STEREOCHEMISTRY

B PHARM II

Prepared by

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Stereochemistry

chemistry in three dimensions

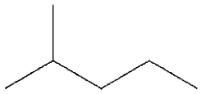
IMPORTANT TERMS IN STEREOCHEMISTRY

- Types of isomers
- Types of Stereoisomers
- Optical Activity
- Chirality
- Internal Plane of Symmetry
- Important role of stereochemistry

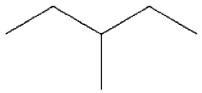
STEREOCHEMISTRY & STEREOISOMERS

- Stereochemistry :That part of the science which deals with structure of molecules in three dimensions is called stereochemistry.
- Stereoisomers:
  - **Isomers** are the compounds having same molecular formula but different structure formula . For example Diethyl ether and ethyl alcohol
  - Same molecular formula, same bonding sequence, different spatial orientation are **Stereoisomers** i.e. these isomers are different from each other only in the way the atoms are oriented in space.

Structural (constitutional) Isomers - Compounds of the same molecular formula with different connectivity (structure, constitution)

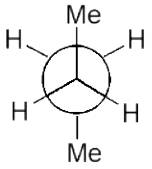


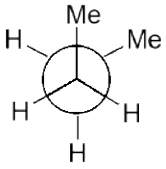
2-methylpentane



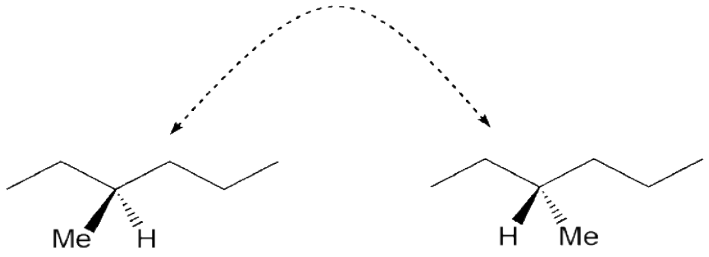
3-methylpentane

Conformational Isomers - Compounds of the same structure that differ in rotation around one or more single bonds





Configurational Isomers or **Stereoisomers** - Compounds of the same structure that differ in one or more aspects of stereochemistry (how groups are oriented in space - enantiomers or diastereomers



3-methylhexane 3-methylhexane

We need a a way to describe the stereochemistry!

Isomers – different compounds with the same molecular formula.

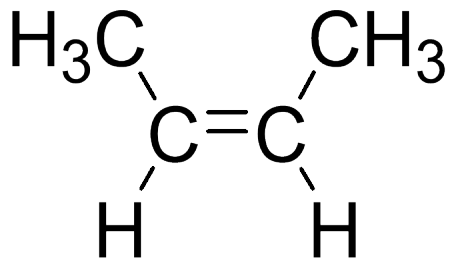
Structu ers that differ in which atoms are bonded t

eg. C_4H $_2CH_2CH_3$ CH_3CHCH_3

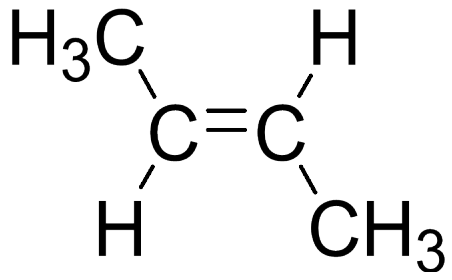
ane isobutane

Stereoisomers – isomers that differ in the way the atoms are oriented in space, but not in which atoms are bonded to which atoms.

eg. *cis*-2-butene



trans-2-butene



Difference between Configurational Isomers &Conformational Isomers

Difference between Configurational &Conformational Isomers is that **Configurational Isomers** cannot be obtained by rotation of molecuies around a single bond whereas **Conformational Isomers** can be obtained by rotation of molecuies around a single bond

