ORGANIC CHEMISTRY

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REFERENCES

[1] Nam T. S. Phan, Hoa T. V. Tran '*Organic chemistry*', VNU-HCMC Publisher, 2011

[2] Nam T. S. Phan, '*Study guide to organic chemistry*', VNU-HCMC Publisher, 2011

[3] Paula Y. Bruice, *'Organic chemistry',* fifth edition, Pearson Prentice Hall, 2007

[4] Francis A. Carey, *'Organic chemistry*', fifth edition, McGraw-Hill, 2003

[5] Paula Y. Bruice, *'Study guide and solutions manual - Organic chemistry',* fifth edition, Pearson Prentice Hall, 2007

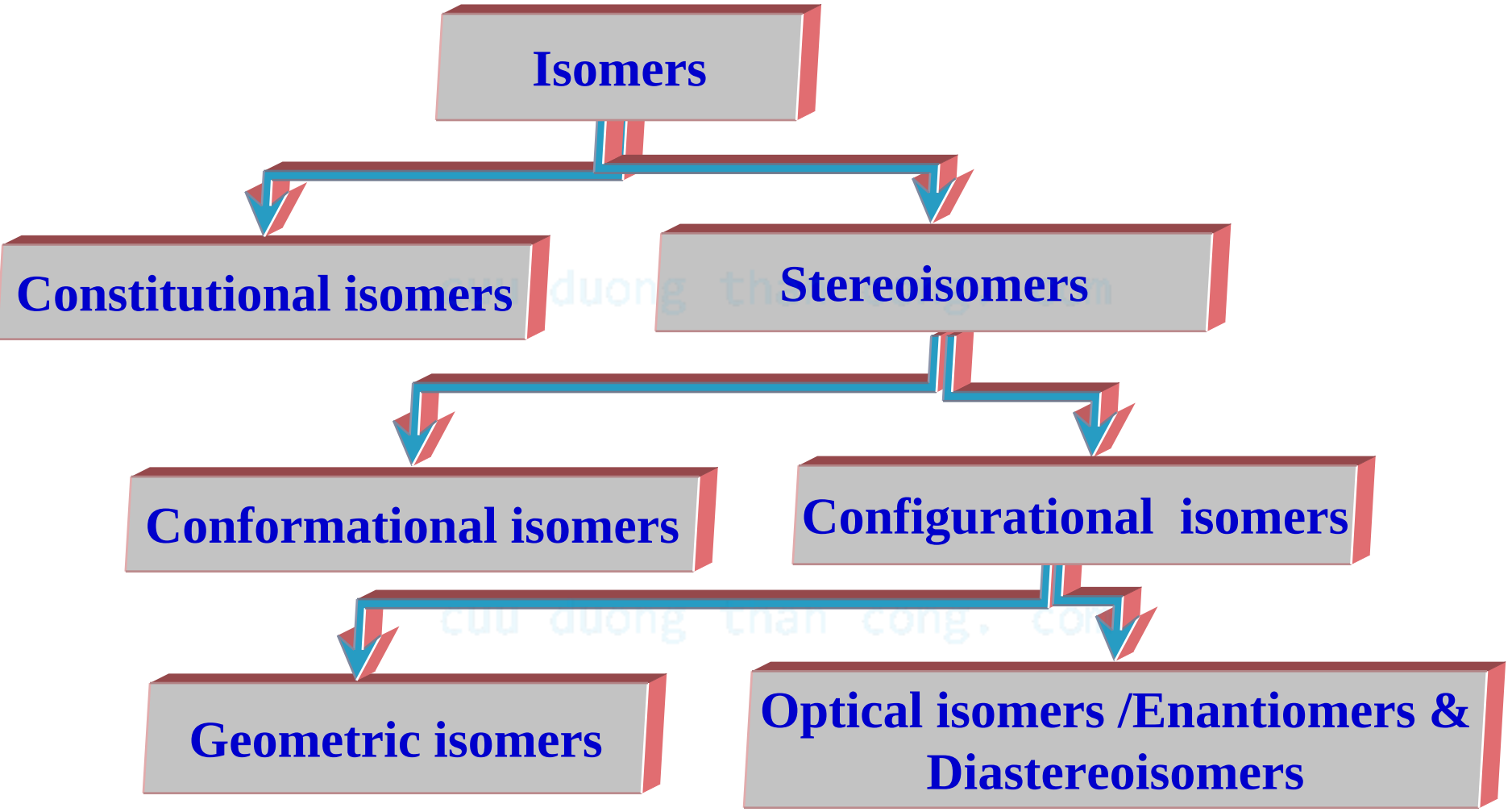
[6] Graham T.W. Solomons, Craig B. Fryhle, *'Organic chemistry',* eighth edition, John Wiley & Sons, 2004

COURSE OUTLINE

- Isomerism
- Electronic & steric effects
- Introduction to reaction mechanisms
- Alkanes
- Alkenes
- Alkadienes
- Alkynes
- Aromatic hydrocarbons
- Alkyl halides
- Alcohols & phenols
- Aldehydes & ketones
- Carboxylic acids
- Amines & diazoniums

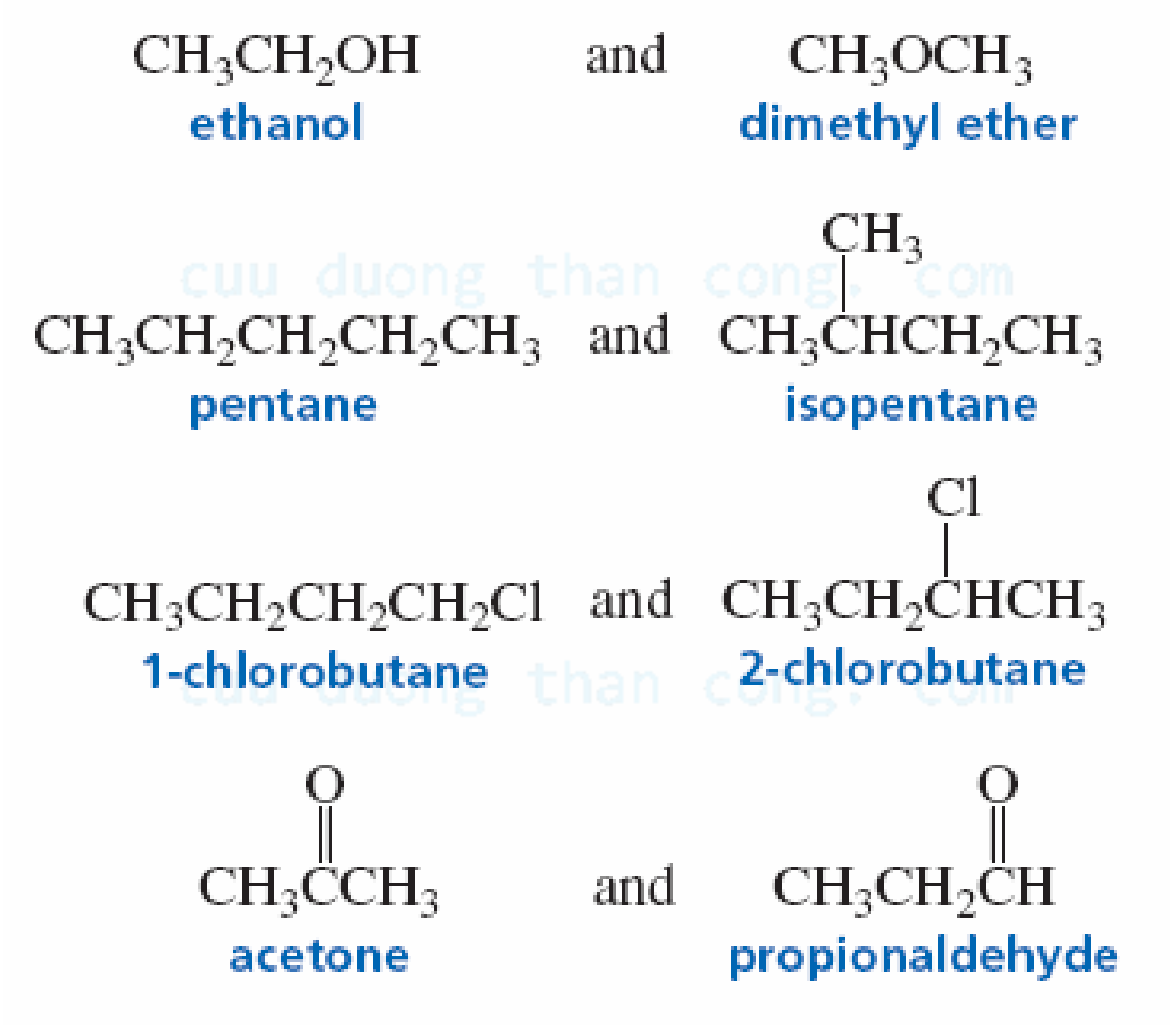
Chapter 1: ISOMERISM

Isomers: Compounds with the same molecular formula but different structural formulas



CONSTITUTIONAL ISOMERS

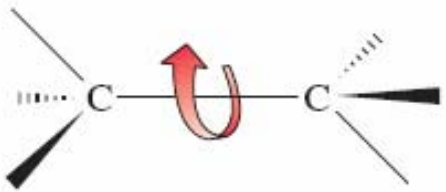
Different compounds that have the same molecular formula – but differ in their connectivity



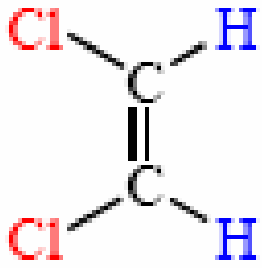
STEREOISOMERS

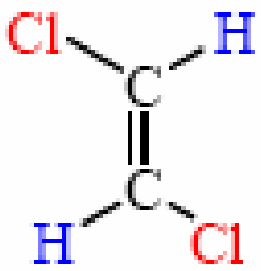
Isomers that differ in the way their atoms are arranged in space

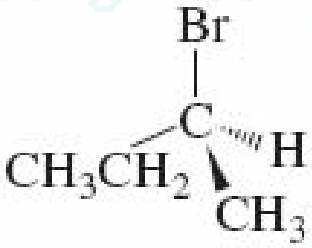
Conformational isomers

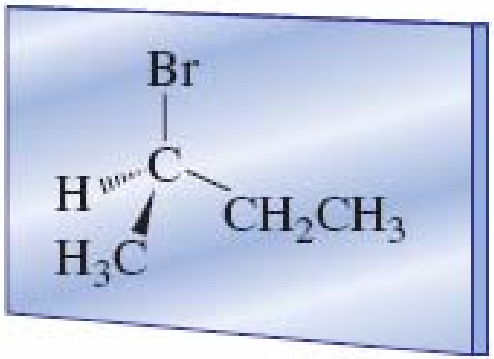


Configurational isomers



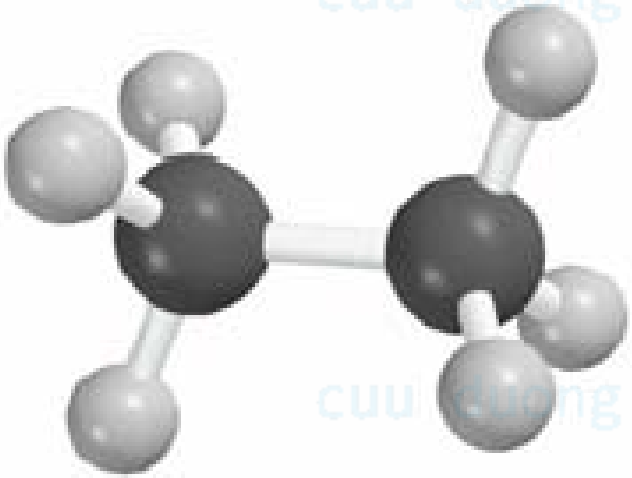




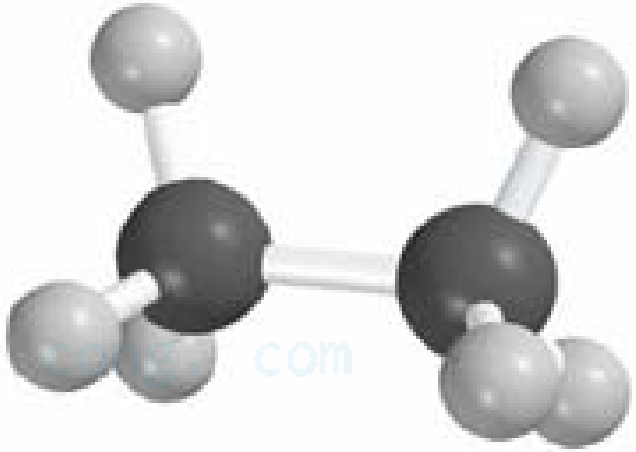


CONFORMATIONAL ISOMERS

- **Different shapes of the same molecule resulting from rotation around a single C-C bond**
- **Conformational isomers are not different compounds**



