

Stereochimica

Molecole nelle tre dimensioni

Isomeri

Composti differenti con la stessa formula molecolare

Isomeri costituzionali

Isomeri i cui atomi hanno una diversa connettività



Stereoisomeri

Isomeri i cui atomi hanno la stessa connettività, ma un diverso orientamento nello spazio

Stereoisomeri conformazionali

Stereoisomeri configurazionali

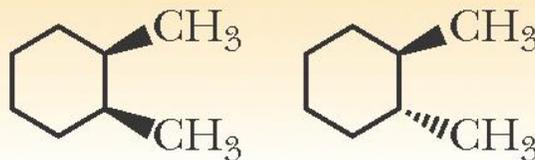
Enantiomeri

Stereoisomeri le cui molecole sono immagini speculari non sovrapponibili



Diastereoisomeri

Stereoisomeri le cui molecole non sono immagini speculari



Stereoisomeri: definizioni

- Stereoisomeri conformazionali: si interconvertono per rotazione attorno a un legame
- Stereoisomeri configurazionali: non possono interconvertirsi senza rompere legami:
 - Enantiomeri: stereoisomeri che sono immagini speculari *non* sovrapponibili.
 - Diastereomeri: stereoisomeri che non sono immagini speculari.

Isomeri conformazionali

- Sono strutture che risultano dalla libera rotazione attorno a un legame singolo.
- Possono differire in energia.
 - Prevalere il conformero a energia più bassa.
- Le molecole ruotano costantemente attraverso tutte le conformazioni possibili.

Stereoisomeria configurazionale

CHIRALITA'

- Ogni oggetto ha un'immagine speculare: le due immagini speculari possono o non possono essere sovrapponibili
- Alcune molecole sono come le mani. La mano destra e la sinistra sono immagini speculari, ma non sono identiche: non sono sovrapponibili



Achiralità

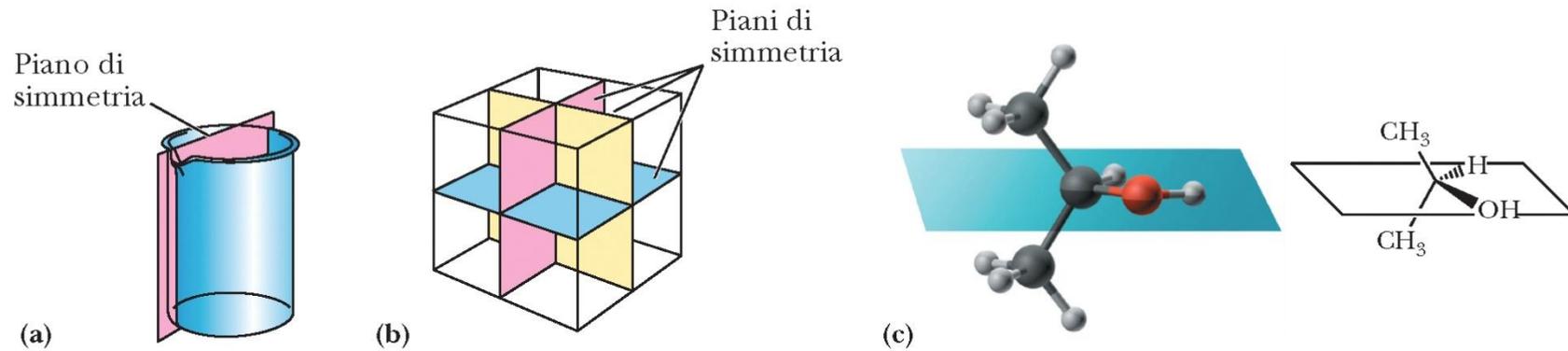
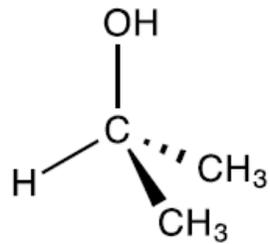


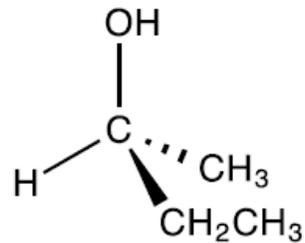
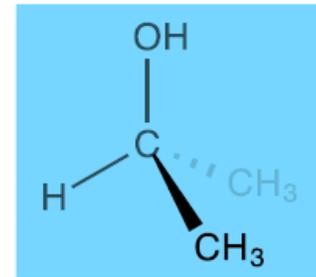
FIGURA 6.2 Piani di simmetria in (a) un beaker, (b) in un cubo e (c) nel 2-propanolo. Il beaker e il 2-propanolo hanno un solo piano di simmetria; il cubo ha diversi piani di simmetria, dei quali sono mostrati solo tre in figura.

Se un oggetto o una molecola ha un piano di simmetria, è achirale e le due immagini speculari sono sovrapponibili, sono identiche, sono lo stesso oggetto

Chiralità e Simmetria



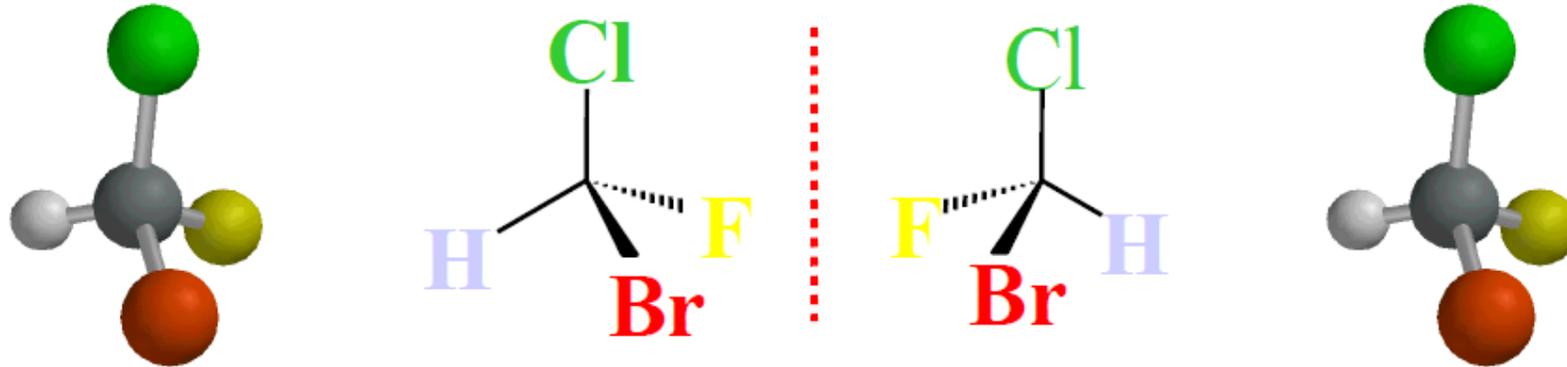
ha un piano di simmetria:
achirale



non ha piani di simmetria
chirale

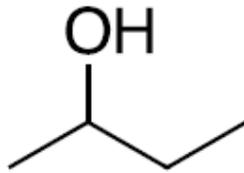
Carbonio stereogenico o stereocentro

- Un carbonio stereogenico è *tetraedrico* (sp^3) ed ha quattro sostituenti diversi:



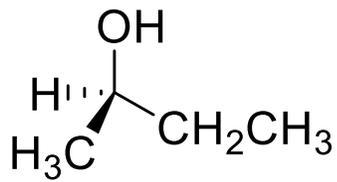
- Una molecola chirale ha uno stereocentro, è *dissimmetrica*.
- Esiste in due forme, immagini speculari non sovrapponibili, che formano una *coppia di enantiomeri*

Enantiomeri

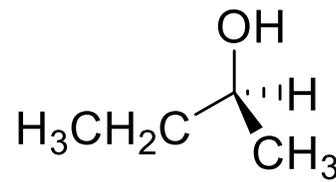


2-butanolo

specchio

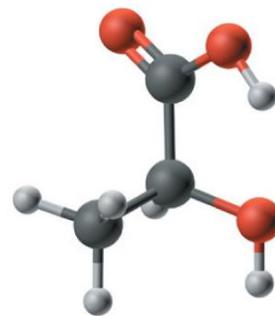
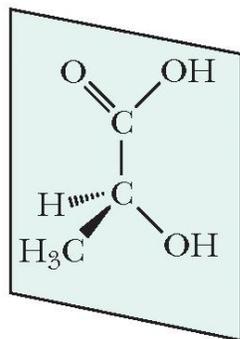
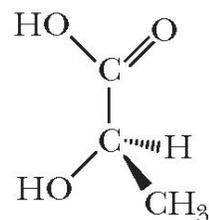
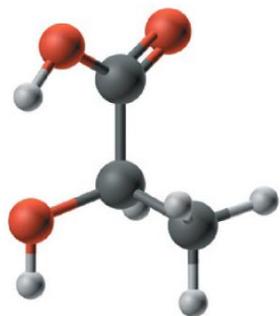


Enantiomero 1

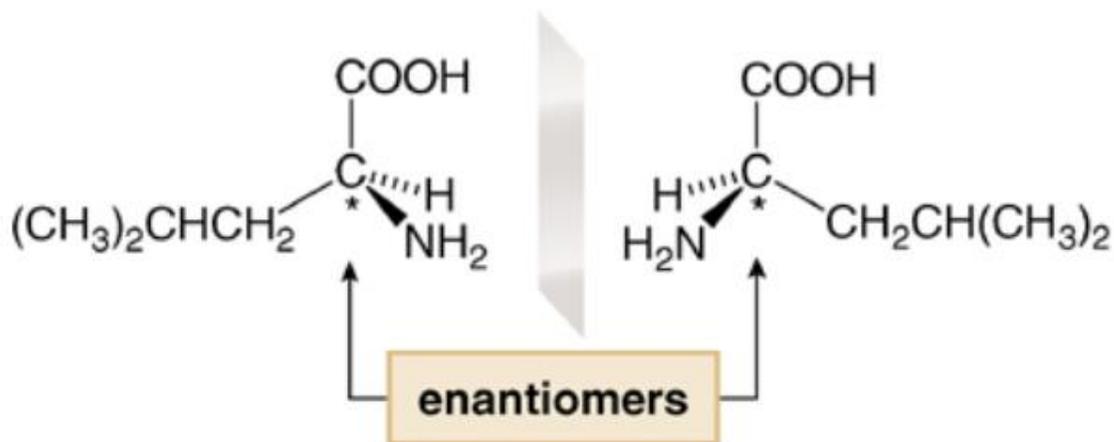


Enantiomero 2

Esempi di molecole chirali



Acido lattico



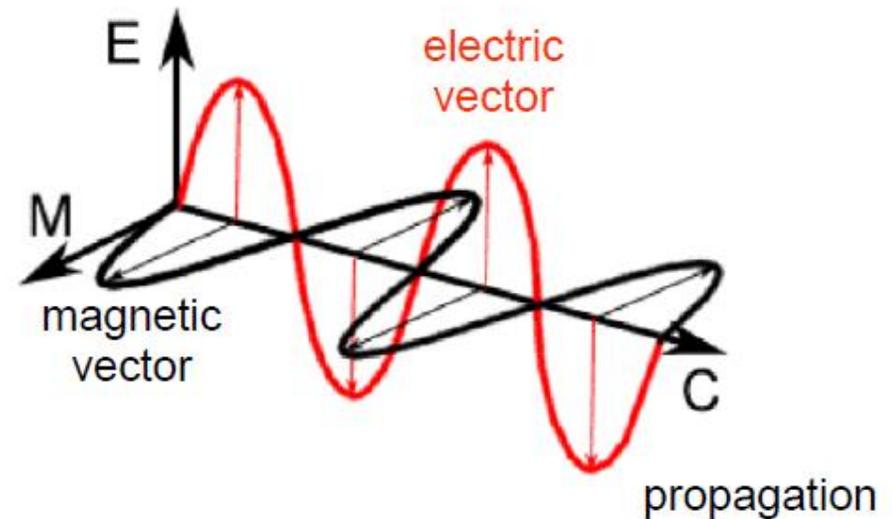
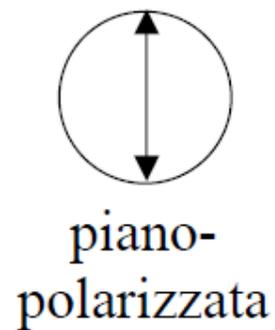
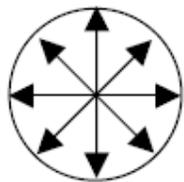
Leucina, un amminoacido

Attività ottica

- Le proprietà *fisiche* degli enantiomeri sono identiche (punto di ebollizione, punto di fusione, densità, indice di rifrazione, etc.) tranne che per la direzione in cui ruotano il piano della luce piano polarizzata.
- Gli enantiomeri sono isomeri ottici o otticamente attivi

