POLITECNICO DI MILANO

Scuola di Ingegneria Industriale e dell'Informazione

Insegnamento di Chimica Generale

083424 - CCS *CHI* e *MAT*





Stereochemistry.

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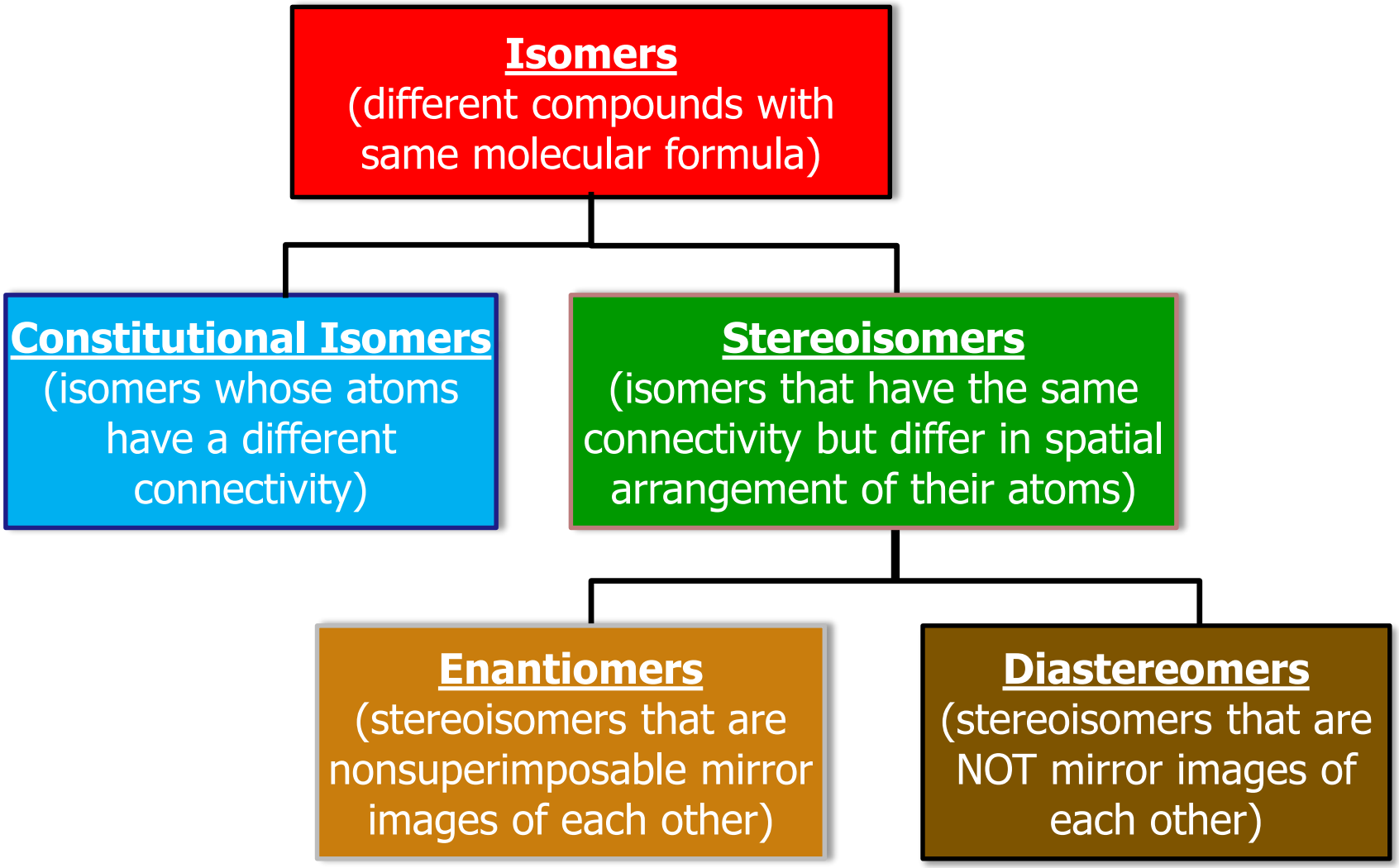
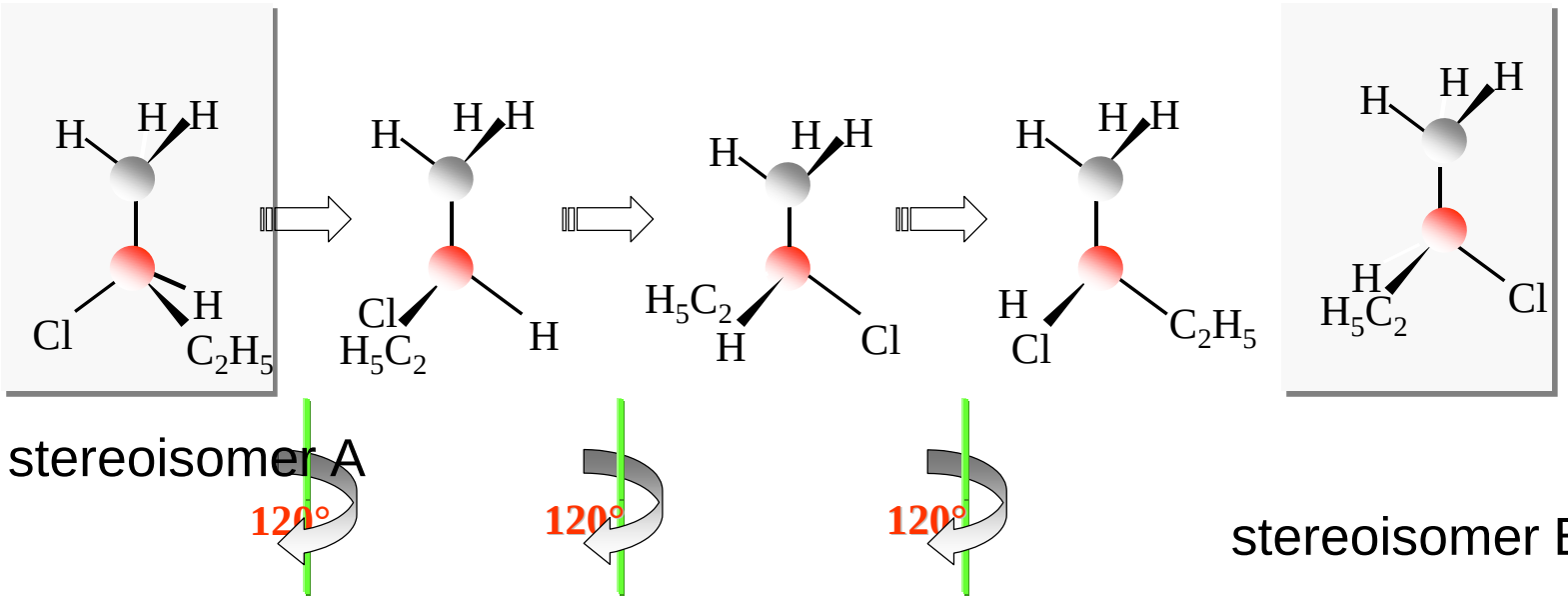
Dipartimento CMIC "Giulio Natta"

https://iscamapweb.chem.polimi.it/citterio/it/education/course-topics/

Classification of Isomers.



Configurational Isomers.



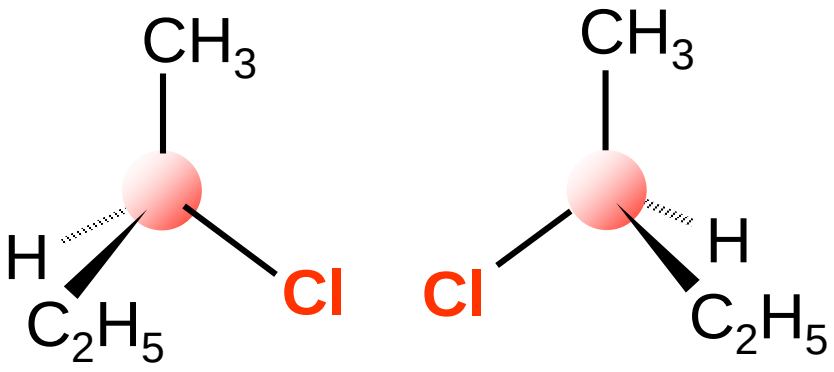
Different conformations of stereoisomer A

No one conformation of A corresponds to B

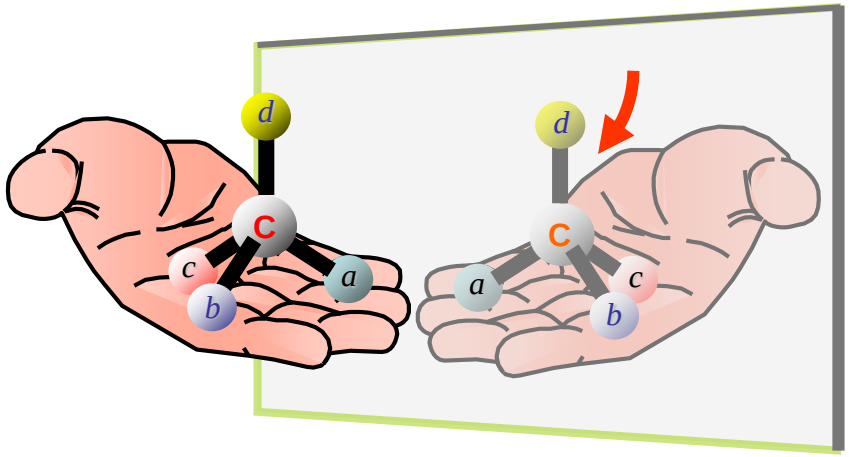
The two compounds are not two different conformations

The two compounds are Configurational Isomers

Two Enantiomers.



