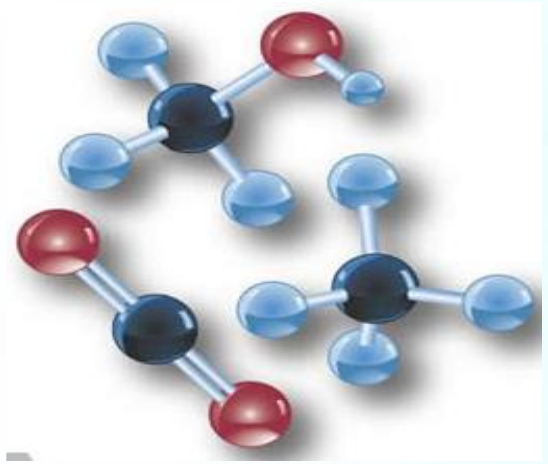
Organic Chemistry

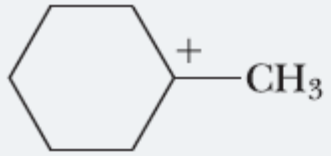


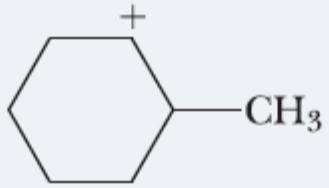
Le Liu

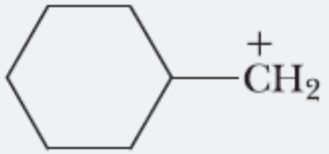
E-mail: le.liu@xjtu.edu.cn

要点复习—例题解析

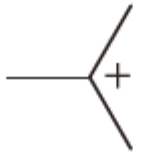
Arrange these carbocations in order of increasing stability:

(a) 

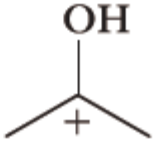
(b) 

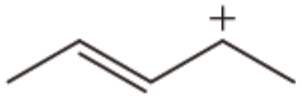
(c) 

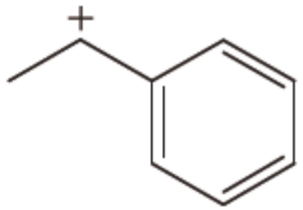
5.52 Each of the following 2° carbocations is more stable than the tertiary-butyl carbocation shown:



a tertiary carbocation

(a) 

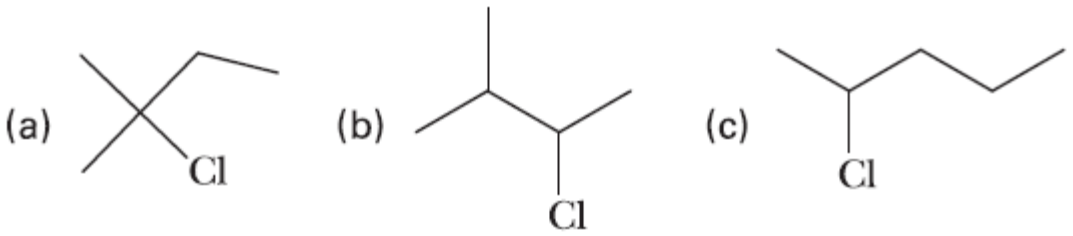
(b) 

(c) 

Provide an explanation for each cation's enhanced stability.

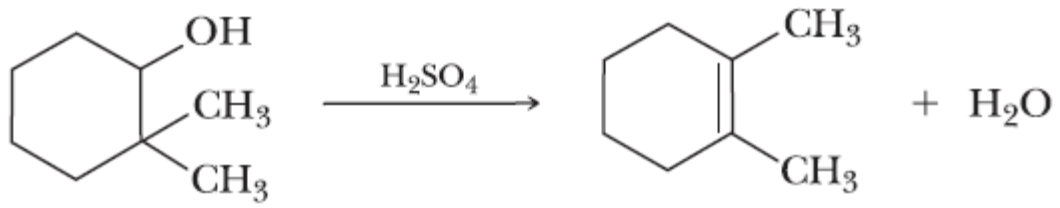
要点复习—例题解析

5.25 Draw the structural formula for an alkene with the molecular formula C_5H_{10} that reacts with HCl to give the indicated chloroalkane as the major product:



要点复习—例题解析

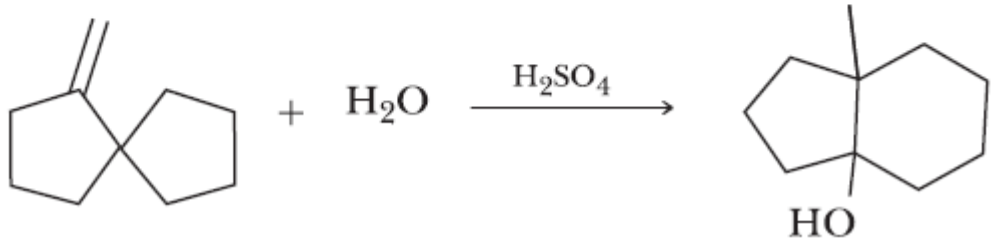
5.30 Propose a mechanism for the following acid-catalyzed dehydration. **(See Examples 5.6, 5.8)**



5.31 Propose a mechanism for each of the following transformations. **(See Examples 5.4, 5.6, 5.8)**

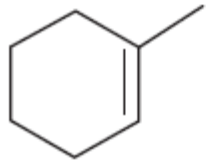
(a)

(b)



要点复习—例题解析

5.37 Treatment of 1-methylcyclohexene with methanol in the presence of a sulfuric acid catalyst gives a compound with the molecular formula $C_8H_{16}O$. Propose a structural formula for this compound and a mechanism for its formation.

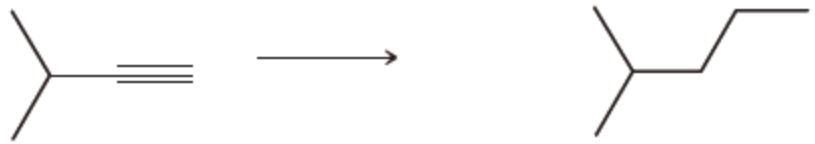


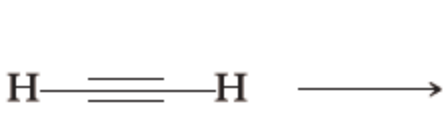
$$+ \quad CH_3OH \xrightarrow{H_2SO_4} C_8H_{16}O$$

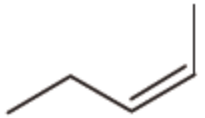
$$R{-}C{\equiv}C{-}H \xrightarrow{NaNH_2} R{-}C{\equiv}C{:}^{-}\,Na^{+} \xrightarrow{R{-}X} R{-}C{\equiv}C{-}R \xrightarrow{\text{reduce}} R{-}C{=}C{-}R \xrightarrow[\text{reactions}]{\text{various}} \text{alcohols, haloalkanes, dihaloalkanes, alkanes, and others}$$

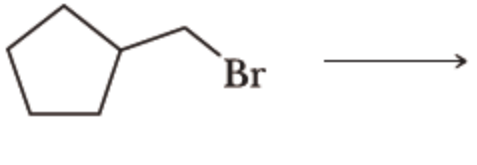
要点复习—例题解析

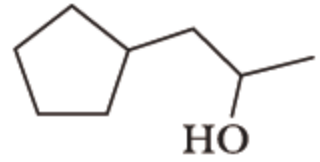
5.51 Test your cumulative knowledge of the reactions learned thus far by completing the following chemical transformations. Note that some will require more than one step.

(a) 

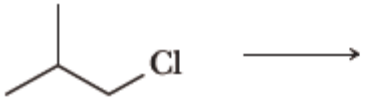
(b) 

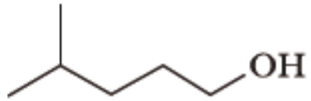


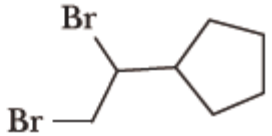
(c) 



(d) 

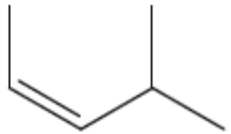
(e) 

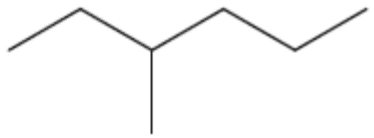


(f) 


要点复习—例题解析

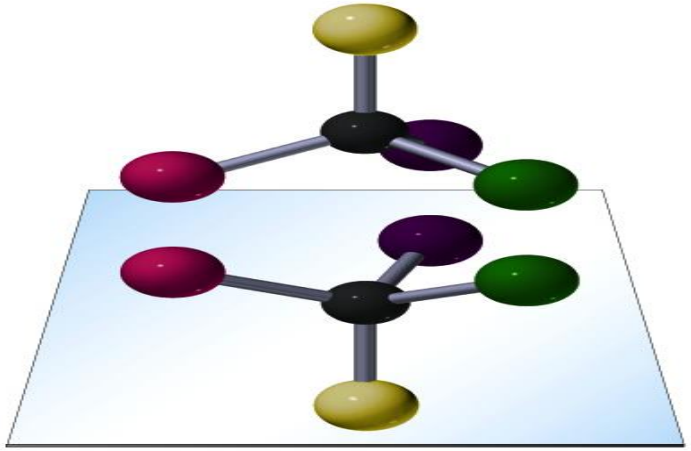
5.44 Determine the alkyne that would be required in the following sequences of reactions.

(a) ? $\xrightarrow[2)\ CH_3CHBrCH_3]{1)\ NaNH_2}{3)\ H_2/Lindlars}$ 

(b) ? $\xrightarrow[2)\ CH_3I]{1)\ NaNH_2}{3)\ H_2/Ni}$ 

Chapter 7

Stereoisomerism



Outline:

1. What are stereoisomers?
2. What are enantiomers?
3. How do we designate the configuration of a stereocenter?
4. What is the 2^n rule?
5. How to determine whether two compounds are the same, enantiomers, or diastereomers?

“真实的物体” 跟“镜子里的物体”是相同的吗?

“真实的物体” 跟 “镜子里的物体” 是相同的吗?