Types of Stereoisomers

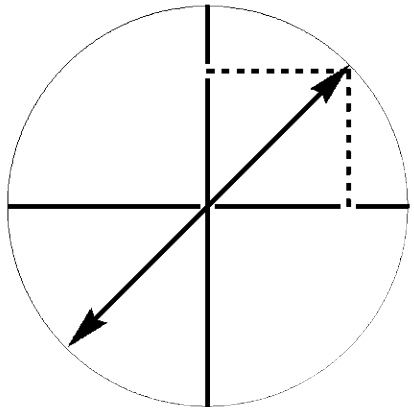
- Two types of stereoisomers:
  - enantiomers

    Two compounds that are non superimposable mirror images of each other

  - Diastereomers
    - Two stereoisomers that are not mirror images of each other
    - Geometric isomers (cis-trans isomers) are one type of diastereomer.

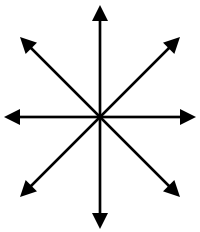
Optical activity
Plane-polarized light

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.

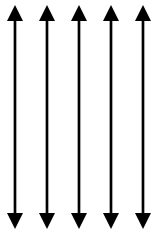


One of these components of ordinary light when passed through a polarizer - Polaroid filter. The resulting light is said to be polarized - all its vibrations are parallel to a single plane.

plane polarized light – Ordinary light when passed through a nicol prism or other polarizing medium ,all of the vibrations are in the same plane called **plane polarized light** or in simple words we can say Ordinary light can be converted to plane polarized light by passing through nicol prism.(it is the lens made up of polaroid or calcite)



non-polarized



polarized

Optical activity

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

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

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

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

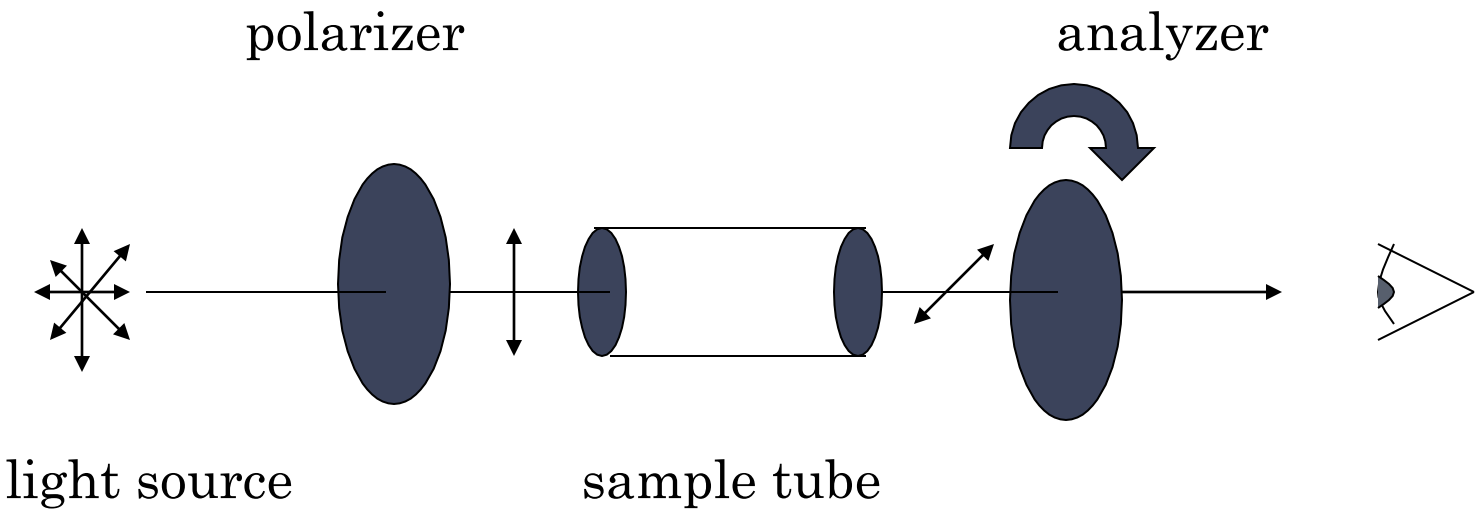
By optical rotation

An enantiomer can be named by the direction in which it rotates the plane of polarized light. If it rotates the light clockwise (as seen by a viewer towards whom the light is traveling), that enantiomer is labeled (+). Its mirror-image is labeled (−). The (+) and (−) isomers have also been termed *d*- and *l*-, respectively (for *dextrorotatory* and *levorotatory*). Naming with *d*- and *l*- is easy to confuse with D- and L- labeling and is therefore discouraged by IUPAC.