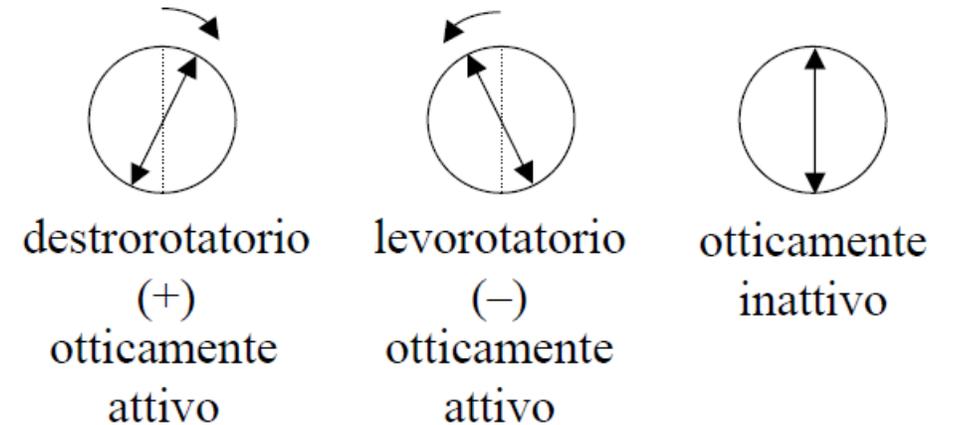
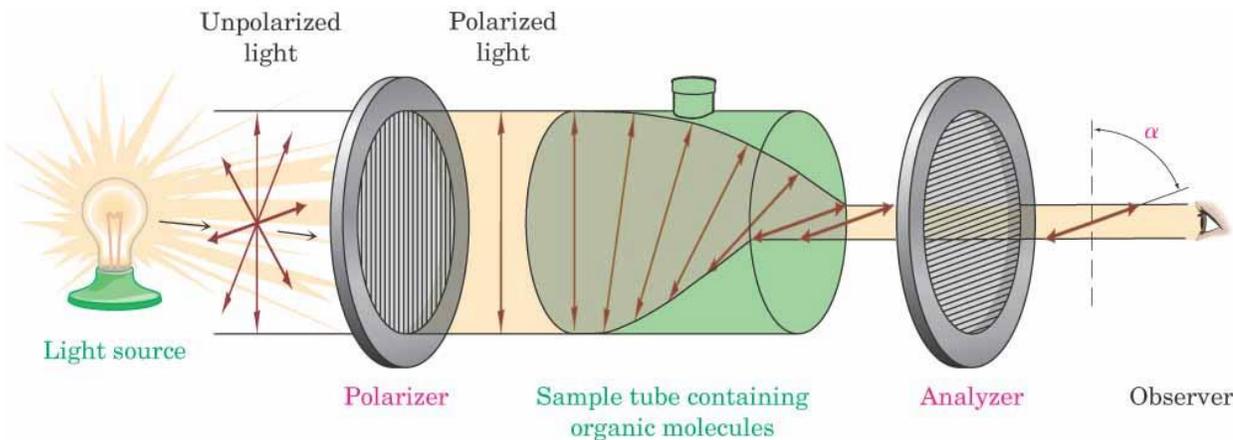
Tipi di luce

- Luce ordinaria consiste di onde che vibrano in tutti i piani perpendicolari alla direzione di propagazione
- Luce piano polarizzata consiste di onde che vibrano in un solo piano



Polarimetro

- È lo strumento che misura il grado di rotazione del piano della luce piano polarizzata.



Attività ottica

- Composto otticamente inattivo:
 - a. molecola achirale
 - b. miscela racema, (\pm), miscela 50/50 dei due enantiomeri
- Composto otticamente puro: 100% di un enantiomero
- Purezza ottica (*eccesso enantiomerico, e.e.*)
= per cento di un enantiomero – per cento dell'altro
 - es. 80% di un enantiomero e 20% dell'altro = 60% *e.e.* o purezza ottica

Attività ottica

- Rotazione specifica $[\alpha]_D^T$

temperatura

rotazione osservata ($^\circ$)

$$[\alpha]_D^T = \frac{\alpha}{cl}$$

cammino ottico (dm)

concentrazione (g/mL soluzione)

riga D del sodio

riga D del sodio = 589 nm

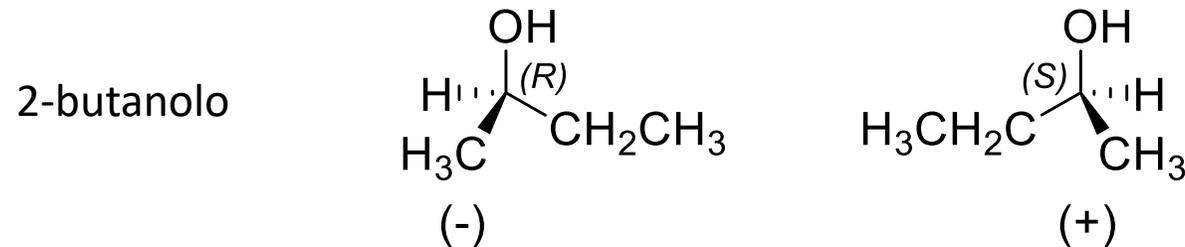
The diagram shows the formula $[\alpha]_D^T = \frac{\alpha}{cl}$ with arrows pointing to each part: 'temperatura' points to the superscript T; 'rotazione osservata (°)' points to the numerator alpha; 'cammino ottico (dm)' points to the denominator c; 'concentrazione (g/mL soluzione)' points to the denominator l; and 'riga D del sodio' points to the subscript D. A separate note on the left states 'riga D del sodio = 589 nm'.

es. (+)-2-butanolo $[\alpha]_D^{27} = +13.5^\circ$
(-)-2-butanolo $[\alpha]_D^{27} = -13.5^\circ$

La rotazione specifica calcolata in questo modo è una proprietà fisica caratteristica di ogni composto otticamente attivo.