左手的镜像是右手

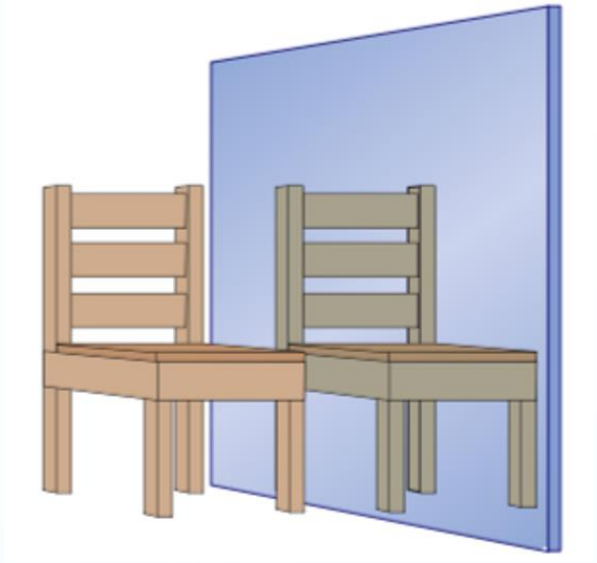
右手的镜像是左手

左手与右手真是一摸一样的吗?

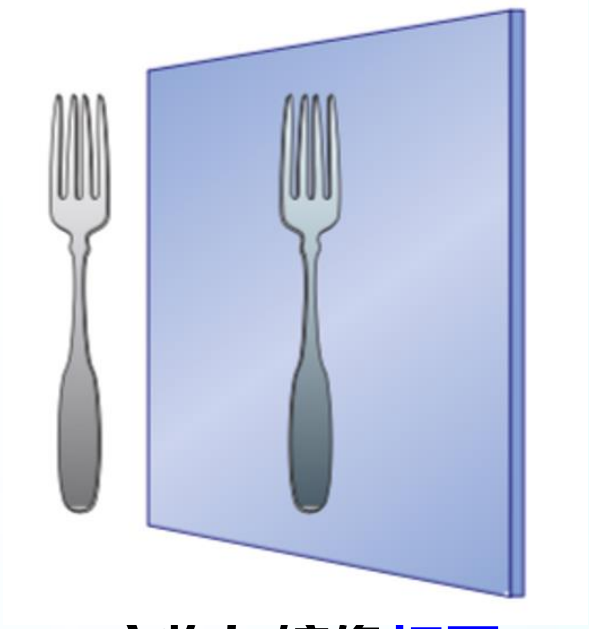
彼此不能重合，并不相同。

结论：“真实的手”与“镜子里的手”并不相同。

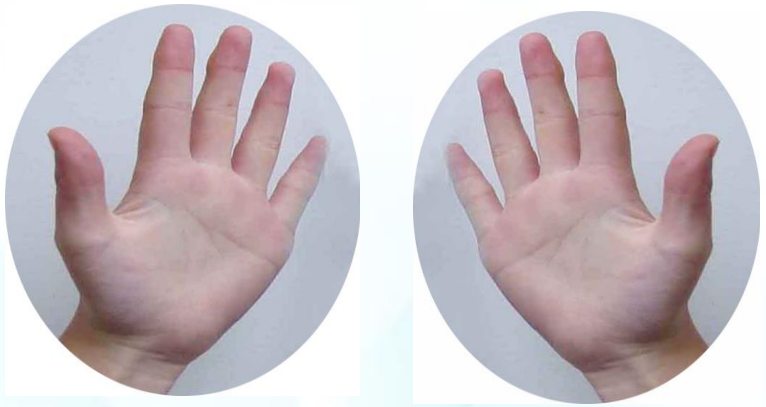
下列物体与它们的镜像是否相同?



实物与镜像**相同**



实物与镜像**相同**



实物与镜像**不同**

“真实的物体” 跟“镜子里的物体”是相同的吗?

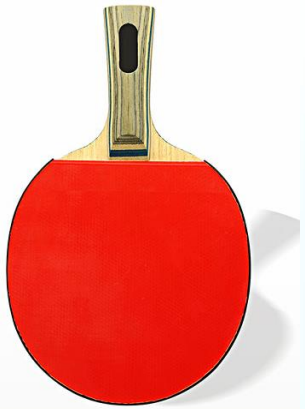
1. 手性

手性（chirality）：实物与镜像不能重合的性质。

手性是三维物体的基本属性。如果一个物体不能与其镜像重合，该物体就称为**手性物体**，否则为**非手性物体**。

判断下列物件是否有手性：

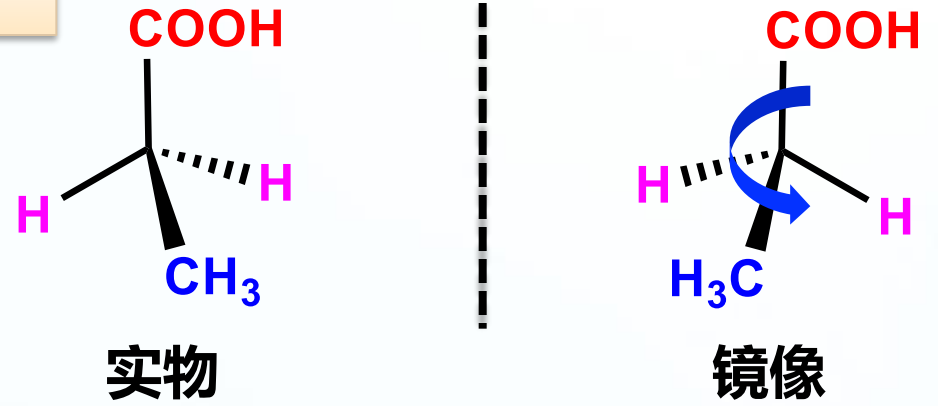
手性



非手性

2. 手性分子和对映异构体

丙酸

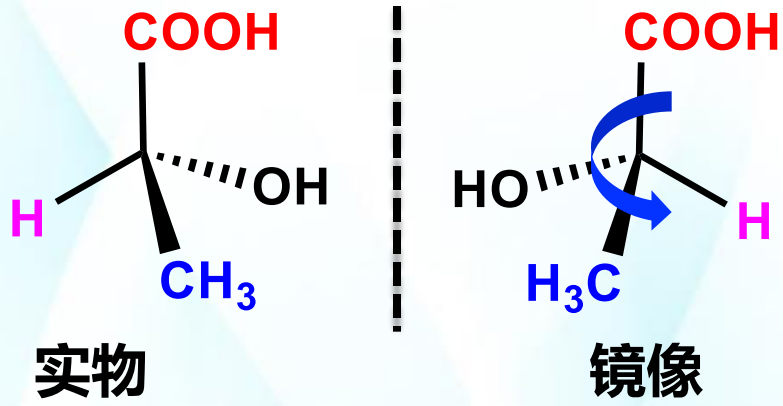


实物　　镜像

稍作旋转

实物与镜　　非手性分子。

乳酸



实物　　镜像

稍作旋转

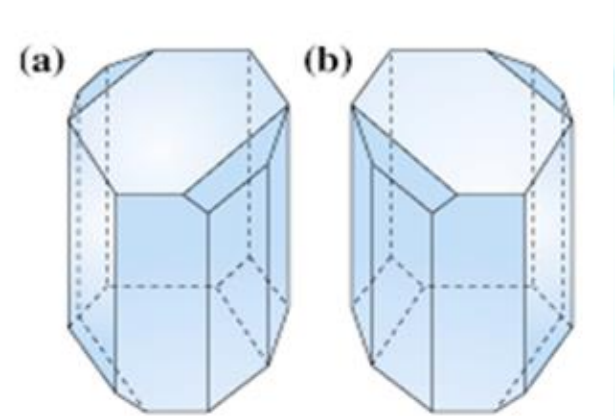
实物与镜像　　称为手性分子。

手性分子的实物与镜像属于不同的立体异构体，称之为对映异构体，简称对映体。

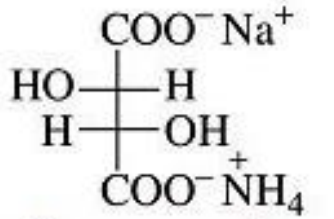
对映异构现象是如何发现的?

巴斯德酒石酸盐对映体分离实验（1848年）

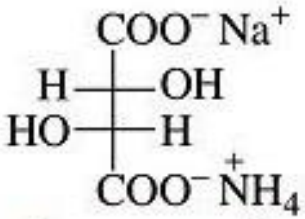
化学史上最美的实验



人类首次发现分子的对映异构现象，并成功地通过手工分离出对映异构体。



sodium ammonium tartrate
left-handed crystals



sodium ammonium tartrate
right-handed crystals

巴斯德

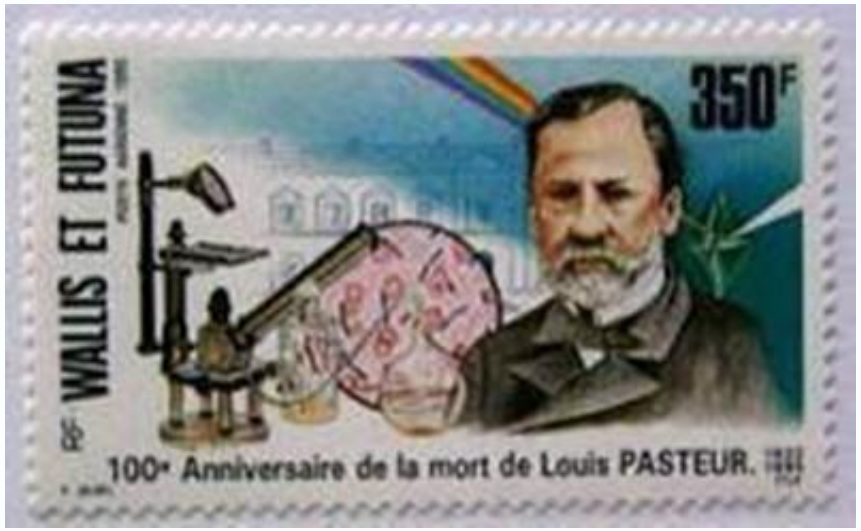
2. 手性分子和对映异构体

为什么巴斯德的实验是化学史最美实验?