Staggered conformation of ethane

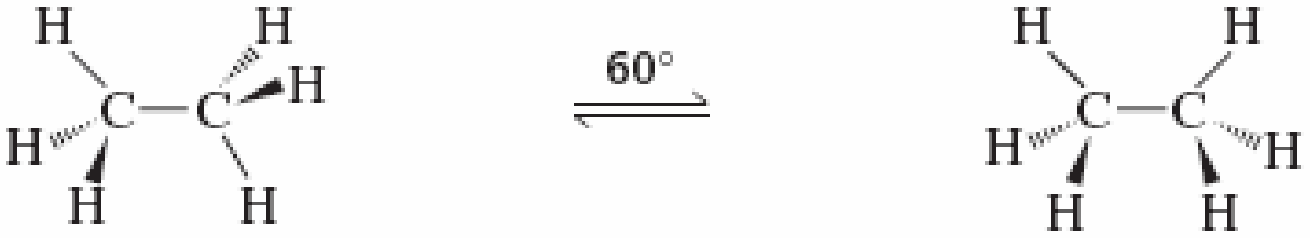


Eclipsed conformation of ethane

staggered conformation for rotation about the carbon–carbon bond in ethane

eclipsed conformation for rotation about the carbon–carbon bond in ethane

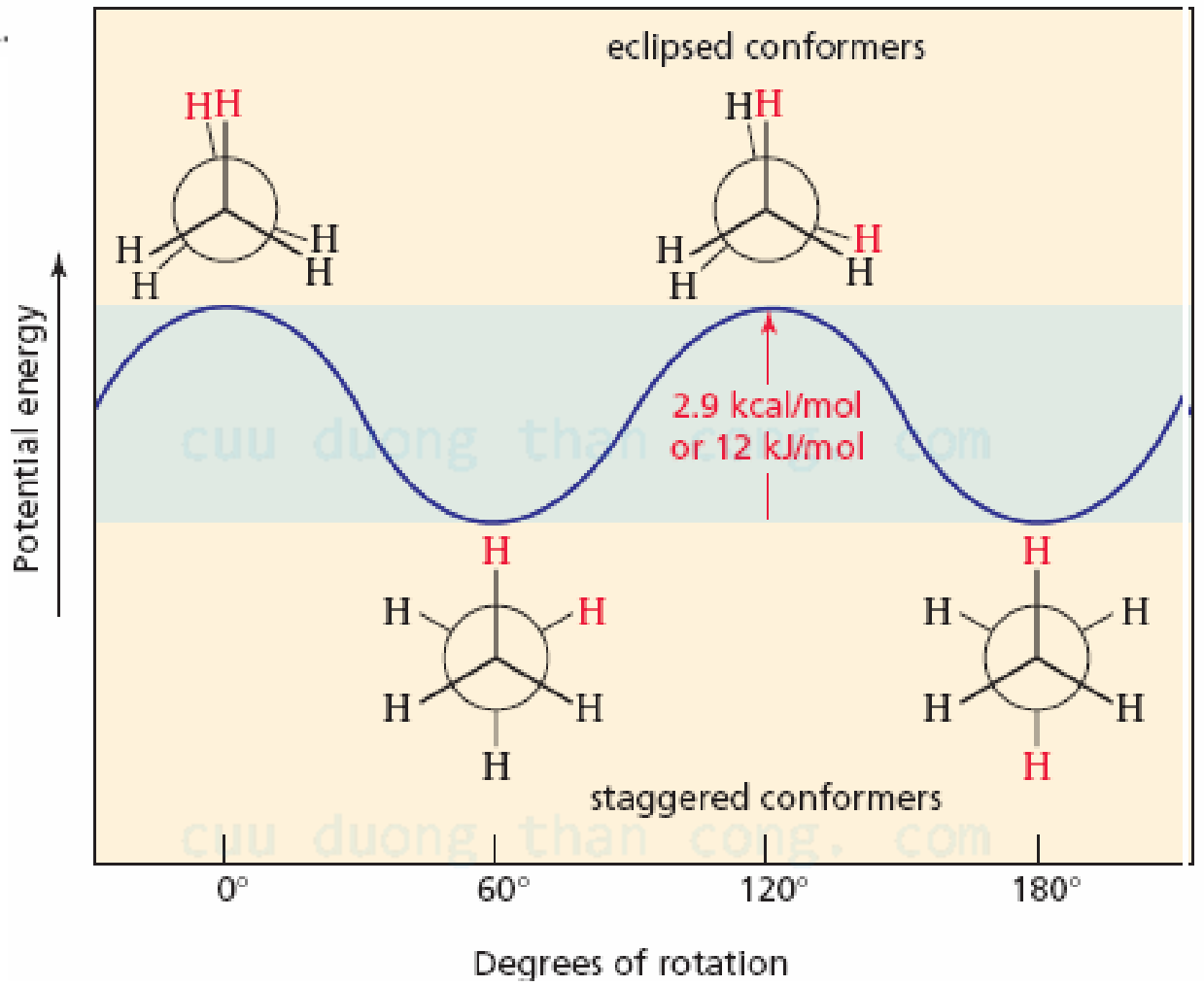
perspective formulas



sawhorse projections

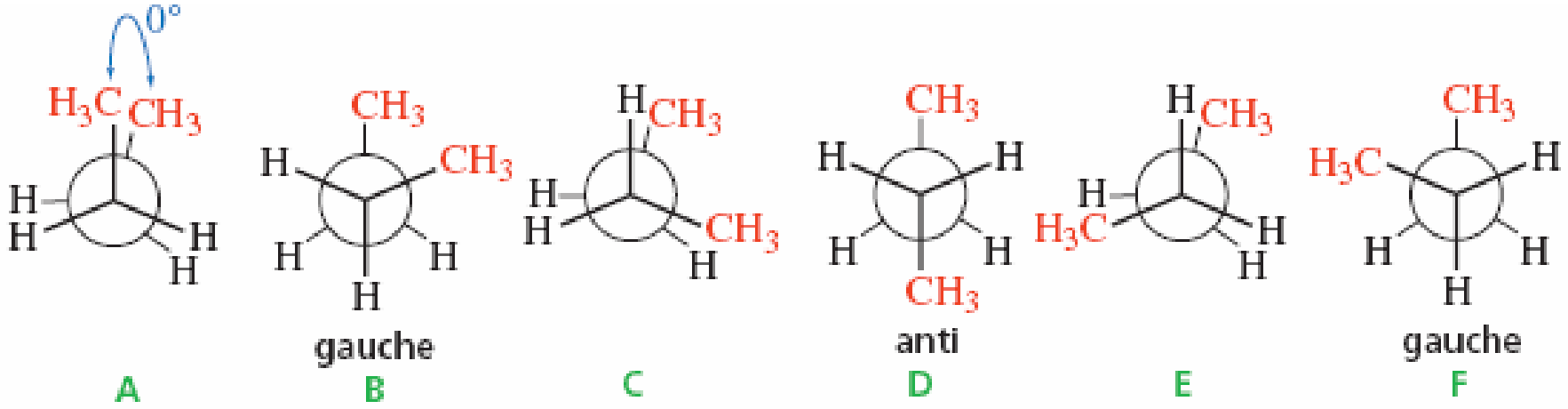
Newman projections

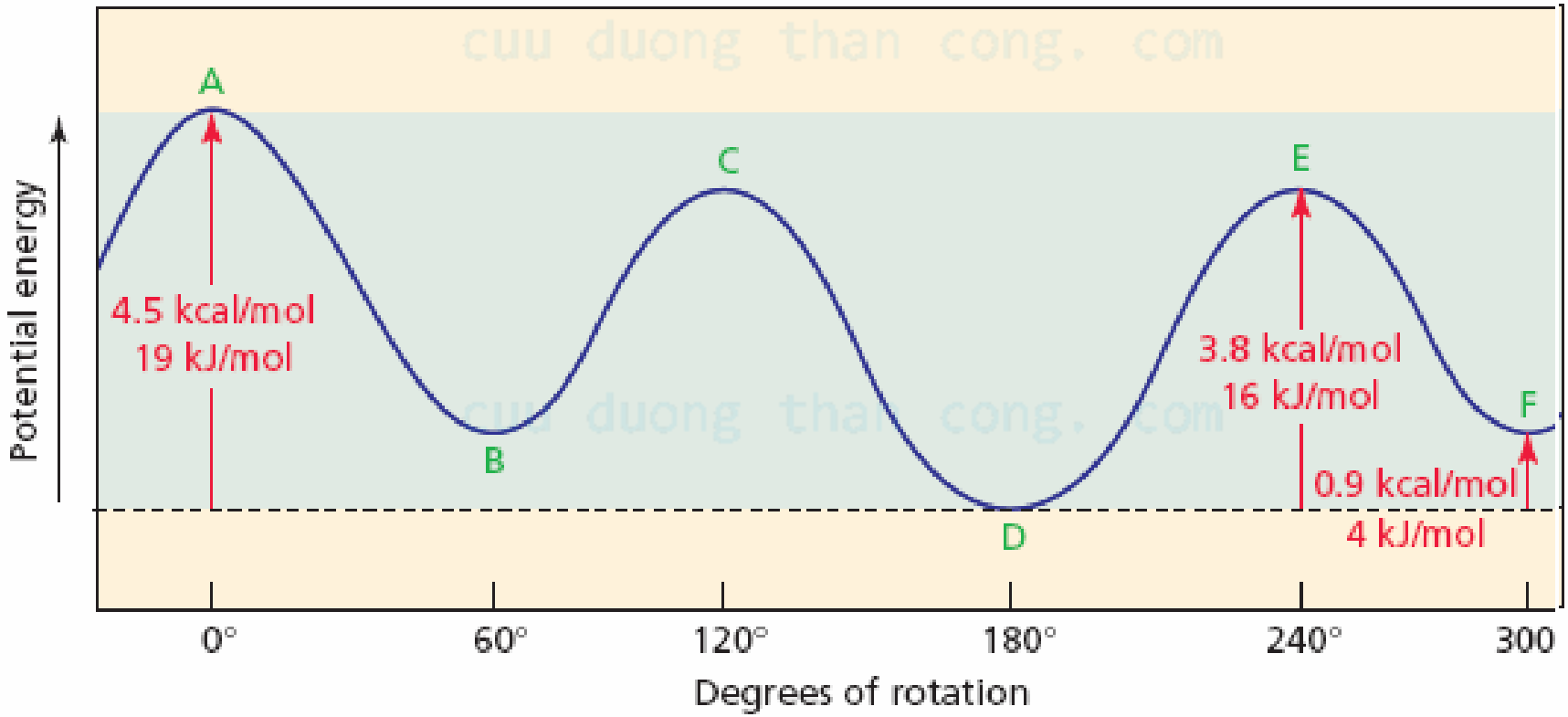
Eclipsed conformation: **maximum repulsive interaction** between the electron pairs of the six C—H bonds ⇒ has the **highest energy** ⇒ **least stable** conformation.



Staggered conformation: allows the **maximum separation** of the electron pairs of the six C—H bonds ⇒ has the **lowest energy** ⇒ **most stable** conformation.

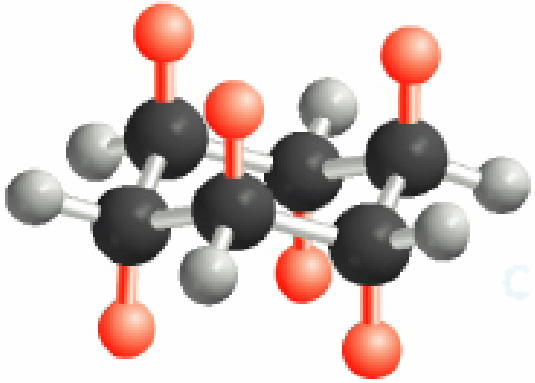
Conformations of butane

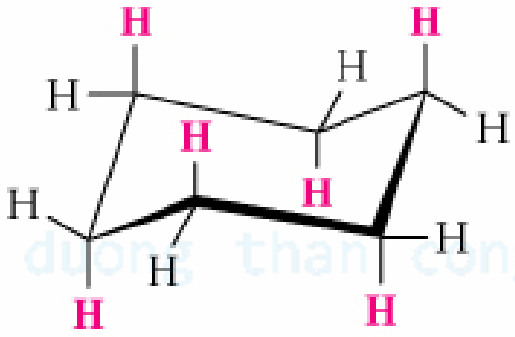




Conformations of cyclohexane

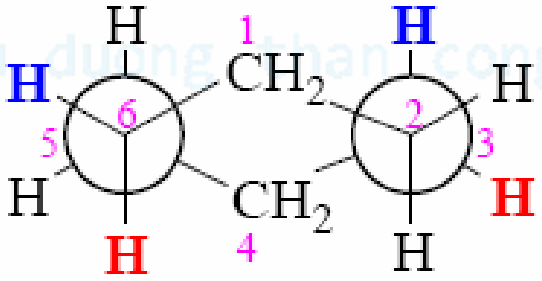
The **most stable** conformation of the cyclohexane ring is the "**chair**" conformation:



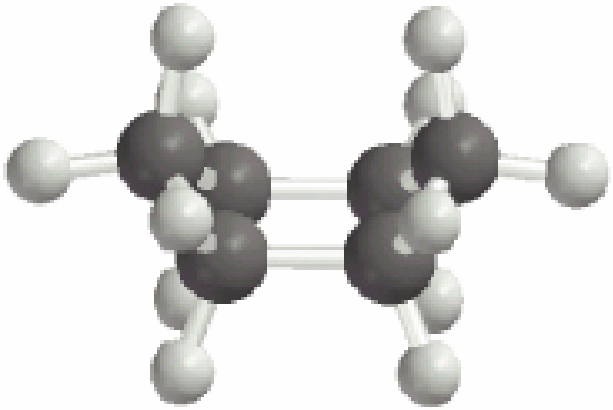


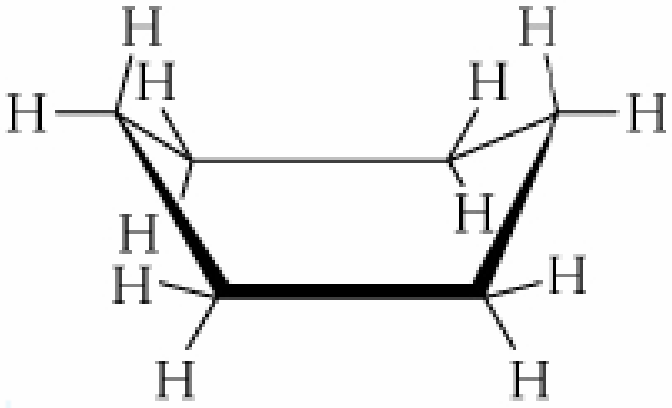
The **C**—**C** bond angles are all 109.5° ⇒ **free** of angle strain

When viewed along any **C**—**C** bond, the atoms are seen to be perfectly **staggered**

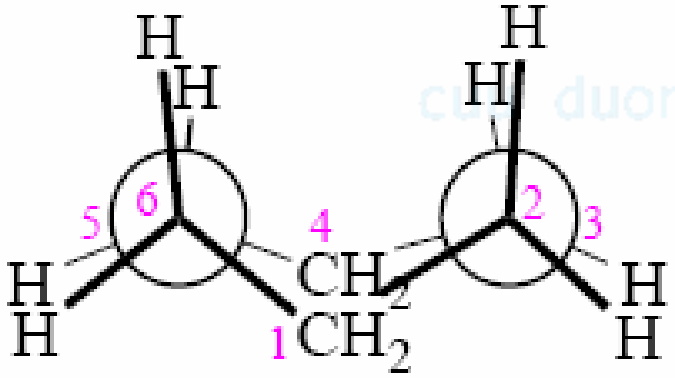


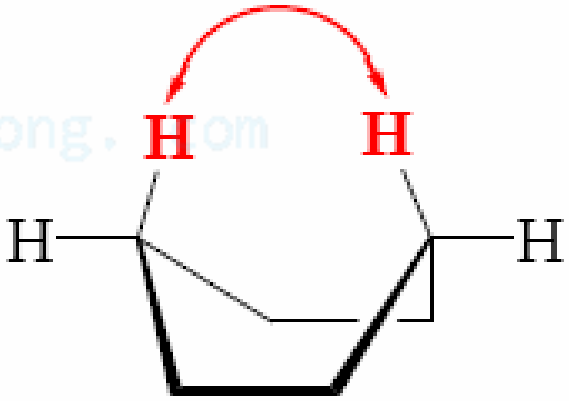
Boat conformation of cyclohexane:

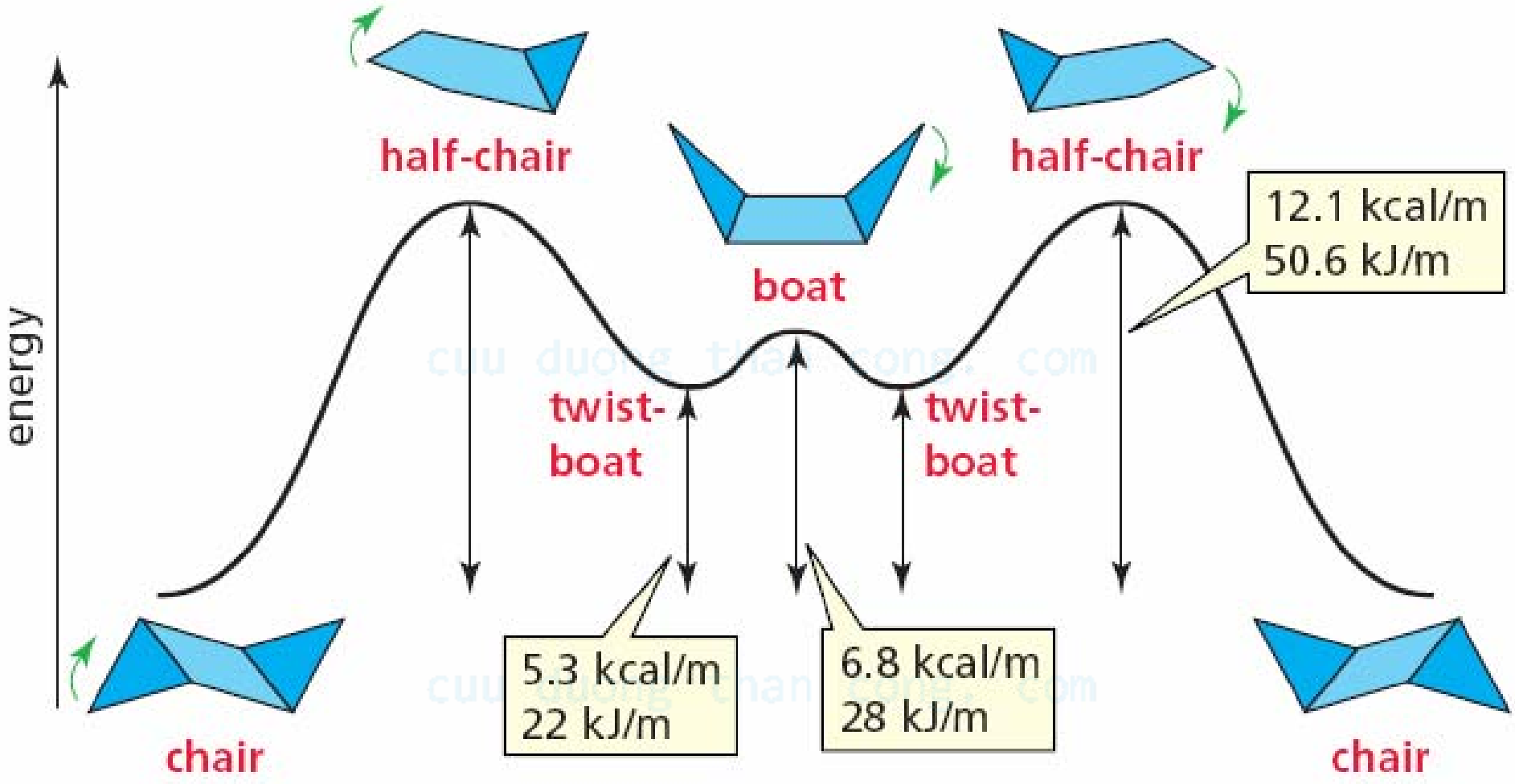




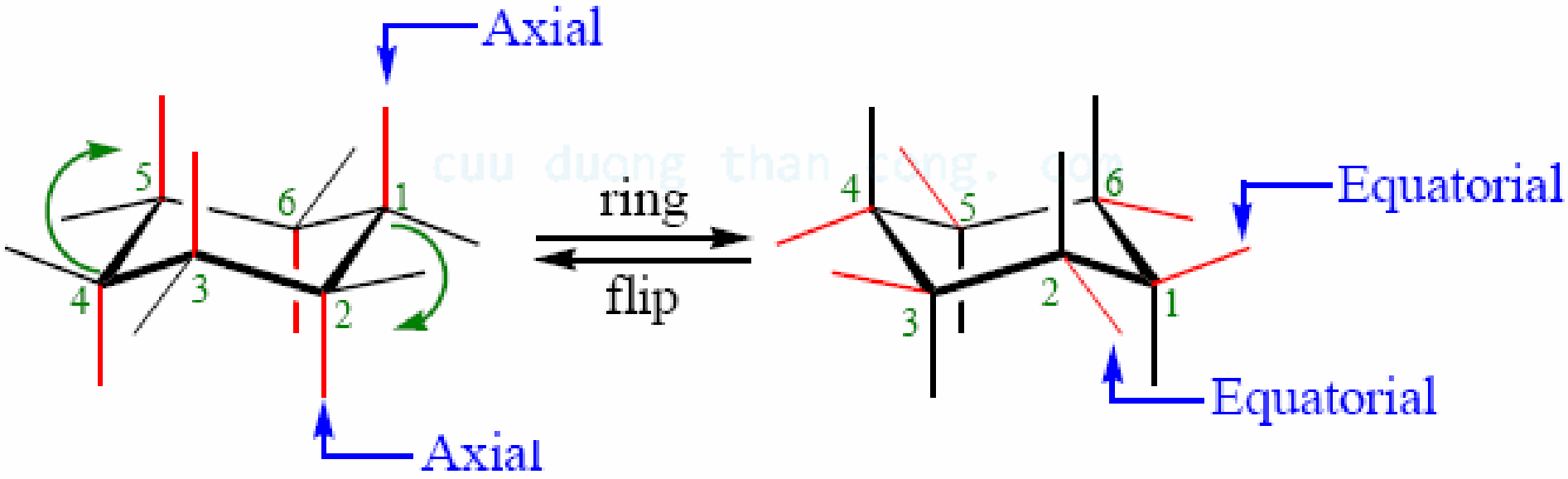
When viewed along the **C—C** bond on either side, the atoms are found to be **eclipsed**





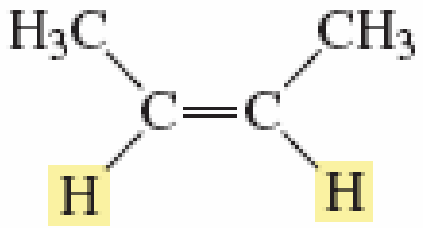

energy
half-chair
boat
half-chair
12.1 kcal/m
50.6 kJ/m
twist-
boat
twist-
boat
5.3 kcal/m
22 kJ/m
6.8 kcal/m
28 kJ/m
chair
chair

The cylohexane ring rapidly flips back and forth between two *equivalent* chair conformation via partial rotations of C—C bonds

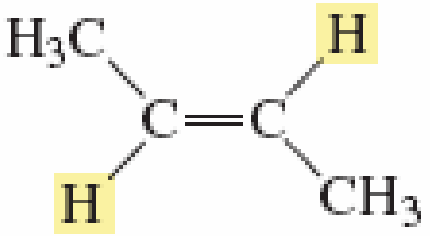


When the ring flips, all of the bonds that were axial become equatorial and vice versa

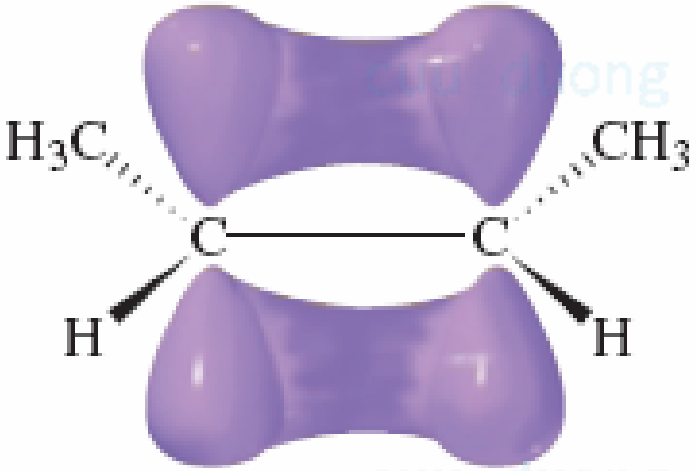
GEOMETRIC ISOMERS



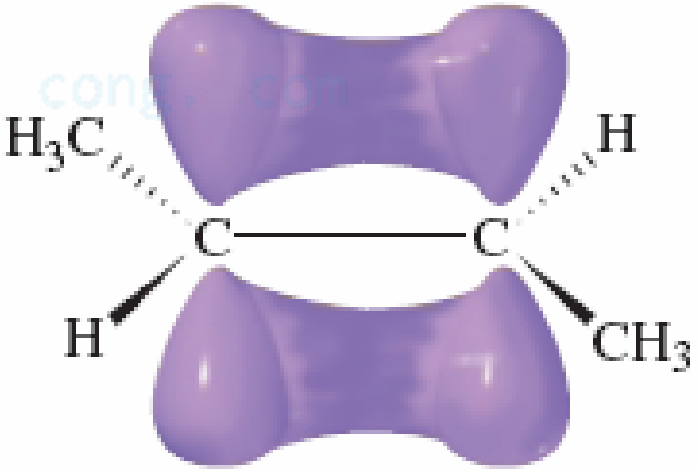
cis-2-butene



trans-2-butene



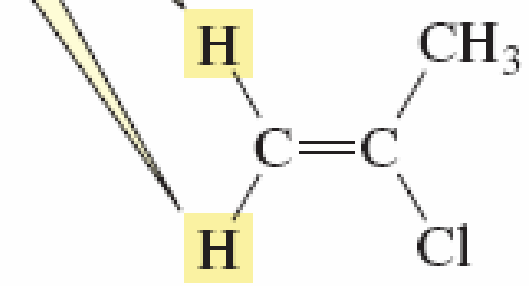
cis isomer

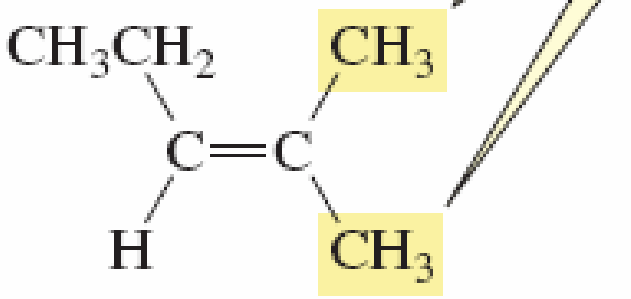


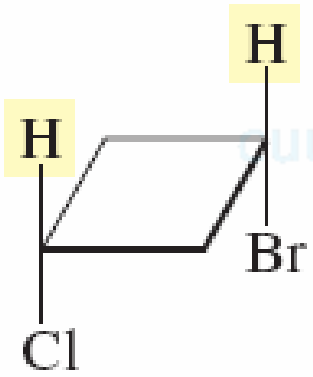
trans isomer

There is no rotation around the C=C bond

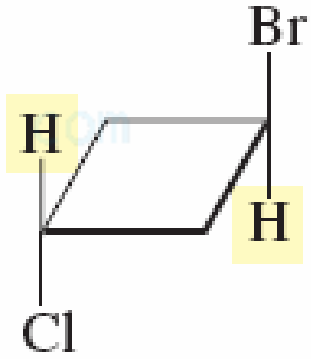
cis and trans isomers are not possible for these compounds because two substituents on an sp^2 carbon are the same