Configurazioni *R* e *S*

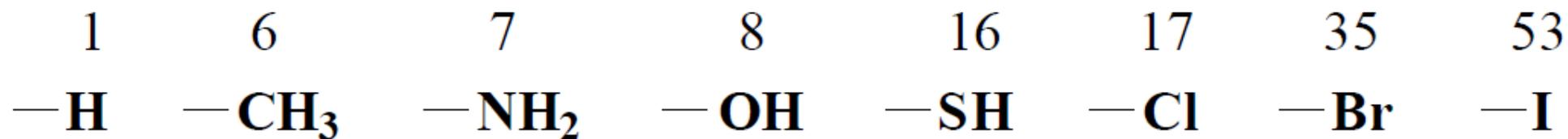
- *R* e *S* sono due descrittori che definiscono la configurazione di uno stereocentro attraverso un set di regole.



- Tale assegnazione non dice quale enantiomero è destrogiro e quale levogiro.
- Non c'è relazione tra la configurazione assoluta di una molecola e il segno della sua rotazione ottica.

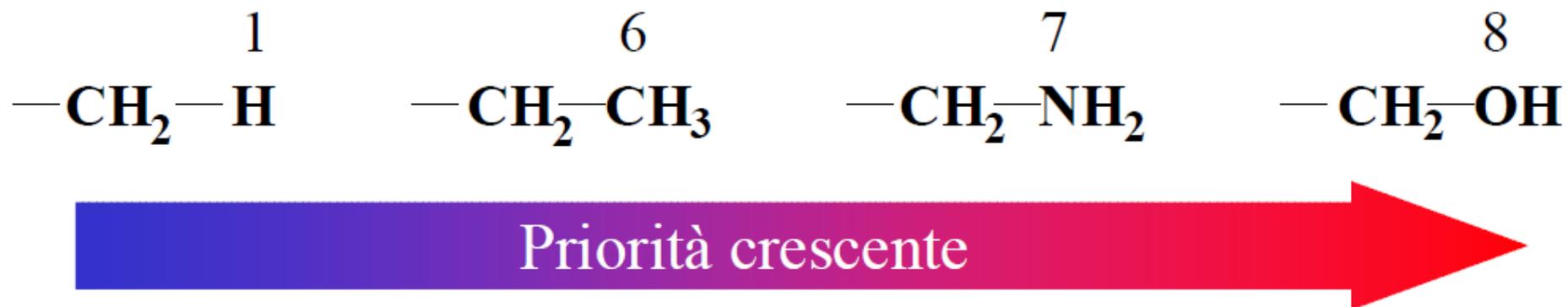
Convenzione *R,S*

- Regole di Priorità (Cahn, Ingold, Prelog)
- Ad ogni *atomo* legato direttamente allo stereocentro viene assegnata una priorità, sulla base del **numero atomico**. Più alto è il numero atomico, più alta la priorità



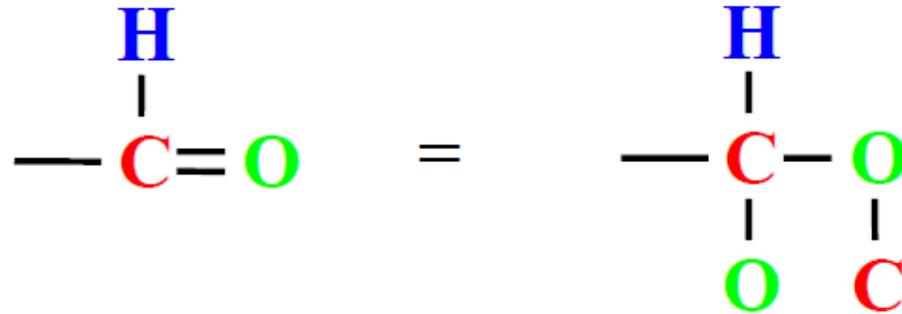
Convenzione *R,S*

- Se non si può assegnare una priorità sulla base del numero atomico dell'atomo legato allo stereocentro, si va al set di atomi successivi.
- La priorità viene assegnata alla prima differenza.



Convenzione R,S

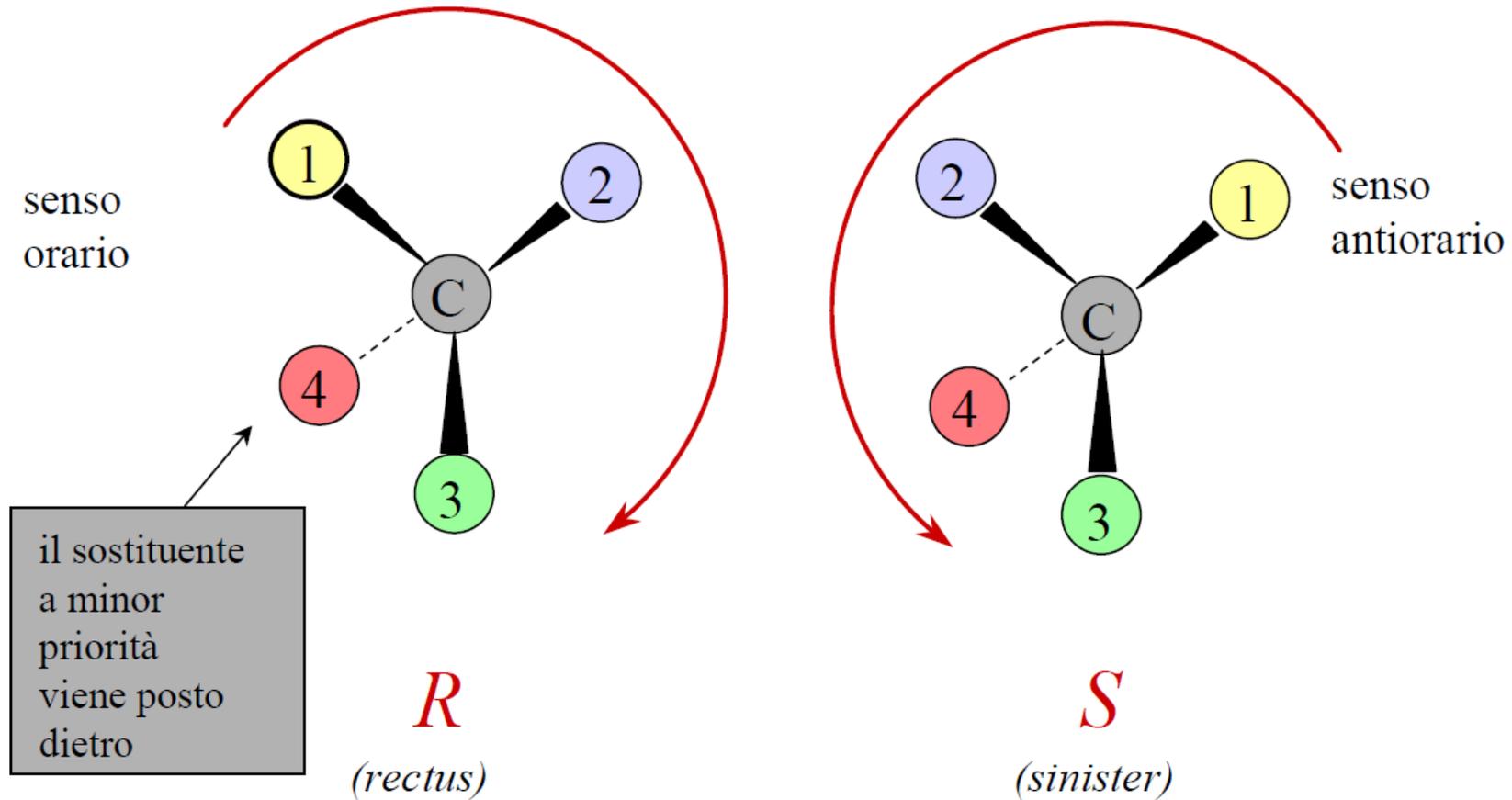
- Gli atomi che possiedono doppi o tripli legami sono considerati legati ad un numero equivalente di atomi simili con legami singoli