美国化学会解释：“elegantly simple but significant”

即：巴斯德的实验一方面优雅简洁，另一方面意义重大。

这两点充分体现了科学的美学意义。

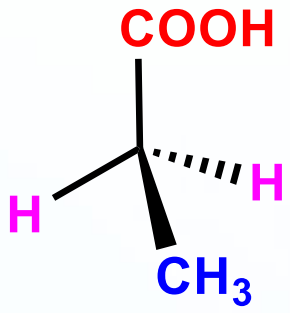


诠释了偶然性与必然性的辩证关系

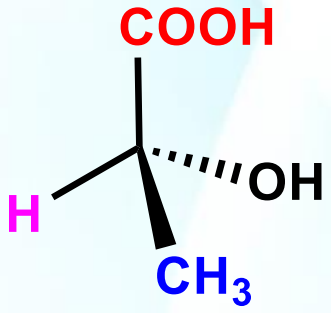
2. 手性分子和对映异构体

观察：丙酸分子和乳酸分子的结构差别在哪里？

丙酸：非手性分子



乳酸：手性分子



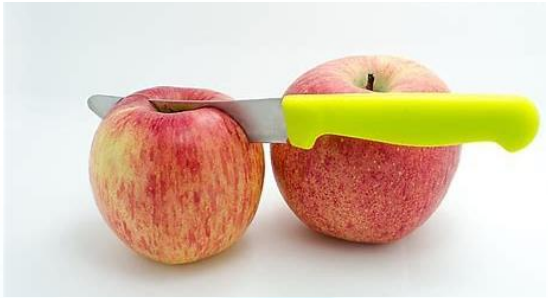
丙酸分子具有对称性。

分子是否有手性，与分子的对称因素有关。

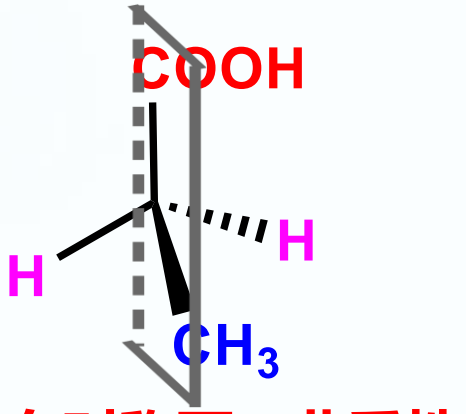
3. 对称因素与手性

(1) 对称面

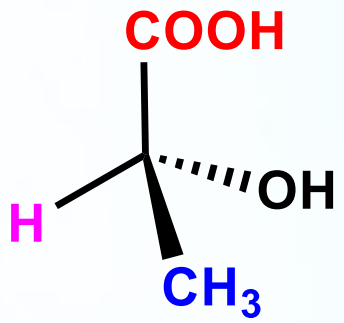
假想分子中有一个平面，可以将分子分割成互为实物与镜像关系的两部分，这个平面就称为分子的对称面。



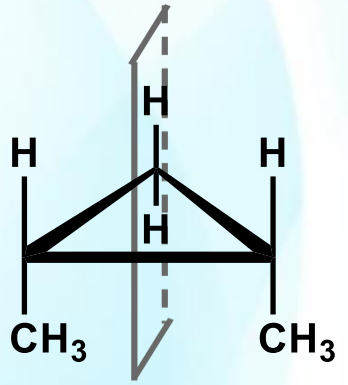
- 有对称面的分子为非手性分子。



有对称面，非手性



无对称面，手性



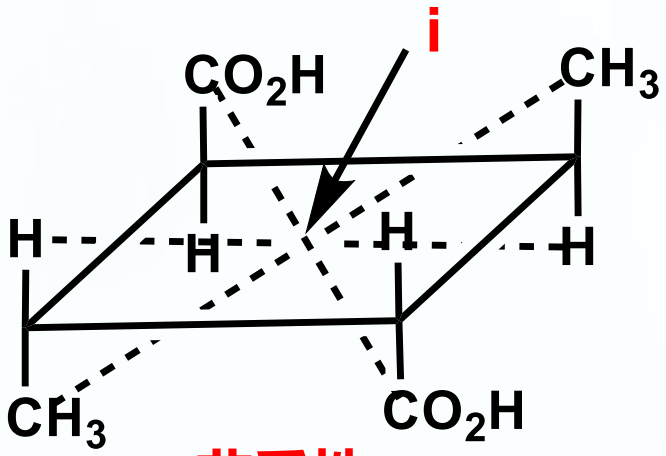
有对称面，非手性

3. 对称因素与手性

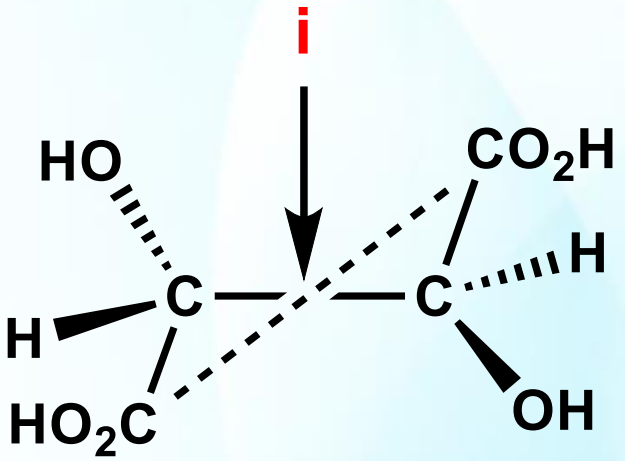
(2) 对称中心

假想分子中有一个点，在经过此点直线的等距离处两端遇到的都是相同的原子或基团，这个点称为分子的对称中心。

- 有对称中心的分子也是非手性分子。



非手性

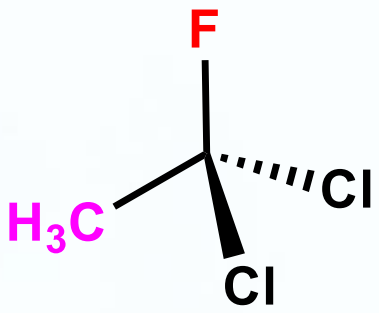


非手性

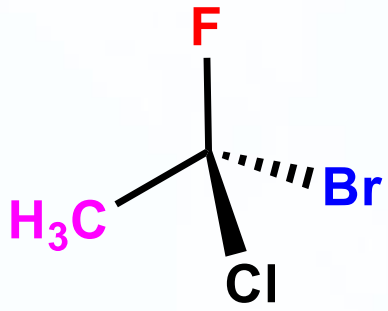
如何判断分子是否是手性分子?

- 实物与其镜像不能重合，是判断手性分子的充分必要条件。
- 方便起见，可如下判断：如果分子不存在对称面或对称中心，则是手性分子。

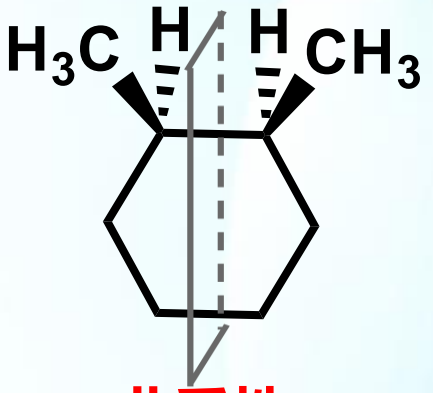
练习：下列分子是否具有手性?



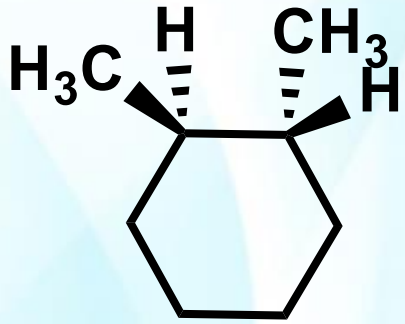
非手性



手性



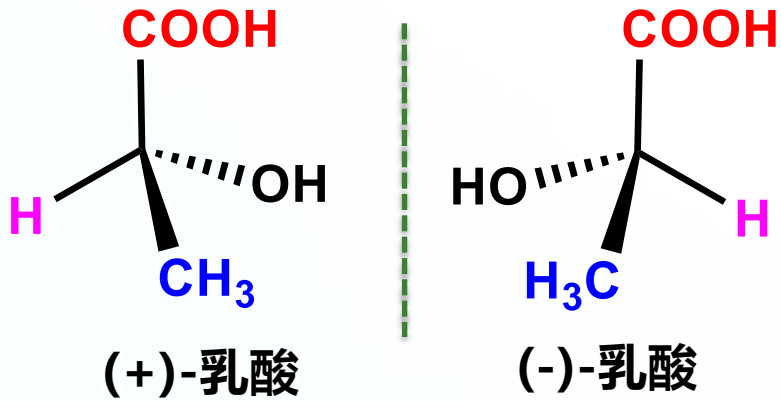
非手性



?

该方法同样适合于宏观物体手性的判断，如：手（手性）、乒乓球拍（非手性）。

4. 对映异构体的性质差异



乳酸的物理性质

物质	mp℃	pK_a	$[\alpha]_D^{20}$
(+)-乳酸	53.0	3.79	+3.82
(-) -乳酸	53.0	3.79	-3.82
(±)-乳酸	18.0	3.79	/

- 除了旋光性质之外，对映体几乎具有相同的物理、化学性质;
- 对映体的比旋光度大小相等，方向相反，对映体又称之为旋光异构体。

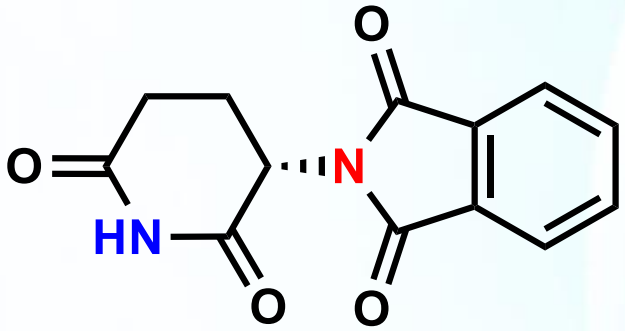
外消旋体（Racemate）：等量对映异构体的混合物称为外消旋体，用(±)表示 。

在手性环境(如生命体)中，对映体会表现出相同的生物活性吗?