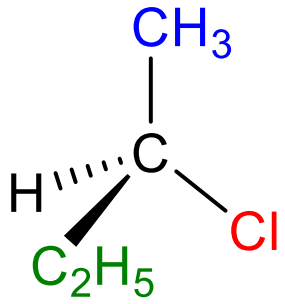
B **A**

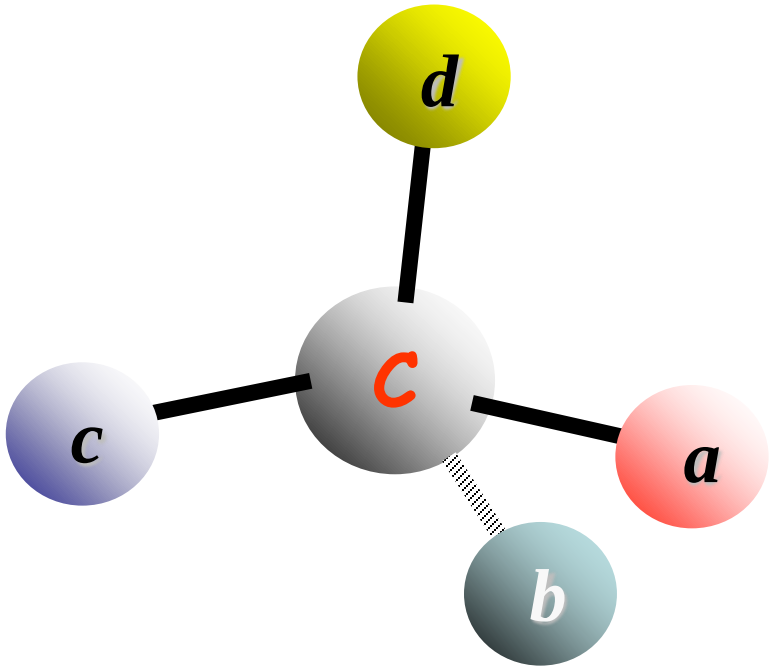


The two compounds are Specular Images
NOT superimposable

They are defined
ENANTIOMERS

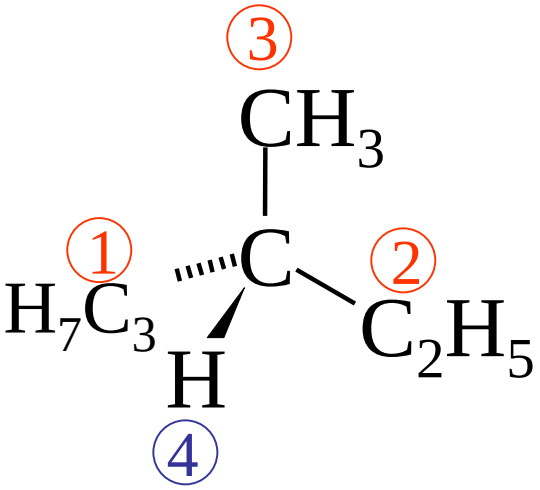
Asymmetric (Chiral) Carbon Atom

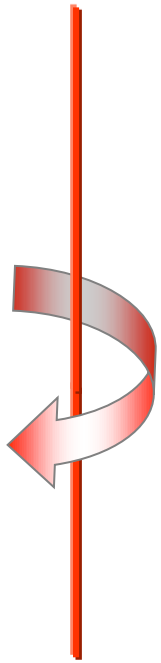


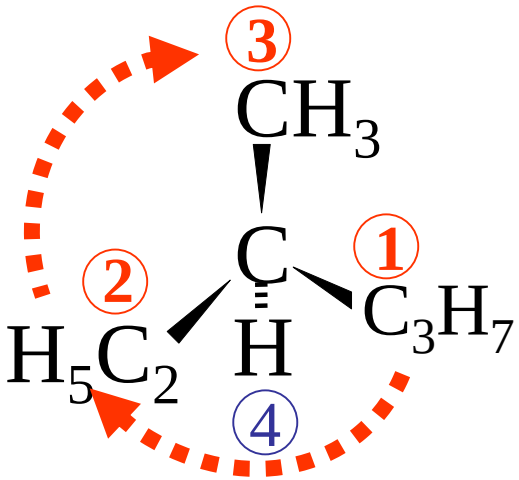


The Carbon atom is hybridized sp^3 and is bound to four different substituents

R,S Cahn-Ingold-Prelog Convention





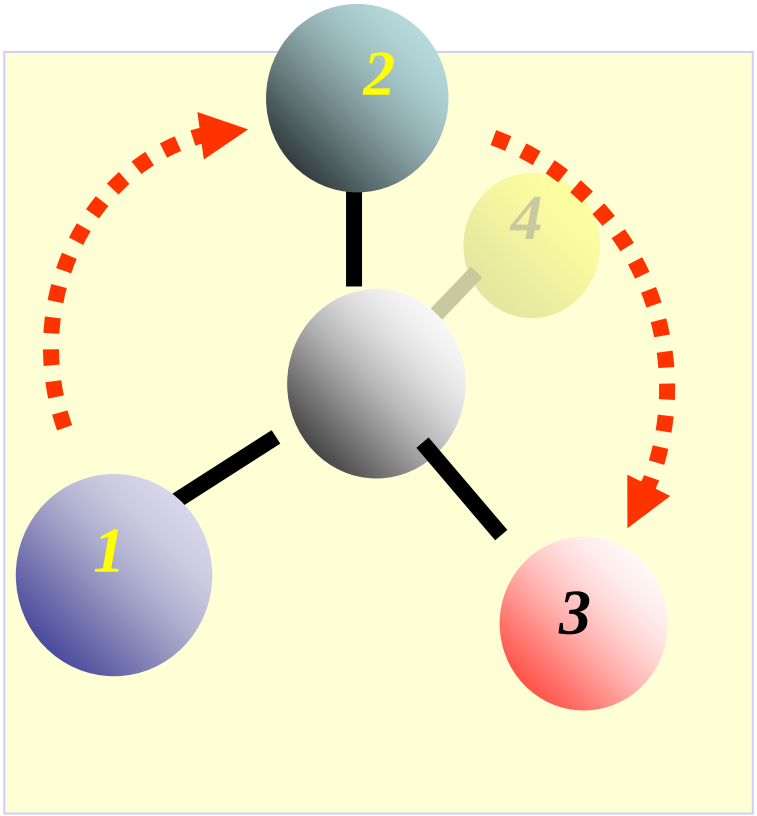


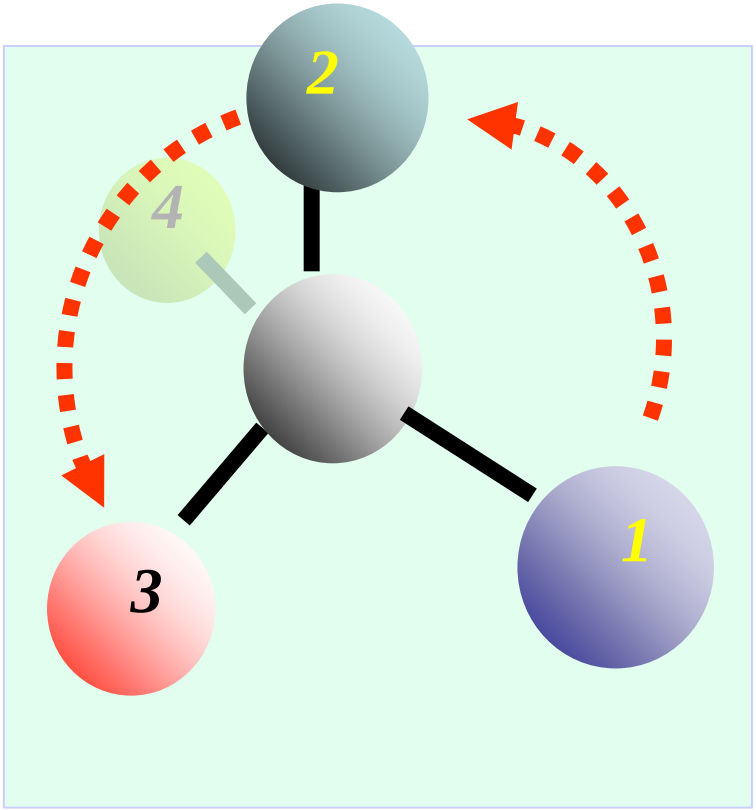
The group with lower priority must be placed far from the observer

***R*ectus**

"clockwise"

Cahn-Ingold-Prelog Convention. R,S Nomenclature System



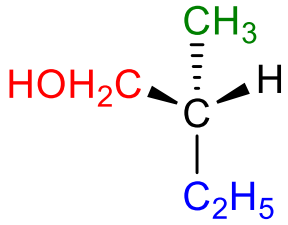


R *Rectus*

S *Sinister*

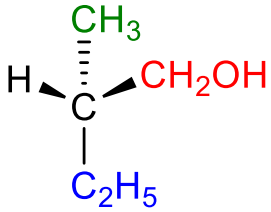
Specific Rotation and R,S –Configuration.

No necessary correlation exists between the (R) and (S) designation and the direction of rotation of plane-polarized light.



(R)-(+)-2-Methyl-1-butanol

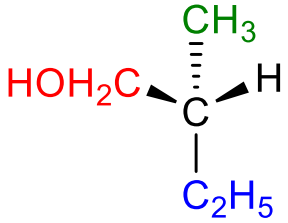
$[\alpha]_D^{25} = +5.756°$



(S)-(−)-2-Methyl-1-butanol

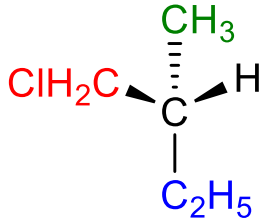
$[\alpha]_D^{25} = -5.756°$

Relative vs. Absolute Configuration (5.15A)

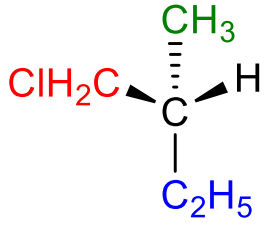


(R)-(+)-3-Methyl-1-butanol

Same Configuration

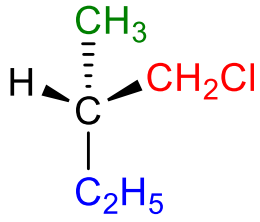


(R)-(−)-1-Chloro-3-methylbutane



(R)-(−)-1-Chloro-3-methylbutane

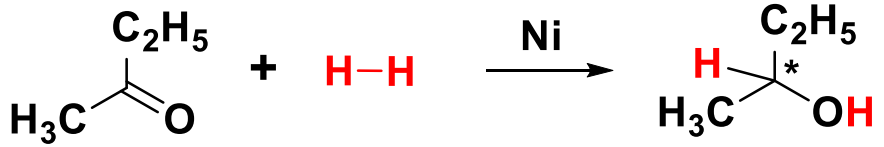
$[\alpha]_D^{25} = +1.64°$



(S)-(+)-1-Chloro-3-methylbutane

$[\alpha]_D^{25} = -1.64°$

Racemic Forms (Racemate).

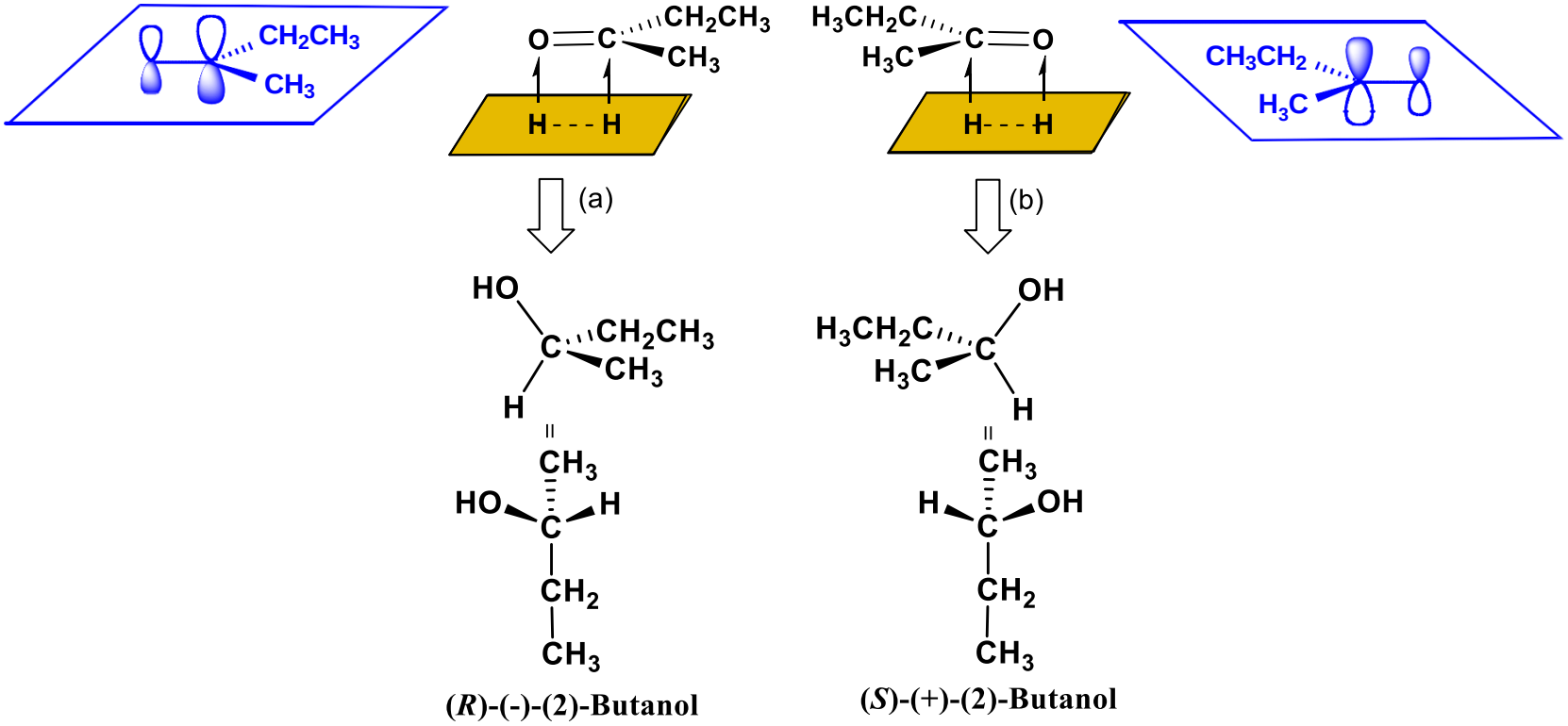


Butanone achiral molecule)

Hydrogen achiral molecule)

(±)-2-Butanol (chiral molecule but 50:50 mixture (*R*) and (*S*)

Racemate

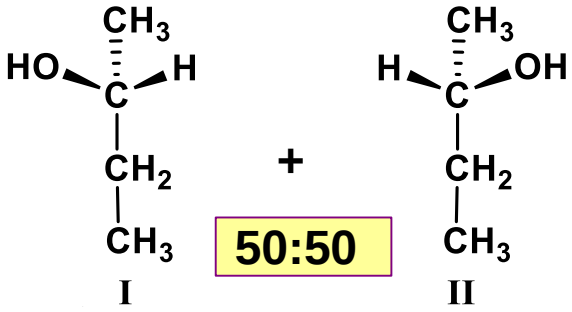


(*R*)-(-)-(2)-Butanol

(*S*)-(+)-(2)-Butanol

Racemic Forms (Racemate).

