台灣大學開放式課程

# 有機化學乙

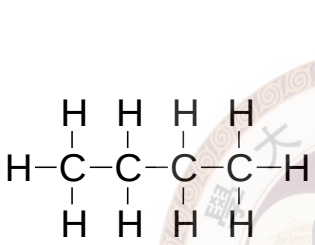
蔡蘊明　教授

# Chapter S Stereochemistry (立體化學): chiral molecules (掌性分子)

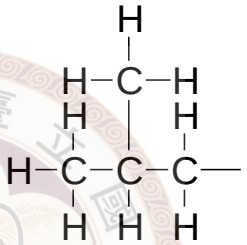


## ※ Isomerism

### ◎ constitutional isomers



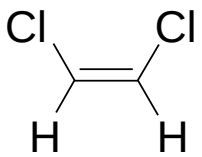
butane



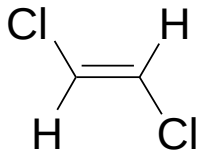
isobutane

分子式相同但鍵結方式不同

### ◎ stereoisomers (立體異構物)



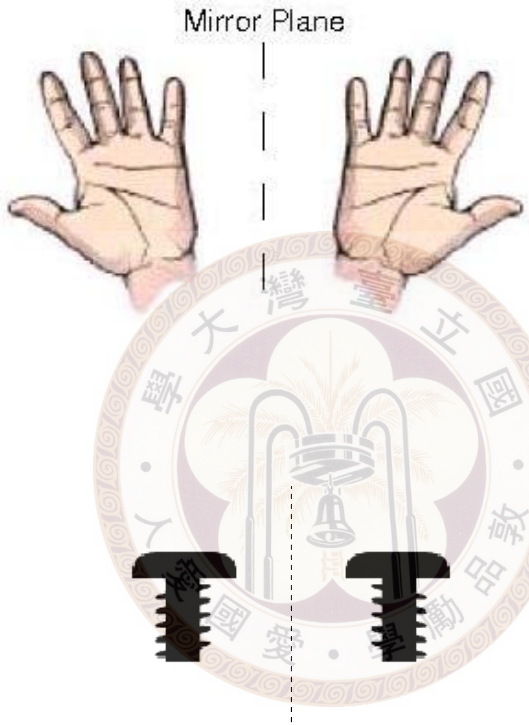
*cis*-1,2-dichloroethene

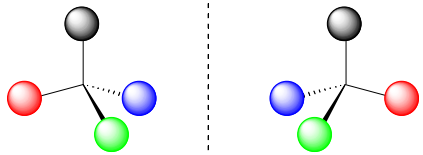


*trans*-1,2-dichloroethene

分子式相同，鍵結方式相同，但是在空間中的安排方式不同

# ※ 鏡像與掌性(chirality)

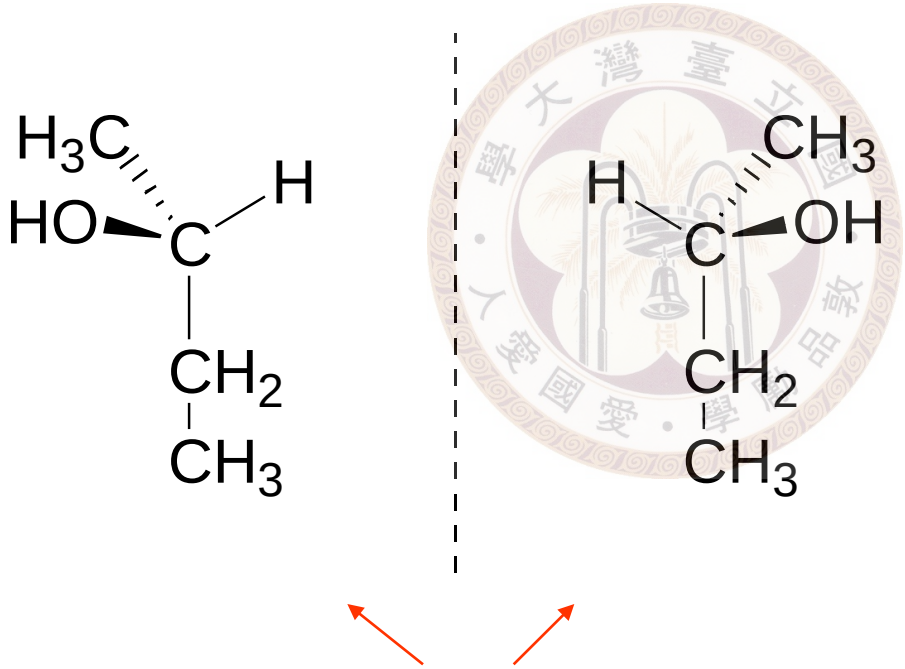


# ※ Enantiomers (鏡像異構物；對掌體 )

$CH_3CHCH_2CH_3$ (OH) 2-butanol

此分子具有掌性
(this molecule is chiral)




Two mirror images not superposable

The two mirror images are enantiomers
(鏡像異構物；對掌異構物)

# ◎ Chiral molecule

A molecule that is not superposable (重疊) on its mirror image is called a chiral molecule

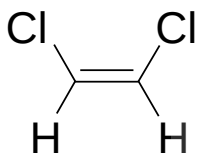
反之則稱為achiral

Enantiomers are differed by the arrangement of the groups in space

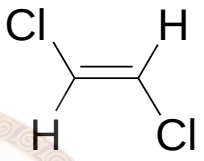
⟹ Enantiomers are stereoisomers

◎ Stereoisomers that are not enantiomers

⟶ Diastereomers (非鏡像異構)




*cis*-1,2-dichloroethene



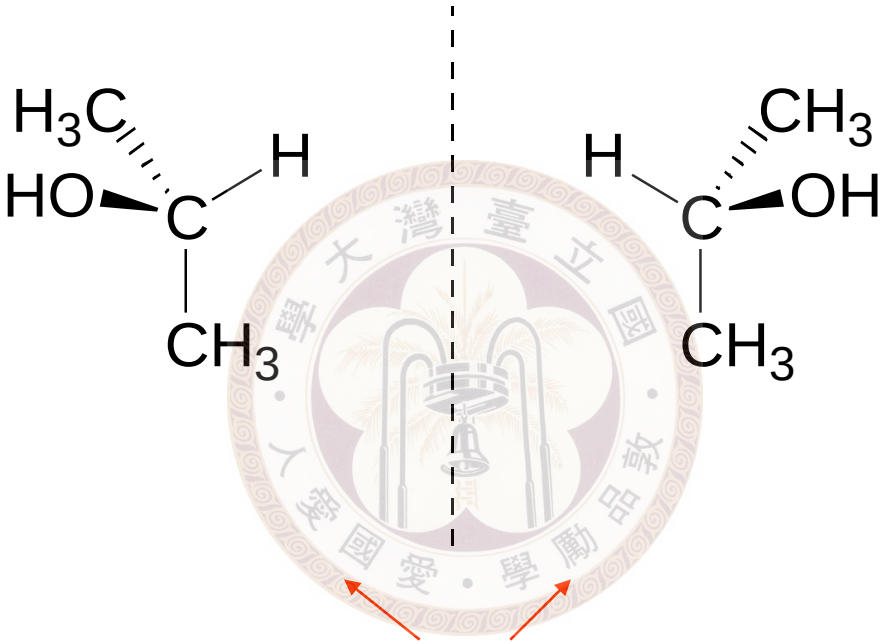

*trans*-1,2-dichloroethene

diastereomers

stereoisomers { enantiomers

diastereomers

Q: $CH_3CHCH_3$ (OH) 2-propanol Chiral?