5. 对映异构体的不同生物活性

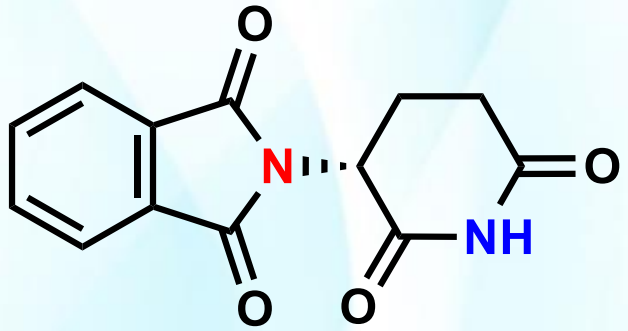
“反应停”事件—— 医药史上的悲剧

20世纪50年代，德国一家公司开发出一种镇静药“反应停”，该药对于消除孕妇妊娠反应效果很好，但是大量使用后却造成了12000多名畸形“海豹儿”的出生。



(S)-thalidomide

致畸作用

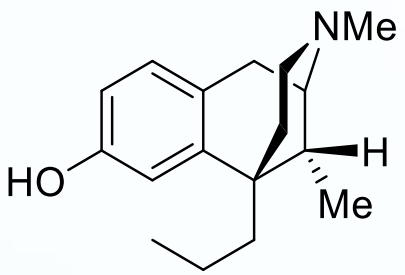


(R)-thalidomide

镇静作用

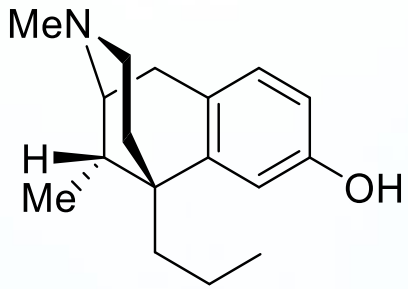
“反应停”药物当时以消旋体出售!

5. 对映异构体的不同生物活性



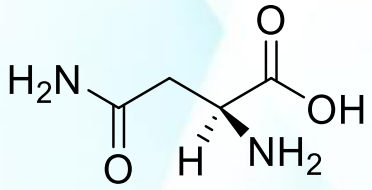
(-)-benzomorphia

止痛，不成瘾



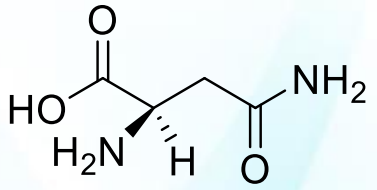
(+)-benzomorphia

弱止痛，成瘾



(*S*)-天冬酰胺

苦味

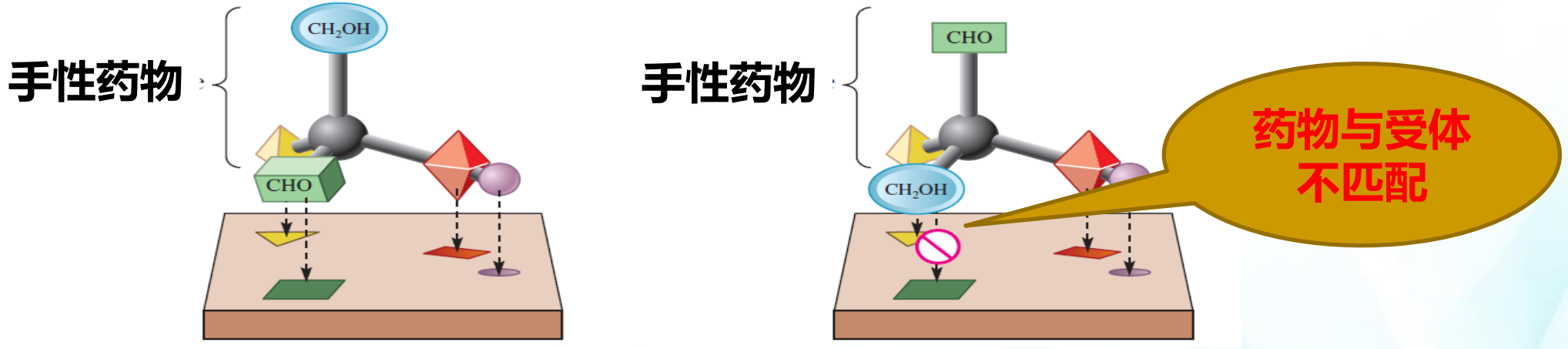


(*R*)-天冬酰胺

甜味

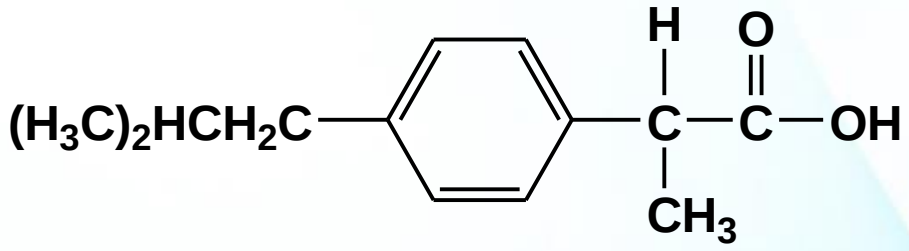
5. 对映异构体的不同生物活性

为什么对映异构体中基团排列的小小差异，竟会引起不同的生理作用呢?

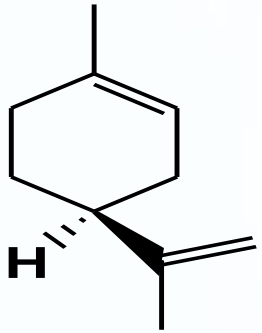


Importance of Chirality

half of pharmaceuticals are chiral compounds!

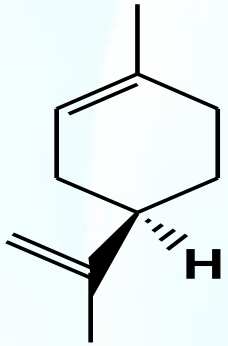


(S)-Ibuprofen (responsible for pain relief)



(S)-Limonene

Lemon smell

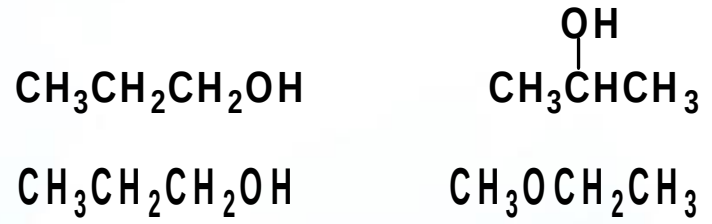


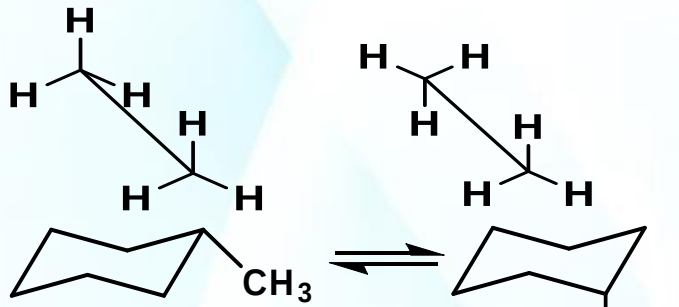
(R)-Limonene

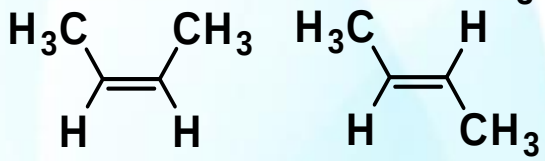
Orange smell

1. What are stereoisomers?

- Isomers
  - Constitutional isomers
    - Skeletal isomers
    - Positional isomers
    - Functional isomers
  - Stereo-isomers
    - Conformational isomers
    - Configurational isomers
      - Cis-trans isomers
      - Optical isomers
        - Enantionmers
        - Diastereomers



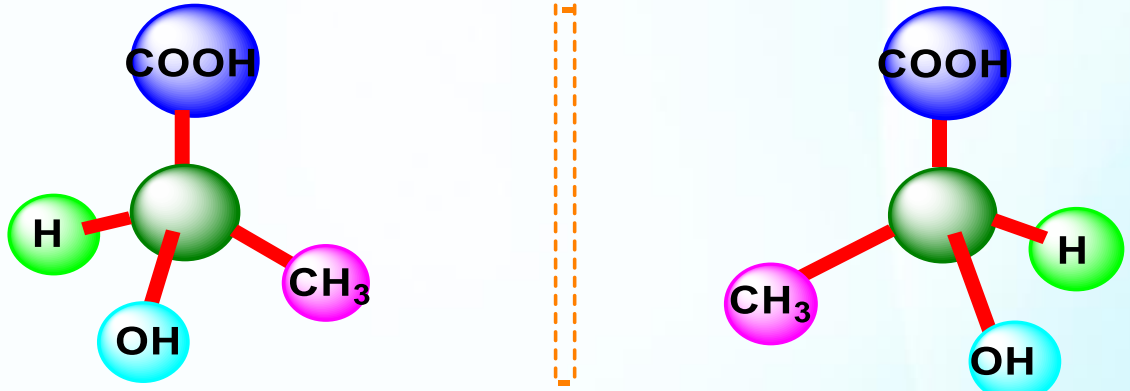




立体异构体的定义：分子中的原子或原子团互相连接的次序相同，但在空间的排列方向不同而引起的异构体。

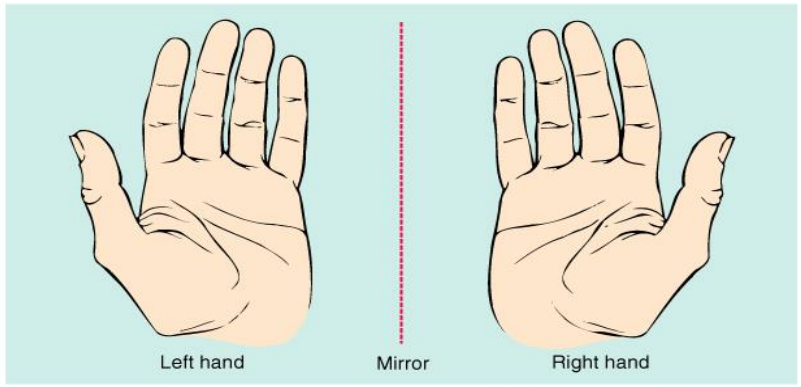
Stereoisomers have the same molecular formula and the same connectivity of atoms in their molecules, but different three-dimensional orientations of their atoms in space.