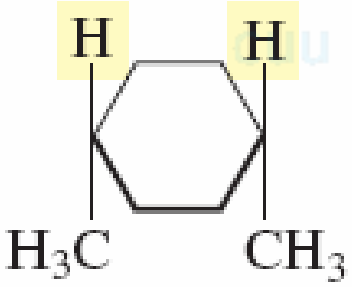




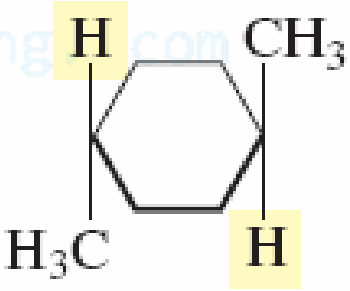
cis-1-bromo-3-chlorocyclobutane



trans-1-bromo-3-chlorocyclobutane

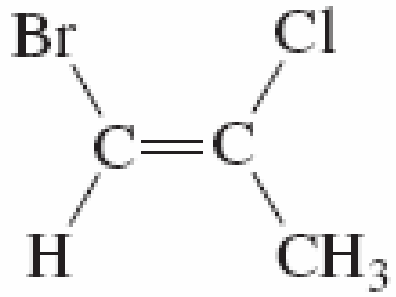


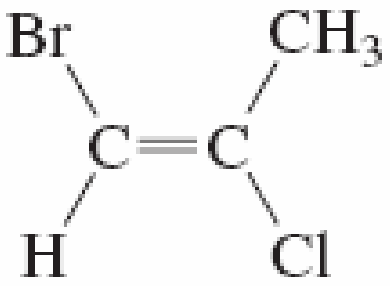
cis-1,4-dimethylcyclohexane



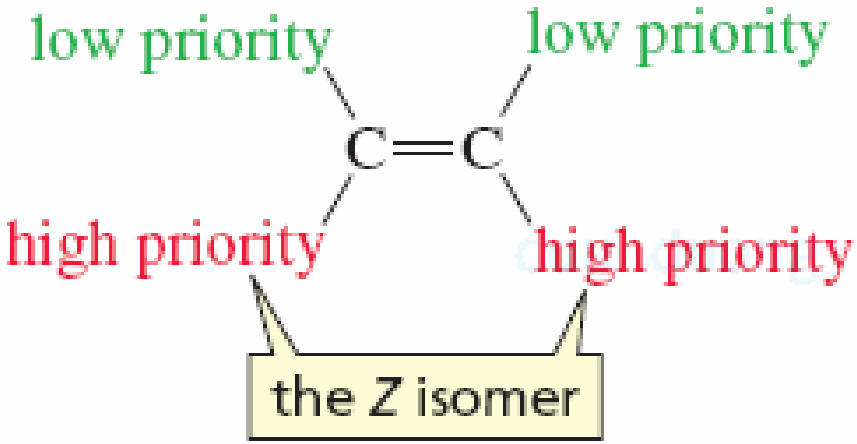
trans-1,4-dimethylcyclohexane

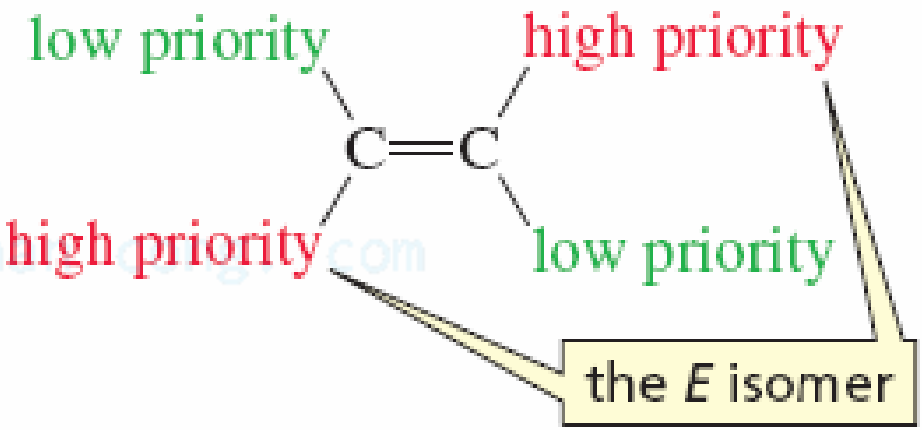
The *E,Z* system of nomenclature



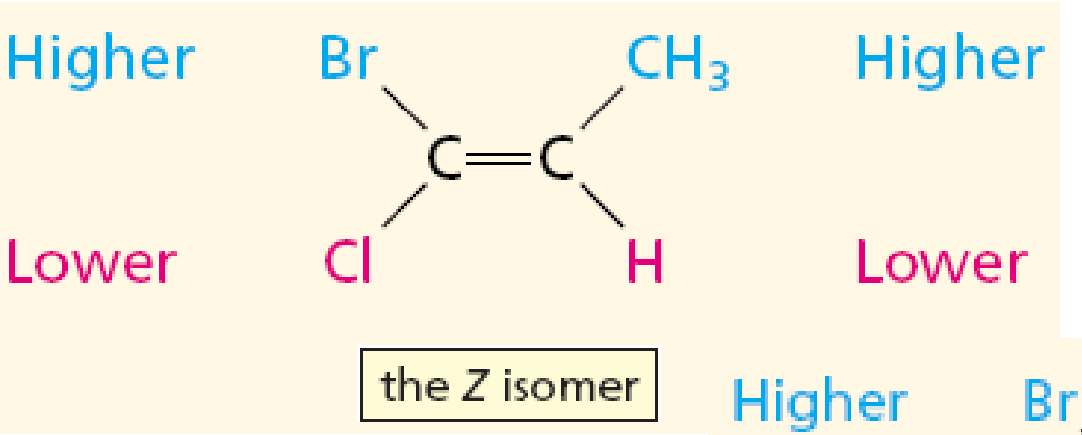


Which isomer is cis and which is trans?

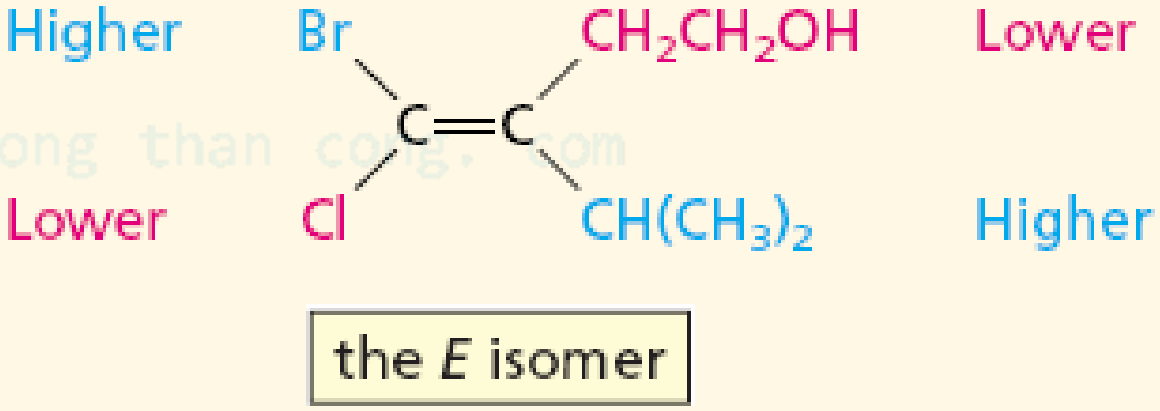




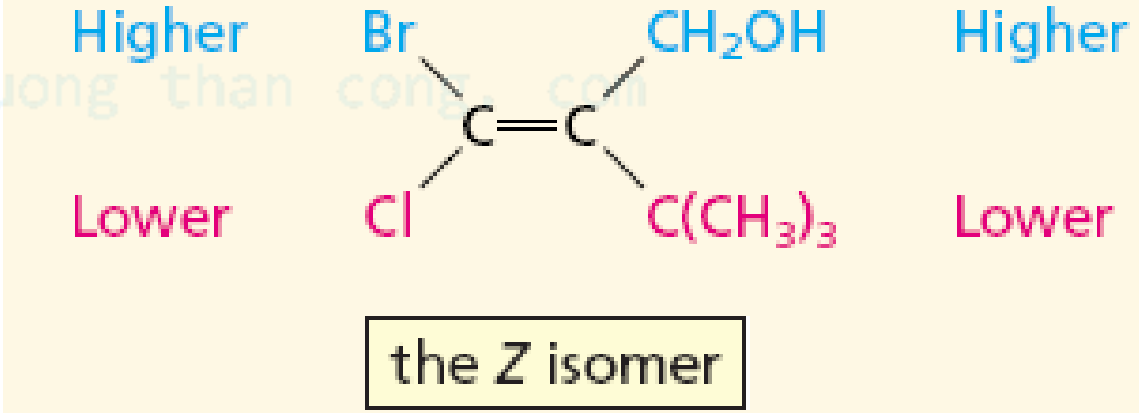
Cahn-Ingold-Prelog priority rules



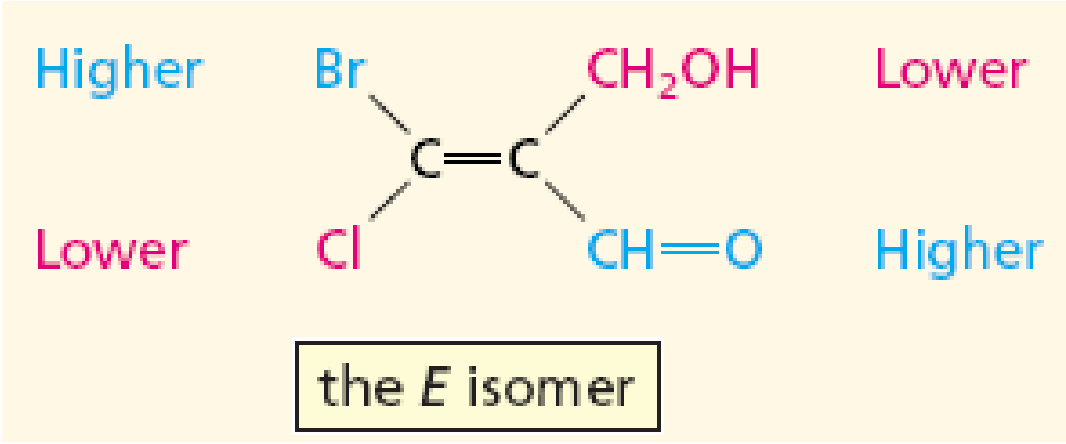
Rule 1

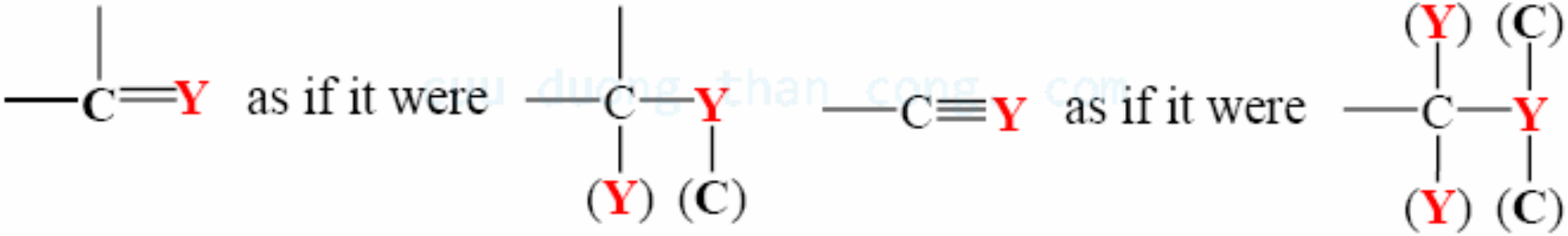


Rule 2

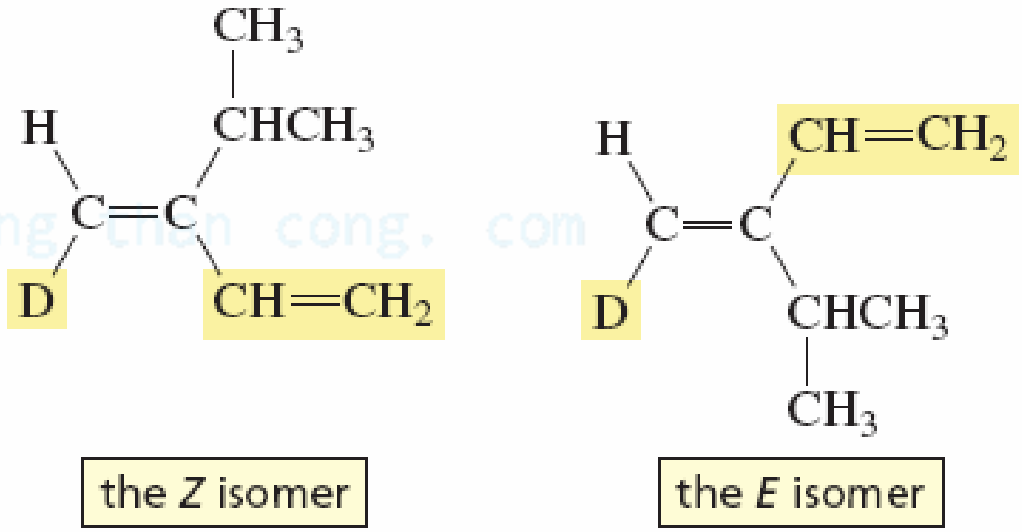


Rule 3


Higher
Br
CH2OH
Lower
C=C
Lower
Cl
CH=O
Higher
the E isomer


C=Y
as if it were
C—Y
(Y) (C)
C≡Y
as if it were
(Y) (C)
C—Y
(Y) (C)