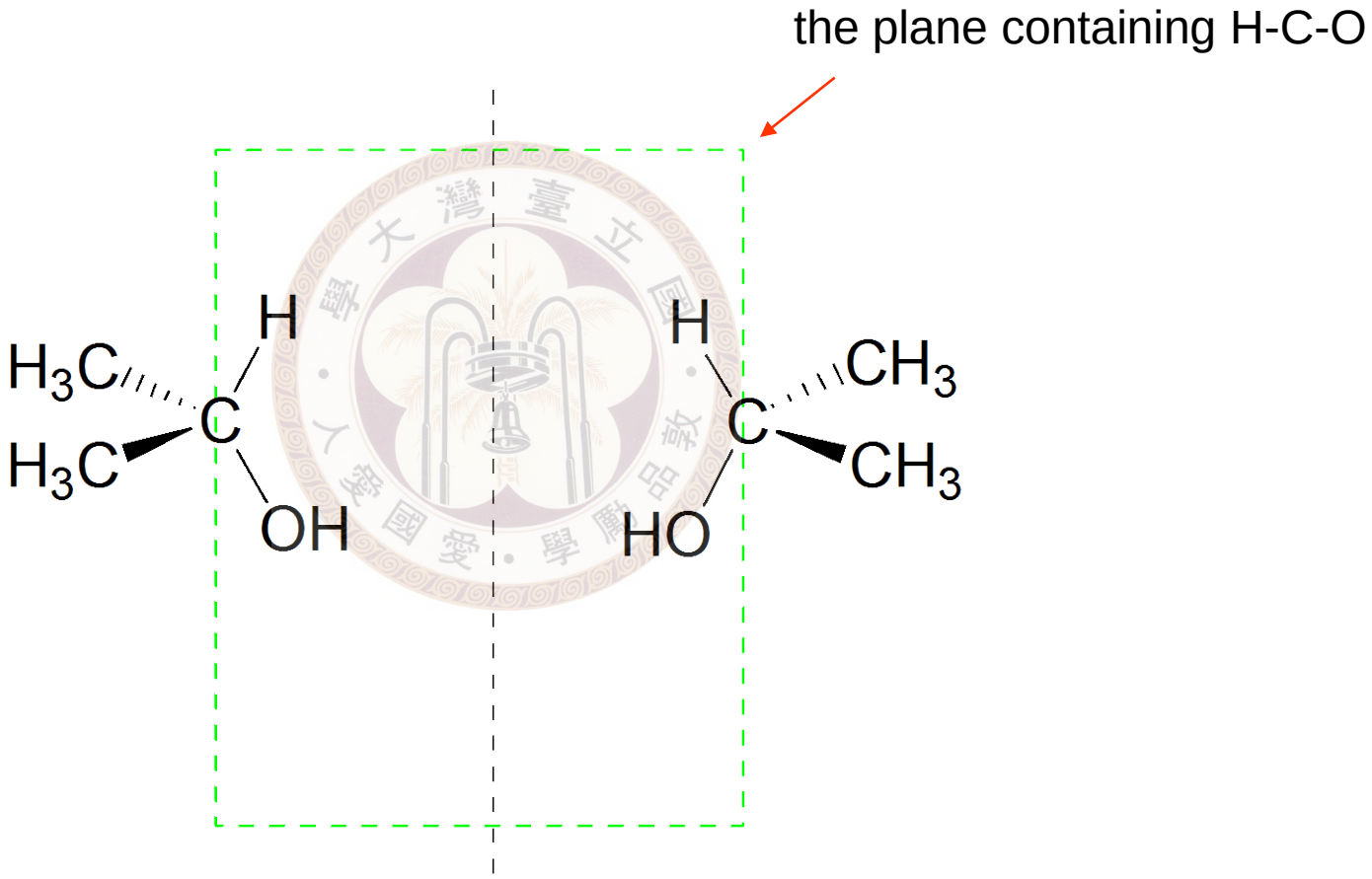

superposable

⇒ same molecule

⇒ achiral

★ In fact, 2-propanol has a plane of symmetry

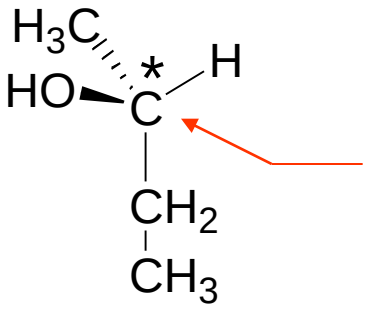
⟹ must be achiral



# Why is 2-butanol chiral?

The presence of a tetrahedral carbon
with four different groups attached

⟹ the presence of a stereocenter
or a chiral center (chirality center)
or a stereogenic center
or an asymmetric center



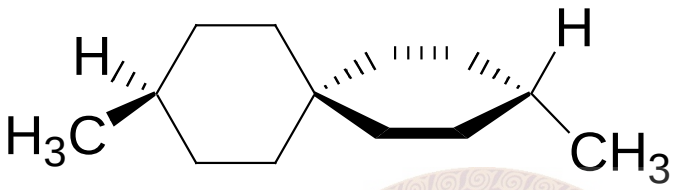

chiral center, 常用星號標記

★ with one stereocenter → must be chiral

with more than one stereocenter → may not be chiral

with no chiral center → may be chiral

Problem for practice:

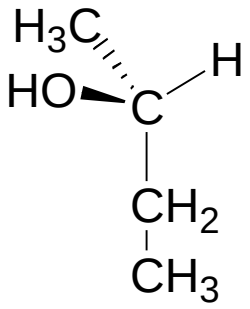



Is there any chiral center?
Is it chiral?

Cahn-Ingold-Prelog system (*R,S*-system):

<1> Priority of the four groups on chiral center

- 先比第一個接在chiral center上的原子序數
  原子序高者priority高(同位素質量高者優先)

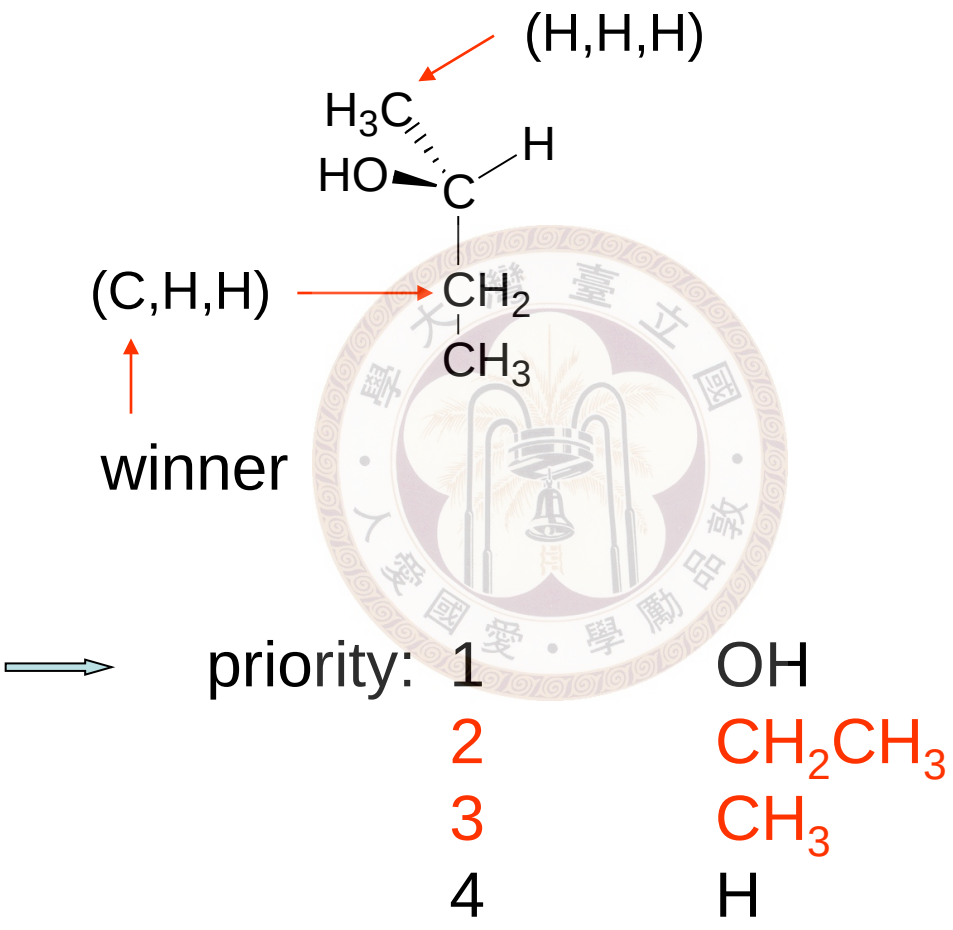



four atoms: O, C, C, H

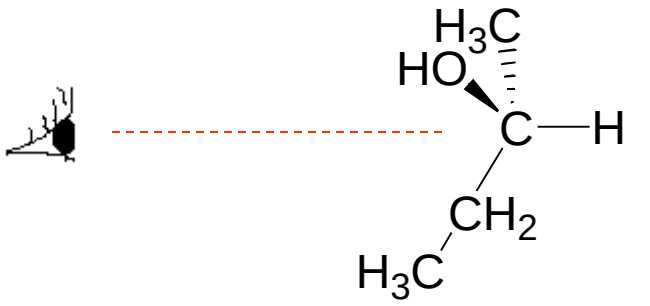
highest

lowest

- 第一個原子相同時，比其上priority高者依此原則一直比到分出高下

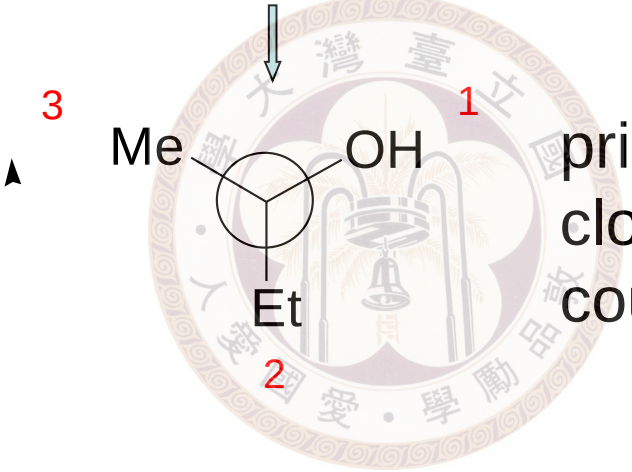


<2>

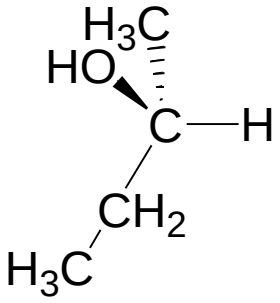



priority最低者
反對觀察者

<3>




priority 1→2→3
clockwise: (*R*)
counterclockwise: (*S*)