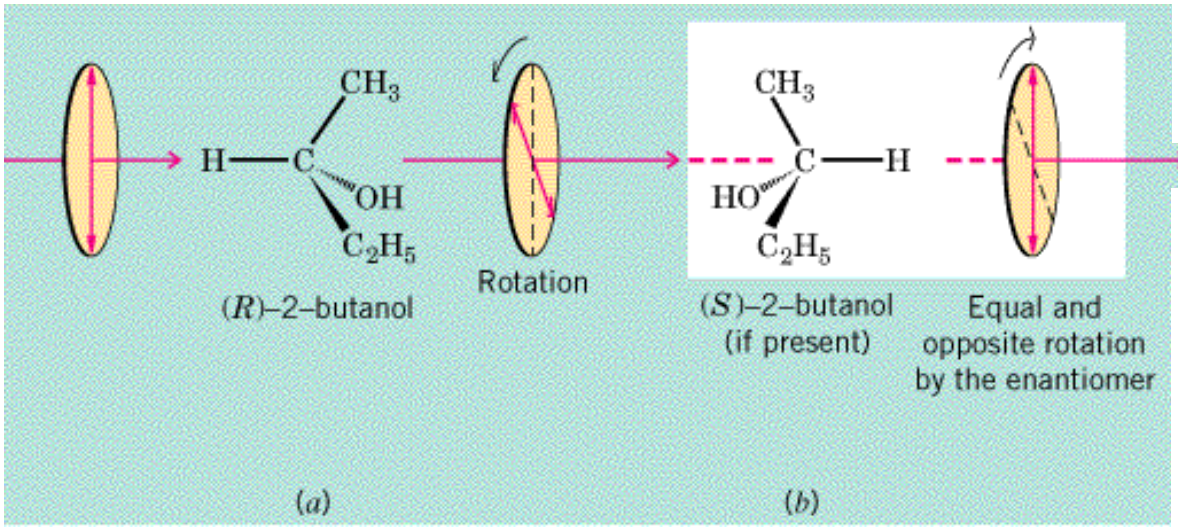
(R)-2-butanol



(S)-2-butanol

Racemate = Equimolar mixture of *(R)* and *(S)* enantiomer

Optically inactive



0 rotation

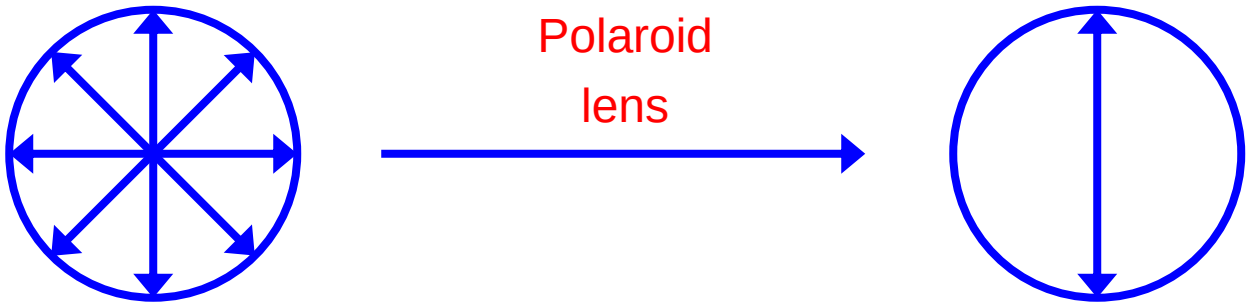
Physical Properties of Stereoisomers.

Enantiomers also:

- Have the same chemical properties (except reaction/interactions with chiral substances)
- Show different behavior only when they interact with other chiral substances (enzymes)
- Rotate **plane-polarized light** in equally in opposite directions - this property of enantiomers is called optical activity

Optical Activity.

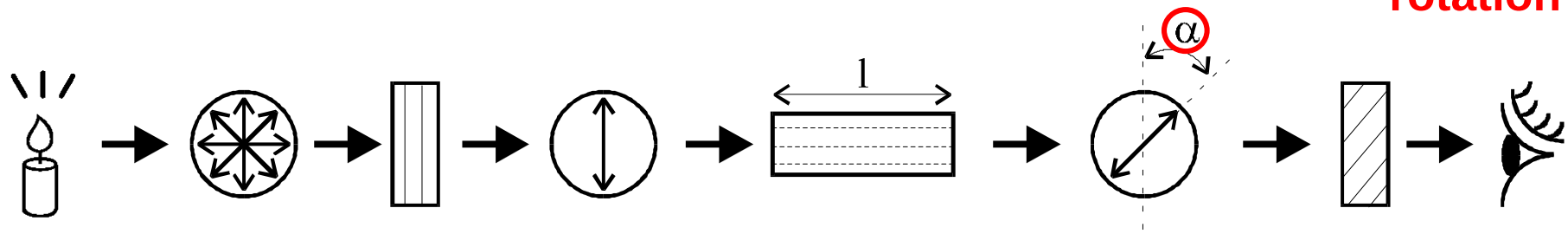
- The property possessed by chiral substances of rotating the plane of polarization of plane-polarized light
- The electric field (like the magnetic field) of light is oscillating in all possible planes
- When this light passes through a polarizer (Polaroid lens), we get plane-polarized light (oscillating in only one plane)



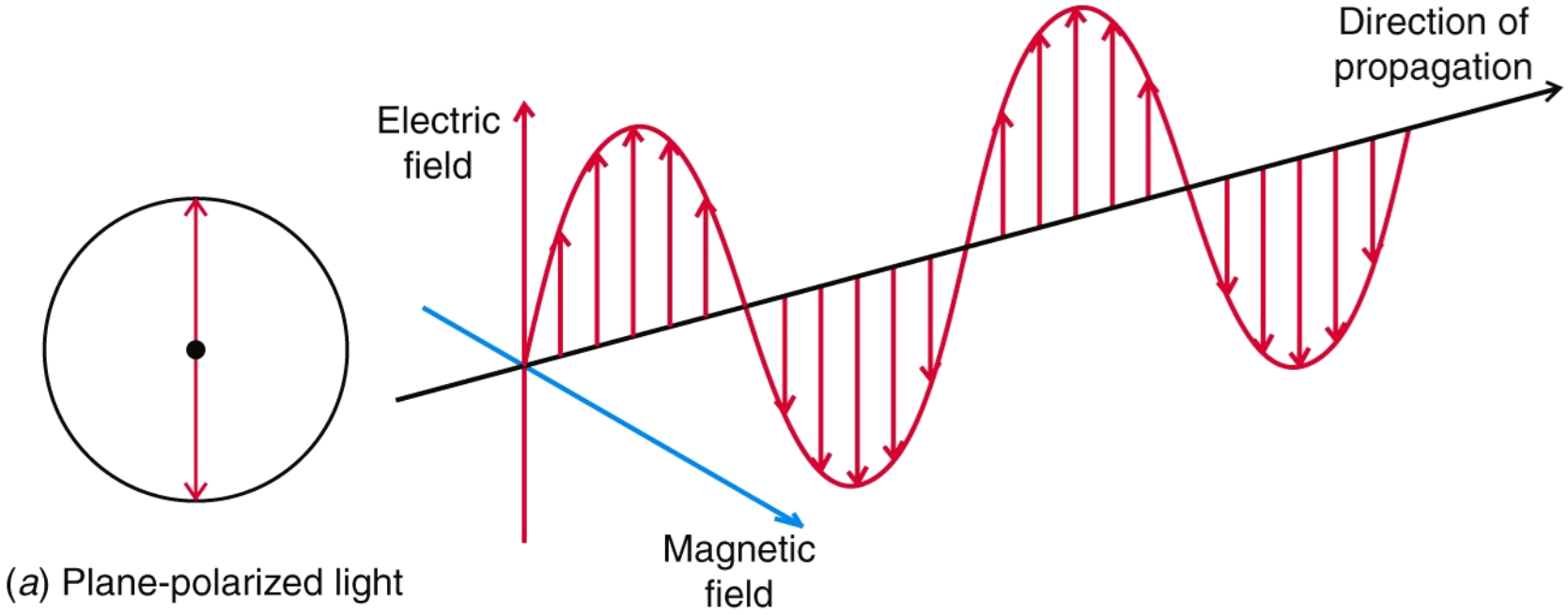
Optical Activity and Polarimeter (2).

Polarimeter – instrument to measure optical activity

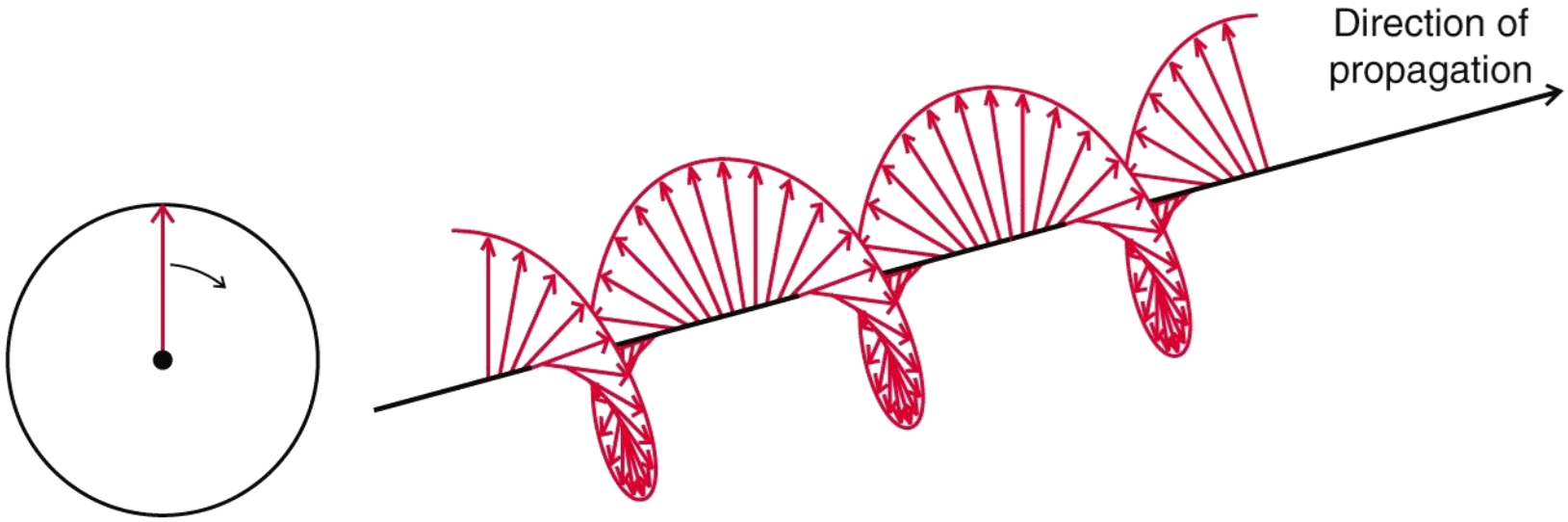
α = observed optical rotation



Optical Activity – Measuring on Polarimeter.

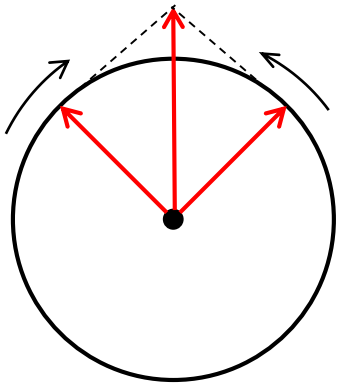


Optical Activity – Measuring on Polarimeter (2).

