

Molecules

Enantiomers

Molecule and it's mirror image
(non-superimposable)

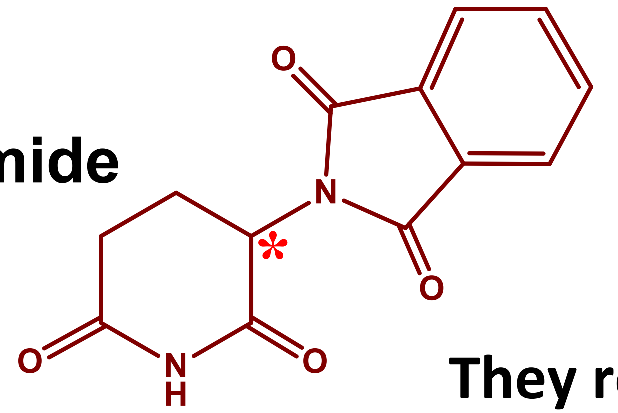
Diastereomers

Not a mirror image of the molecule

Enantiomers - Properties

Different in chiral medium

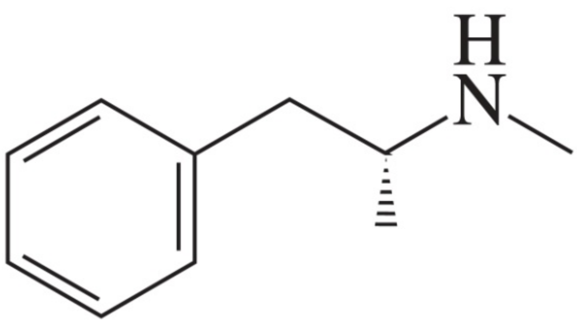
E.g. 1 **Thalidomide**



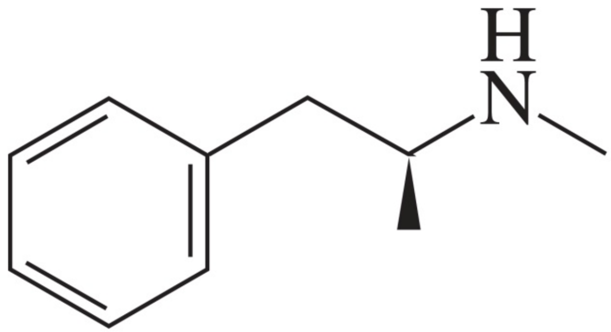
- R against nausea
- S cause fetal damage

They react with chiral enzymes

E.g. 2



the active ingredient in Vicks Vapor Inhaler®

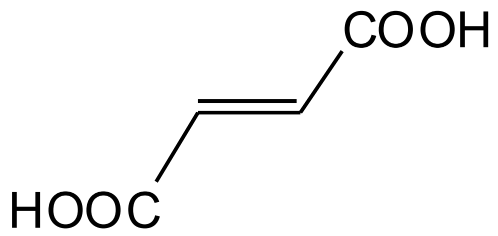


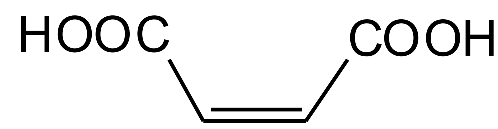
methamphetamine

Crystal meth of "Breaking Bad"

Diastereomers

- **They are chemically (and physically) different**
- **Can be chiral or achiral**