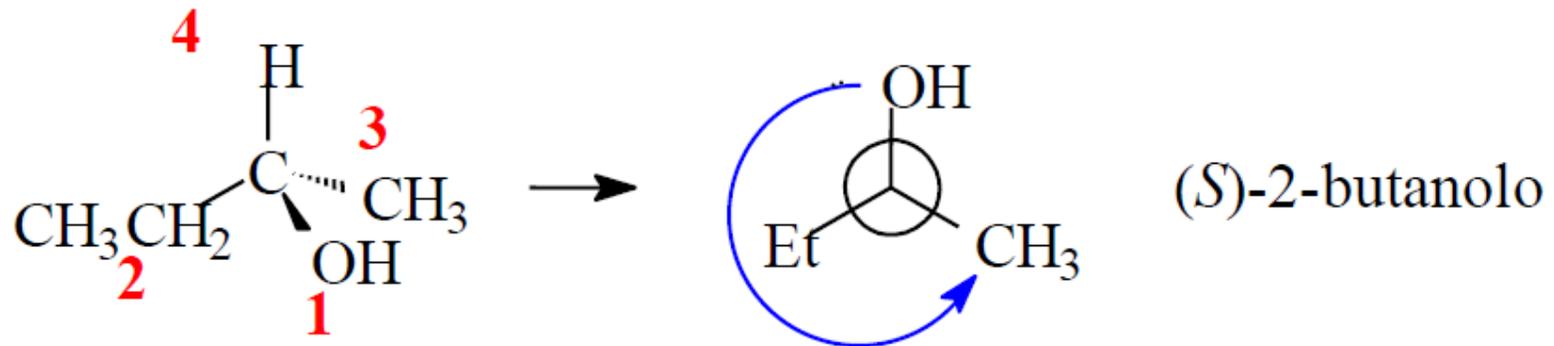
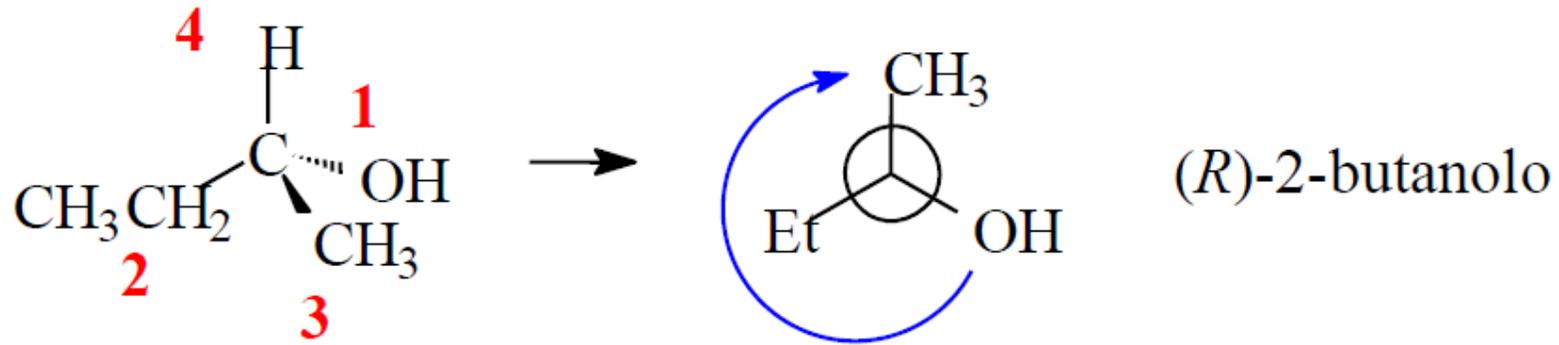
Convenzione *R,S*

- Assegnare la priorità ai quattro sostituenti secondo le Regole di Priorità.
- Orientare la molecola in modo che il gruppo a priorità più bassa sia lontano dall'osservatore.
- Determinare la direzione di precessione degli altri tre gruppi cominciando da quello con la massima priorità:
 - senso orario = ***R*** (*rectus*)
 - senso antiorario = ***S*** (*sinister*)

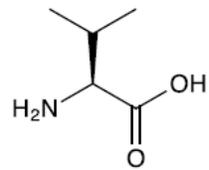
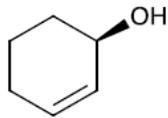
Convenzione R,S