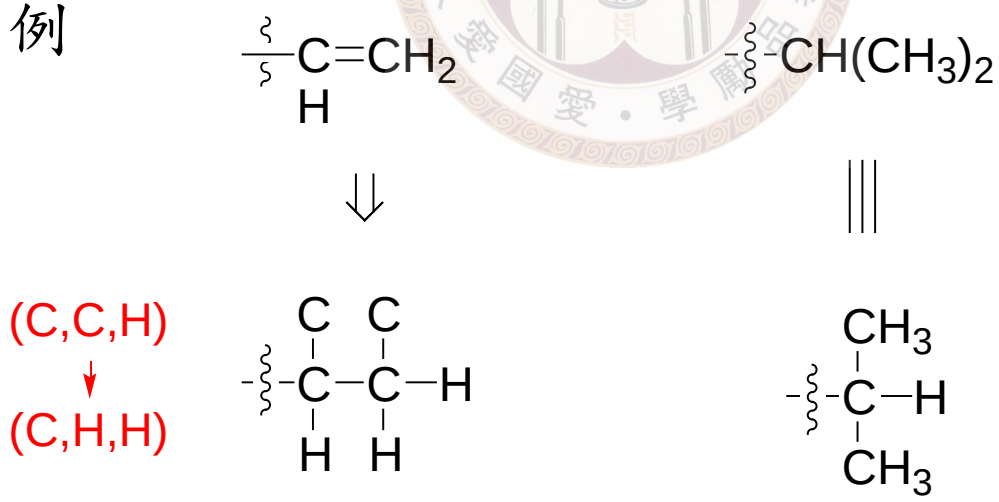



(*R*)-2-butanol

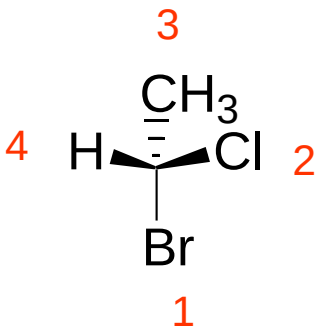
## <4> Multiple bonds

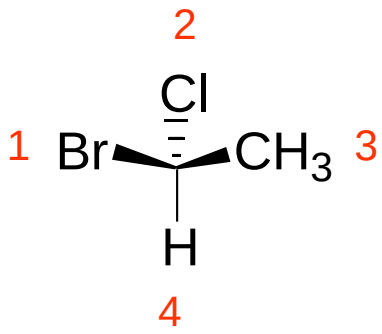


例



Practice:




(*R*) (*R*)

must be the same molecule

# ※ Properties of enantiomers

Most properties are the same:
bp, mp, density…….
(unless in a chiral environment)

The most distinct property:
they rotate plane-polarized light (平面偏極光) in opposite direction

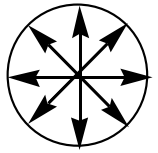
⟹ they are optically active

⟹ they are optical isomers (光學異構物)

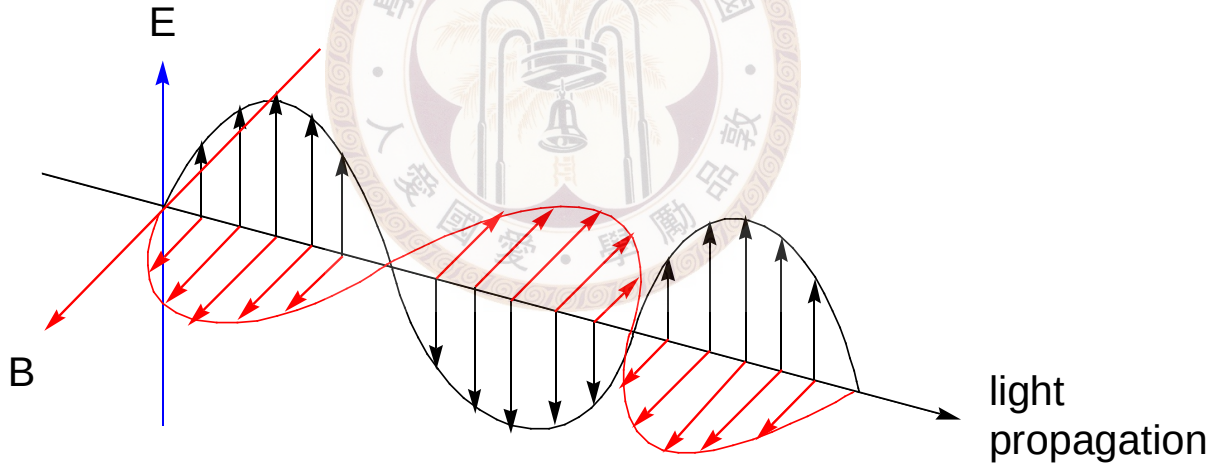
# ◎ Plane-polarized light?

Ordinary light — 由無數個平面光所組成

end on view:

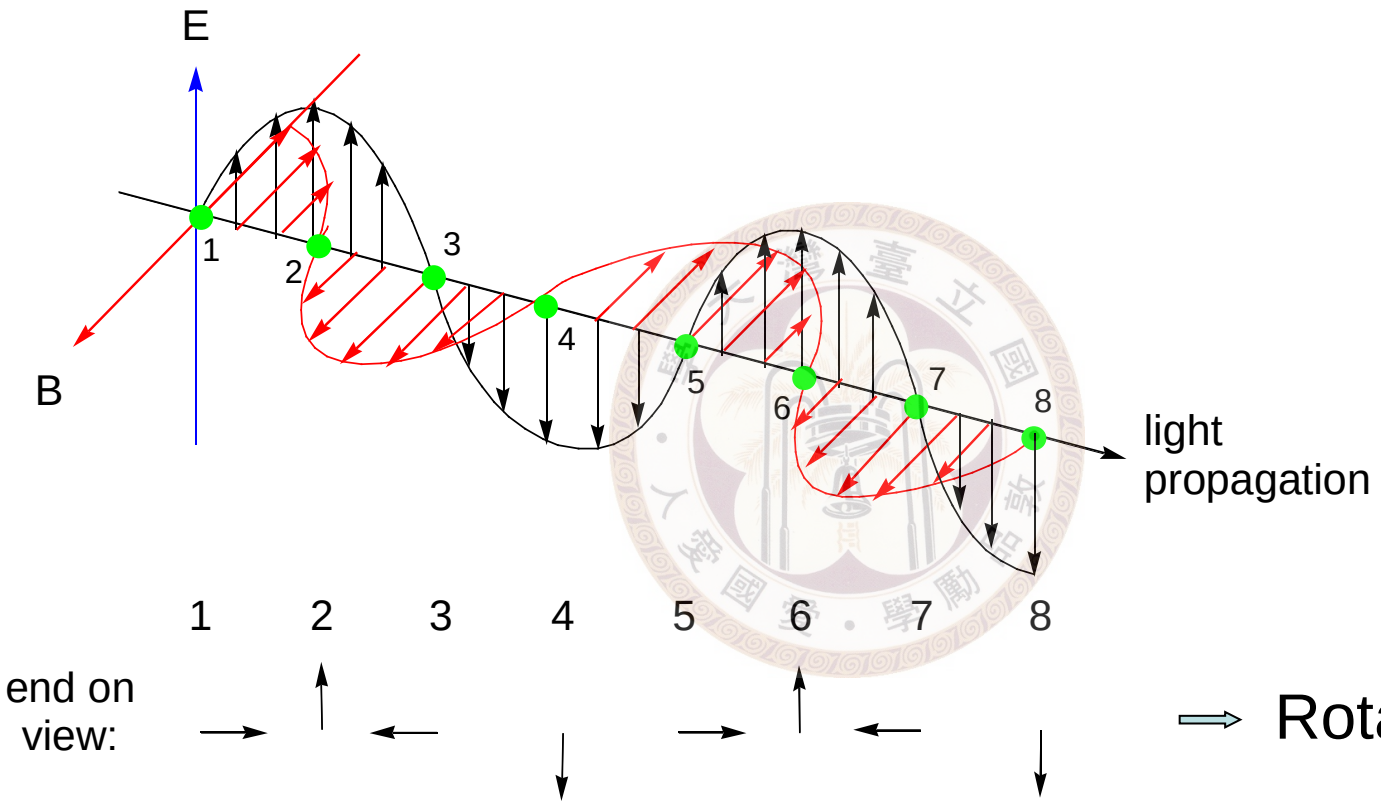


光是一種電磁波，每一平面光亦可拆解為相互垂直的電波和磁波




當光通過某些被稱為polarizer的物質時，光會與之作用而只有一平面光通過，此一平面光就被稱為平面偏極光(plane-polarized light)