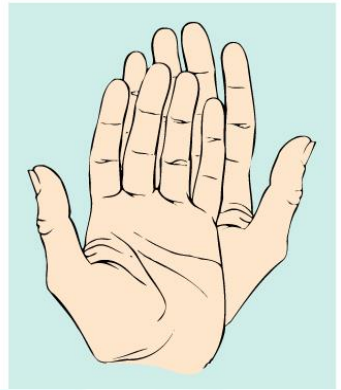
立体化学的任务：研究分子的立体形象及与立体形象相联系的特殊物理性质和化学性质的科学。



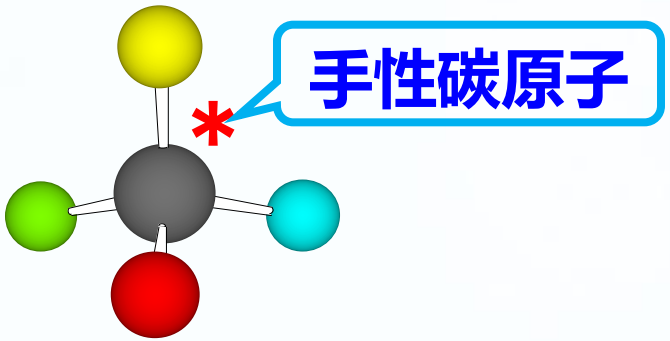
2. What are enantiomers?

Enantiomers are stereoisomers that are nonsuper-imposable mirror images.

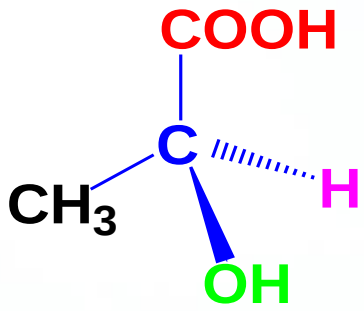


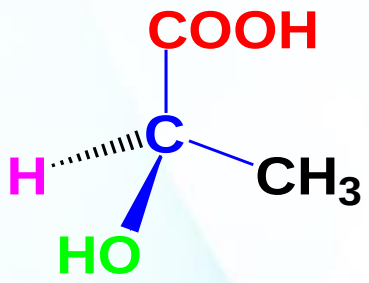


A molecule that is nosuperposable on its mirror image is termed as a chiral molecule.



手性碳原子（不对称碳原子或手性中心）——与4个不相同的原子或基团相连的碳原子，用*标记。





(*S*)-(+)-乳酸

m.p: 53°C

$[\alpha]_D$ = +3.82

*p*Ka=3.79 (25°C)

(*R*)-(-)-乳酸

m.p: 53°C

$[\alpha]_D$ = -3.82

*p*Ka=3.83 (25°C)

一个可使平面偏振光向右旋，称为**右旋体(+)**；另一个可使平面偏振光向左旋，称为**左旋体(-)**。二者旋转角度相同。因此**对映异构**也叫做**旋光异构**。

对映异构体的特点：

1)结构：镜影与实物关系;

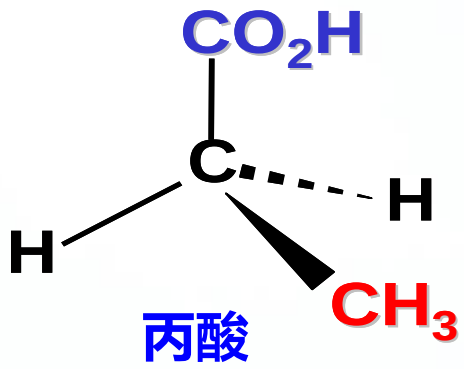
2)内能：内能相同;

3)物理性质和化学性质在非手性环境中相同，在手性环境中有区别;

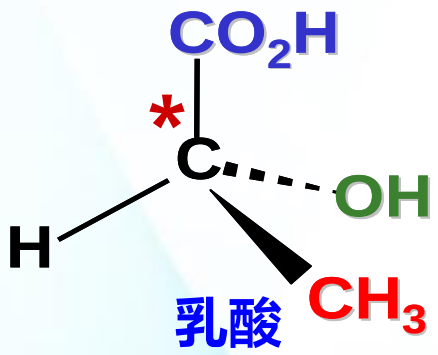
4)旋光能力相同，旋光方向相反。

一对对映体结构差别很小，因此它们具有相同的b.p，m.p，溶解度等，化学性质也基本相同，很难用一般的物理或化学方法区分。

3. Symmetry and chirality



丙酸



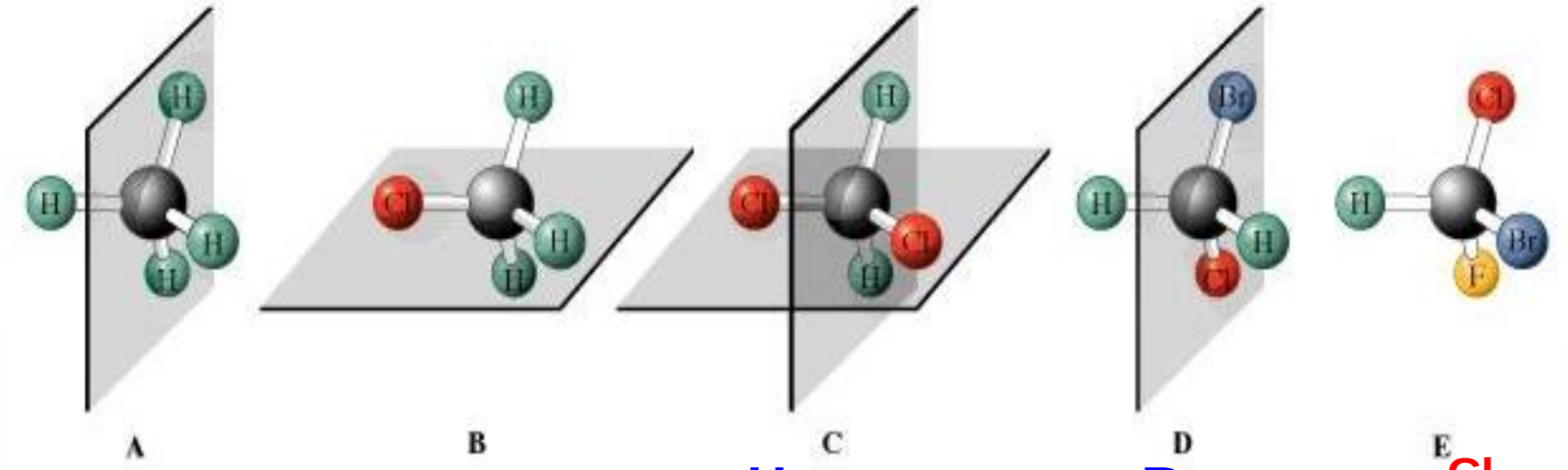
乳酸

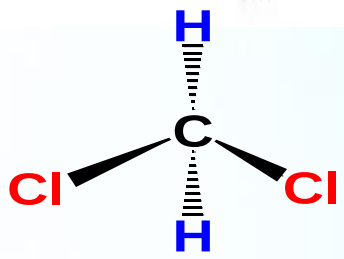
问题：对于无手性的丙酸分子和有手性的乳酸分子，它们的结构差异是什么?

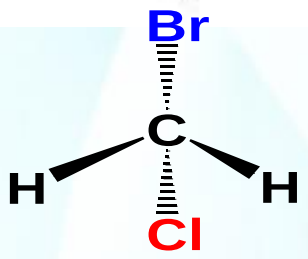
分子与其镜像能否互相叠合决定于分子本身的对称性。
即分子的手性与分子的对称性有关。考察分子的对称性就能判断它是否具有手性。

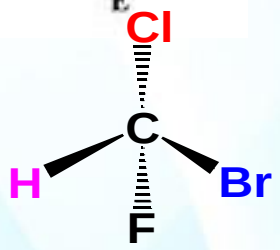
对称元素：对称面、对称中心。

Plane of symmetry





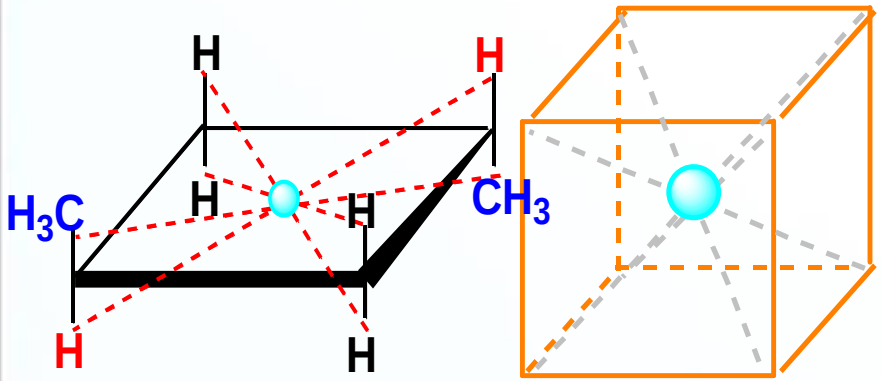


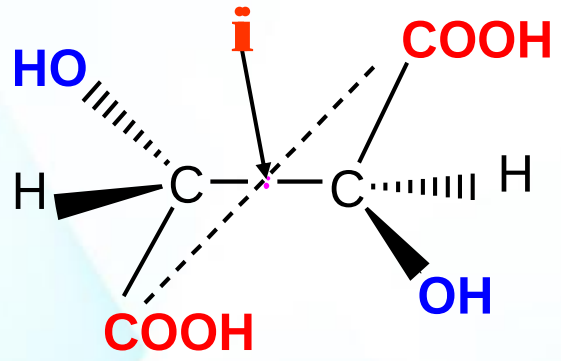


Plane of symmetry: An imaginary plane passing through an object and dividing it such that one half is the mirror image of the other half.