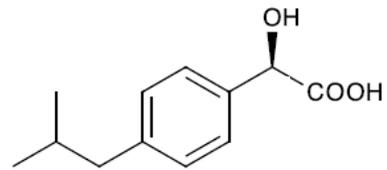
Esempi



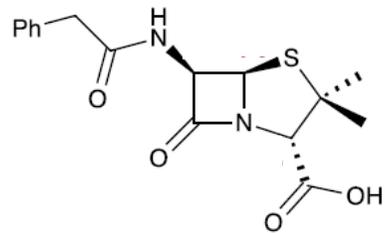
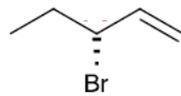
Esercizi



valina

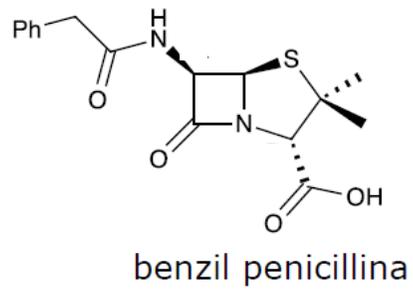
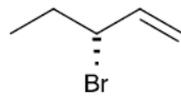
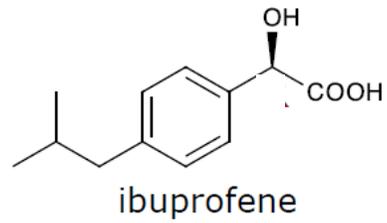
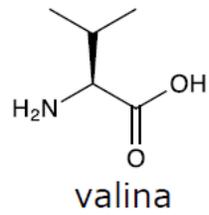
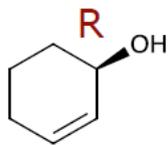


ibuprofene

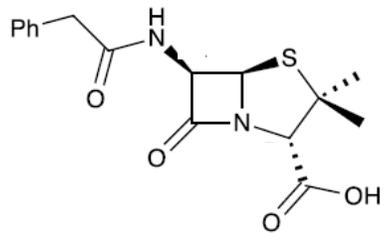
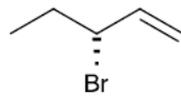
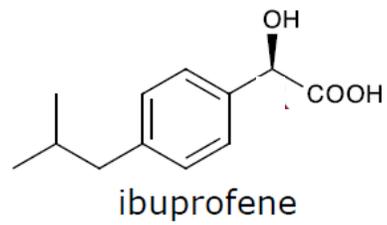
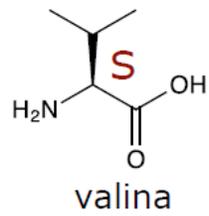
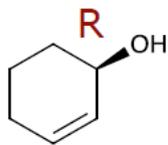


benzil penicillina

Esercizi

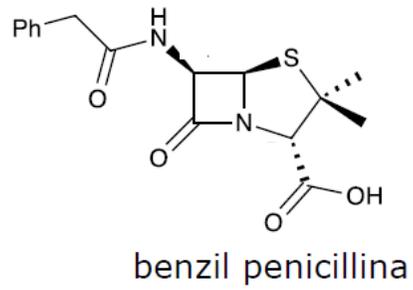
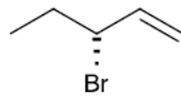
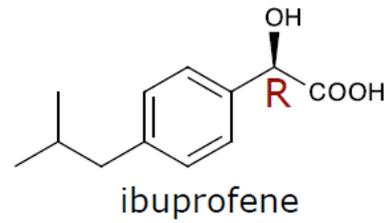
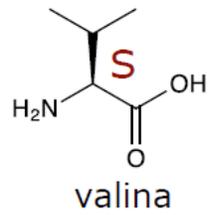
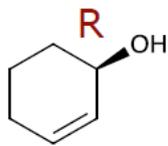


Esercizi

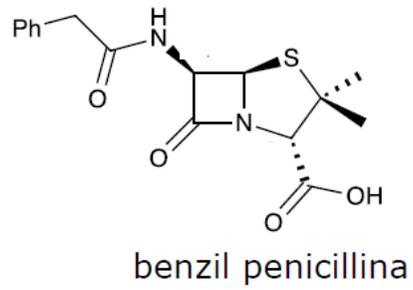
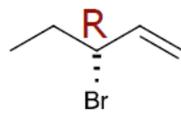
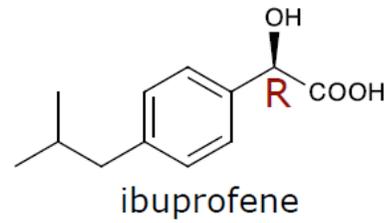
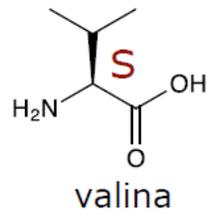
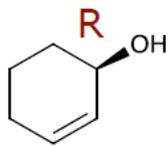


benzil penicillina

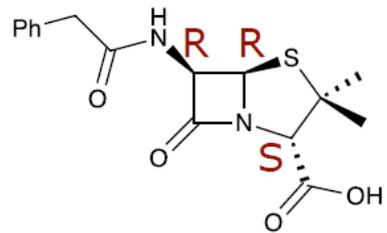
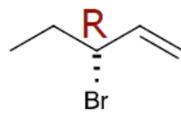
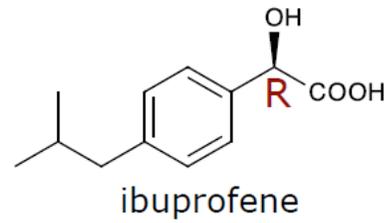
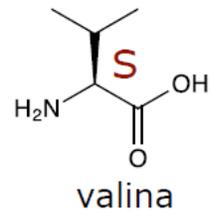
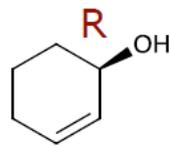
Esercizi



Esercizi



Esercizi



benzil penicillina

Talidomide

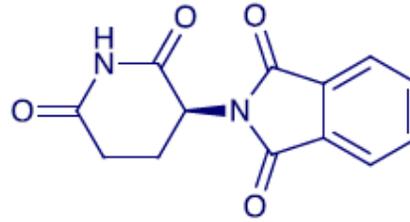
1953: scoperto in Germania

1957: commercializzato come farmaco da banco

1957-1961: ampiamente usato contro le nausee mattutine nelle donne in gravidanza

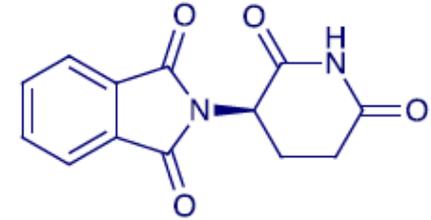
1957-1960: abnorme incidenza di focomelia: 10.000 - 20.000 casi al mondo. 50% mortalità

1961-1962: ritirato dal mercato



(-)

sedativo



(+)