平面偏極光在通過由單一對掌體所構成的溶液時，會與之作用而產生電波和磁波的相位差(phase difference)

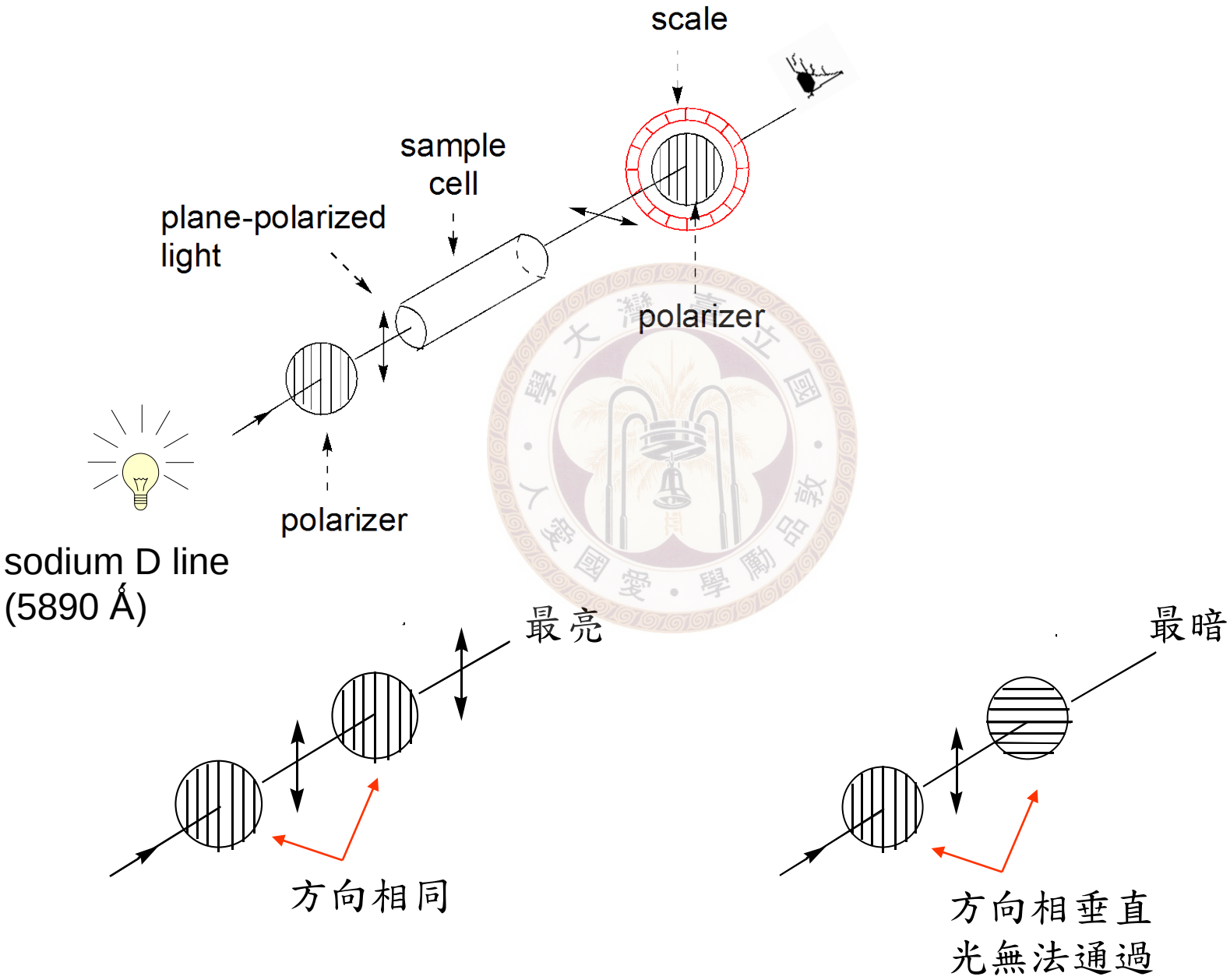



⇨ Rotation occurs

順時針旋轉 — dextrorotatory or *d* or (+)

逆時針旋轉 — levorotatory or *l* or (–)

# Polarimeter (偏光儀 )



◎ Specific rotation (比旋光度)

observed rotation

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

specific rotation

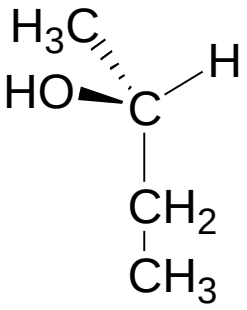
cell length in dm (公寸)

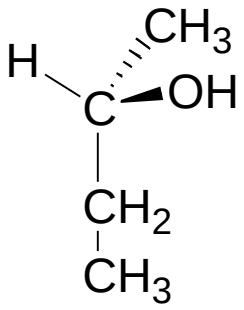
concentration in g/mL

Problem: 若測得 +90°
怎知不是 –270°？

Solution: 將濃度減半 +90° → +45°
–270° → –135° } 可區別了

⟹ Usually requires to measure at two different conc.




$[\alpha]_D^{25} = -13.52^o$ $[\alpha]_D^{25} = +13.52^o$

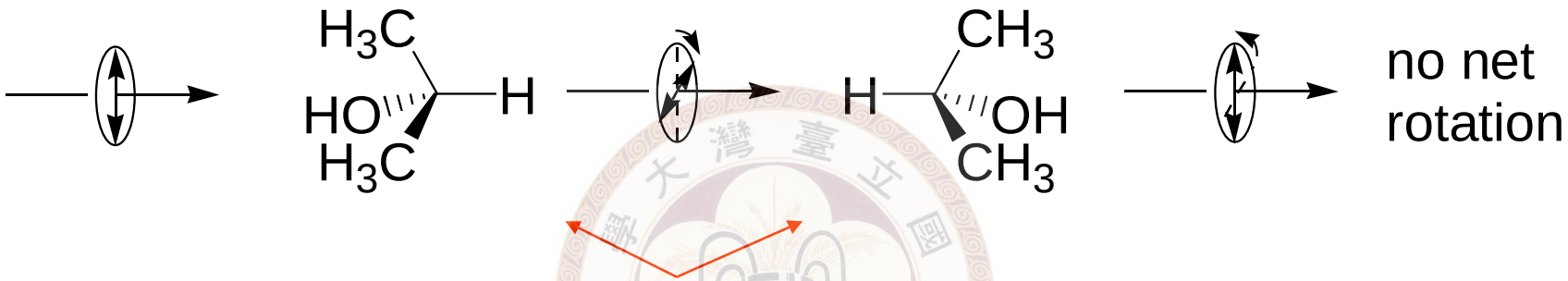
(*R*)-(–)-2-butanol (*S*)-(+)-2-butanol

互為鏡像，旋光方向相反，幅度相同

★ (R), (S) 為命名，人為決定
(+), (–) 為性質，無法預測
} 二者無關

# ※ The origin of optical activity

For achiral compound:

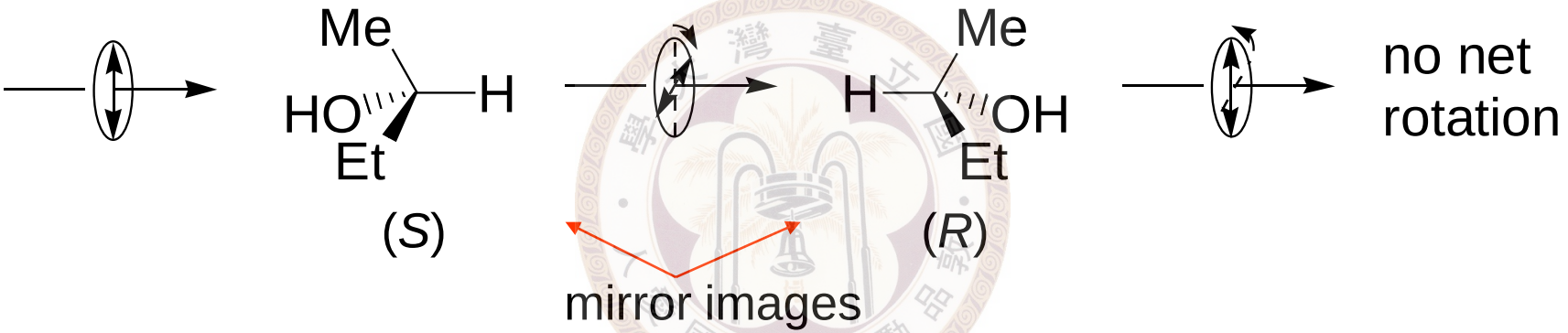



Mirror images: must present
Rotate light in opposite direction

For a mixture of 50% *d* form, 50% *l* form

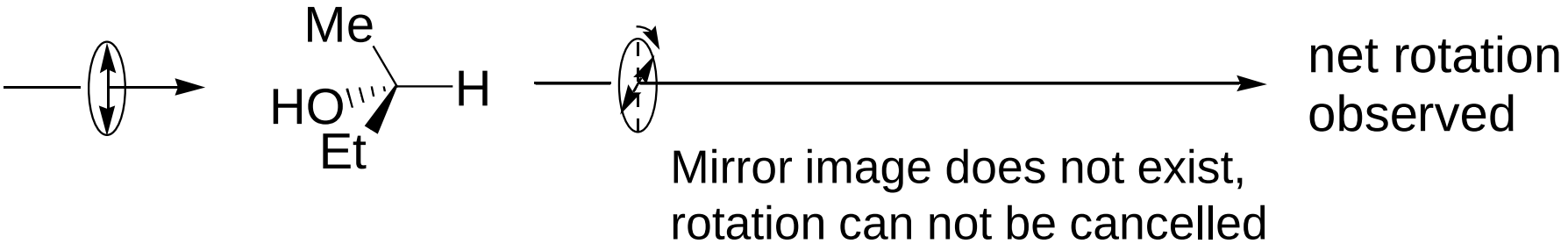
⟹ a racemic mixture (外消旋)
or a racemate
or a racemic modification