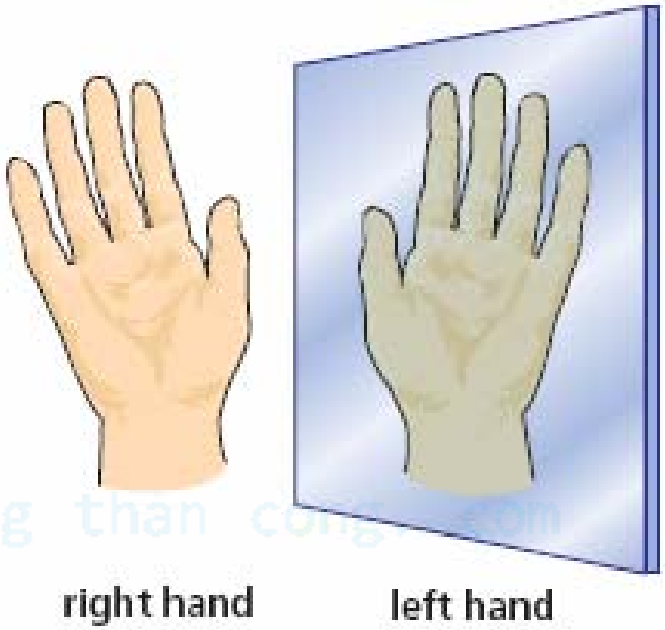
Rule 4


CH3
H
CHCH3
C=C
D
CH=CH2
the Z isomer
H
CH=CH2
C=C
D
CHCH3
CH3
the E isomer

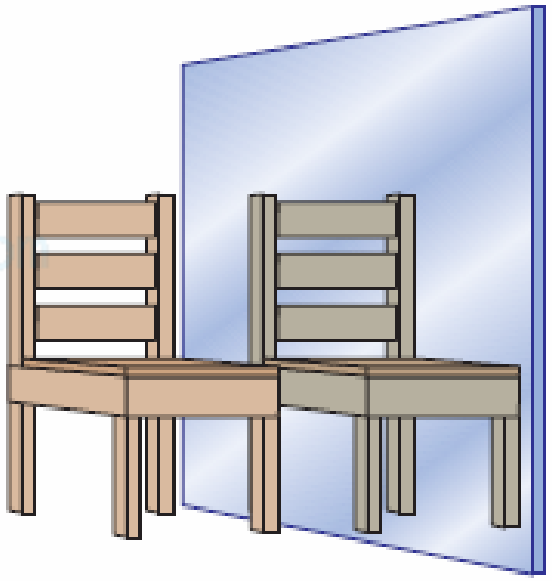
OPTICAL ISOMERS

A chiral opbject

Nonsuperimposable mirror image



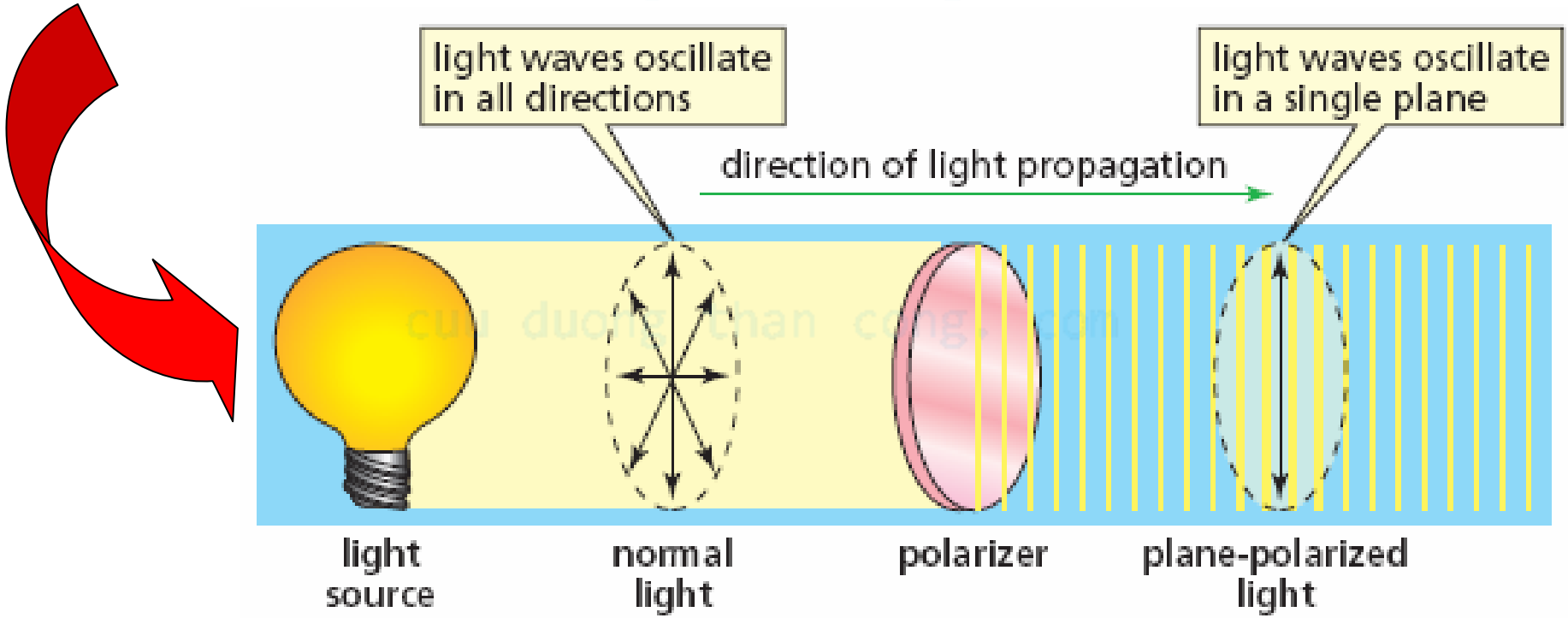
An achiral object



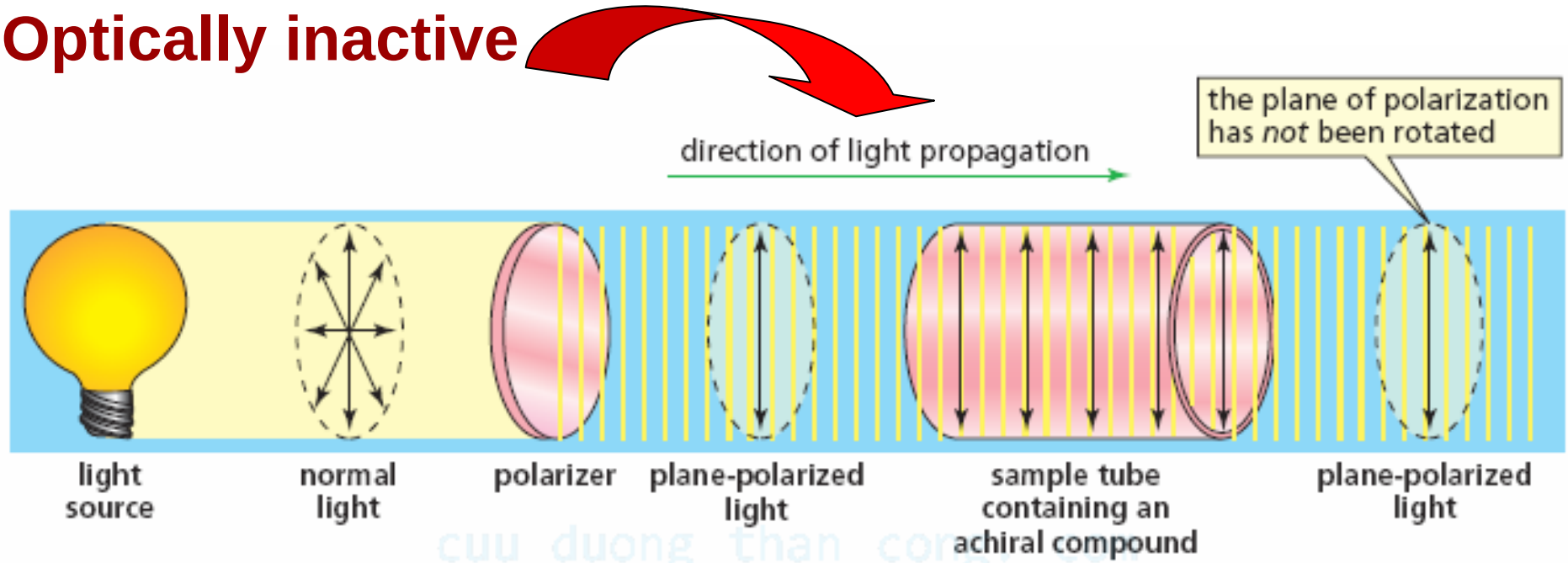
OPTICAL ISOMERS

Optical isomers are configurational isomers which are able to rotate plane-polarized light clockwise or anticlockwise

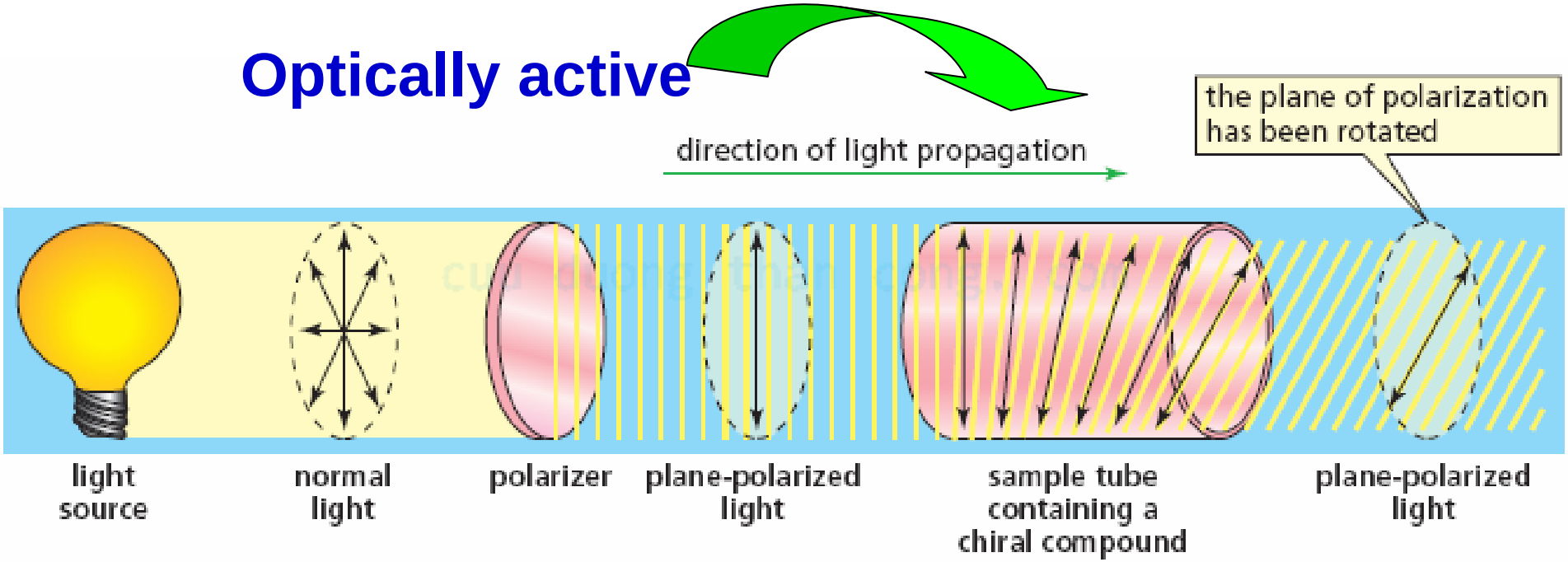
plane-polarized light



Optically inactive

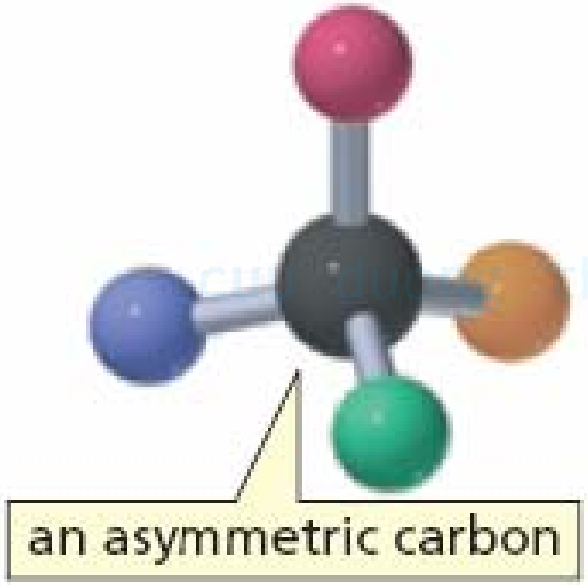


Optically active

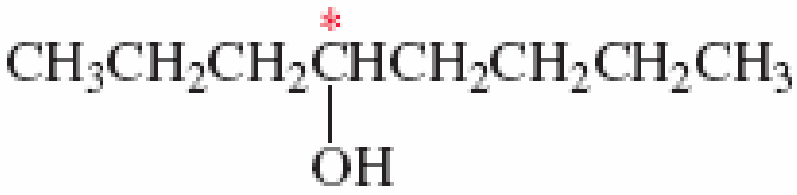


Asymmetric carbon

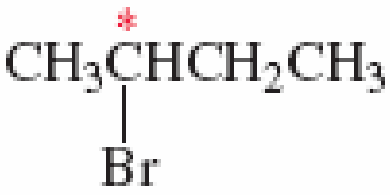
An asymmetric carbon is a carbon atom that is bonded to 4 different groups



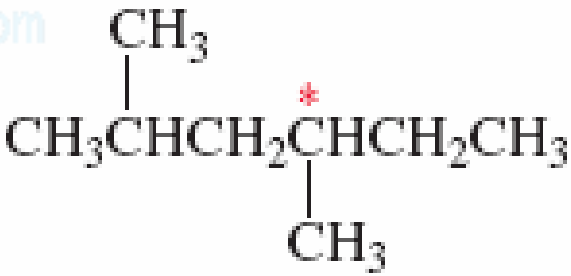
Optically active (chiral)



4-octanol

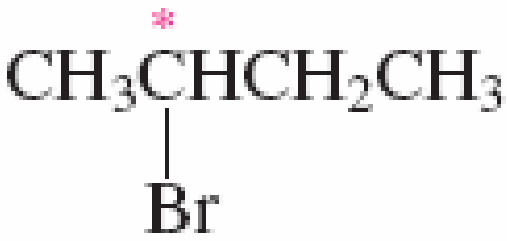


2-bromobutane

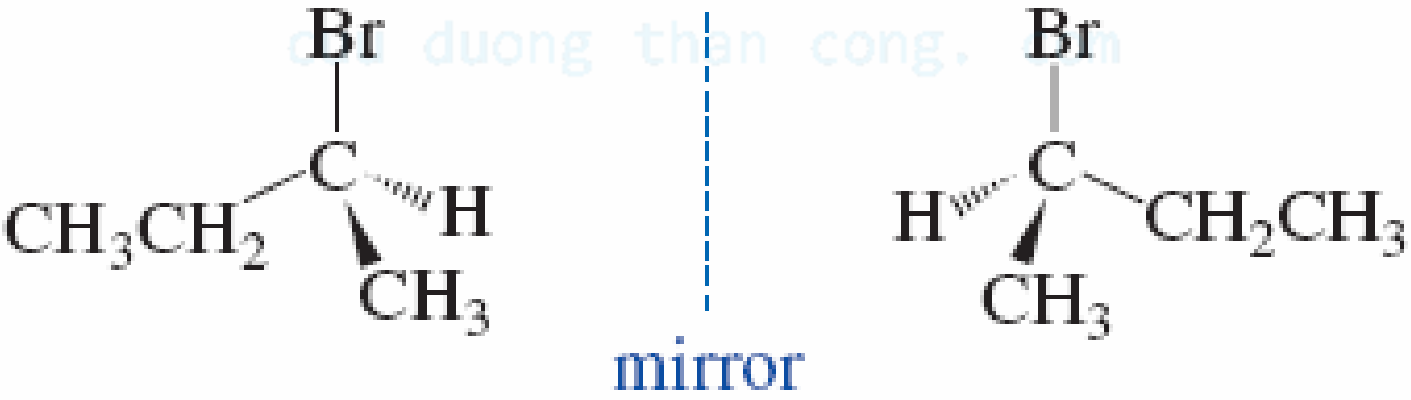


2,4-dimethylhexane

Isomers with one asymmetric carbon



2-bromobutane



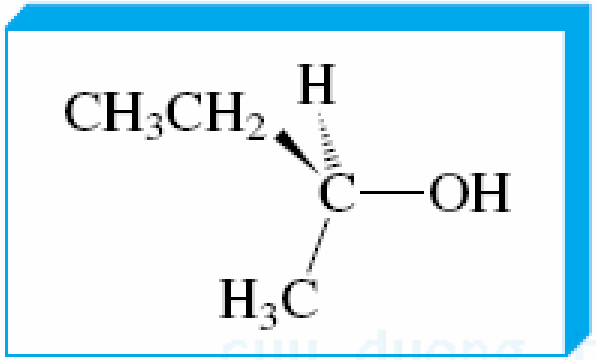
the two isomers of 2-bromobutane

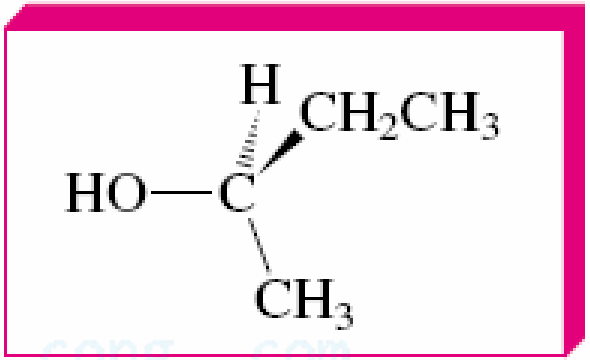
enantiomers

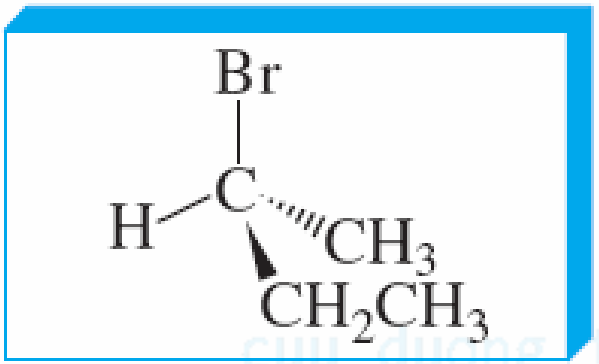
Nonsuperimposable mirror-image molecules are called enantiomers