Teratogeno

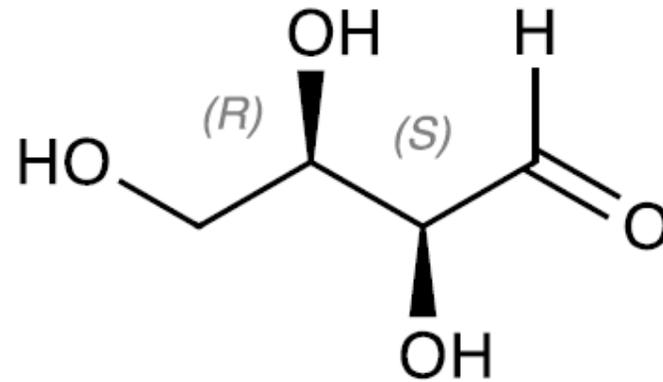
produce anomalie nell'embrione

Composti con due o più stereocentri

- Diastereomeri o diastereoisomeri: stereoisomeri che non sono immagini speculari.
- I diastereomeri hanno differenti proprietà fisiche.
- n carboni chirali $\Rightarrow 2^n$ possibili stereoisomeri

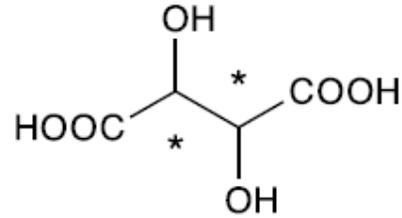
Diastereoisomeri

- Quando un composto ha più di uno stereocentro, le configurazioni R e S devono essere assegnate a ognuno di essi.

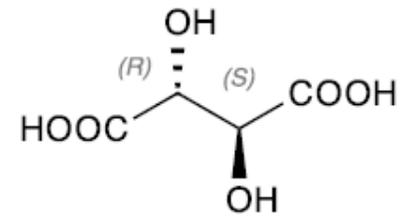
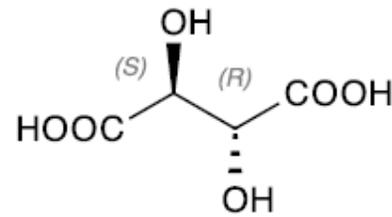
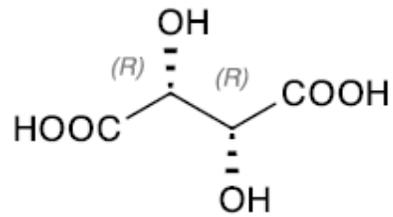
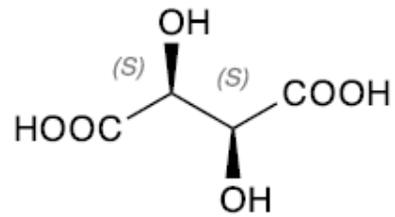


(2S,3R)-2,3,4-triidrossibutanale (treosio)