(±)-2-butanol




must present in this orientation in equal amount by probability

If only (*S*)-form present:



## ※ Optical purity or enantiomeric purity

Only one enantiomer present: optically pure
or enantiomerically pure
or enantiopure

Estimation of optical purity: enantiomeric excess (ee)
鏡像超越值

$$\%\ ee = \frac{\text{moles of one enant.} - \text{moles of the other}}{\text{moles of both}} \times 100$$

$$= \frac{|\ \text{observed rotation}\ |}{|\ \text{specific rotation}\ |} \times 100$$

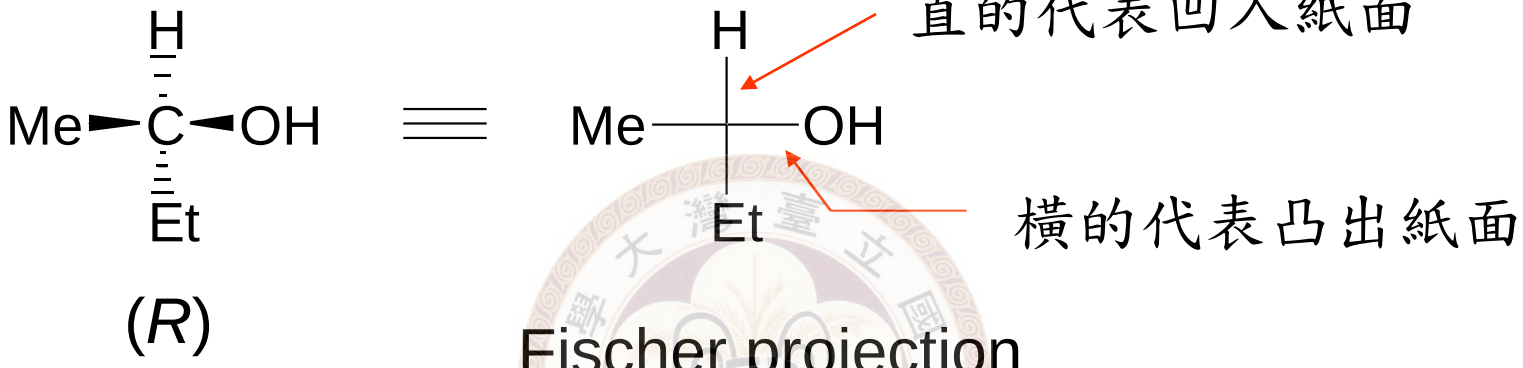
例　A sample of 2-butanol: $[\alpha] = +6.76^{o}$

$$\text{optical purity} = \frac{6.76}{13.52} = 50\%$$

This mixture consists of 75% (+)-form,
25% (–)-form

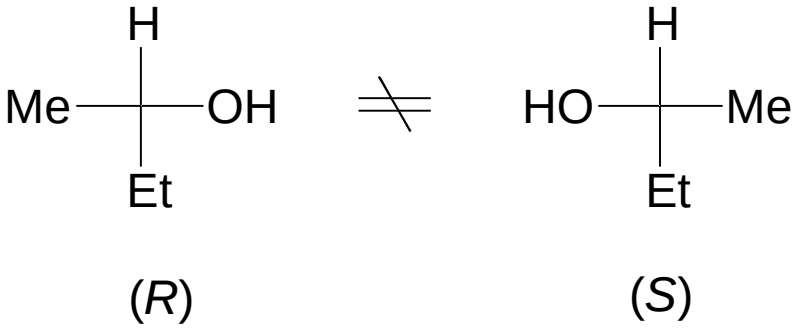
% ee = 50

# ※ Fischer projection formulas

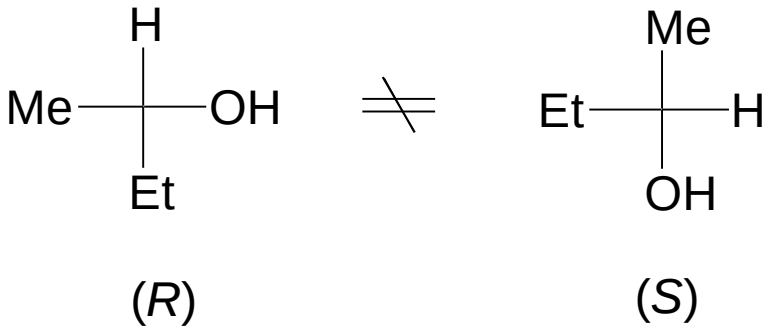



使用規則:

<1> 不可翻面

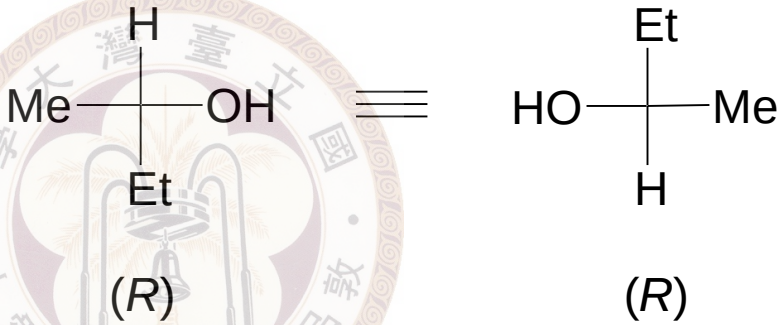


<2> 不可轉90°




(*R*) (*S*)

<3> 可以轉180°

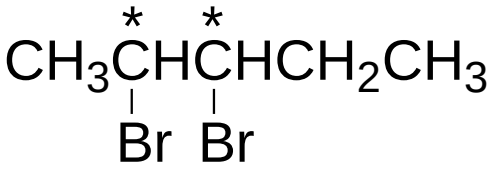



(*R*) (*R*)

例

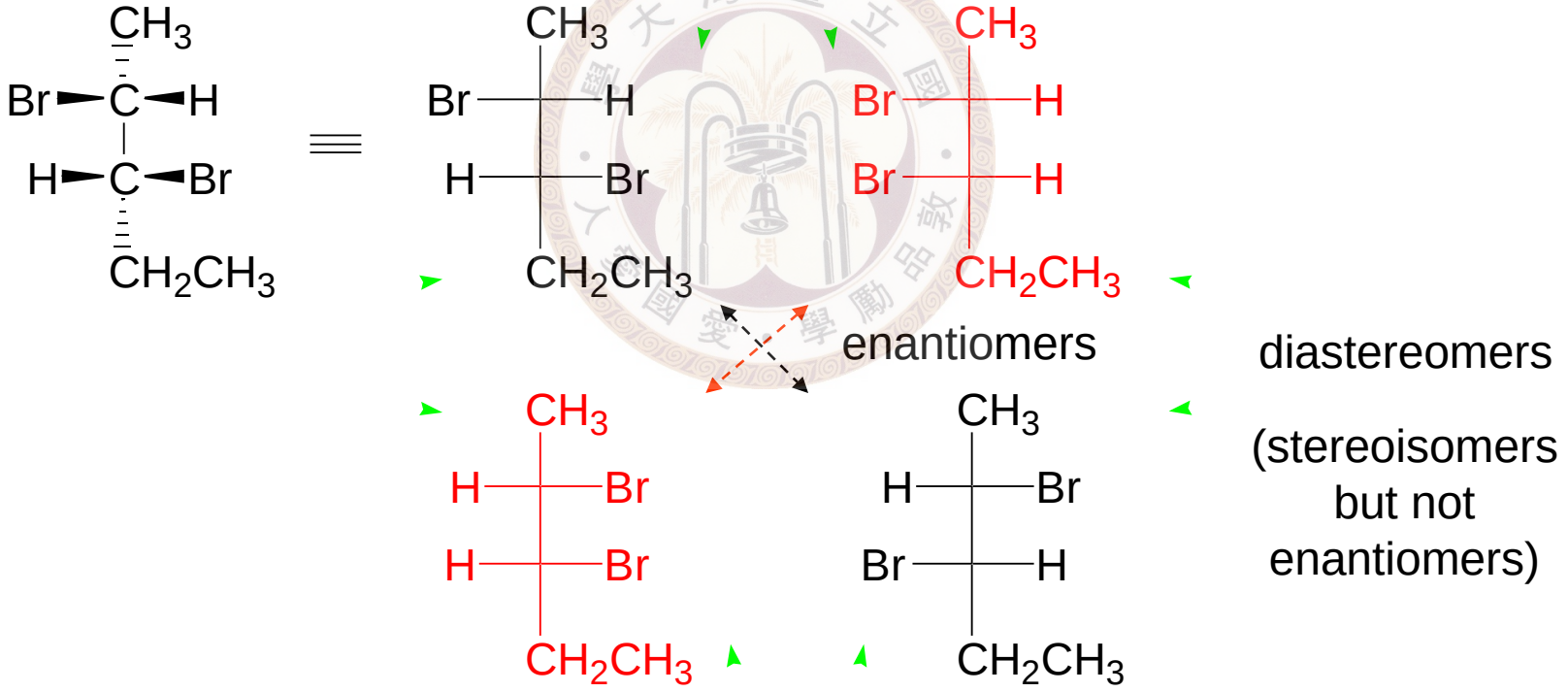

(*R*) (*S*)