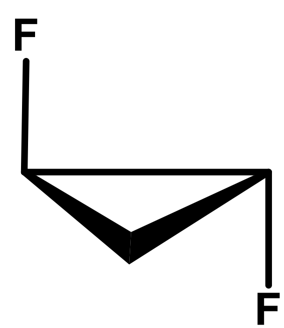
Fumaric Acid

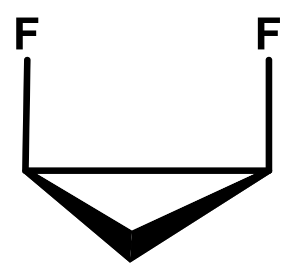
MP: 299-300 ºC

Maleic Acid

MP: 140-142 ºC

Forms anhydride upon heating





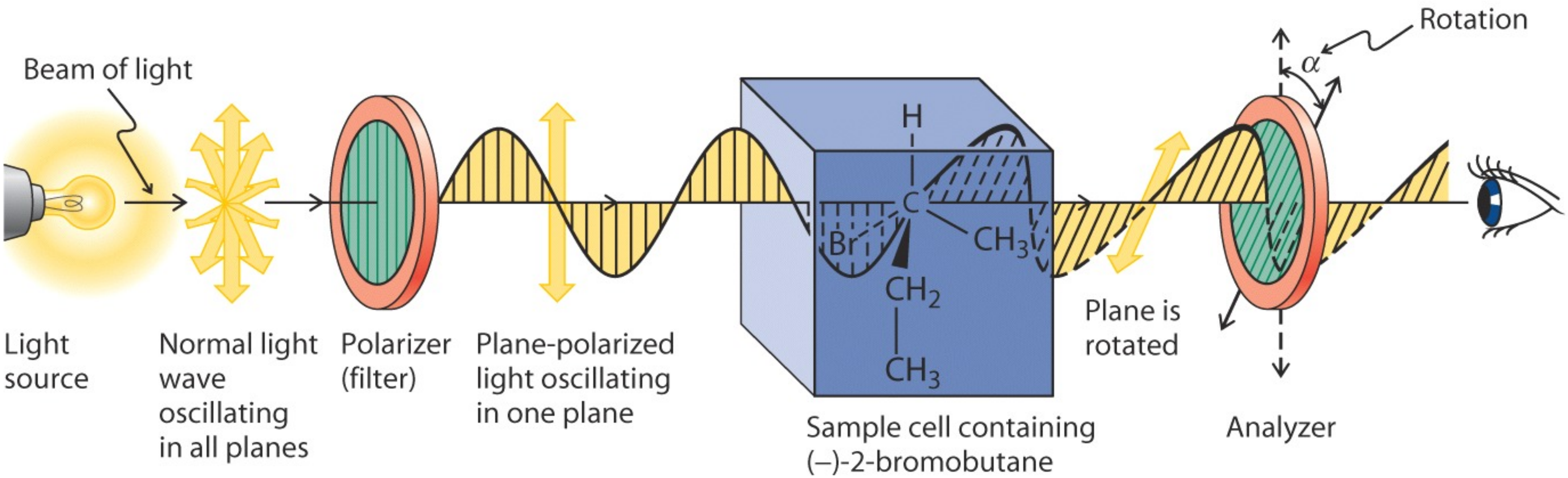
Enantiomers – Optical Activity

Enantiomers: Which is which?

Polarimeter: Optical rotation of plane polarized light:

Image → dextrorotatory (clockwise), (+)-enantiomer

Mirror image → levorotatory (counter-clockwise), (-)-enantiomer.



Enantiomers – Specific Rotation

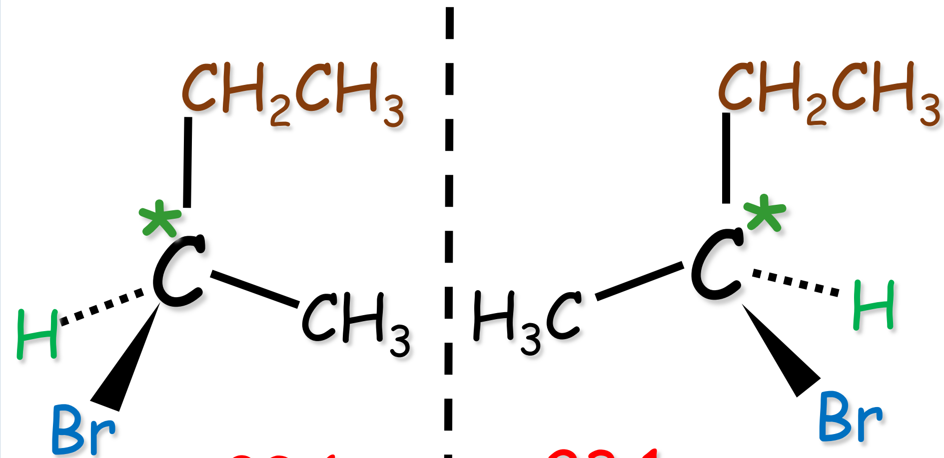
$$[\alpha]_{\lambda}^{t(^{\circ}C)} = \frac{\alpha}{lc}$$

Measured rotation

Length of vessel (in dm usually)

Concentration (g ml^{-1})

[α] is called *specific rotation*



-23.1 +23.1

Note: Sign of rotation does not tell you absolute configuration

Optical Purity

- **Optical purity (o.p.) is sometimes called enantiomeric excess (e.e.).**
- **One enantiomer is present in greater amounts.**

$$\text{o.p.} = \frac{\text{observed rotation}}{\text{sp. rotation of pure enantiomer}} \times 100$$

Calculating optical purity

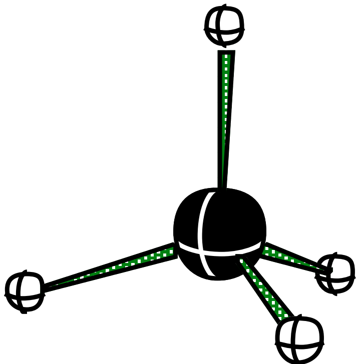
The specific rotation of (*S*)-2-iodobutane is +15.90°. Determine the % composition of a mixture of (*R*)- and (*S*)-2-iodobutane if the observed rotation of the mixture is –3.18°.