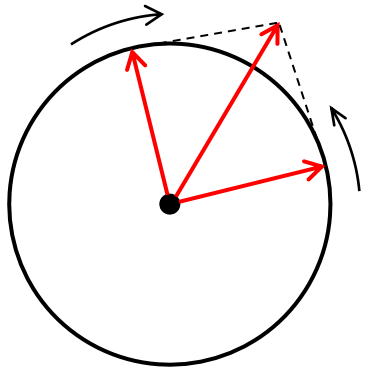


(*b*) Circularly-polarized light

Optical Activity – Measuring on Polarimeter (3).

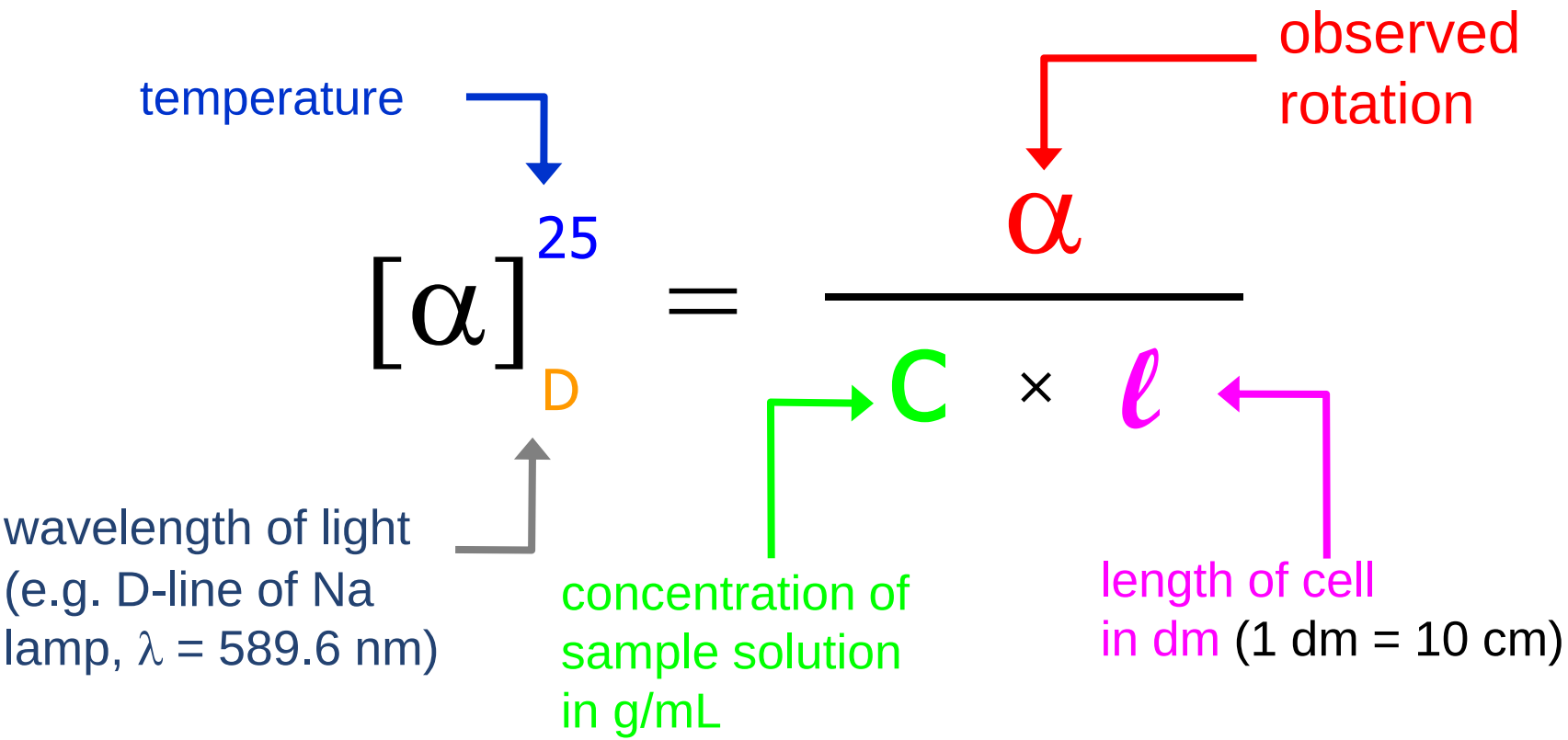


(c) Two circularly-polarized beams counter-rotating at the same velocity (in phase), and their vector sum. The net result is like (a).



(d) Two circularly-polarized beams counter-rotating at the different velocities, such as after interaction with a chiral molecule, and their vector sum. The net result is like (b).

Optical Activity – Calculating Specific Rotation.



Enantiomeric Excess (ee).

Non-equimolar mixture of *(R)* and *(S)* enantiomer

→ **Enantiomerically enriched – Optically active**

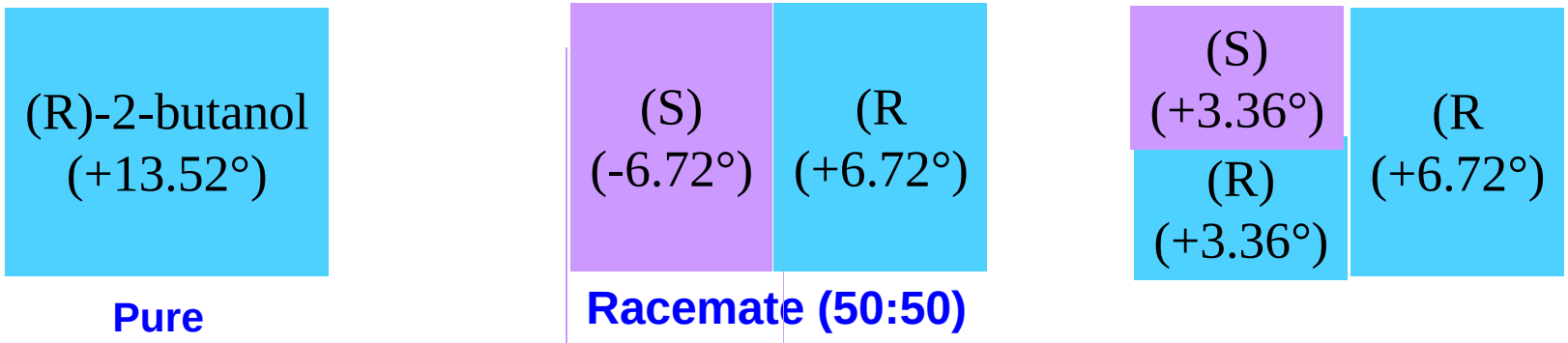
The enantiomeric excess can be calculated from optical rotations:

$$\%\ \text{Enantiomeric excess} = \frac{\text{moles of one enantiomer - moles of other enantiomer}}{\text{total moles of both enantiomers}} \times 100$$

E.g. a mixture of the 2-butanol enantiomers showed a specific rotation of +6.76°

$$\%\ \text{Enantiomeric excess *} = \frac{\text{observed specific rotation}}{\text{specific rotation of the pure enantiomer}} \times 100$$

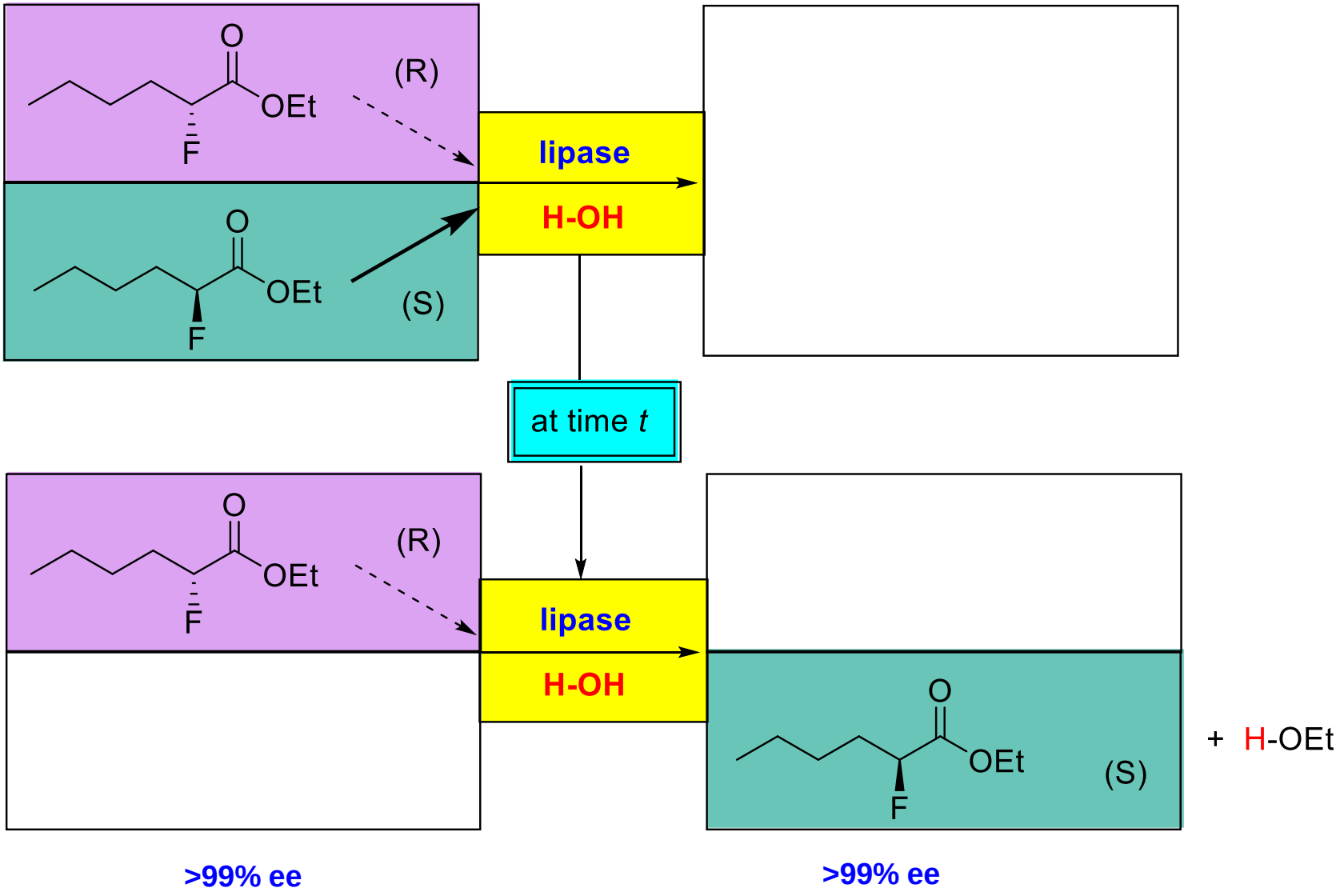
$$\text{Enantiomeric excess} = \frac{+6.76°}{+13.52°} \times 100 = 50\%$$