有对称面的分子,实物和镜象能重叠，为非手性分子。

Center of symmetry





A center of symmetry is a point from which two identical atoms or groups are away from each other at the same length of distance, and through which these two atoms or groups can be connected by a straight line.

有对称中心的分子，实物和镜像能重叠，为非手性分子。

4. How do we designate the configuration?

R / S标记法

IUPAC 规定对映异构体用 R、S命名。R/S标记法是根据手性碳原子上所连的四个原子或原子团在空间的排列方式来标记的。

规则如下：

① 将手性碳原子上相连的四个不同原子或基团（a，b，c，d）按次序规则从大到小排列成序（假定a > b > c > d）；

② 将最低次序的原子或基团（d）远离观察者，置于距观察者最远处；

③ 观察其余三个原子或基团由大到小的排列顺序。

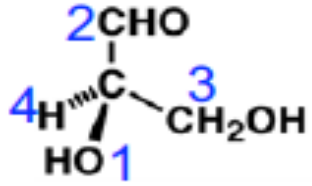
若由 a→b→c为顺时针方向旋转的，为R构型；

若由 a→b→c为逆时针方向旋转的，为S构型。

Assigning Chirality Center Configuration

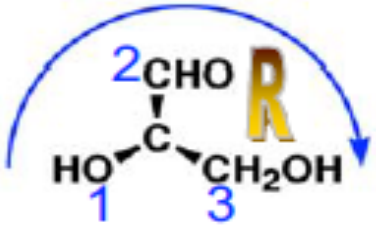
The configuration of chirality centers can be assigned using "R,S" descriptors.

1. Prioritize substituents with #'s 1-4 following Cahn-Ingold-Prelog Rules

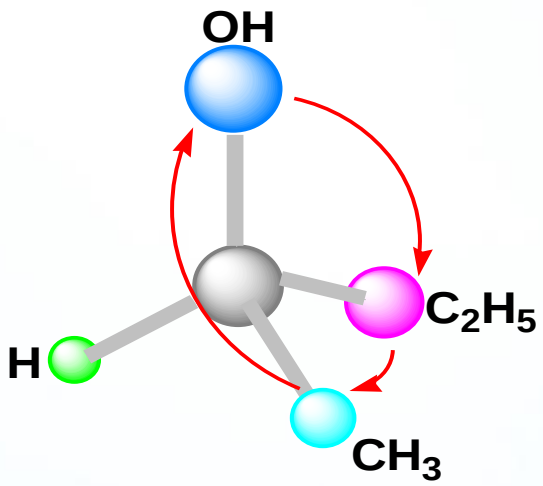


2. Orient molecule so substituent of lowest priority (4) is directed back

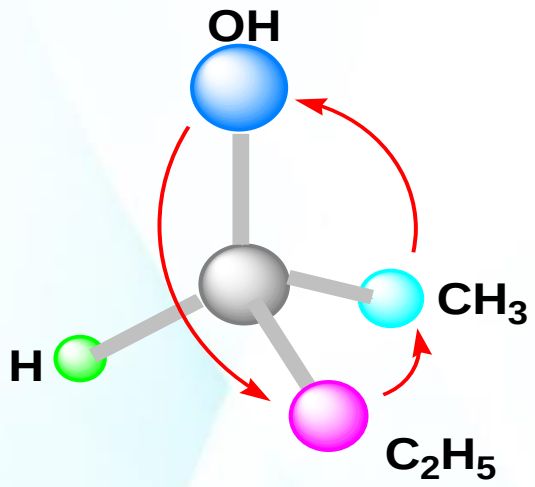
3. Starting from highest priority substituent (1) move to the second highest (2), then to third highest (3)



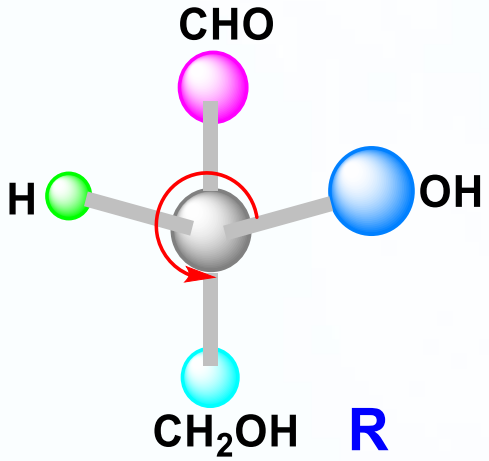
Clockwise movement: R
Counterclockwise movement: S



R

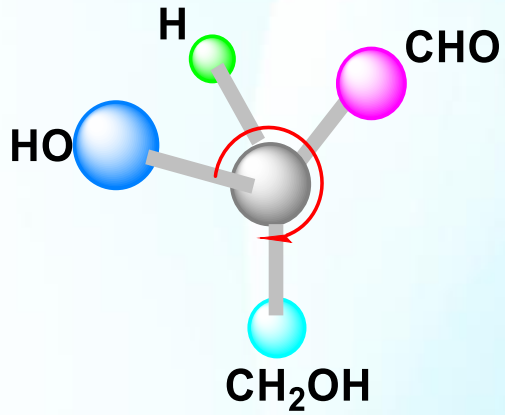


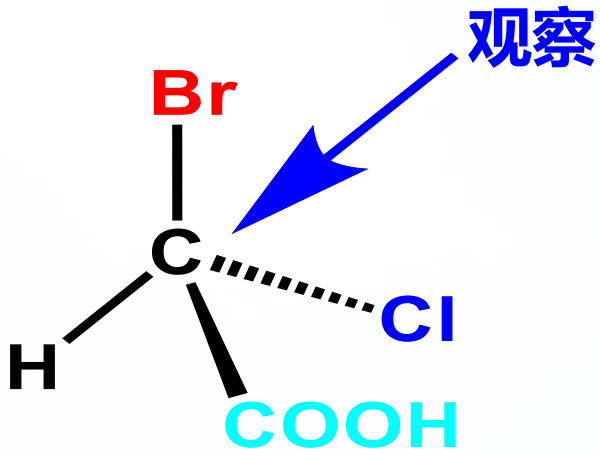
S



R

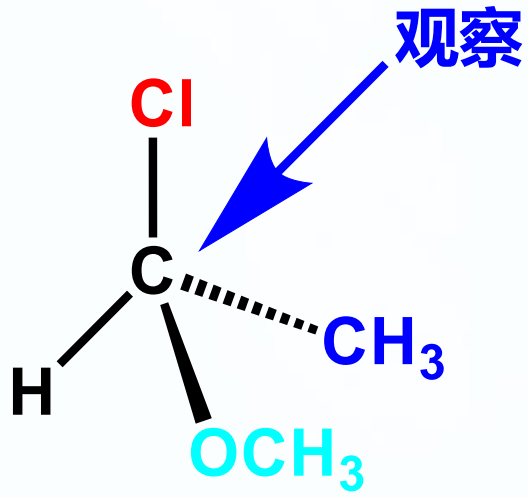
≡





Br → Cl → COOH

R型



Cl → CH_2OH → CH_3

S型

5. What is the 2^n rule?

For molecule with *n* stereocenters, the maximum number of stereoisomers possible is 2^n.

不相同的不对称碳原子数	对映异构体数	外消旋体数
1	2	1
2	4	2
3	8	4
4	16	8
n	2^n	2^{n-1}

外消旋体数目=2^{n-1} (n为不同手性碳的数目)

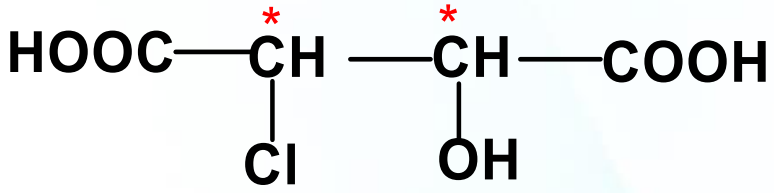
6. How to determine whether two compounds are the same?

Step 1: Verify that the compounds are stereoisomers.

Step 2: Assign R/S configurations to each stereo-center in both compounds.

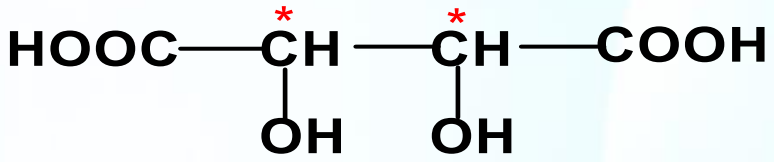
Step 3: Compare the configuration at corresponding stereocenters.

Possible Scenario	Relationship
All configurations the same	Identical compounds
All configurations opposite	enantiomers
Any other scenario	diastereomers