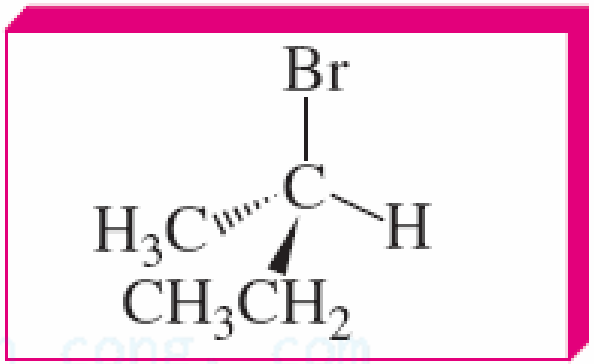
Drawing enantiomers

Using perspective formulas:







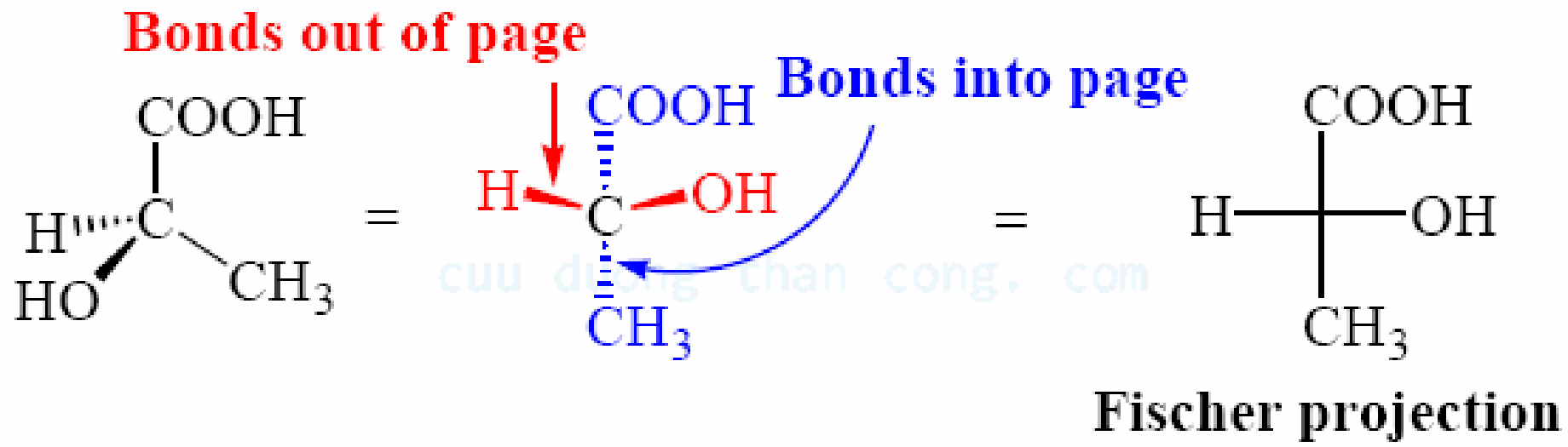


Convention

- **2 bonds in the paper plane**
- **1 bond as a solid wedge**
- **1 bond as a hatched wedge**

Drawing enantiomers

Using Fisher Projection formulas:



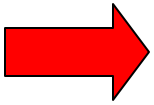
Convention ➡

- **Carbon chain is drawn along the vertical line**
- **Vertical lines: bonds going into the page**
- **Horizontal lines: bonds coming out of the page**

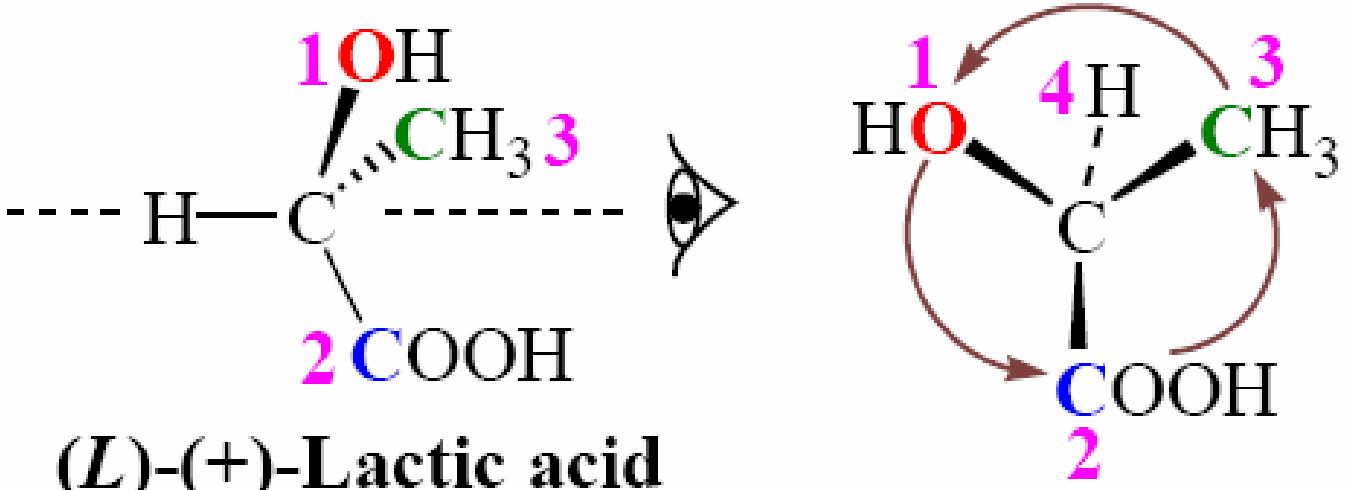
NAMING ENANTIOMERS

ABSOLUTE CONFIGURATION: *R-S* SYSTEM

Convention for perspective formulas

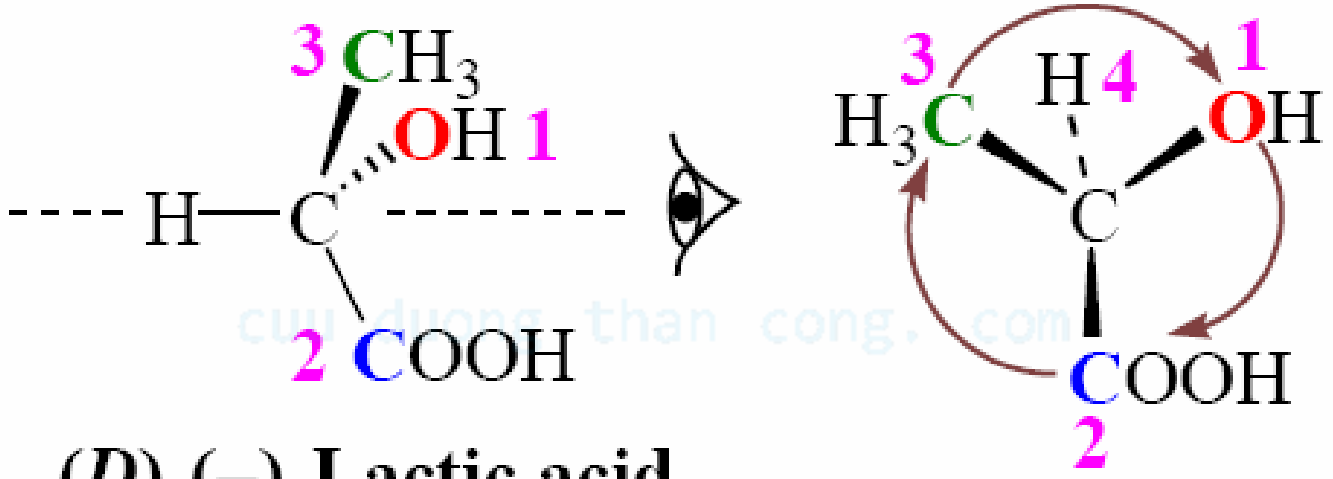


- **Using Cahn-Ingold-Prelog rules**
- **View the molecule with the lowest priority group pointing away**
- **If the direction from highest priority group to the next is clockwise: *R***
- **If the direction is anticlockwise:*S***



(*L*)-(+)-Lactic acid

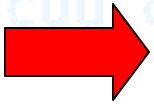
***S* configuration**



(*D*)-(–)-Lactic acid

***R* configuration**

Convention for Fisher Projection formulas

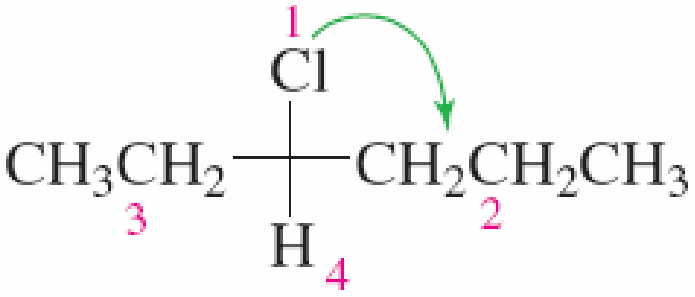


- **Using Cahn-Ingold-Prelog rules**
- **When the lowest priority group is <u>on a vertical bond:</u>**

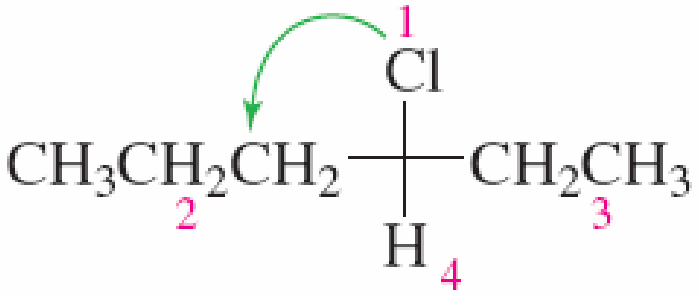
  + If the direction from highest priority group to the next is clockwise: *R*

  + If the direction is anticlockwise:*S*
- **When the lowest priority group is <u>on a horizontal bond:</u>**