Sign is from the enantiomer in excess: levorotatory.

$$\text{o.p.} = \frac{3.18}{15.90} \times 100 = 20\%$$

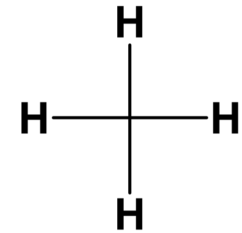
$$l = 60\% \qquad d = 40\%$$

Fischer Representation

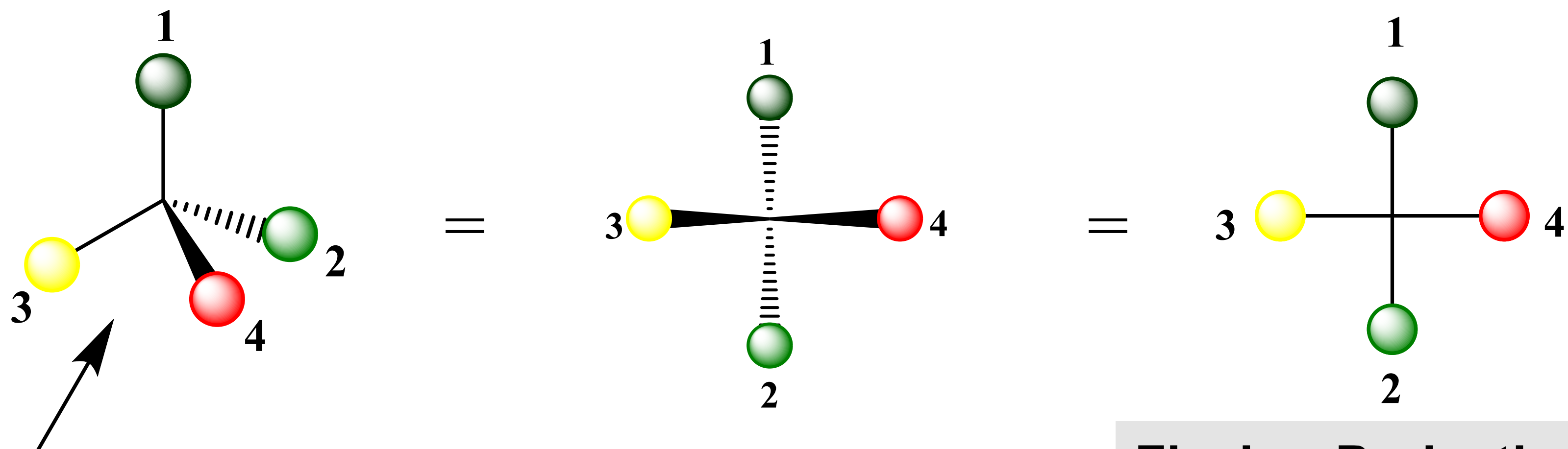


3D Structure

Methane



Fisher projection – 2D



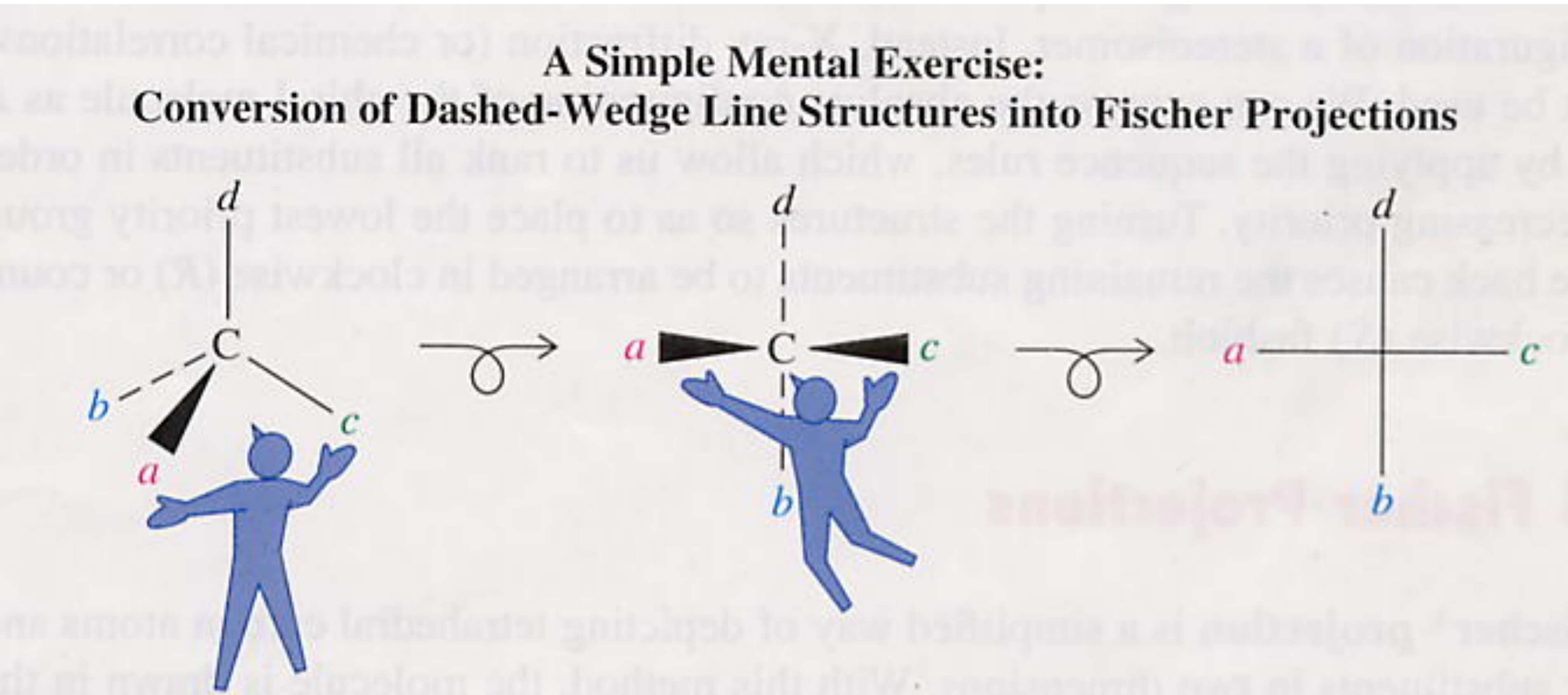
view