## ※ With more than one chiral center

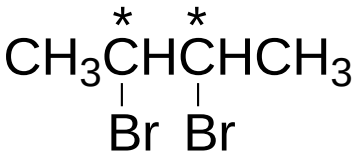



2,3-dibromopentane

Two chiral centers: in principle $2^2 = 4$ isomers

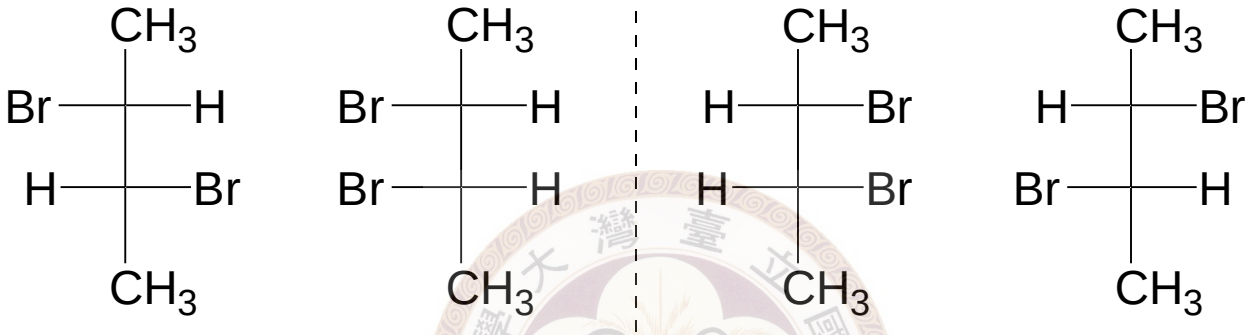



*Diastereomers exhibit completely different properties



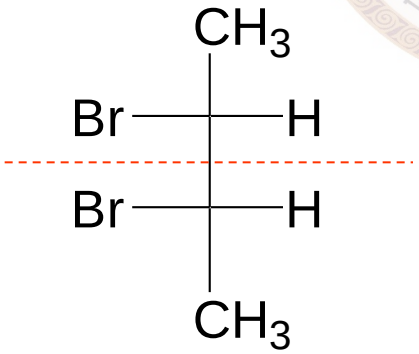

2,3-dibromobutane

enantiomers




same molecule

In fact:




A plane of symmetry exists
→ Must be achiral

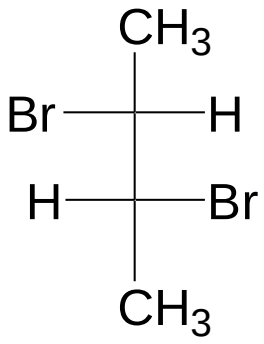
★ A compound with more than one chiral center but is achiral

⟹ A meso compound (內消旋化合物)

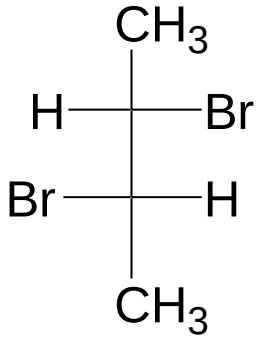
2,3-Dibromobutane with 2 chiral centers
has only 3 stereoisomers

⟹ Compound with n chiral centers
should have $\leqq 2^n$ possible stereoisomers

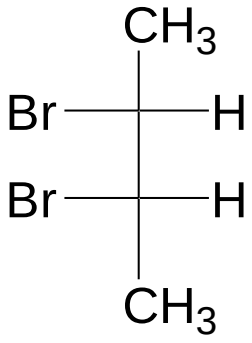
◎ 命名




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



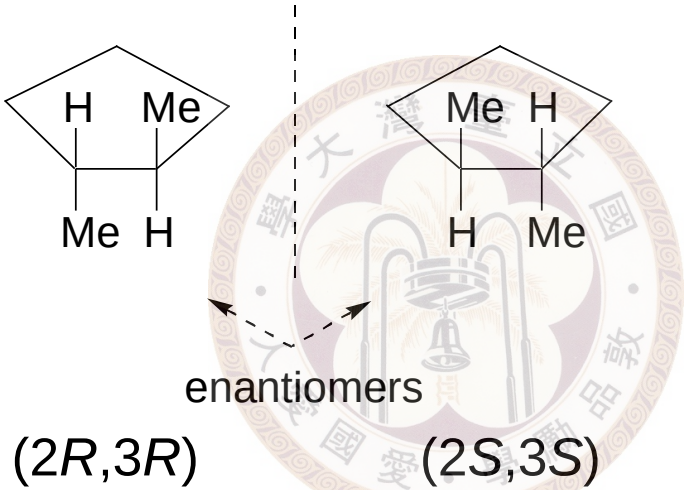

(2*S*,3*S*)-2,3-dibromobutane




*meso*-2,3-dibromobutane

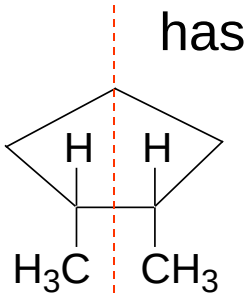
# ※ Cyclic compounds

*trans*-1,2-Dimethylcyclopentane



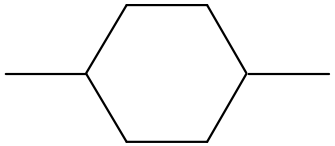

*cis*-1,2-Dimethylcyclopentane

has a plane of symmetry




*meso*

# 1,4-Dimethylcyclohexane



Has a plane of symmetry
→ achiral

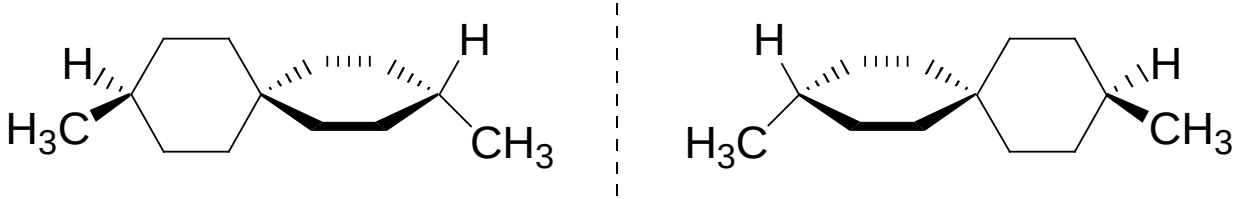
trans

cis

(there is no chiral center: not meso)

Note: 沒有chiral center並不一定為achiral

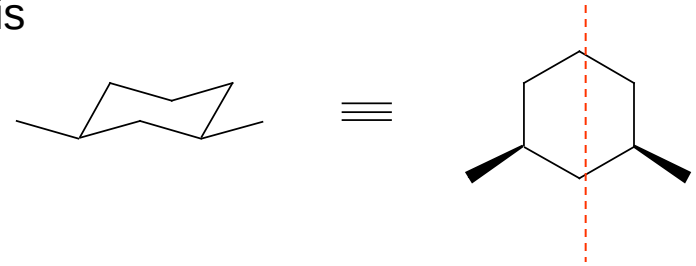
例




enantiomeric
but with no chiral center

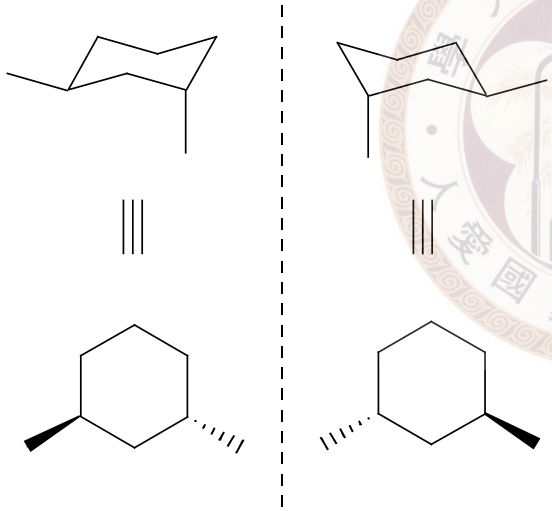
# 1,3-Dimethylcyclohexane

cis



achiral and meso

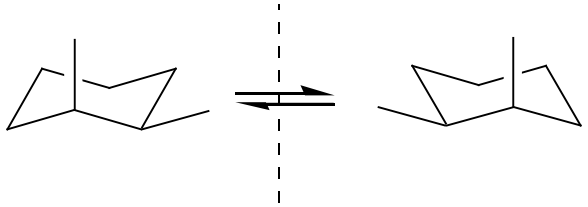
trans



a pair of enantiomers

# 1,2-Dimethylcyclohexane

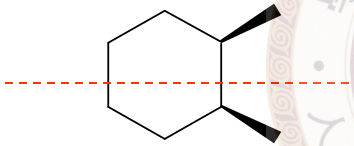
cis



flipping

quickly interconverting
(each conformer is chiral
if fixed)