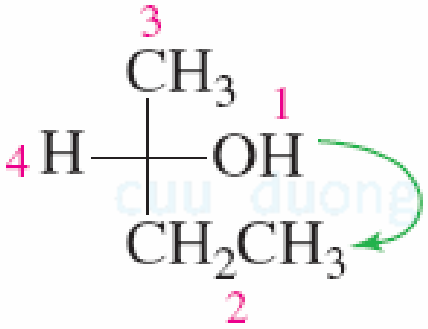
  + opposite answers



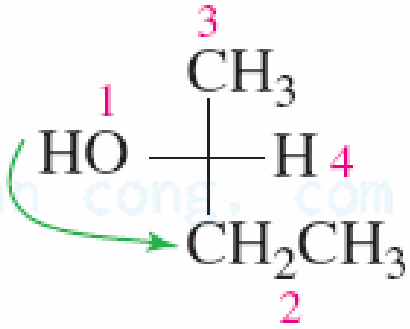
(*R*)-3-chlorohexane



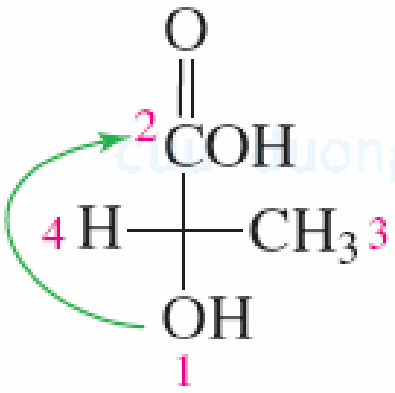
(*S*)-3-chlorohexane



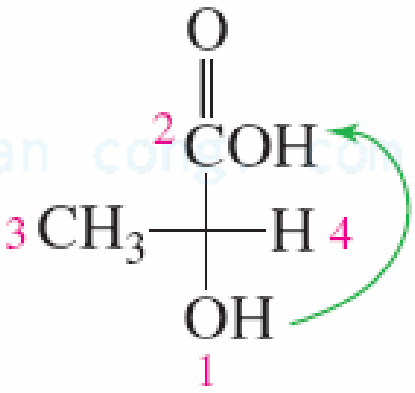
(*S*)-2-butanol



(*R*)-2-butanol



(*S*)-lactic acid

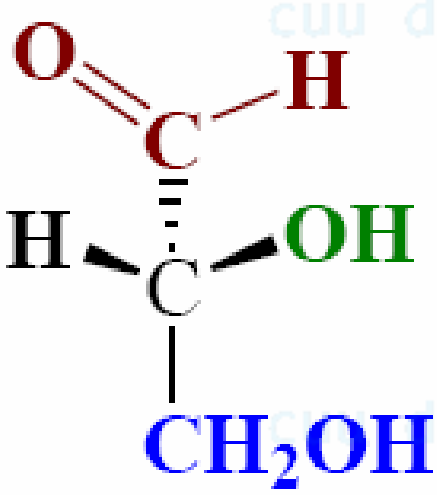


(*R*)-lactic acid

NAMING ENANTIOMERS

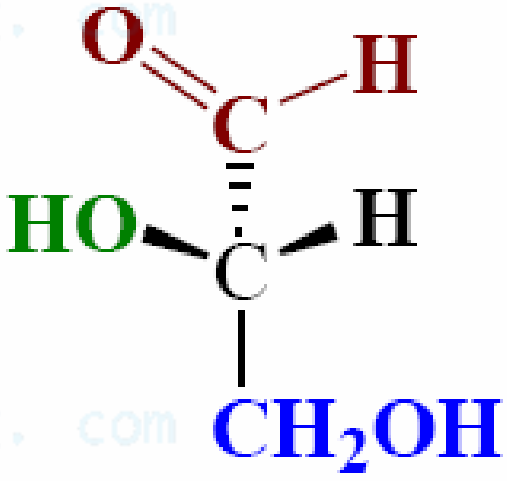
RELATIVE CONFIGURATION: *D-L* SYSTEM

Glyceraldehyde: the standard compound for chemical correlation of configuration



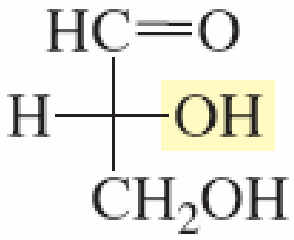
D-Glyceraldehyde

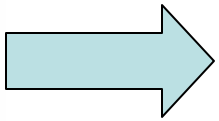
and

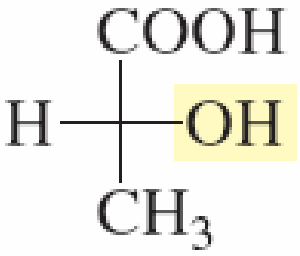


L-Glyceraldehyde

D-L system is only useful for naming sugars & aminoacids

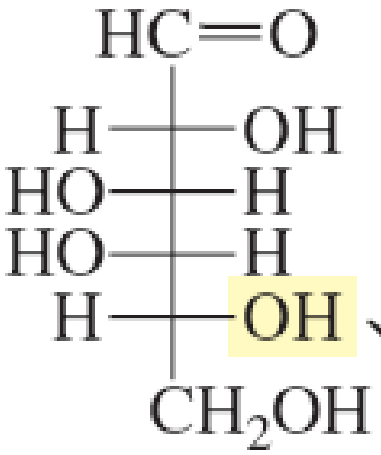






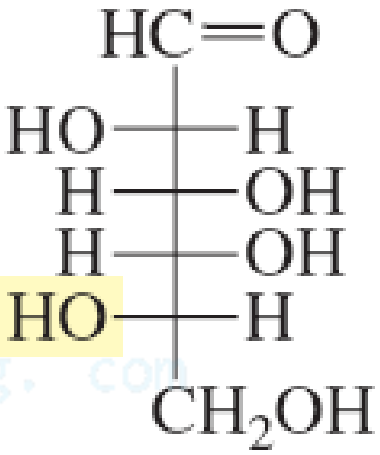
D-(+)-glyceraldehyde

D-(–)-lactic acid



D-galactose

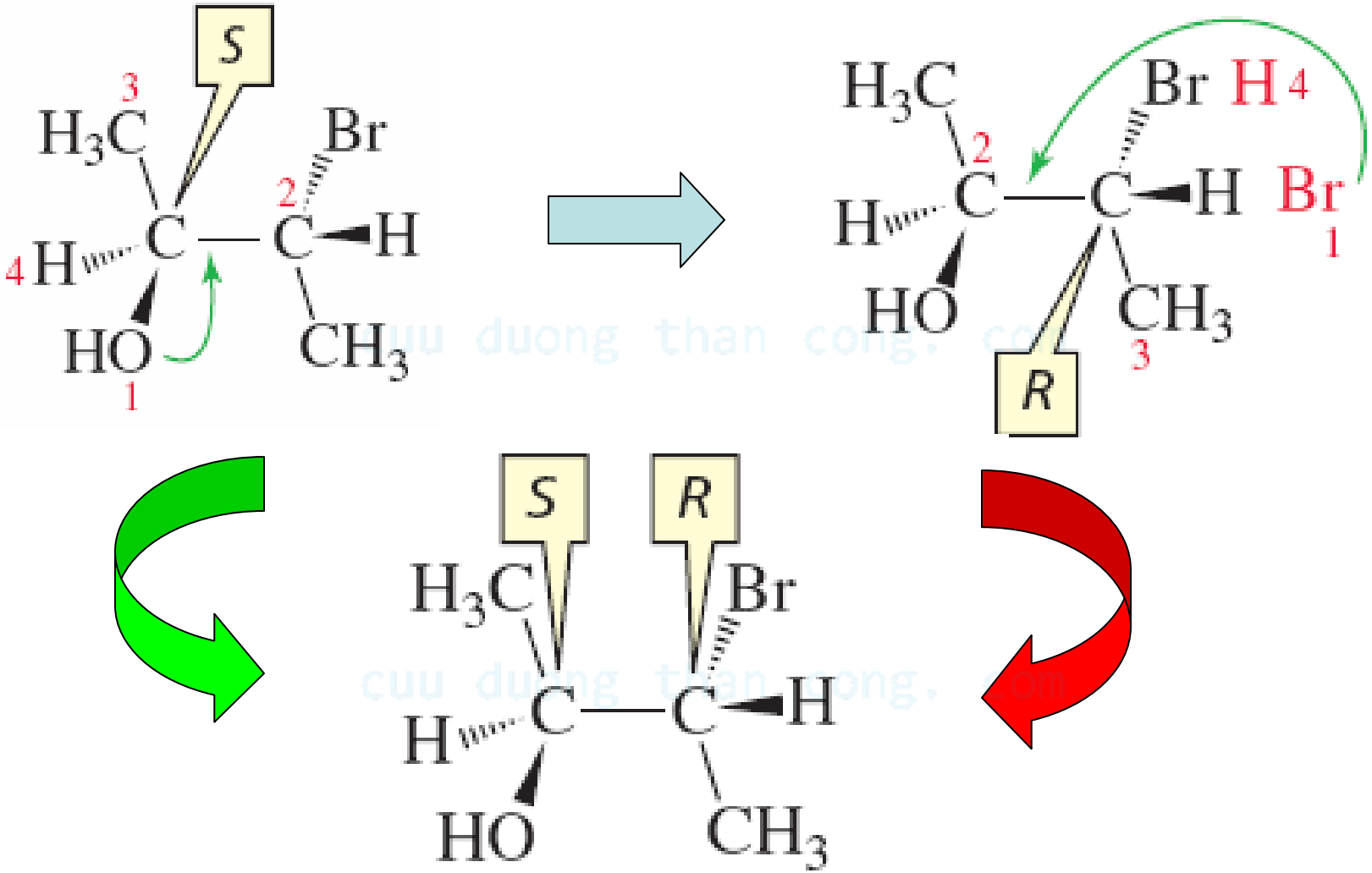
the OH group is on the right



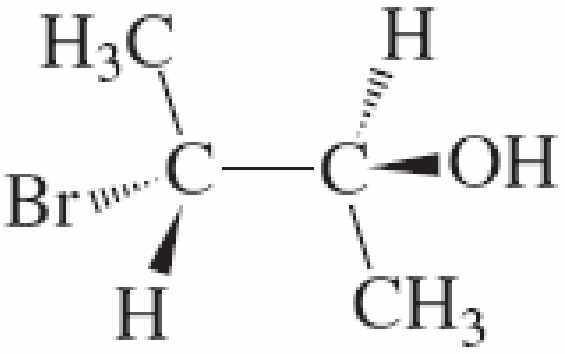
L-galactose

mirror image of D-galactose

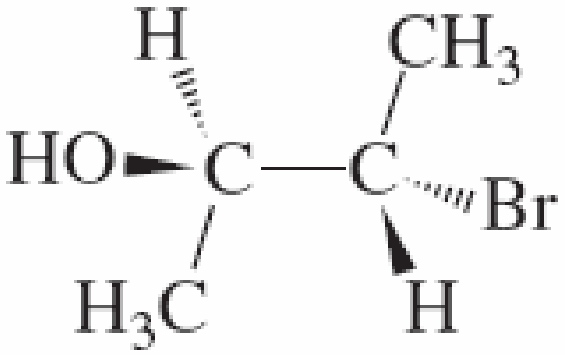
Isomers with more than one asymmetric carbon



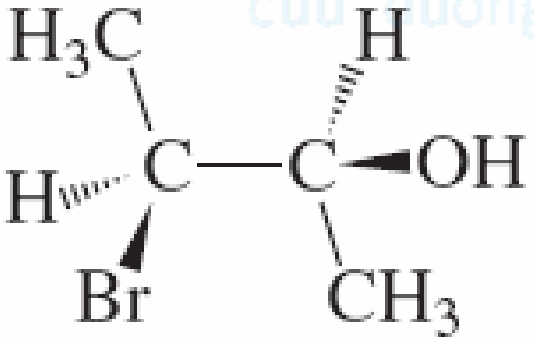
(2*S*,3*R*)-3-bromo-2-butanol



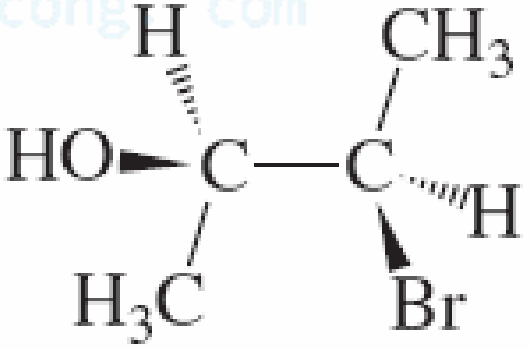
(2*S*,3*R*)-3-bromo-2-butanol



(2*R*,3*S*)-3-bromo-2-butanol

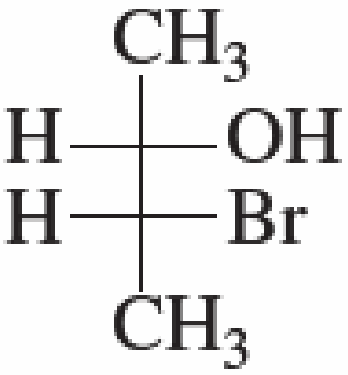


(2*S*,3*S*)-3-bromo-2-butanol

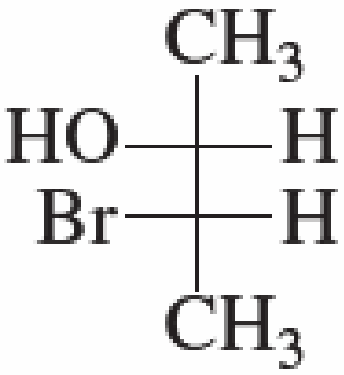


(2*R*,3*R*)-3-bromo-2-butanol

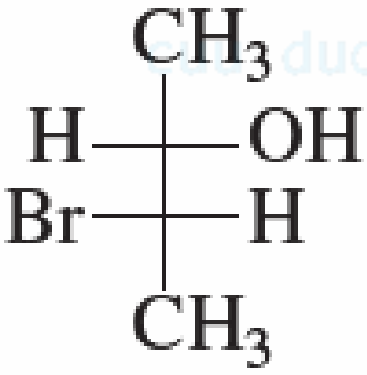
perspective formulas of the stereoisomers of 3-bromo-2-butanol



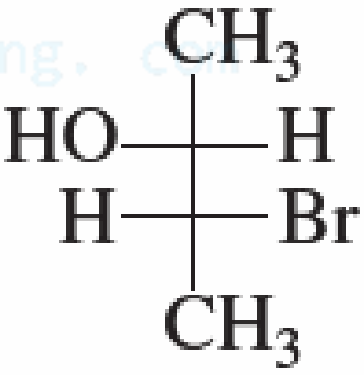
(2*S*,3*R*)-3-bromo-2-butanol



(2*R*,3*S*)-3-bromo-2-butanol



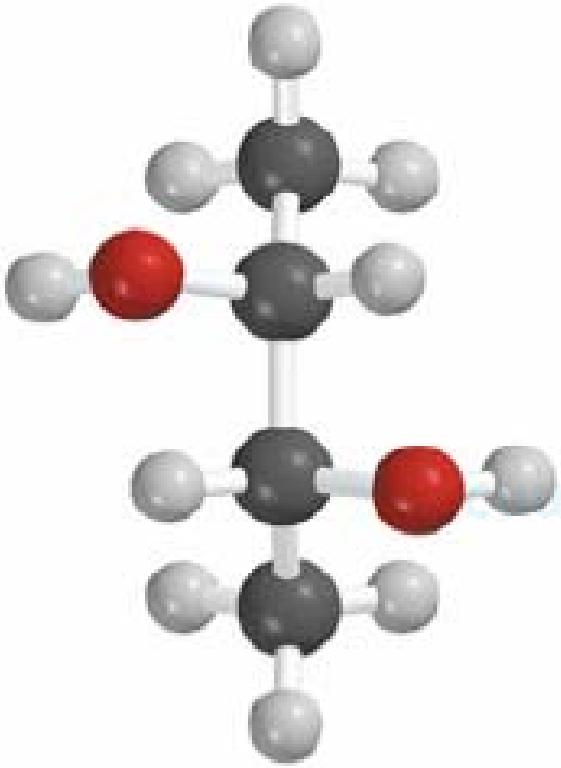
(2*S*,3*S*)-3-bromo-2-butanol

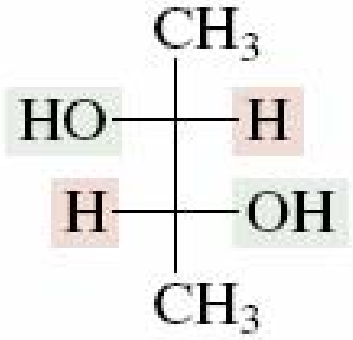


(2*R*,3*R*)-3-bromo-2-butanol

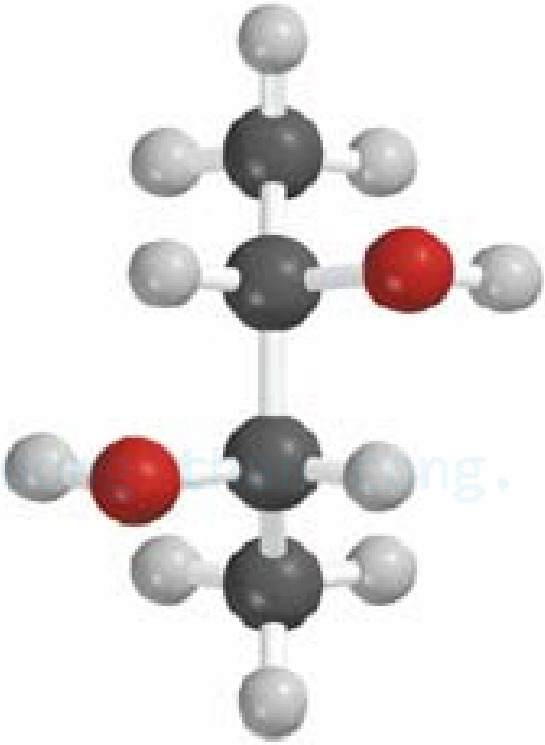
Fischer projections of the stereoisomers of 3-bromo-2-butanol