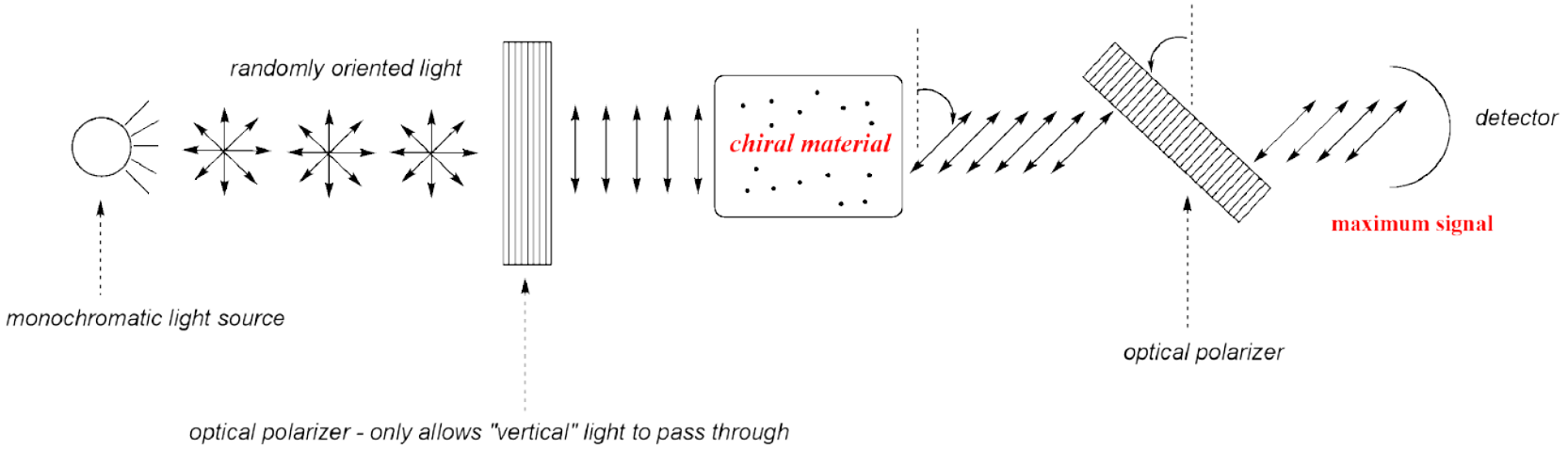
An optical isomer can be named by the spatial configuration of its atoms. The D/L system not to be confused with the *d*- and *l*-system, does this by relating the molecule to glyceraldehyde. Glyceraldehyde is chiral itself, and its two isomers are labeled D and L. Certain chemical manipulations can be performed on glyceraldehyde without affecting its configuration, and its historical use for this purpose has resulted in its use for nomenclature.

Optical activity is measured by a polarimeter, and is dependent on several factors: concentration of the sample, temperature, length of the sample tube or cell, and wavelength of the light passing through the sample. Rotation is given in +/- degrees, depending on whether the sample has d- (positive) or l- (negative) enantiomers. The standard measurement for rotation for a specific chemical compound is called the specific rotation, defined as an angle measured at a path length of 1 decimeter and a concentration of 1g/ml.

polarimeter – an instrument used to measure optical activity.