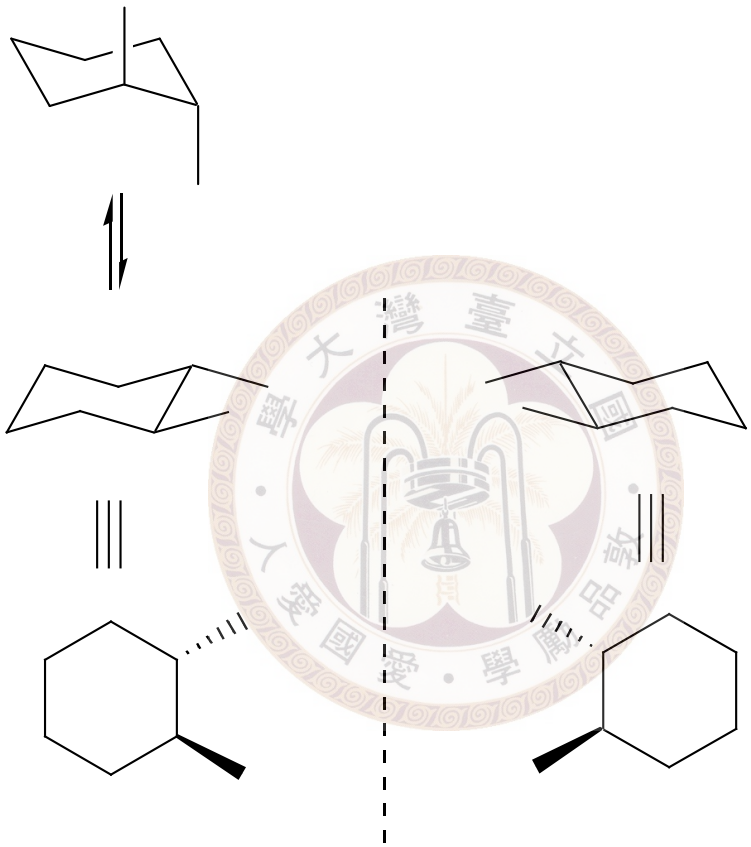
A simple view:



achiral and meso

# 1,2-Dimethylcyclohexane

trans

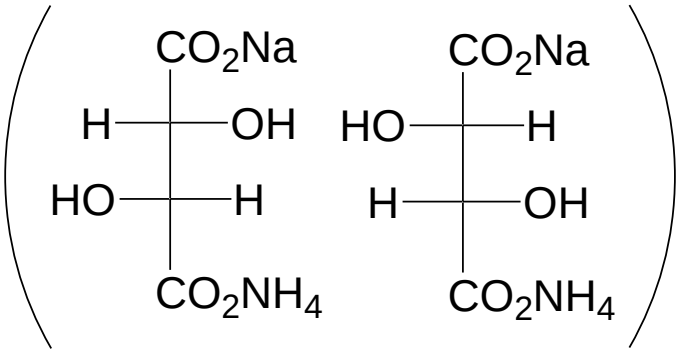


(*S*,*S*) (*R*,*R*)

# ※ Separation of enantiomers: resolution (拆分)

## <1> By hands

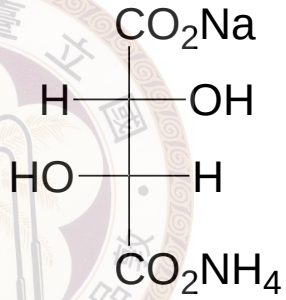
### 1848 Pasteur



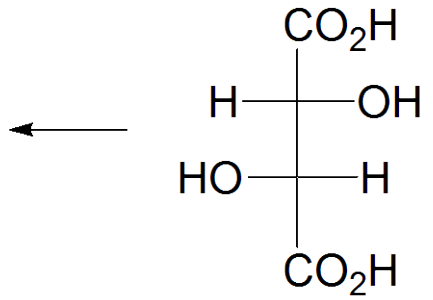

a racemate
of sodium ammonium salt of
(±)-tartaric acid (酒石酸)

separate

two kinds
of crystals

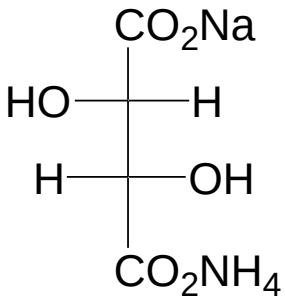



(+)

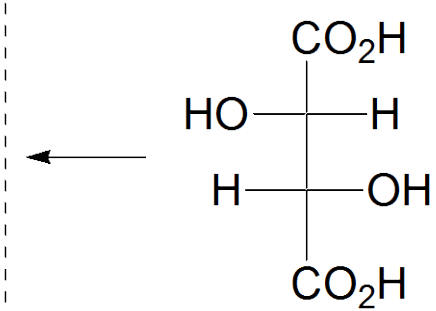



(+)-tartaric acid

Rotation exists even
when crystals dissolved

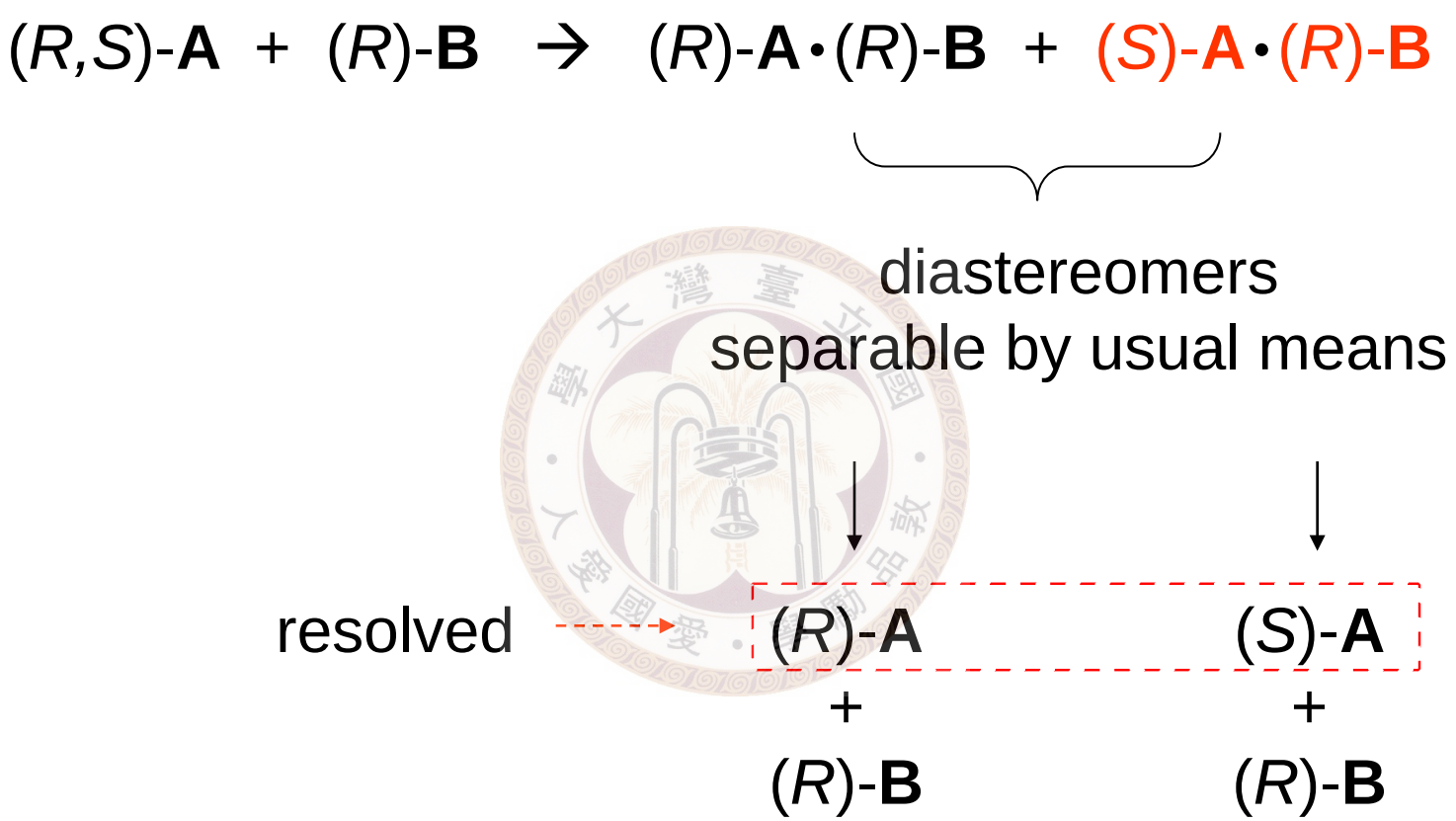



(–)