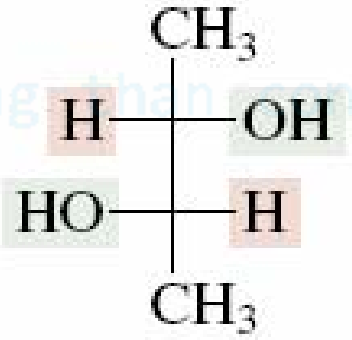
Meso compounds



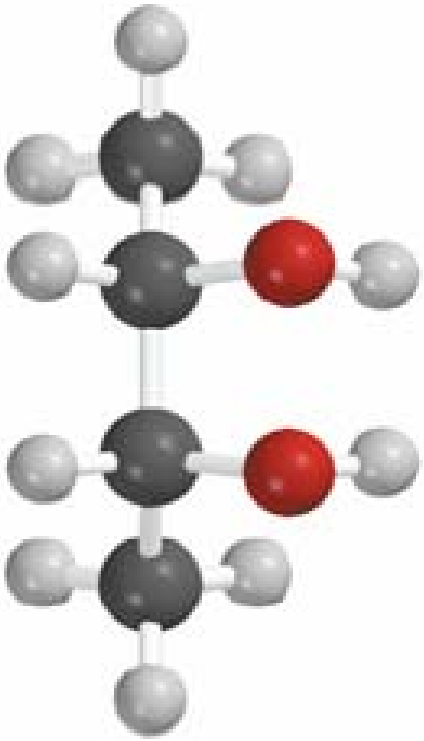


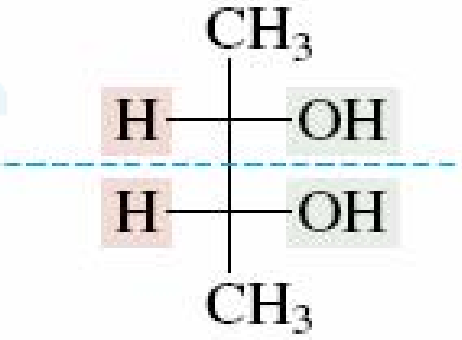
(2*R*,3*R*)-2,3-Butanediol





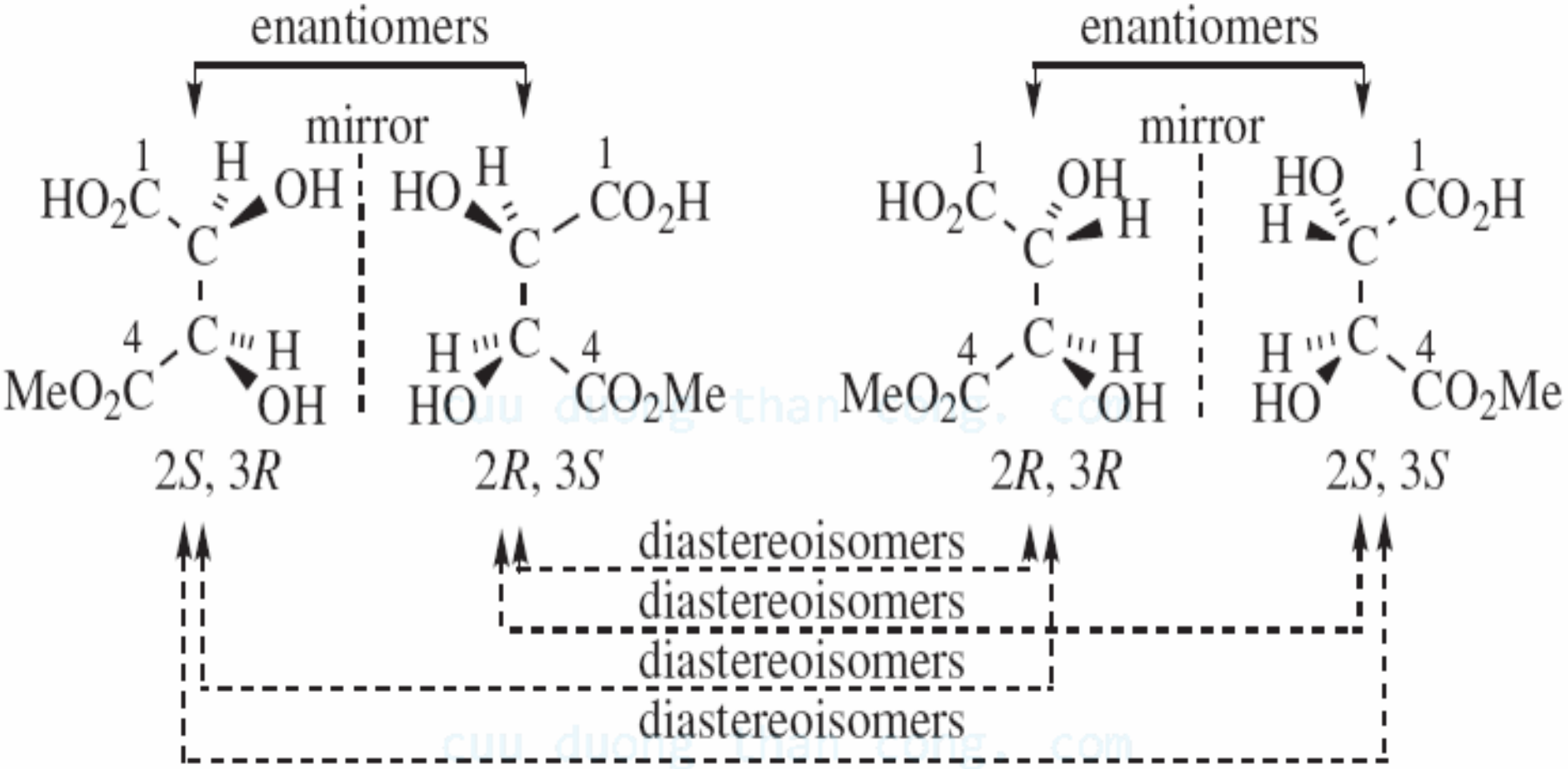
(2*S*,3*S*)-2,3-Butanediol





meso-2,3-Butanediol

Enantiomers *vs* diastereoisomers

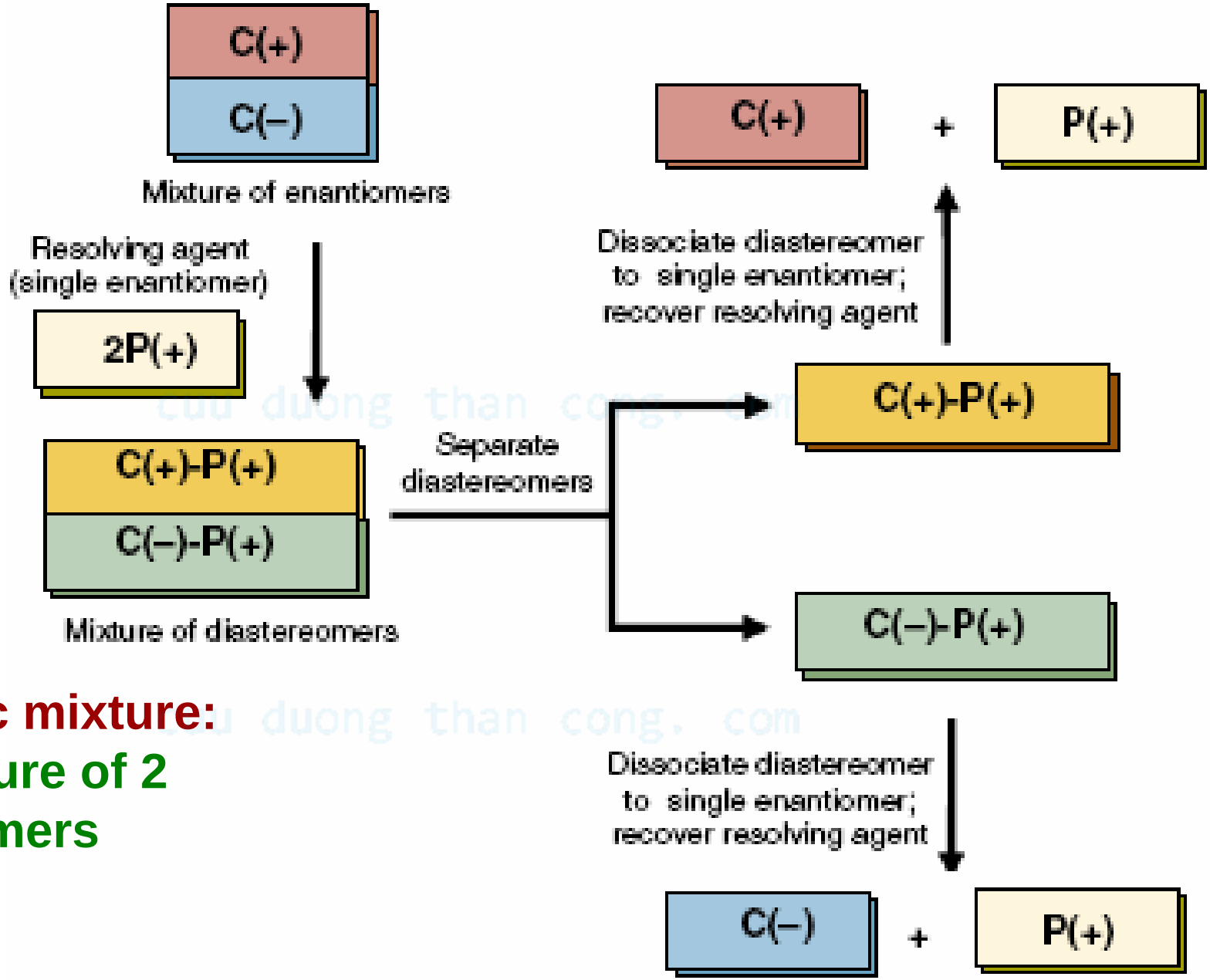


- **Enantiomers: Nonsuperimposable mirror images**
- **Diastereoisomers: not mirror images of each other**

Enantiomers *vs* diastereoisomers

- **Enantiomers normally have identical physical & chemical properties**
- **Enantiomers normally interact differently with other chiral molecules**
- **Diastereoisomers can have different physical & chemical properties**
- **Enantiomers are always chiral**
- **Diastereoisomers can be chiral or achiral (meso compounds)**

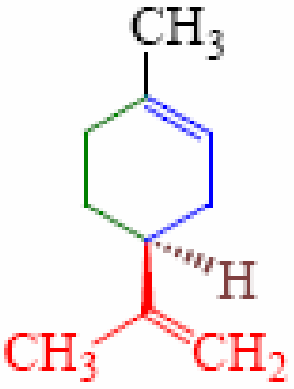
Separating enantiomers



Racemic mixture:
1/1 mixture of 2 enantiomers

CHIRALITY & BIOLOGICAL ACTIVITY

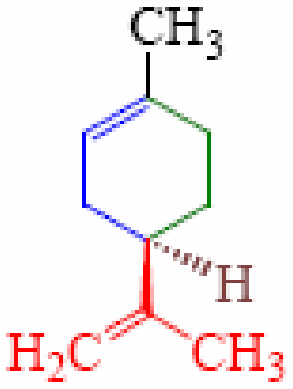
S



lemon odor

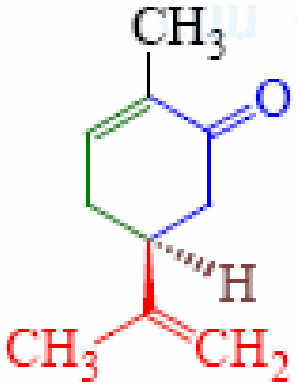
Limonene

R



orange odor

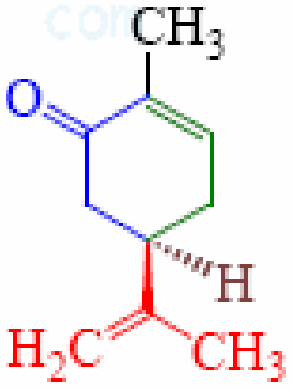
S



spearmint fragrance

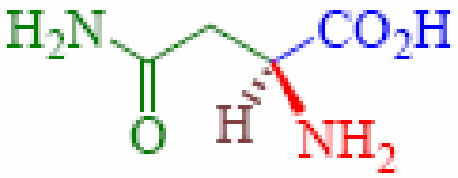
Carvone

R



caraway seed odor

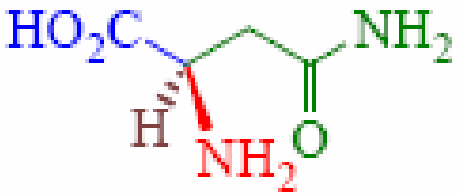
S



bitter taste

Asparagine

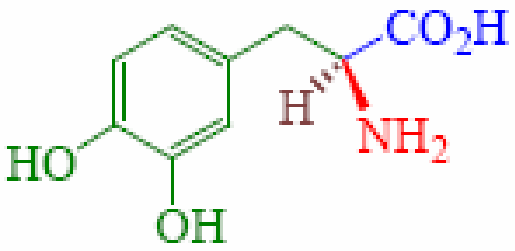
R



sweet taste

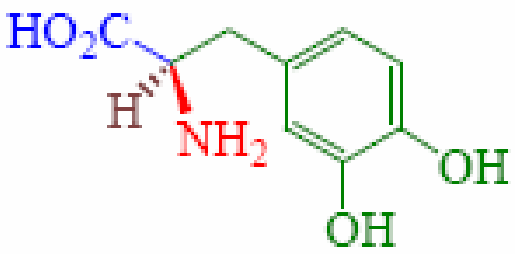
CHIRALITY & BIOLOGICAL ACTIVITY

S



Anti-Parkinson's disease

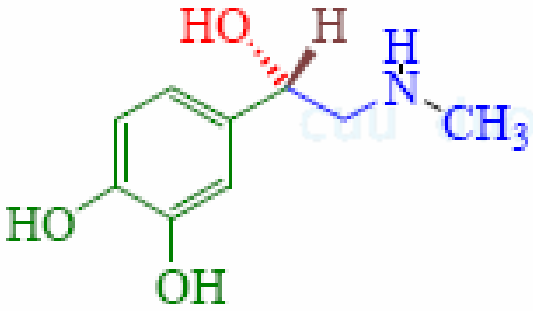
Dopa



Toxic

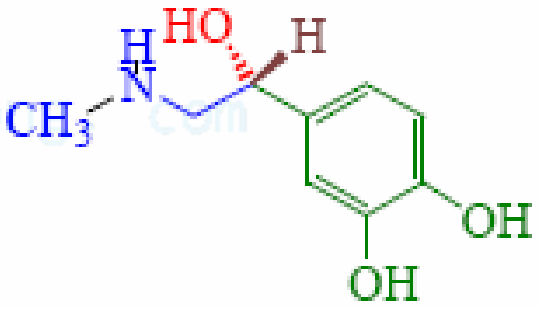
R

S



Toxic

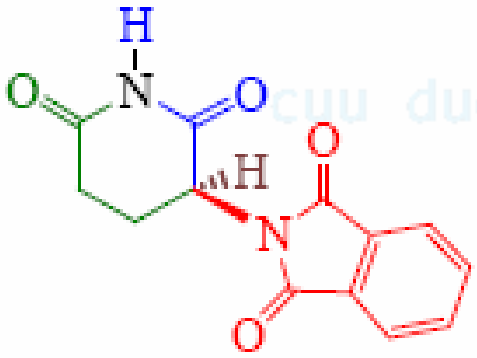
Epinephrine



hormone

R

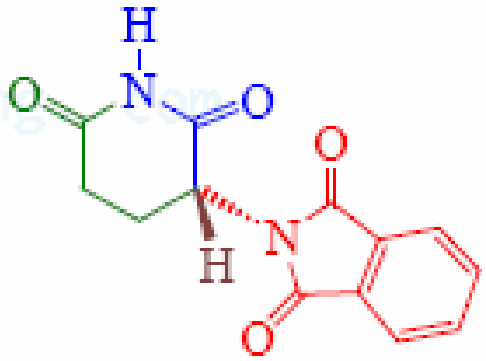
S



teratogenic activity

Thalidomide

sedative, hypnotic



causes **NO** deformities

R