Optical Rotation and Polarimetry



*The amount (in degrees) that a chiral material will rotate light is called the **optical rotation**. Different chiral molecules will have optical rotations that vary in direction and size of the optical rotation. Enantiomers will always have equal optical rotations but in opposite directions.*

*The **optical purity** of a substance can be measured by comparing the optical rotation of the sample to the known optical rotation of a single entantiomer of that compound. Optical purity is usually reported in percent **entantiomeric excess (%ee)**.*

$$\%ee = \frac{\text{sample rotation}}{\text{single enantiomer rotation}} \times 100$$

Enantiomeric excess is the % of the sample that is non-racemic. For example, 80% ee means that there is 90% of one enantiomer and 10% of the other.

Vocabulary

- **(R) or (S):** identifies the configuration of a stereocenter using the CIP priority system

- ***d*- or (+):** indicates that a (chiral) compound rotates light in a clockwise direction (this has no correlation with S or R)

- ***l* or (-):** indicates that a (chiral) compound rotates light in a counterclockwise direction (this has no correlation with S or R)

- ***dl* or (+/-) or *rac*-:** indicates a racemate

So we can see that when a beam of plane polarized light is passed through a optically active compound like 2-chloro butane,glucose,lactic acid,it is found that thr-e beam which emerges out of the solution vibrates in different plane.

Specific Rotation For measurement of optical rotation the term specific rotation is used .It is defined as the angle of rotation [α] in degrees produced by the solution containing 1 gram of optically active substance in 1 ml of solvent taken in polarimeter tube of 1dm (10cm) in length.

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

Chiral

- Enantiomers are chiral:
  - Chiral:

    Not superimposable on its mirror image

- Many natural and man-made objects are chiral:
  - hands
  - scissors
  - screws (left-handed vs. right-handed threads)

Right hand threads slope up to the right.