Fischer Projection

Perspective drawing

Or Flying-wedge formula

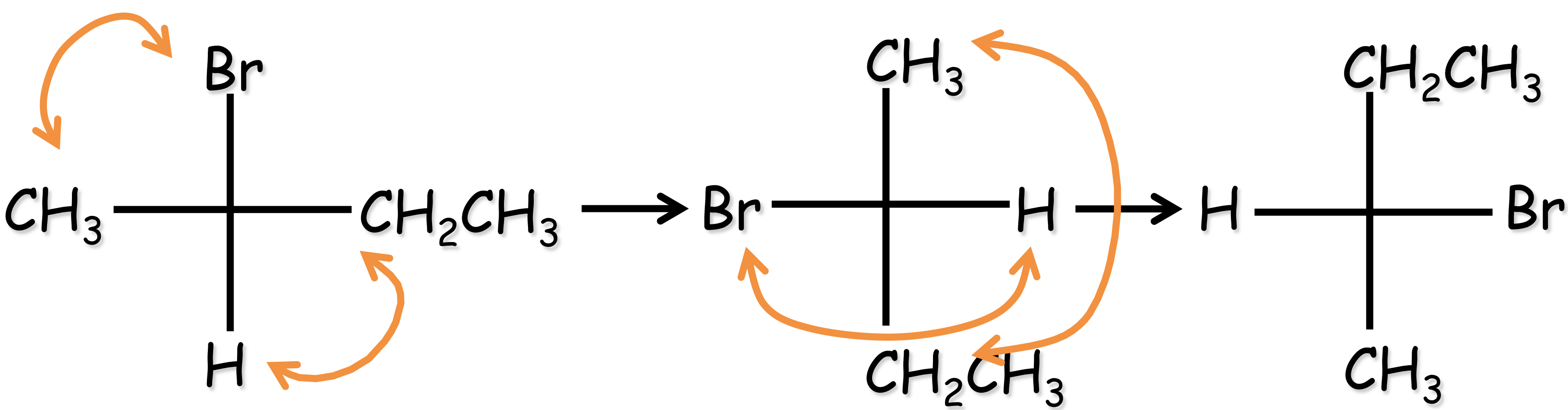
Fischer Representation



Rules for Fischer Projection

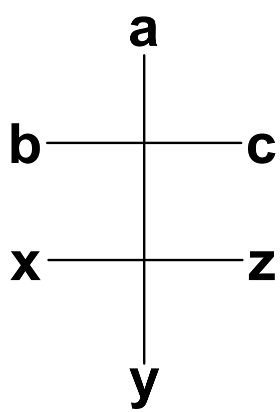
1. Cannot lift projection out of plane of paper.
2. Can be rotated in plane of paper only by 180°
3. **2 pairs** of substituents can be exchanged.