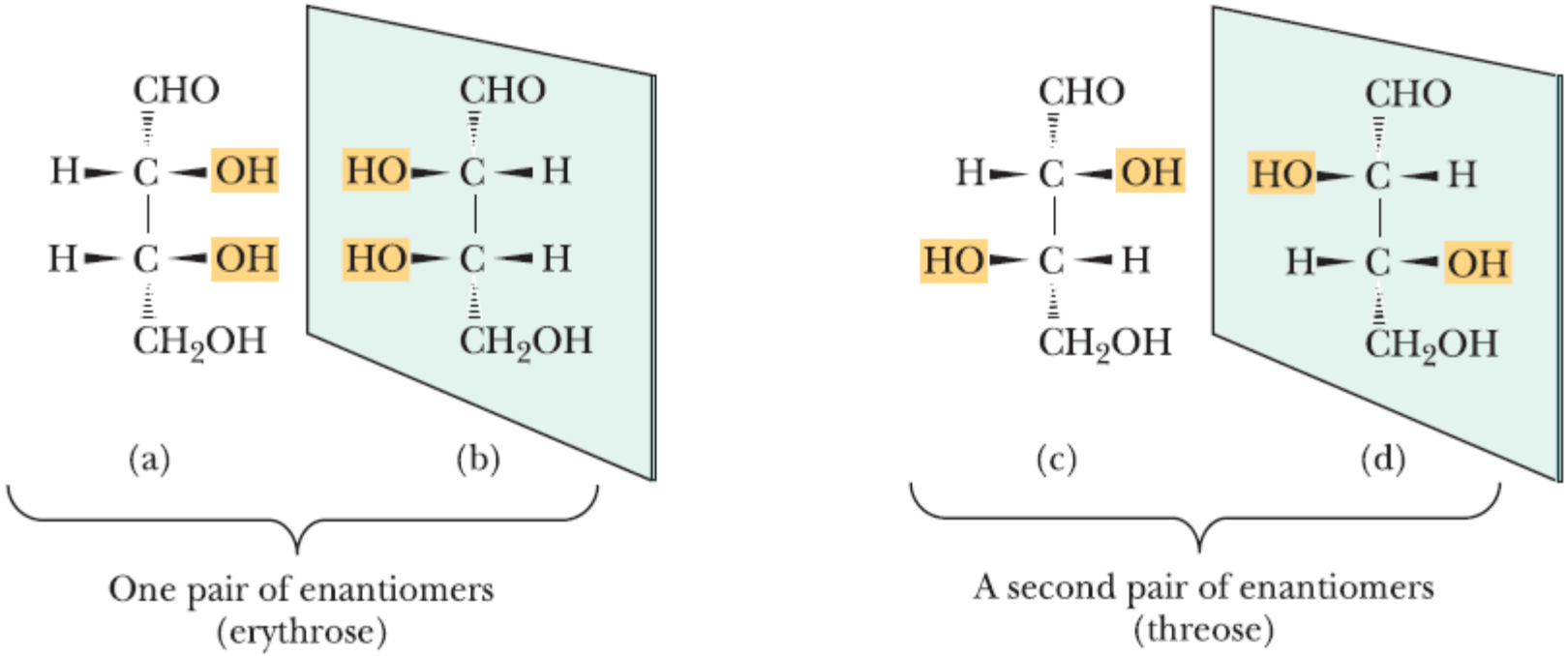
Racemate — A quivalent amount of mixture of a pair of enantiomers is called a racemate.

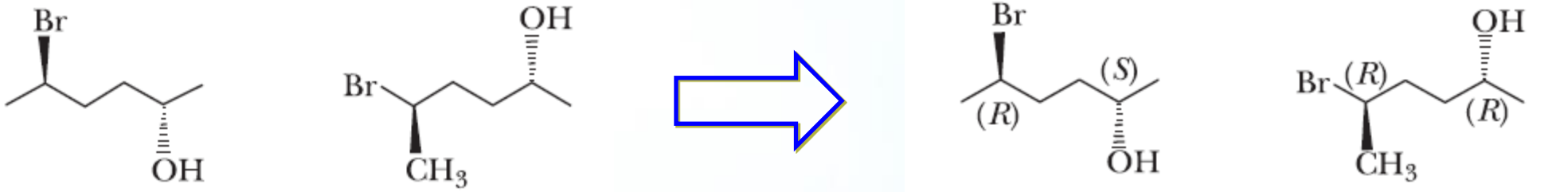
Diastereomers — Stereoisomers that are not mirror images of each other.

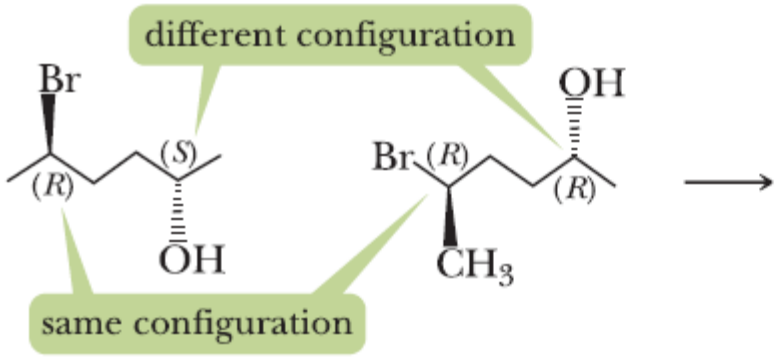


(tartaric acid)

Meso compound—An achiral compound possessing two or more stereocenters.

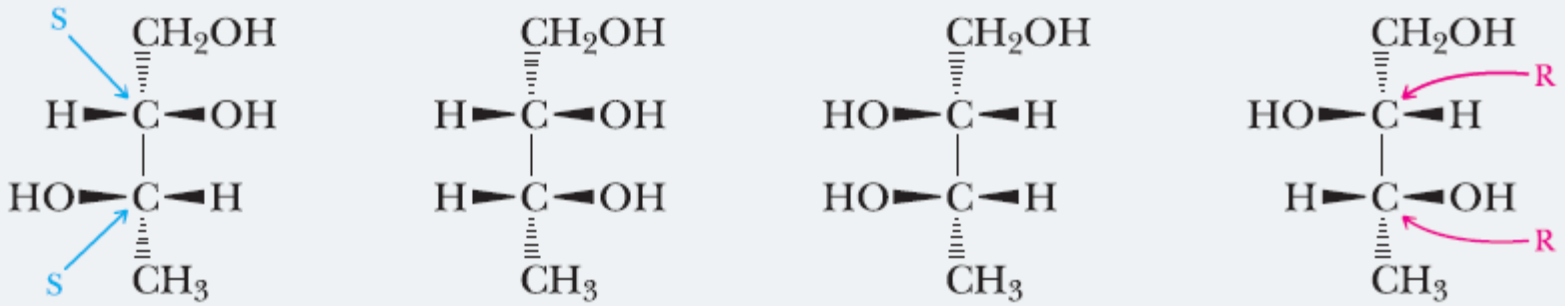

CHO
H C OH
H C OH
CH2OH
(a)
CHO
HO C H
HO C H
CH2OH
(b)
One pair of enantiomers
(erythrose)
CHO
H C OH
HO C H
CH2OH
(c)
CHO
HO C H
H C OH
CH2OH
(d)
A second pair of enantiomers
(threose)





Possible Scenario	Relationship
all configurations the same	identical compounds
all configurations opposite	enantiomers
any other scenario	diastereomers

Following are stereorepresentations of the four stereoisomers of 1,2,3-butanetriol:

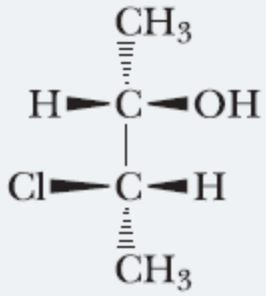


(1) (2) (3) (4)

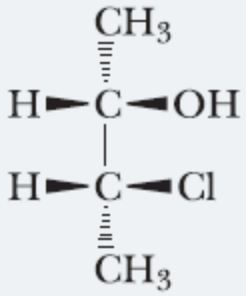
Configurations are given for the stereocenters in (1) and (4).

(a) Which compounds are enantiomers? **(b)** Which compounds are diastereomers?

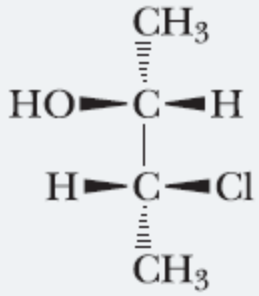
Following are stereorepresentations of the four stereoisomers of 3-chloro-2-butanol:



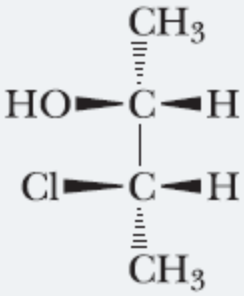
(1)



(2)



(3)



(4)

(a) Which compounds are enantiomers? **(b)** Which compounds are diastereomers?

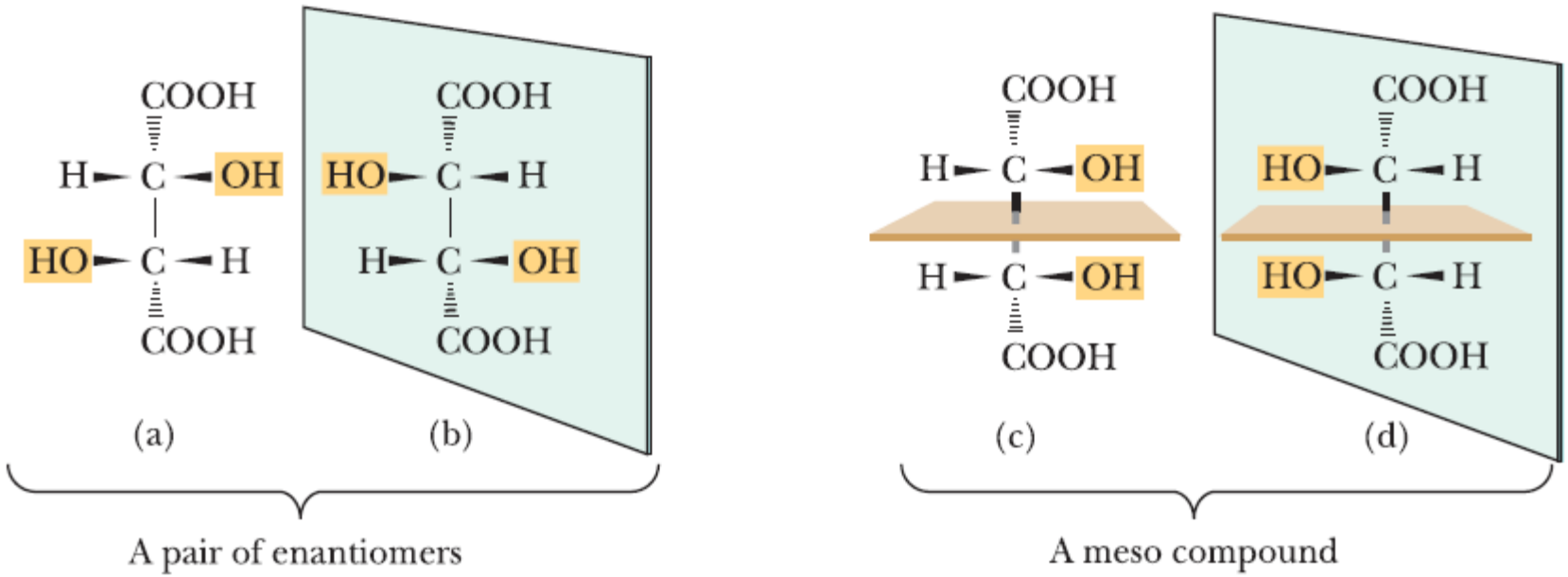
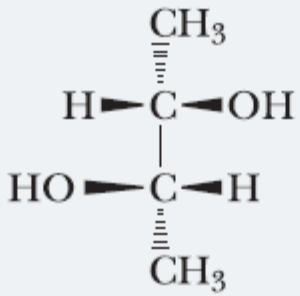
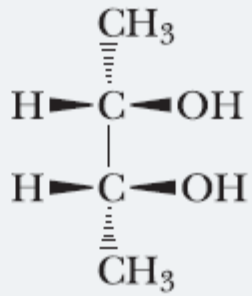


FIGURE 6.5
Stereoisomers of tartaric acid. One pair of enantiomers and one meso compound. The presence of an internal plane of symmetry indicates that the molecule is achiral.