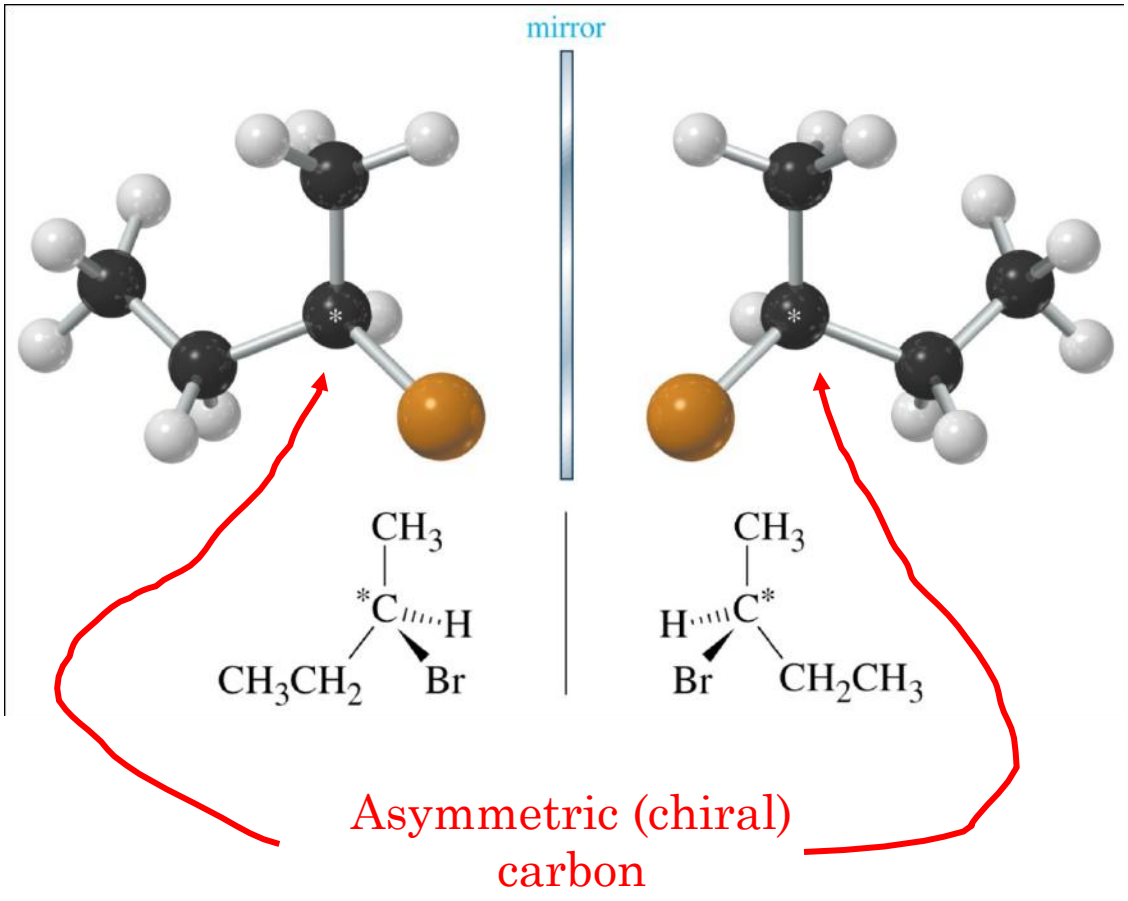
CHIRAL CENTER

Is a carbon that is bonded to four different groups of atoms.

$CH_3CH_2\overset{*}{C}HBrCH_3$

Chiral

- Some molecules are chiral:



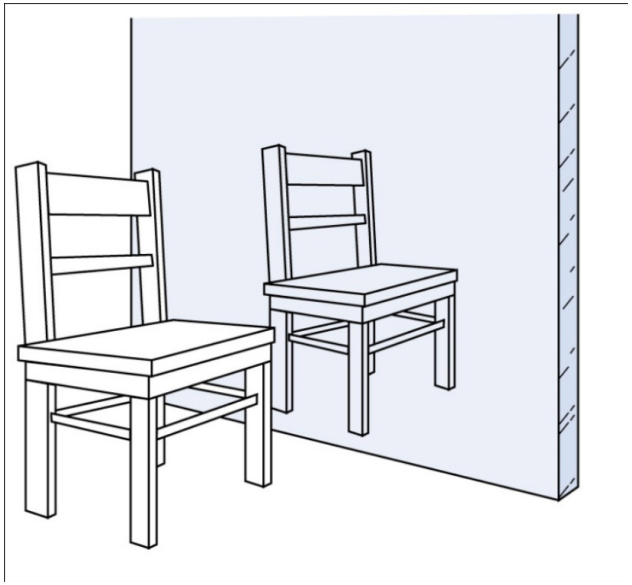
Asymmetric Carbons

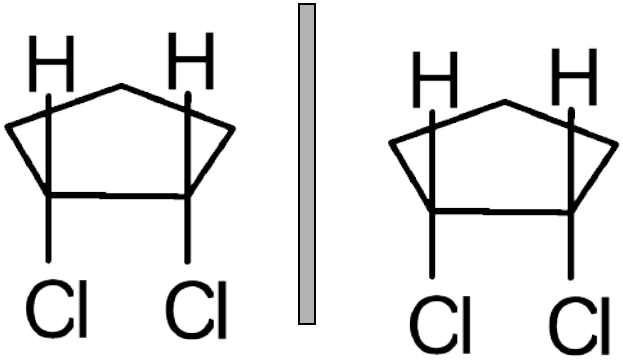
- The most common feature that leads to chirality in organic compounds is the presence of an asymmetric (or chiral) carbon atom.
  - A carbon atom that is bonded to four different groups

- In general:
  - no asymmetric C → usually achiral
  - 1 asymmetric C → always chiral
  - ≥ 2 asymmetric C → may or may not be chiral