Remember - Exchange of only 1 pair gives enantiomer!



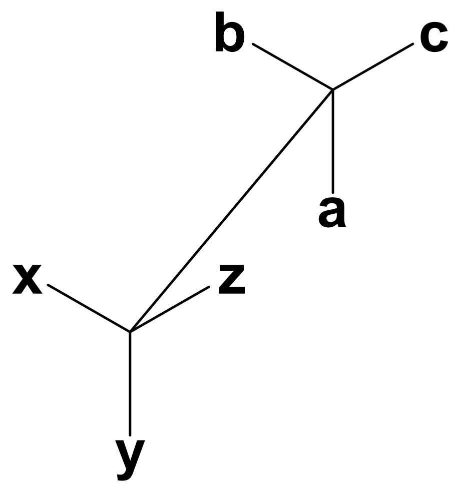
4. One atom can be fixed and the other 3 can be rotated (**DO NOT** change the sequence of 3 you are rotating)

Interconverting Representations



Fischer projection

≡



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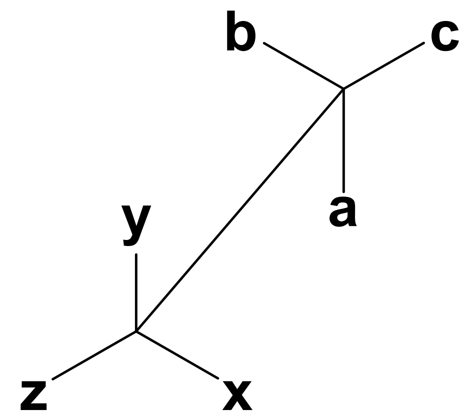
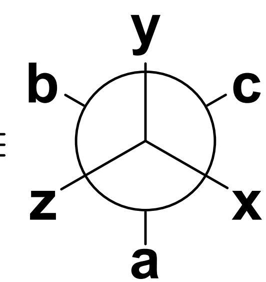