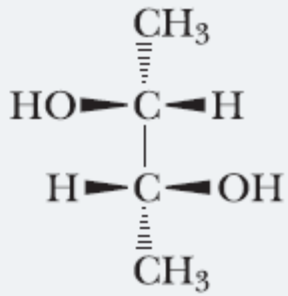
Following are stereorepresentations of the three stereoisomers of 2,3-butanediol:



(1)



(2)



(3)

(a) Which are enantiomers? **(b)** Which is the meso compound?

Summary

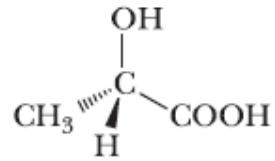
1. 立体异构；
2. 对映异构；
3. 对映异构与手性；
4. 对映异构的构型标记；
5. 2^n规则；
6. 怎样判断立体异构体之间的关系。

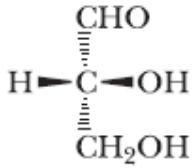
作业：
P192：6.20，6.22，6.24，6.25，6.41(b)、 (c)
6.46(a)

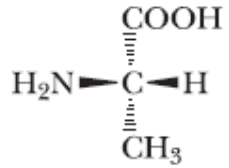
6.17 Which alcohols with the molecular formula $C_5H_{12}O$ are chiral?

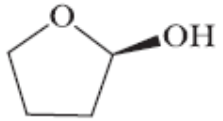
6.18 Which carboxylic acids with the molecular formula $C_6H_{12}O_2$ are chiral?

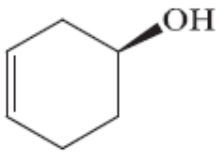
6.19 Draw the enantiomer for each molecule: **(See Example 6.1)**

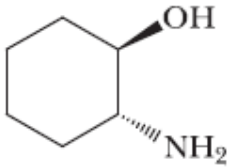
(a) 

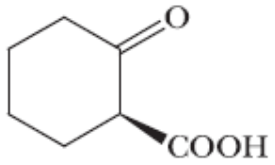
(b) 

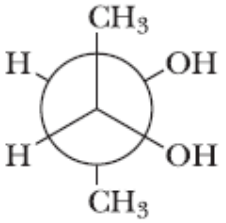
(c) 

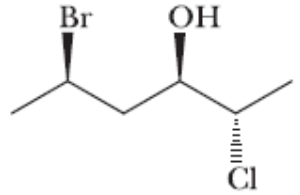
(d) 

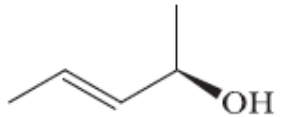
(e) 

(f) 

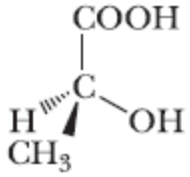
(g) 

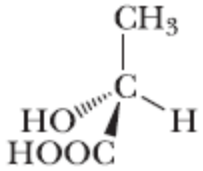
(h) 

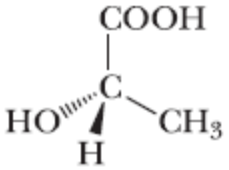
(i) 

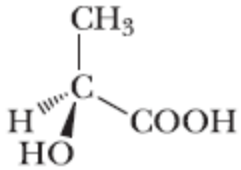
(j) 

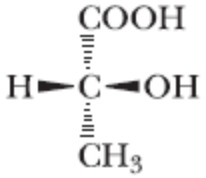
6.23 Following are eight stereorepresentations of lactic acid: **(See Examples 6.3, 6.4)**

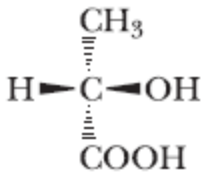
(a) 

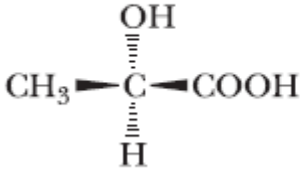
(b) 

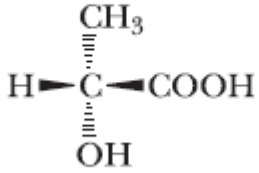
(c) 

(d) 

(e) 

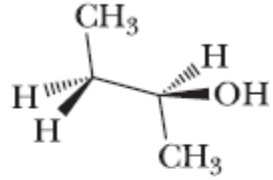
(f) 

(g) 

(h) 

Take (a) as a reference structure. Which stereorepresentations are identical with (a) and which are mirror images of (a)?

6.27 Following is a staggered conformation of one of the stereoisomers of 2-butanol: **(See Example 6.2)**



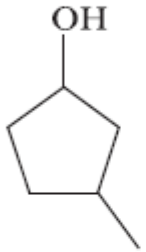
(a) Is this (*R*)-2-butanol or (*S*)-2-butanol?
(b) Draw a Newman projection for this staggered conformation, viewed along the bond between carbons 2 and 3.
(c) Draw a Newman projection for one more staggered conformations of this molecule. Which of your conformations is the more stable? Assume that —OH and —CH_3 are comparable in size.

6.31 Label each stereocenter in these molecules with an asterisk and tell how many stereoisomers exist for each. **(See Examples 6.5, 6.6)**

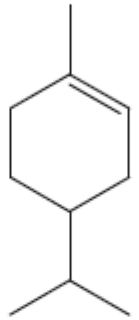
(a) $CH_3CHCHCOOH$ (OH, OH)

(b) $CH_2(COOH)CH(COOH)CH(OH)COOH$

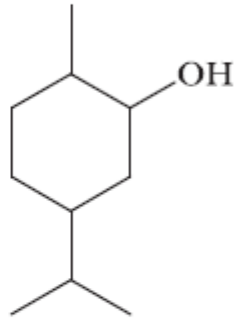
(c)



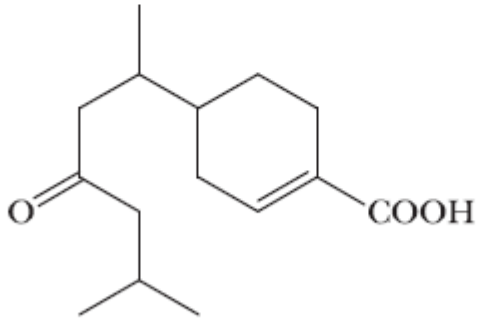
(d)



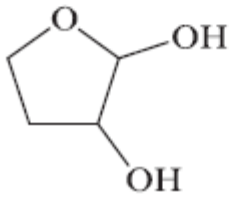
(e)



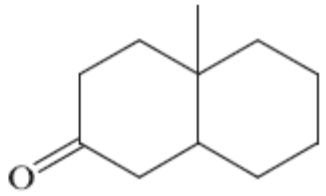
(f)



(g)

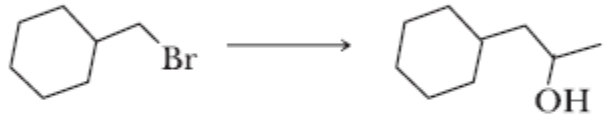


(h)



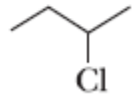
6.41 Test your cumulative knowledge of the reactions learned so far by completing the following chemical transformations. Pay particular attention to the stereochemistry in the product. Where more than one stereoisomer is possible, show each stereoisomer. *Note that some transformations will require more than one step.*

(a)

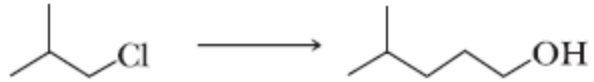


(b) $CH_3CH_2Br \longrightarrow$

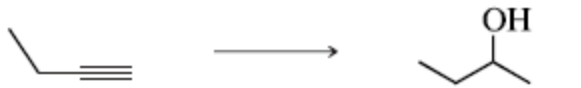
(c) $H{-}{\equiv}{-}H \longrightarrow$



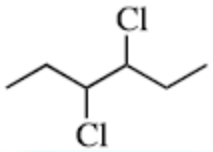
(d)



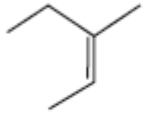
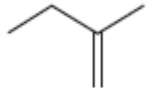
(i)



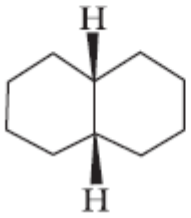
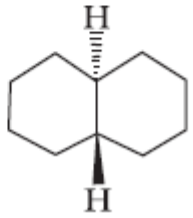
(j) $CH_2{=}CH_2 \longrightarrow$



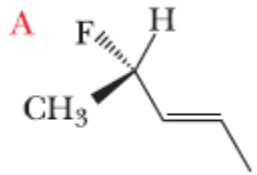
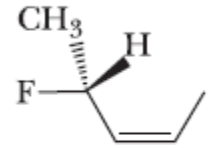
6.42 Predict the product(s) of the following reactions (in cases where more than one stereoisomer is possible, show each stereoisomer):

(a)  $\xrightarrow[Pt]{H_2}$ (b)  $\xrightarrow[H_2SO_4]{H_2O}$

6.43 What alkene, when treated with H_2/Pd, will ensure a 100% yield of the stereoisomer shown?

(a)  (b) 

4. What is the relationship between the following two molecules?

A  B 

(a) They are identical.
(b) They are enantiomers.
(c) They are diastereomers.
(d) They are constitutional isomers.
(e) They are nonisomers.

也许有一天，不知不觉，你将渐渐活出写满答案的人生！