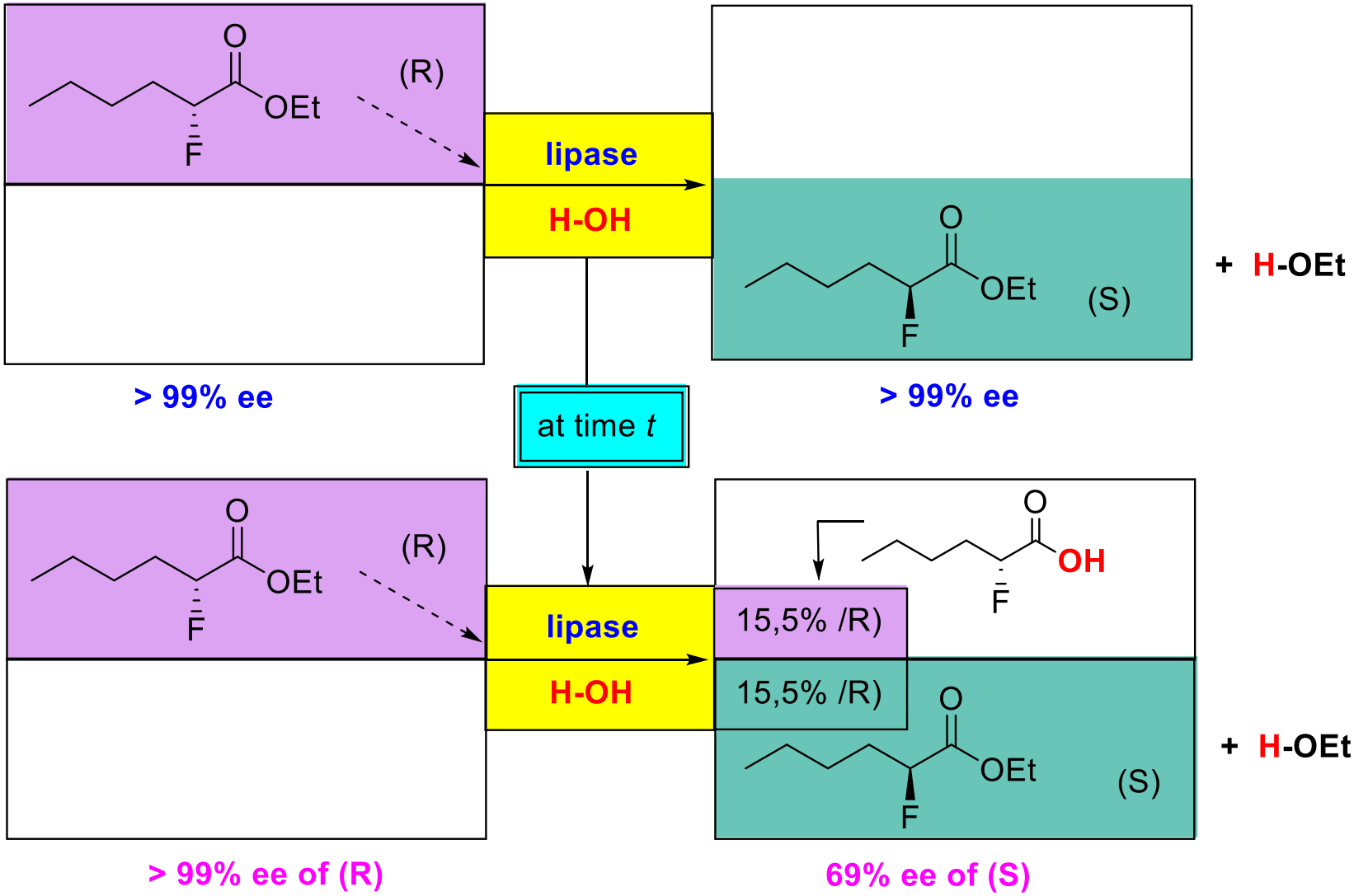
Pure

Racemate (50:50)

Stereo-selective Synthesis (Kinetic Resolution).

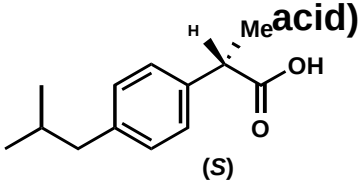


Stereo-selective Synthesis (Kinetic Resolution) (2).



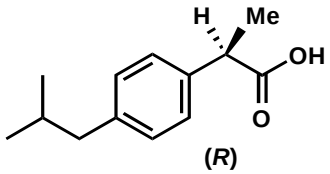
Chiral Drugs (for Chiral Receptor).

Ibuprofen (Isobutyl phenyl pripionic acid)



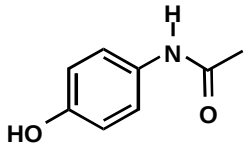
(*S*)

Active anti-inflamatory agent

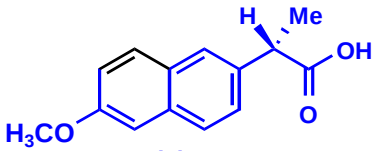


(*R*)

No anti-inflamatory activity



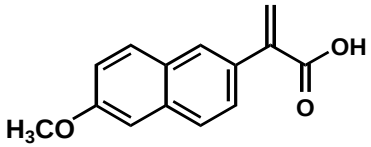
Acetaminophen (Tylenol)



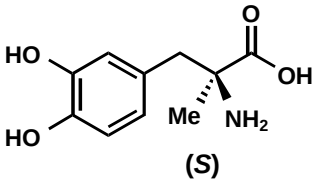
(*S*)-Naproxene

(*S*)-BINAP-Ru(Ac)$_2$

H− H

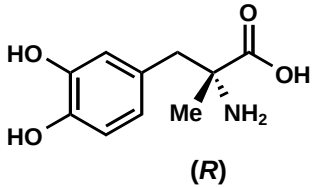


Methyldopa (Aldomet)



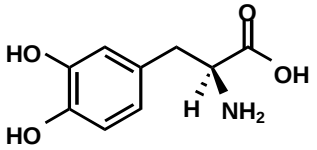
(*S*)

Anti-hypertensivedrug



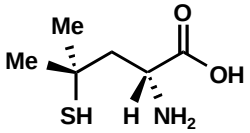
(*R*)

No activity



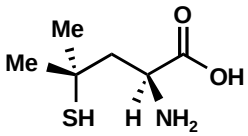
L-DOPA

Penicillamine



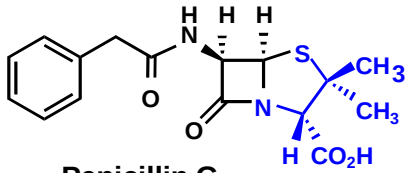
(*S*)

Therapeutic agent
for primary chronic arthritis



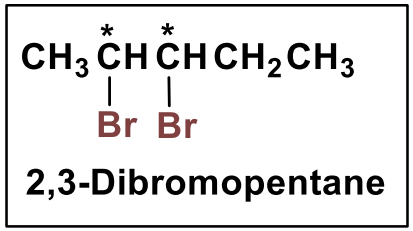
(*R*)

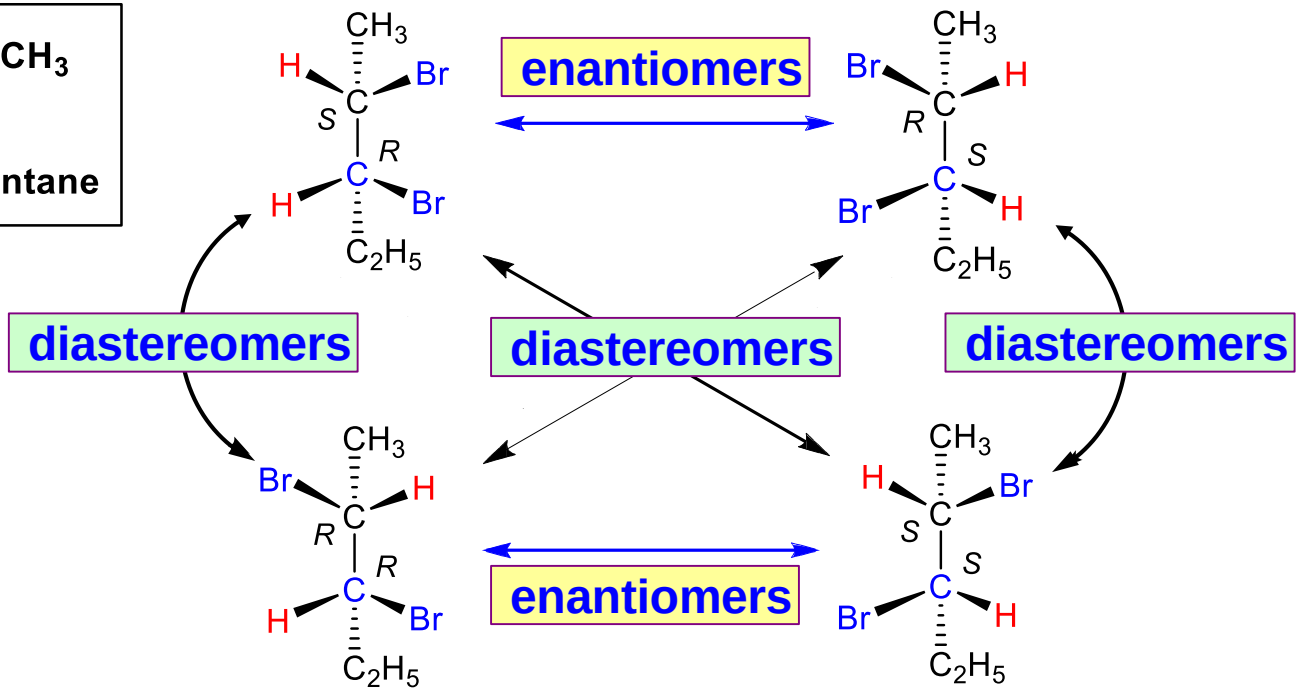
Highly toxic



Penicillin G

Molecules with Multi-Stereogenic Centers.

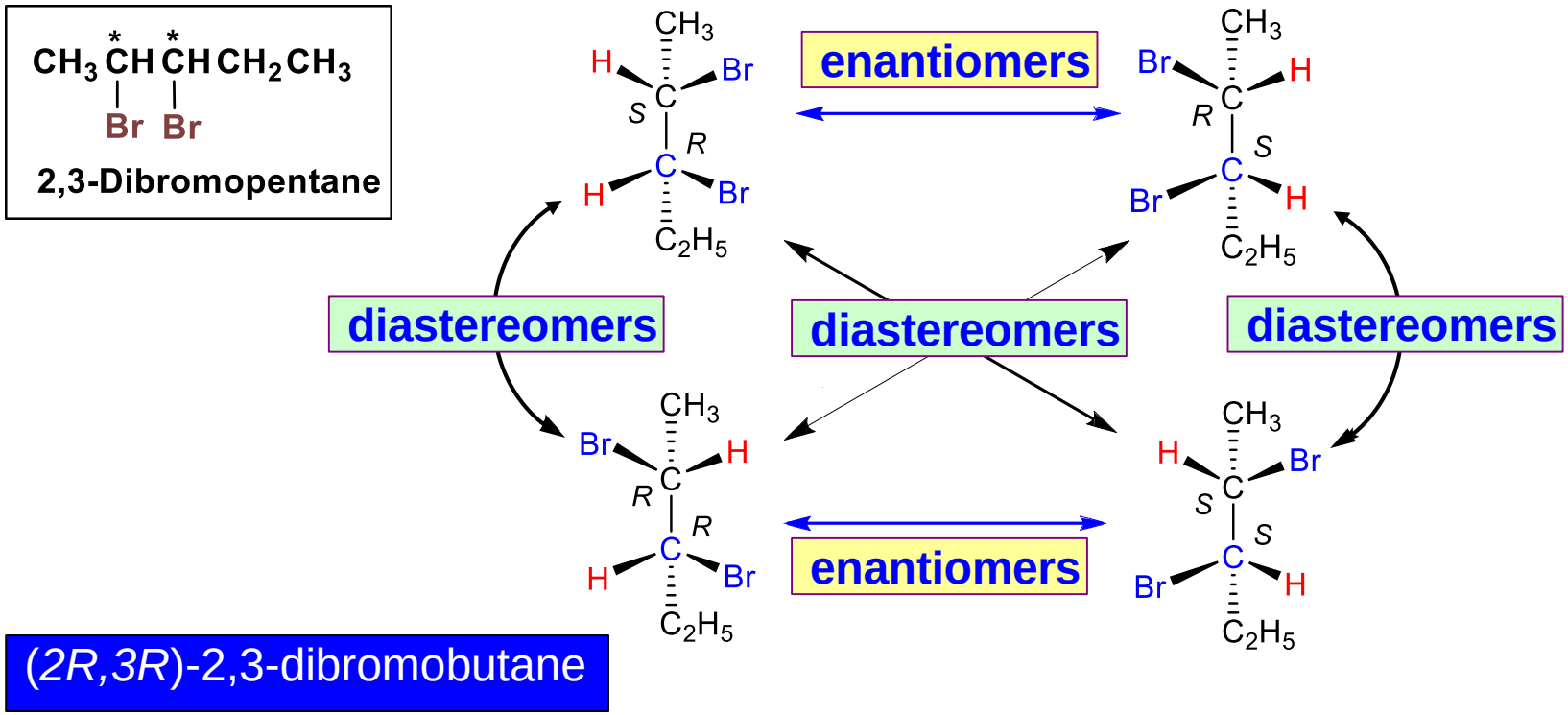




Diastereomers have different physical properties: different m.p. and b.p., different solubilities, and so forth.

Total number of stereoisomers will not exceed 2^n, where n is equal to the number of tetrahedral stereogenic centers.