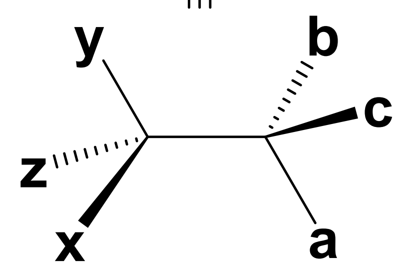
sawhorse

≡



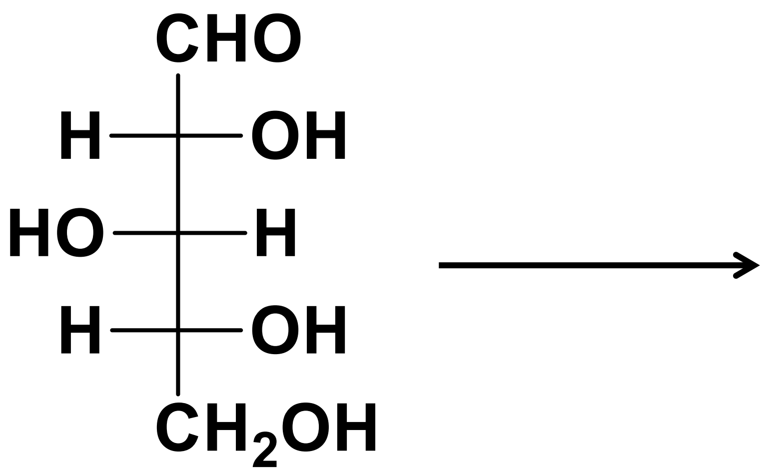
Newmann

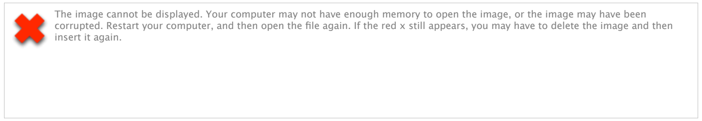
≡



wedges

Small Activity



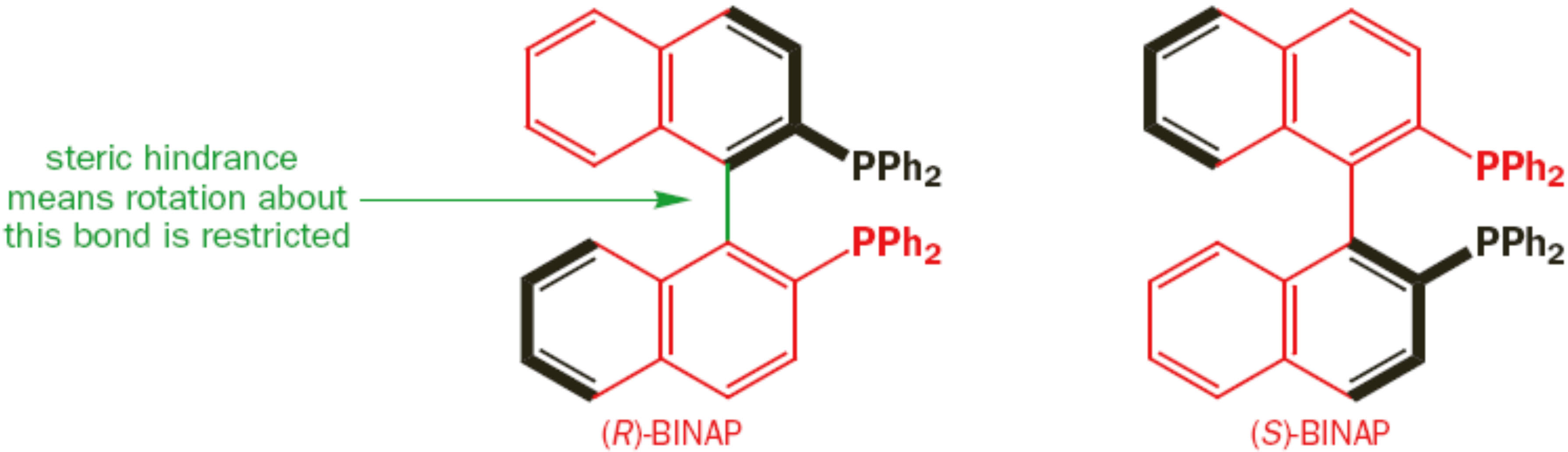


Convert the above structure to flying wedge

You can work in pairs or groups!

Axial Chirality

These molecules are chiral without having chiral centres

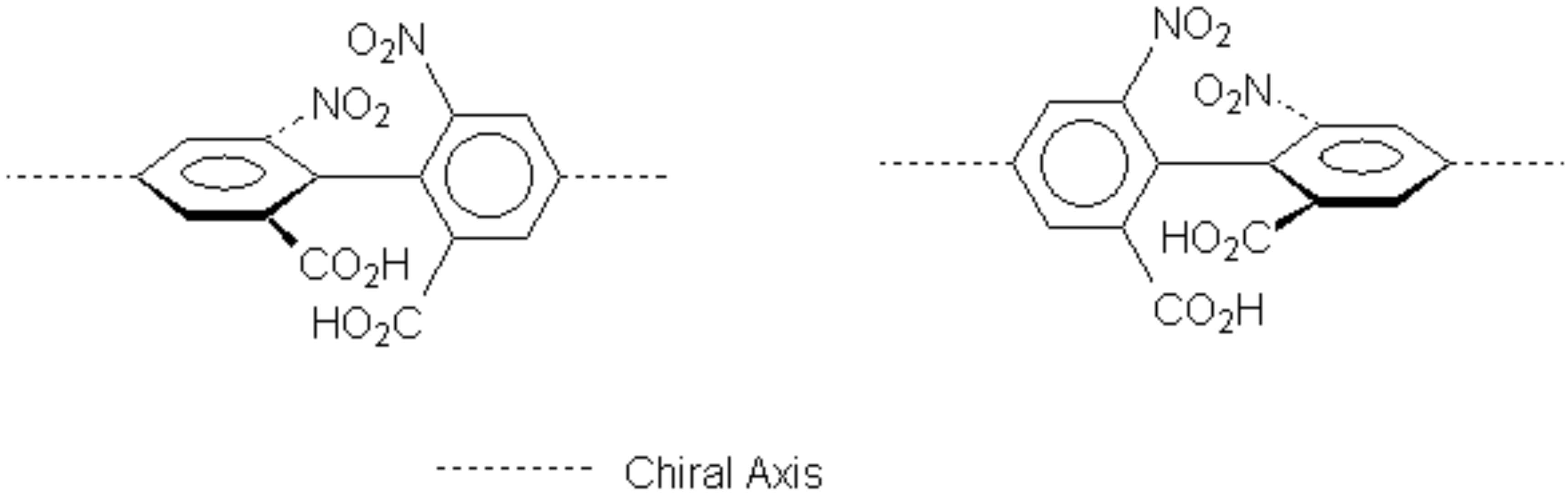


These molecules are axially chiral (axial asymmetry) arises due to restricted rotation around the C-C bond

They need not have 4 different substituents for chirality!
2 is enough!