Achiral

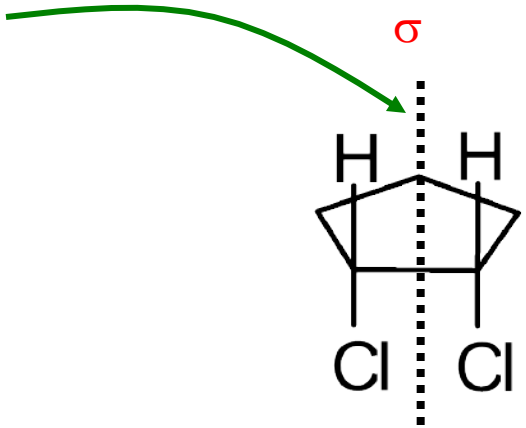
- Many molecules and objects are achiral:
  - identical to its mirror image
  - not chiral





Internal Plane of Symmetry

- Cis-1,2-dichlorocyclopentane contains two asymmetric carbons but is achiral.
  - contains an internal mirror plane of symmetry



- Any molecule that has an internal mirror plane of symmetry is achiral even if it contains asymmetric carbon atoms.

Internal Plane of Symmetry

- Cis-1,2-dichlorocyclopentane is a meso compound:
  - an achiral compound that contains chiral centers
  - often contains an internal mirror plane of symmetry

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.

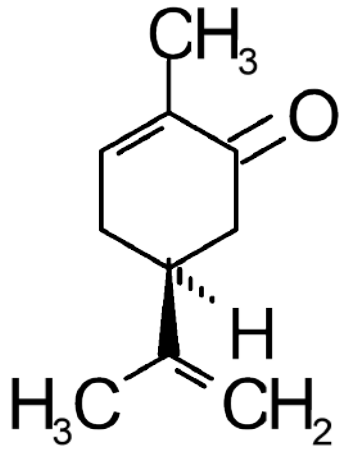
Test for optical activity: chiral molecules are optically active.

- **Racemic modification** – equimolar molar mixture of enantiomers (will be optically inactive) (±).
- compounds with one chiral center will show optical activity
- compounds without chiral centers do not normally show optical acitivity
- compounds with more than one chiral center may or may not show optical activity depending on whether or not they are non-superimposable on their mirror image (chiral) or superimposable (achiral).

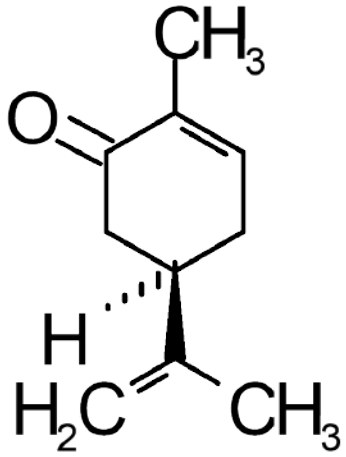
Stereochemistry:

The study of the three-dimensional structure of molecules

- Stereochemistry plays an important role in determining the properties and reactions of organic compounds:



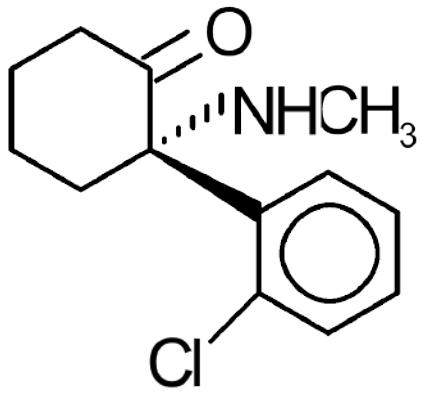
Caraway seed



spearmint

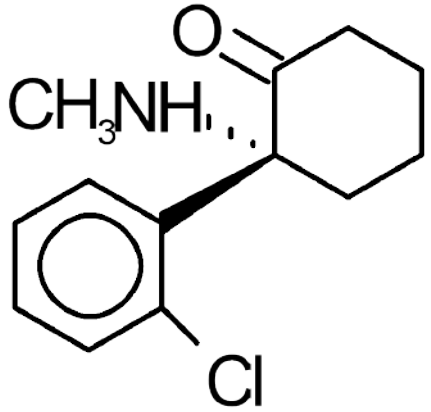
Stereochemistry

- The properties of many drugs depends on their stereochemistry:



(S)-ketamine

anesthetic



(R)-ketamine

hallucinogen

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Thank you---