Naming Molecules with Multi-Stereogenic Centers.



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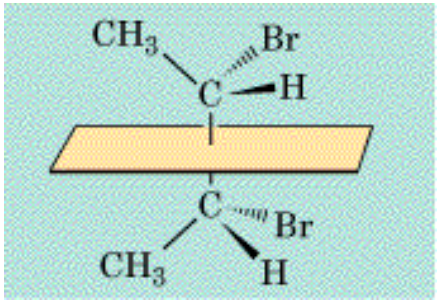
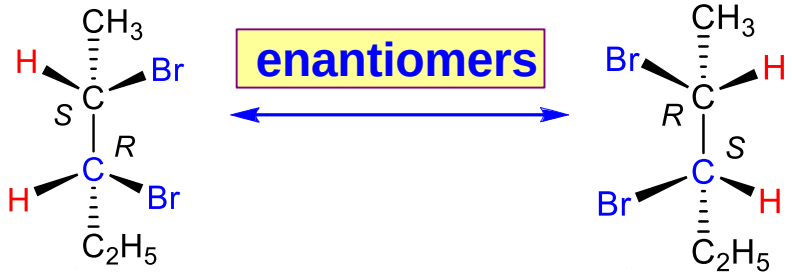
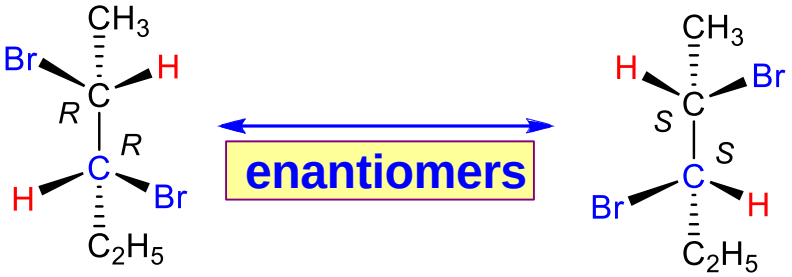
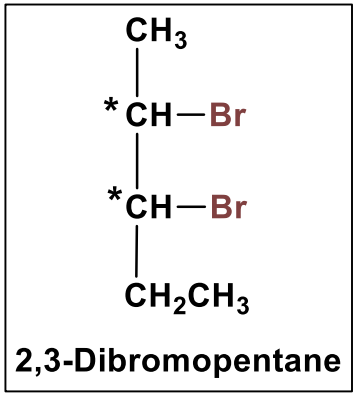
Molecules with Multi-Stereogenic Centers
Meso Compounds.



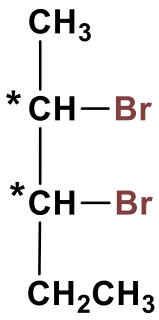
(superimposable)



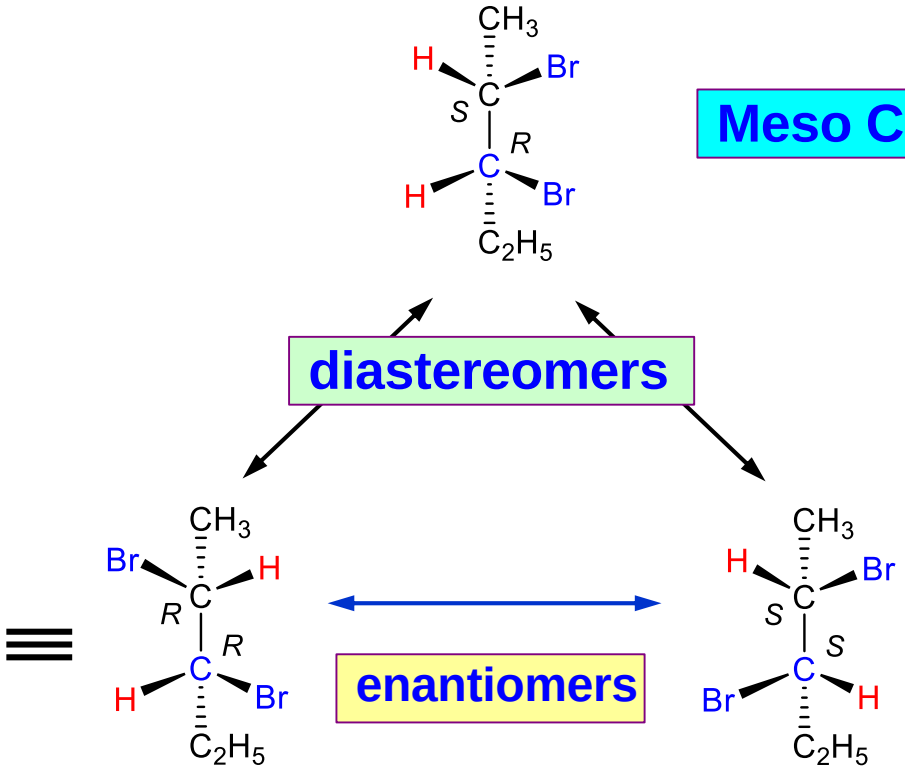




Molecules with Multi-Stereogenic Centers
Meso Compounds (2).

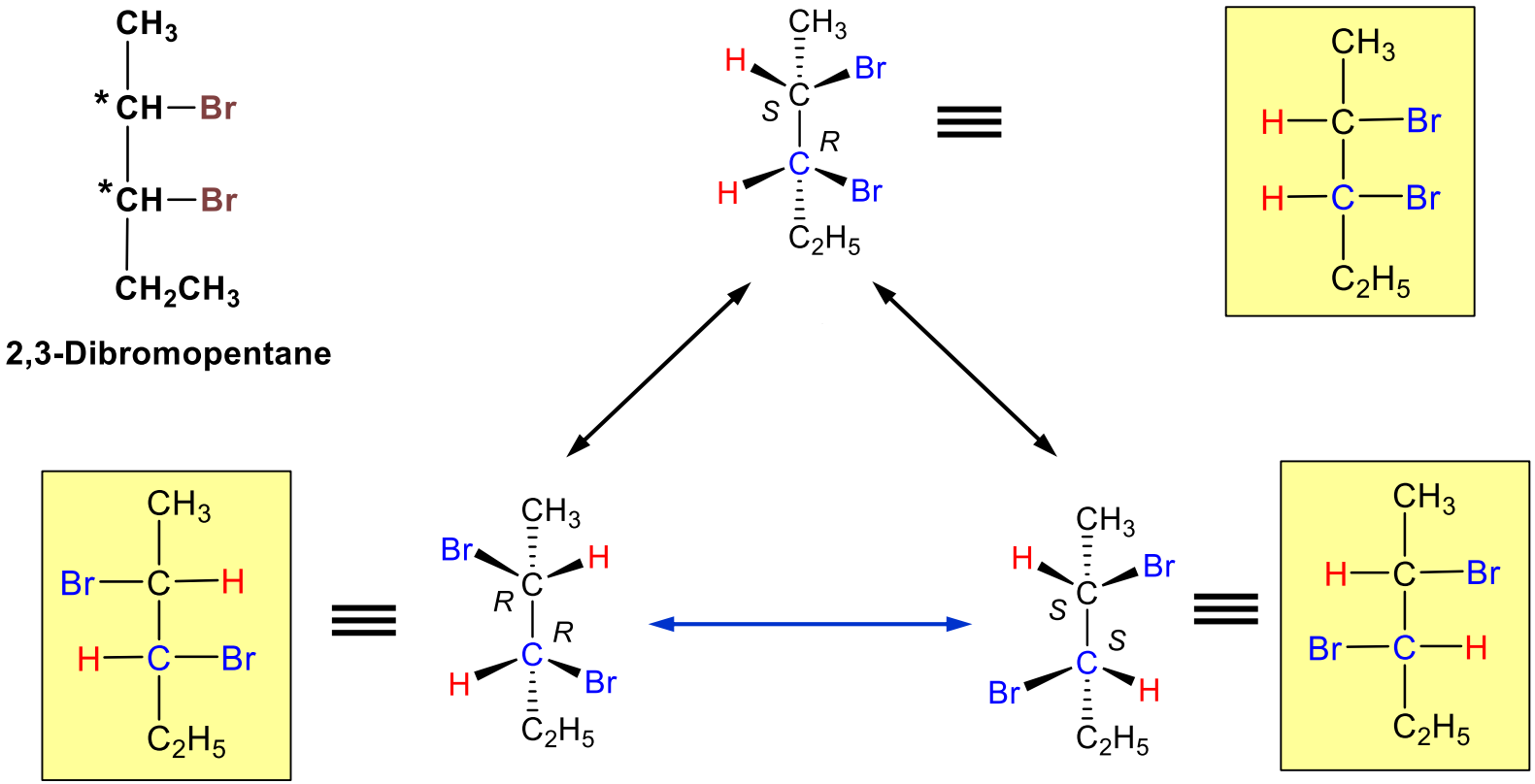


2,3-Dibromopentane



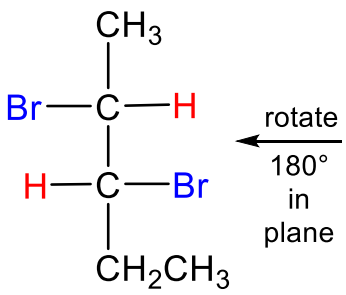
Total number of stereoisomers will not exceed 2^n, where n is equal to the number of tetrahedral stereogenic centers.

Molecules with Multi-Stereogenic Centers
Fisher Projection Formula.



Vertical lines represent bonds that **project behind the plane** of the paper (or that lie in it). **Horizontal** lines represent bonds that **project out of the plane** of the paper.

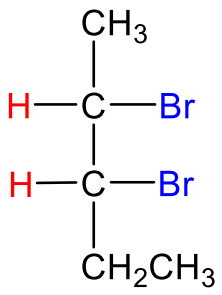
Molecules with Multi-Stereogenic Centers
Fisher Projection Formula (2).



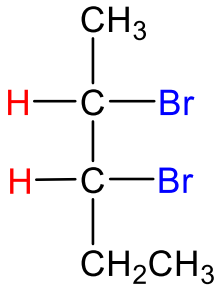
A

Same structure

rotate 180° in plane

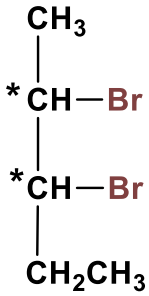


A

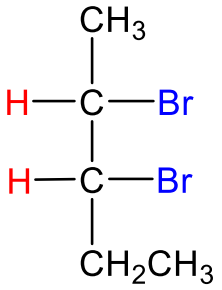


B

Not the same
(Flipping the projection formula over sideways creates the projection formula for the *enantiomer* of A)



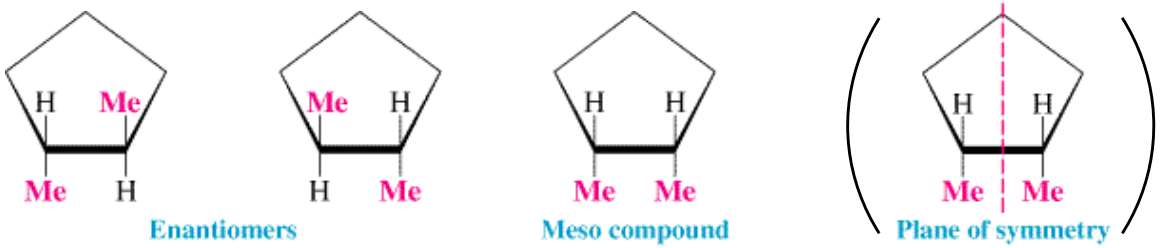
2,3-Dibromopentane

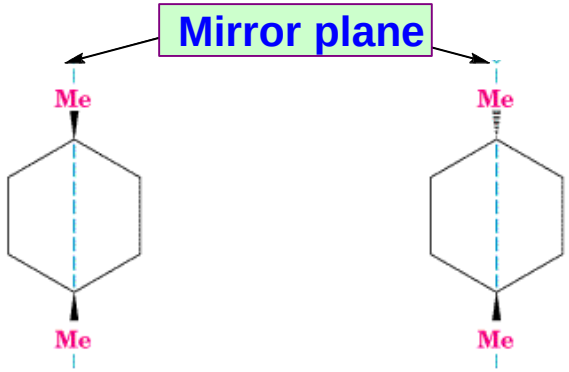


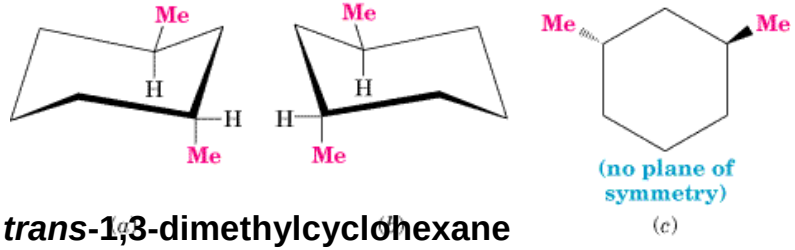
Not the same
(Flipping the projection formula over sideways creates the projection formula for the *enantiomer* of A)

Vertical lines represent bonds that **project behind the plane** of the paper (or that lie in it). **Horizontal** lines represent bonds that **project out of the plane** of the paper.