Atropisomerism

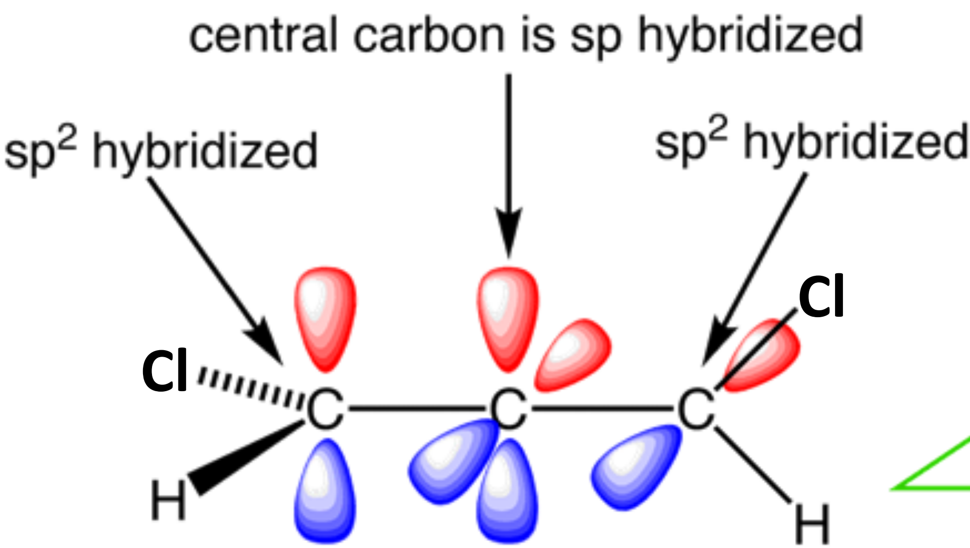
Chirality due to restricted rotation around the bond connecting the two phenyl rings – also referred to as Atropisomerism



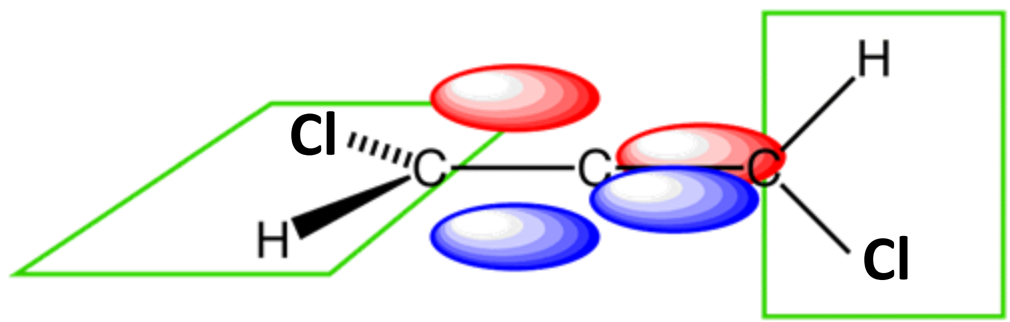
Why are two different substituents enough?

Axial Chirality – Another Example

a chiral allene

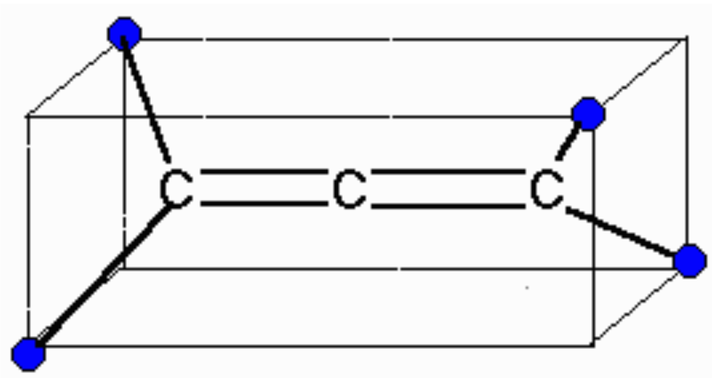


the π bonds formed as a result
of the overlap of the p orbitals
must be at right angles to each other