(–)-tartaric acid

## <2> By conversion to diasteromers



# ※ Absolute configuration
## 絕對構造

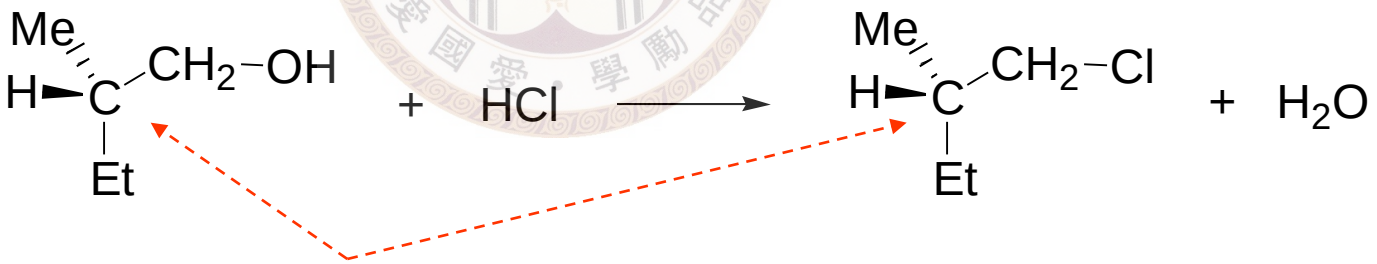
Q: How do we know the absolute configuration?

Before 1951: only relative configurations are known

相對構造

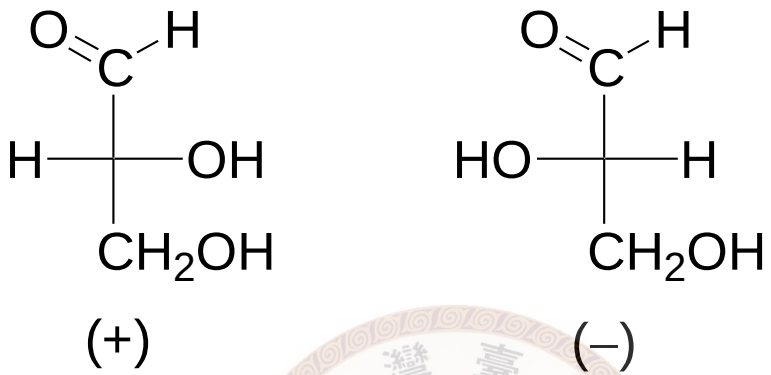
Configurations are correlated with each other through chemical methods (chemical correlation)

例




- No bond at the chiral center is broken
- They have the same configuration (retention of configuration)
- The two structures are correlated
- Know one absolute structure, the other one will be known

Glyceraldehyde was chosen as a standard for correlation

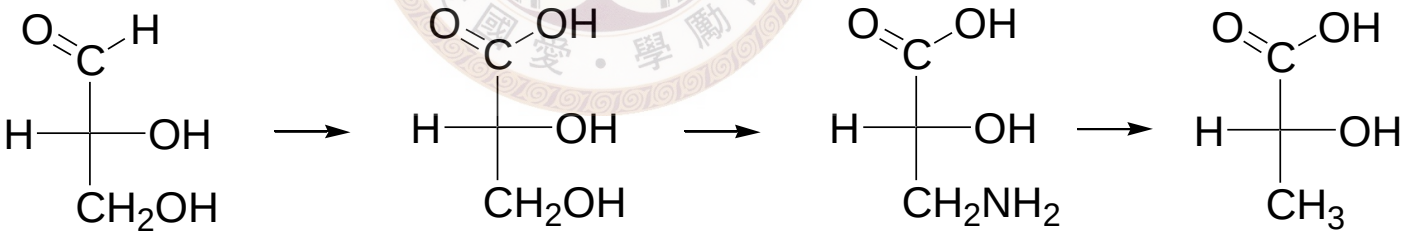


(+) (–)

arbitrarily assigned: (*R*) (*S*)

Other compounds are correlated with glyceraldehyde

例

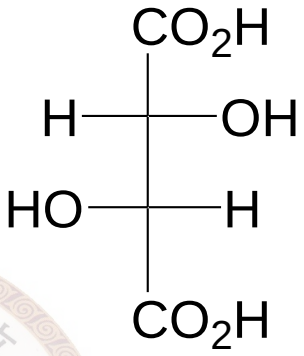


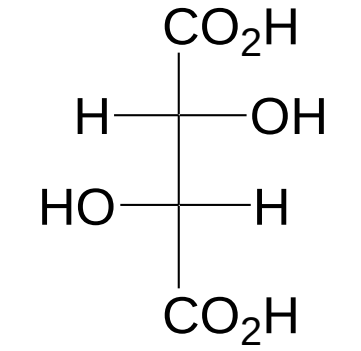

These compounds are correlated with (+)-glyceraldehyde

1951 Bijvoet

X-ray diffraction:

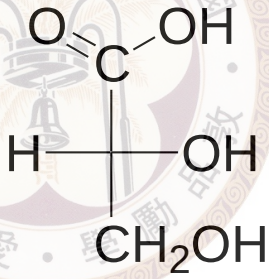
(+)-tartaric acid =



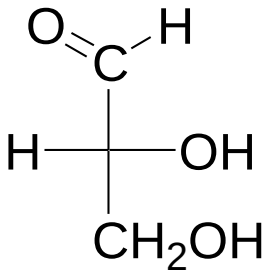




(+)-tartaric acid

correlation



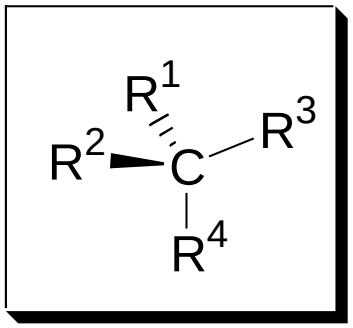

(–)-lactic acid

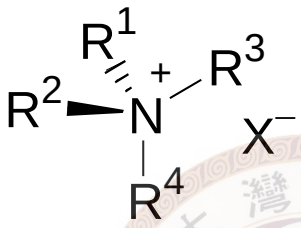



(+)-glyceraldehyde

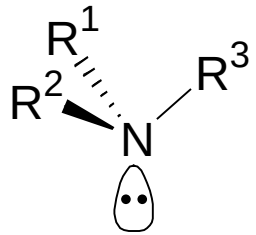
The arbitrary assignment was correct!!

# ※ Stereoceneters other than carbon

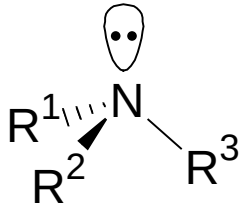


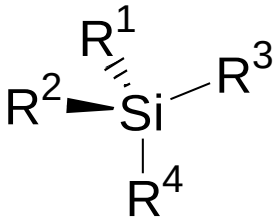



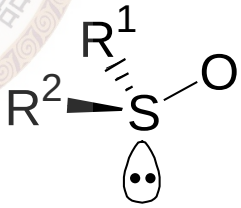

a quaternary ammonium salt
(四級銨鹽)



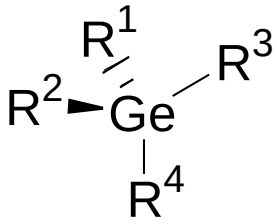

Invert quickly ⇌



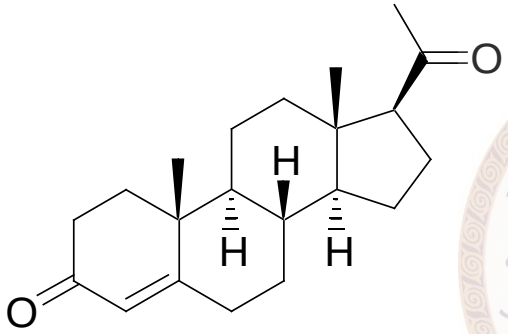




a sulfoxide



# ※ Biological importance

Natural products usually contain multiple chiral centers and exist as one enantiomer




progesterone
(黃體激素)

Enzymes (酶) catalyze many biological reactions and only recognize one enantiomeric form of their substrates through a three-point binding