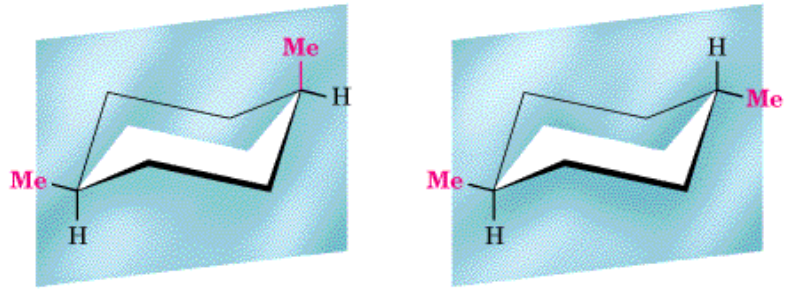
Stereoisomerism of Cyclic Compounds.



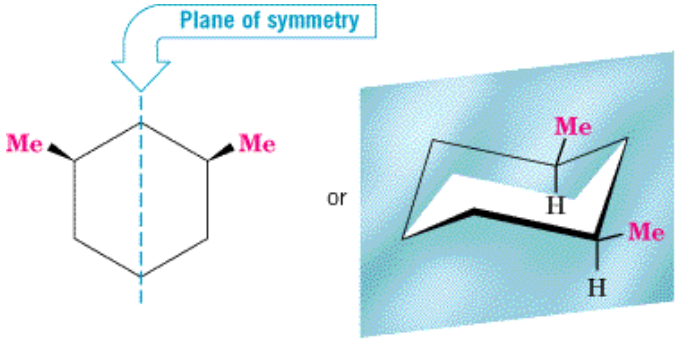




***trans*-1,3-dimethylcyclohexane**



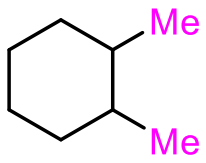
***cis*-1,4-Dimethylcyclohexane** ***trans*-1,4-Dimethylcyclohexane**



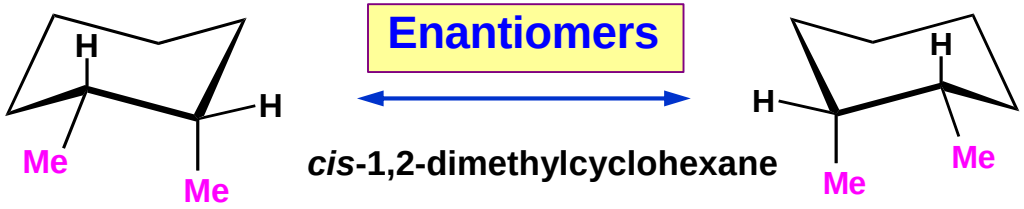
***cis*-1,3-dimethylcyclohexane**

1,2-Dimethylcyclohexane.

***trans*-1,2-dimethylcyclohexane**

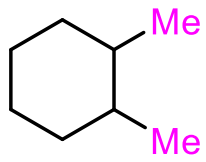


1,2-dimethylcyclohexane



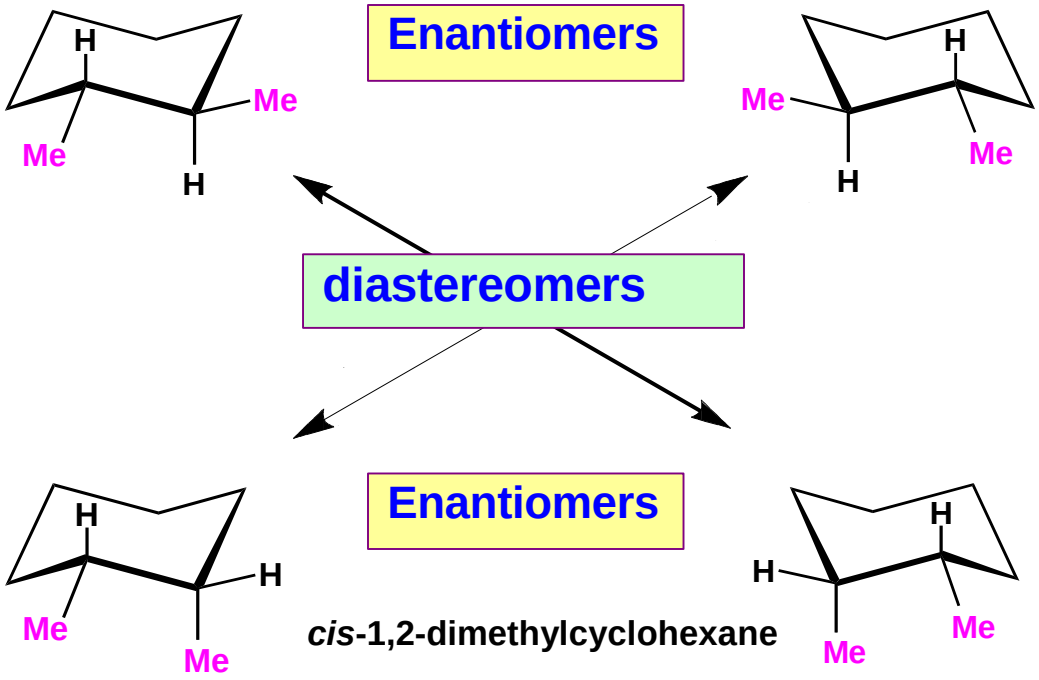
***cis*-1,2-dimethylcyclohexane**

1,2-Dimethylcyclohexane.



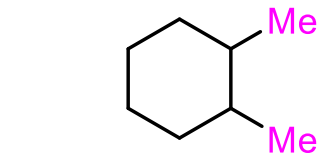
1,2-dimethylcyclohexane

***trans*-1,2-dimethylcyclohexane**



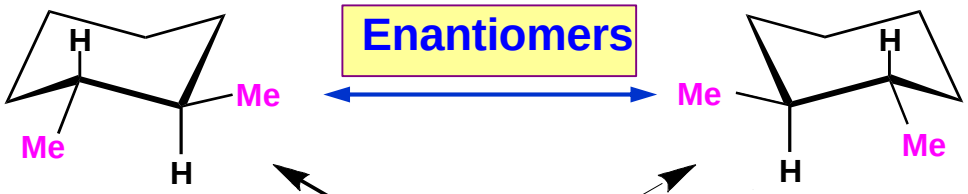
***cis*-1,2-dimethylcyclohexane**

1,2-Dimethylcyclohexane.



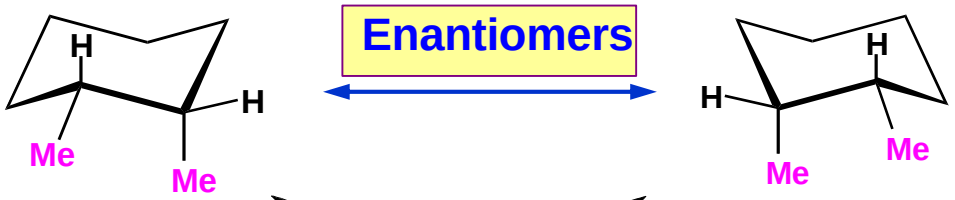
1,2-dimethylcyclohexane

***trans*-1,2-dimethylcyclohexane**

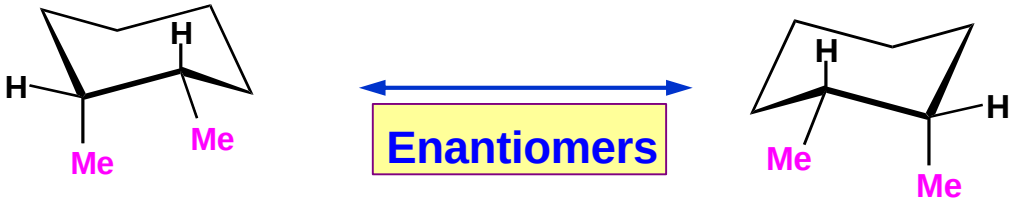


diastereomers

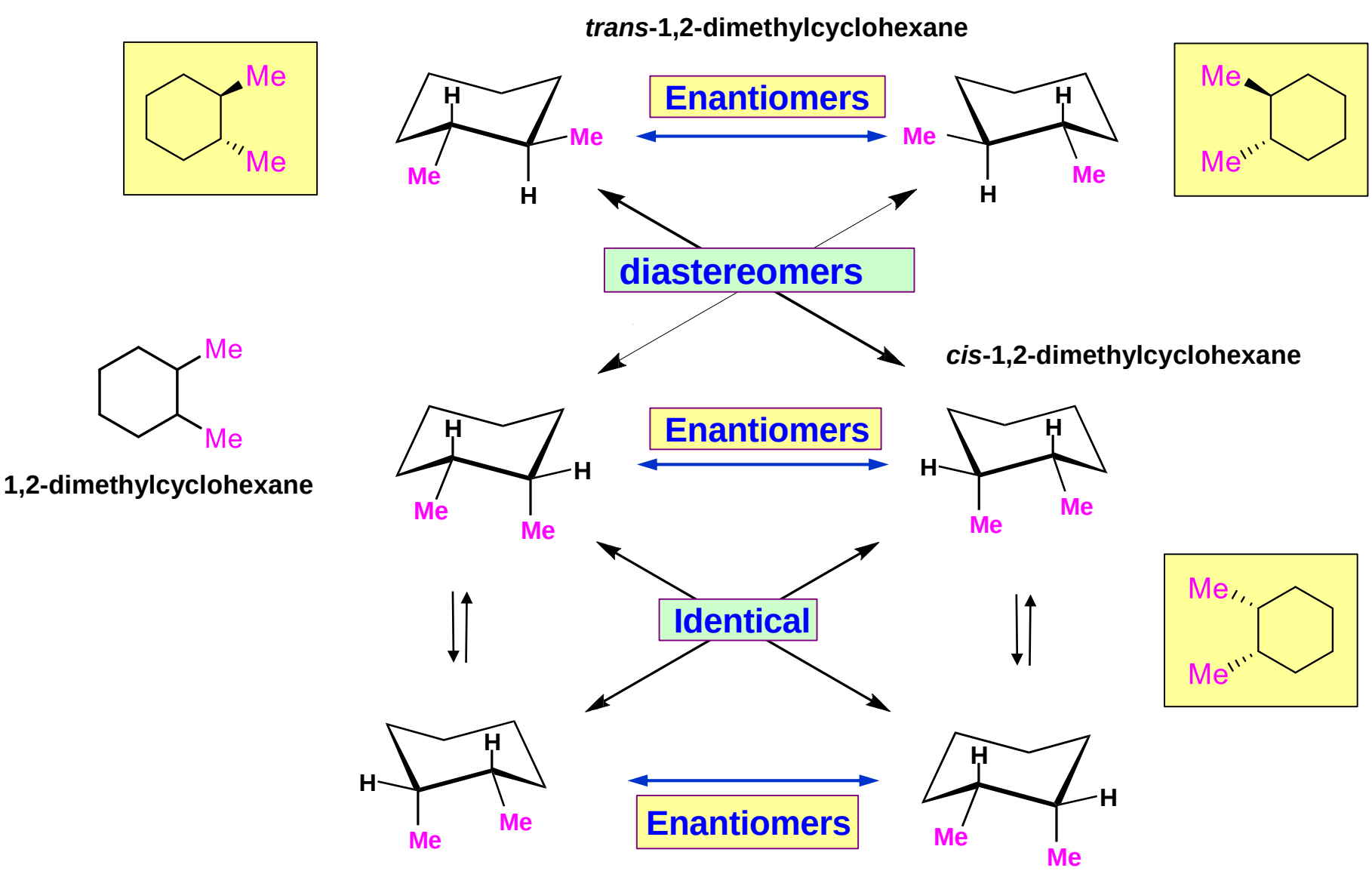
***cis*-1,2-dimethylcyclohexane**



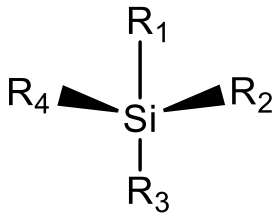
Identical

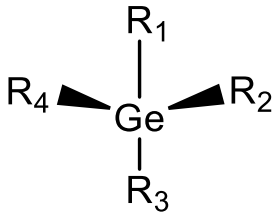


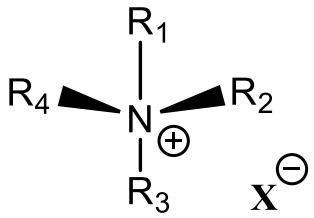
1,2-Dimethylcyclohexane.