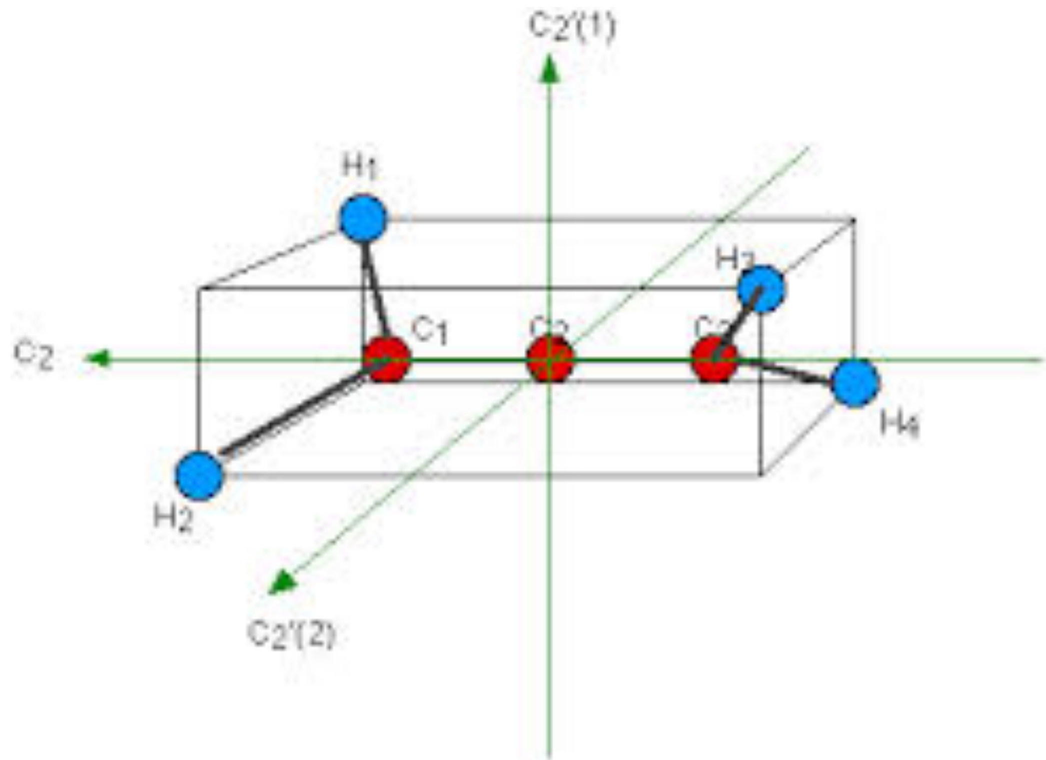


The three Cs form the axis
The perpendicular planes
contain substituents

Allene in a Box



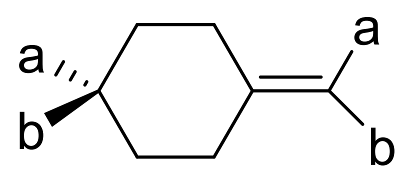
Axis of symmetry in allene



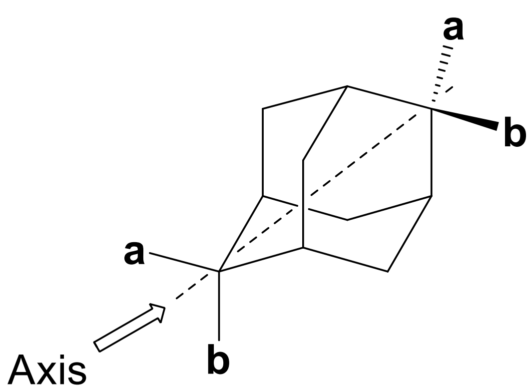
Allene - C2 - Before

Examples of Axial Chirality

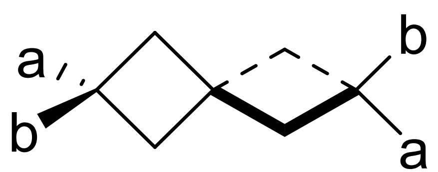
Alkylidine cyclohexane



Adamantanes



Spiranes



Summary

Isomers – Different molecules with the same molecular formula

Bonding connectivity same?

No → **Constitutional Isomers**

Yes → **Stereoisomers**

Mirror images?

Yes → **Enantiomers**

No → **Diastereomers**

Meso compounds They have a plane of symmetry in the molecule

Learning Outcomes

At the end of this module you should be able to….

- **Recognize** the elements of symmetry present in a molecule or object and **determine** if it is chiral
- **Differentiate** between various types of stereoisomers
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Thank you