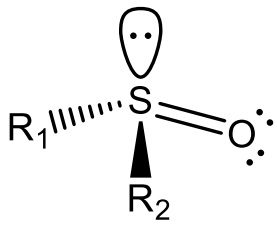


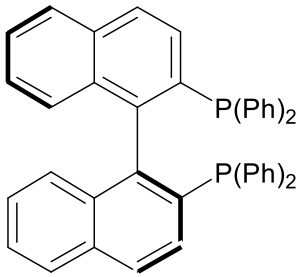
Compounds with Stereogenic Centers Other than Carbon or No Stereogenic Centers.



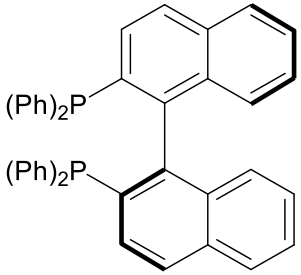




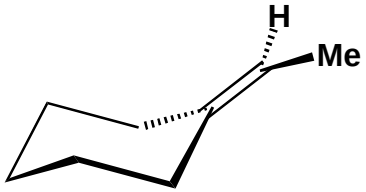


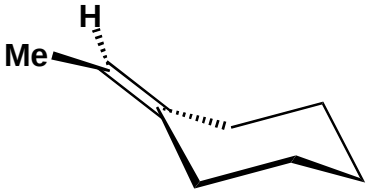


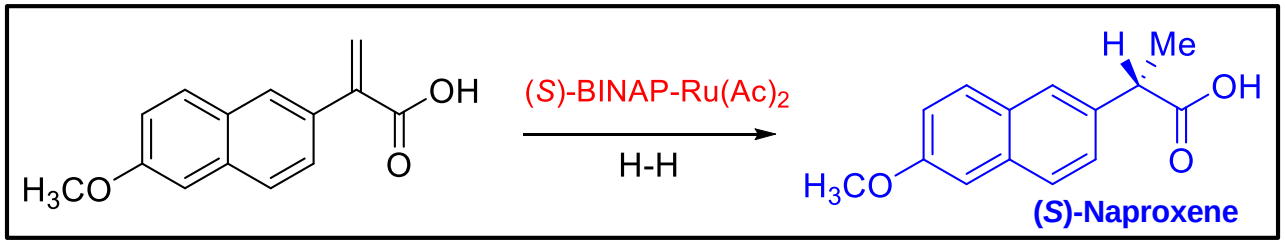
(S)-BINAP

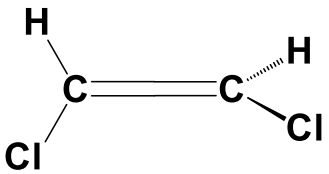


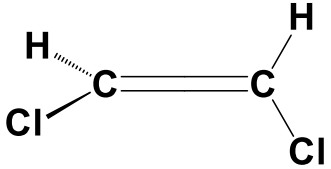
(R)-BINAP



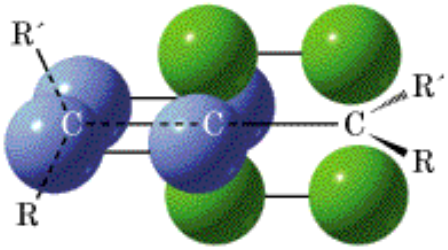




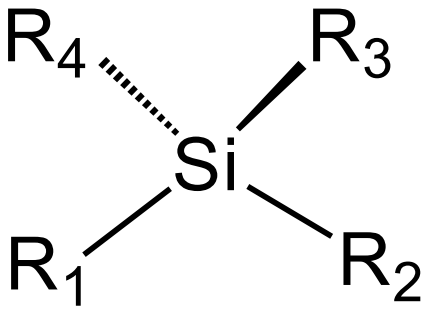


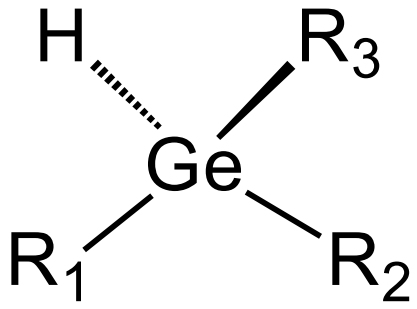


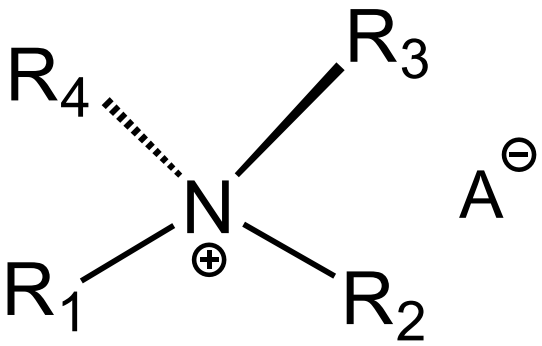
Mirror

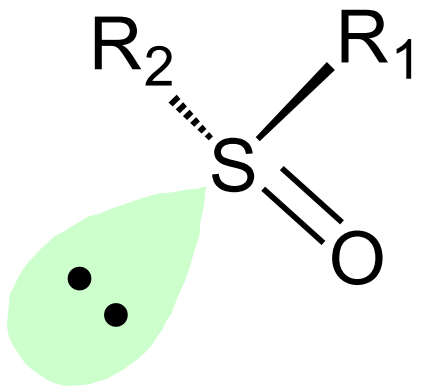


Other Chirality in Organic Chemistry.

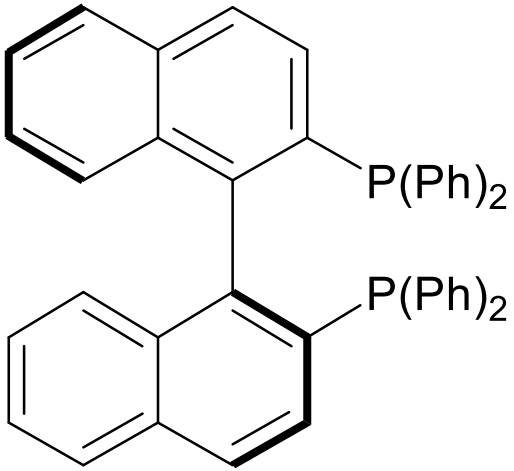








Other Chirality in Organic Chemistry.



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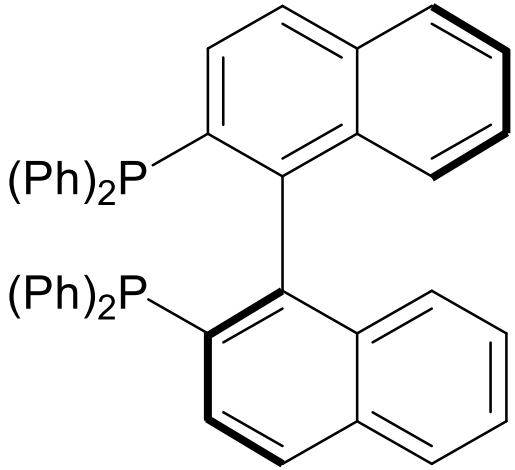
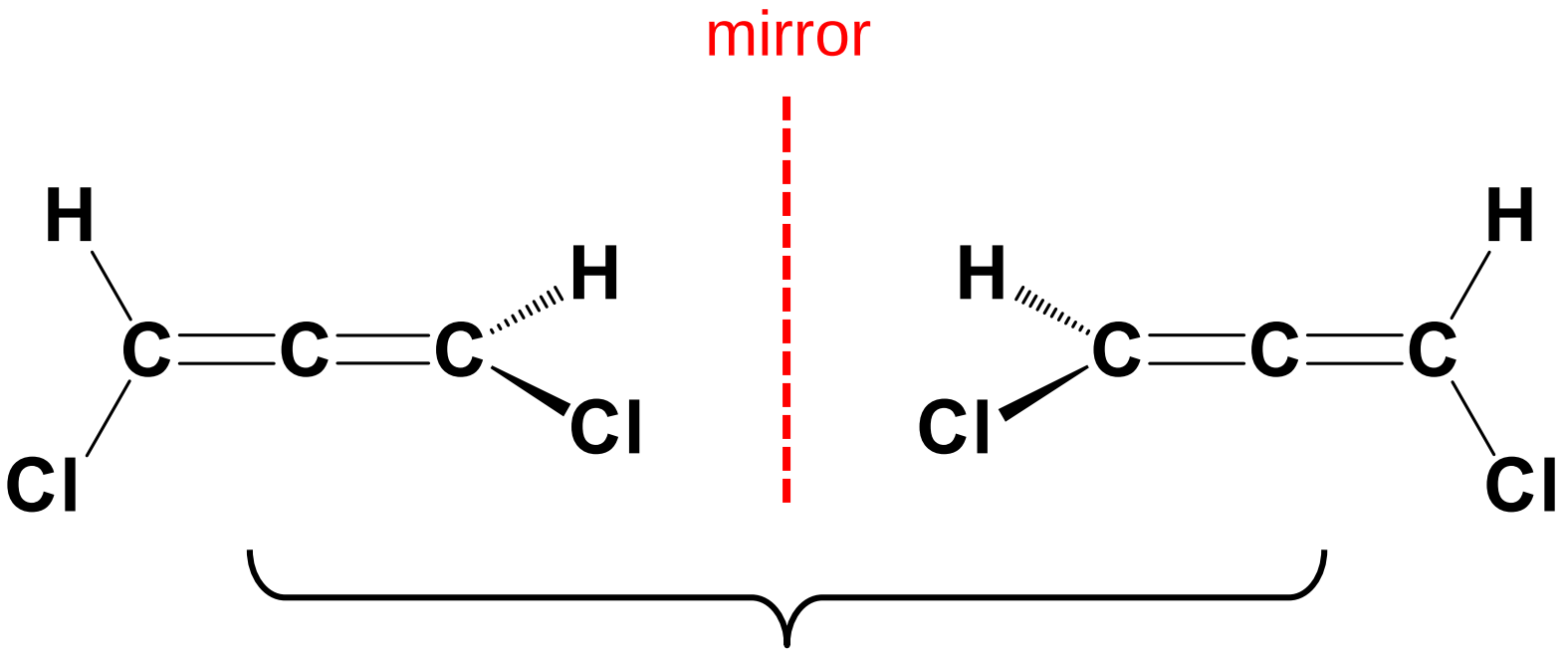


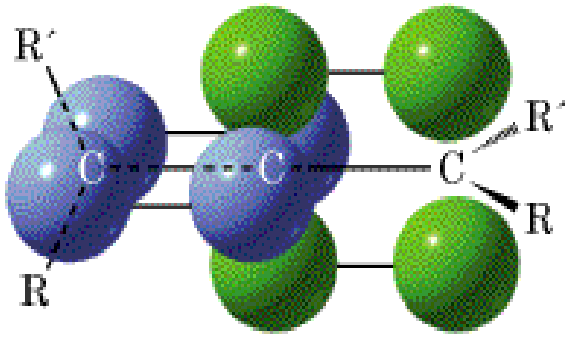
(R)-BINAP

enantiomers

Other Chirality in Organic Chemistry.



enantiomers



allene