Composti meso



acido tartarico

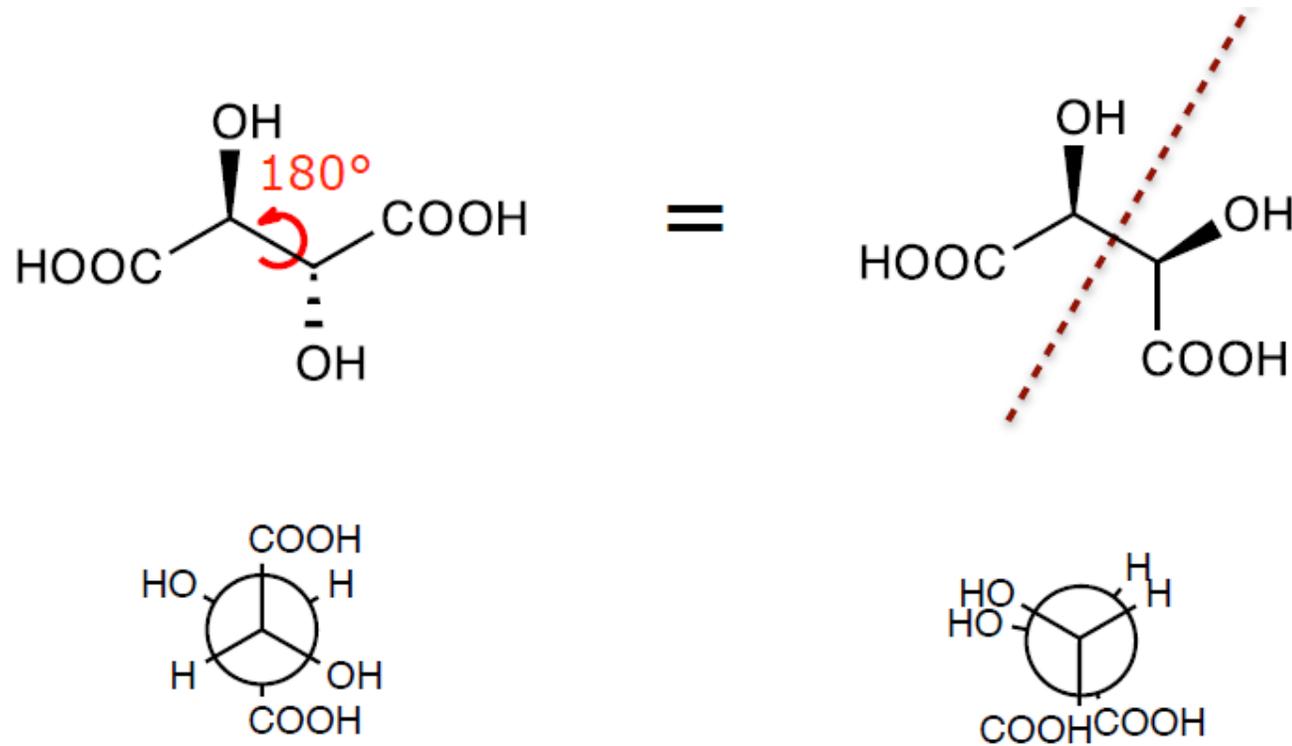


enantiomeri

identici

diastereoisomeri

Composti meso



I composti meso posseggono un piano di simmetria e sono achirali

Acido tartarico

acido (–)-tartarico

$$[\alpha]_D = -12.0$$

pf 168 – 170 °C

solubilità di 1 g

0.75 mL H₂O

1.7 mL metanolo

250 mL etere

insolubile in CHCl₃

d = 1.758 g/mL

acido (+)-tartarico

$$[\alpha]_D = +12.0$$

pf 168 – 170 °C

solubilità di 1 g

0.75 mL H₂O

1.7 mL metanolo

250 mL etere

insolubile in CHCl₃

d = 1.758 g/mL

acido *meso*-tartarico

$$[\alpha]_D = 0$$

pf 140 °C

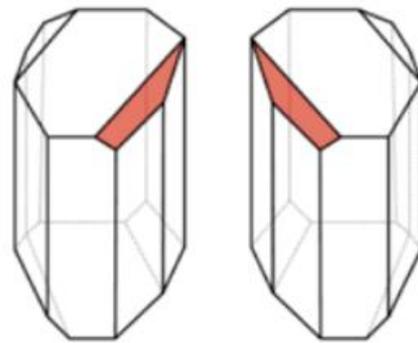
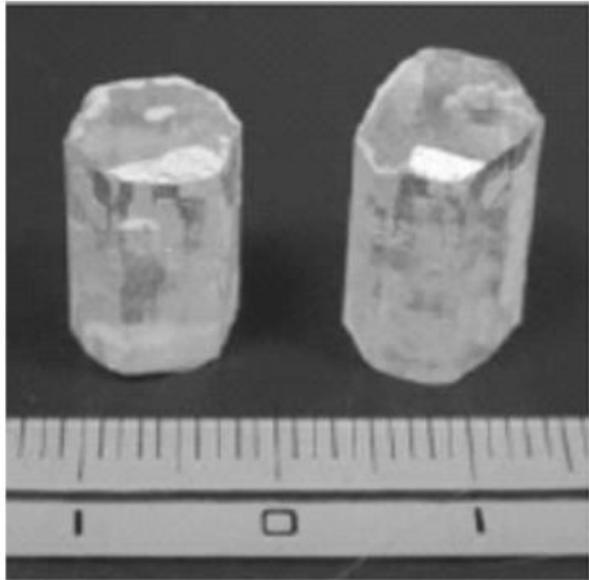
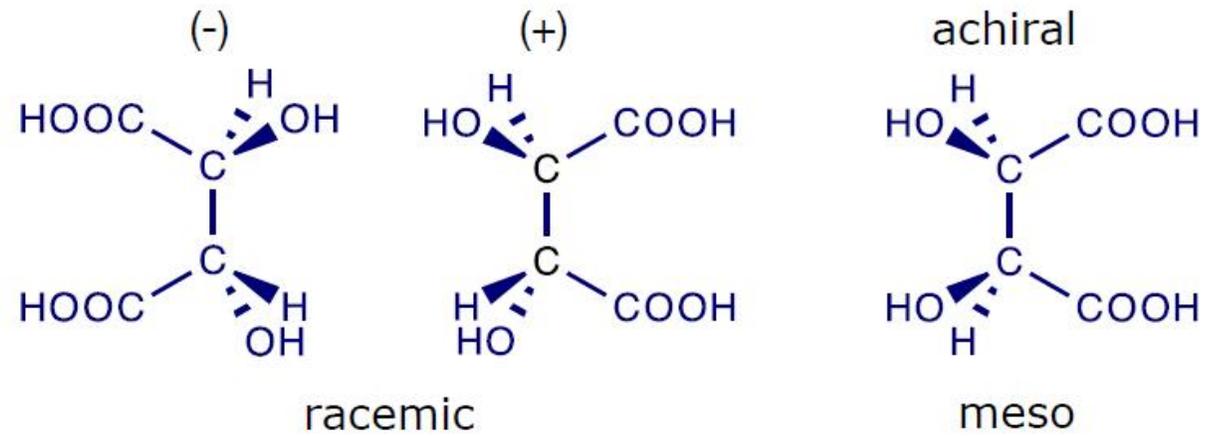
solubilità di 1 g

0.94 mL H₂O

insolubile in CHCl₃

d = 1.666 g/mL

Louis Pasteur 1822-1895



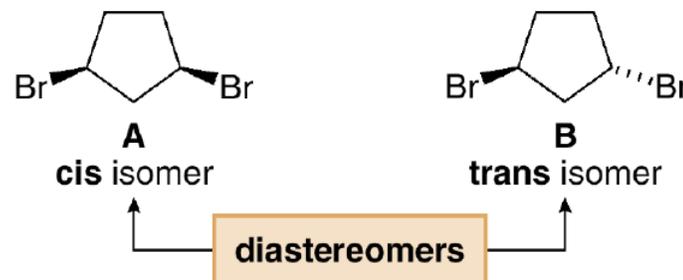
Sali dell'acido tartarico

Composti ciclici

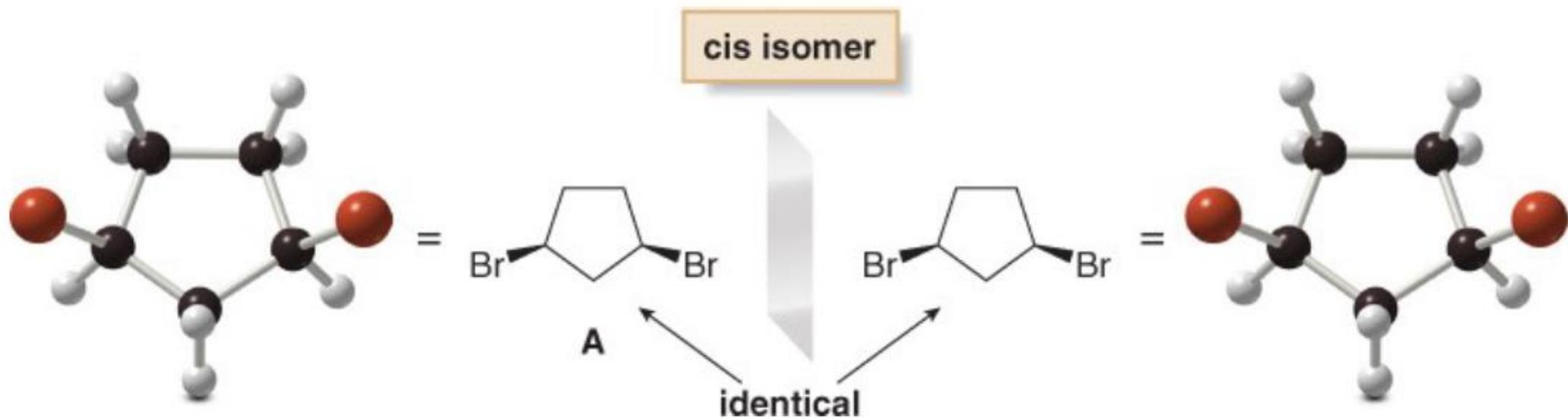
- 1,3-dibromociclopentano, 2 stereocentri, al massimo 4 stereoisomeri (2^n)



- L'isomero *cis* A e l'isomero *trans* B sono stereoisomeri ma non immagini speculari, sono diastereoisomeri

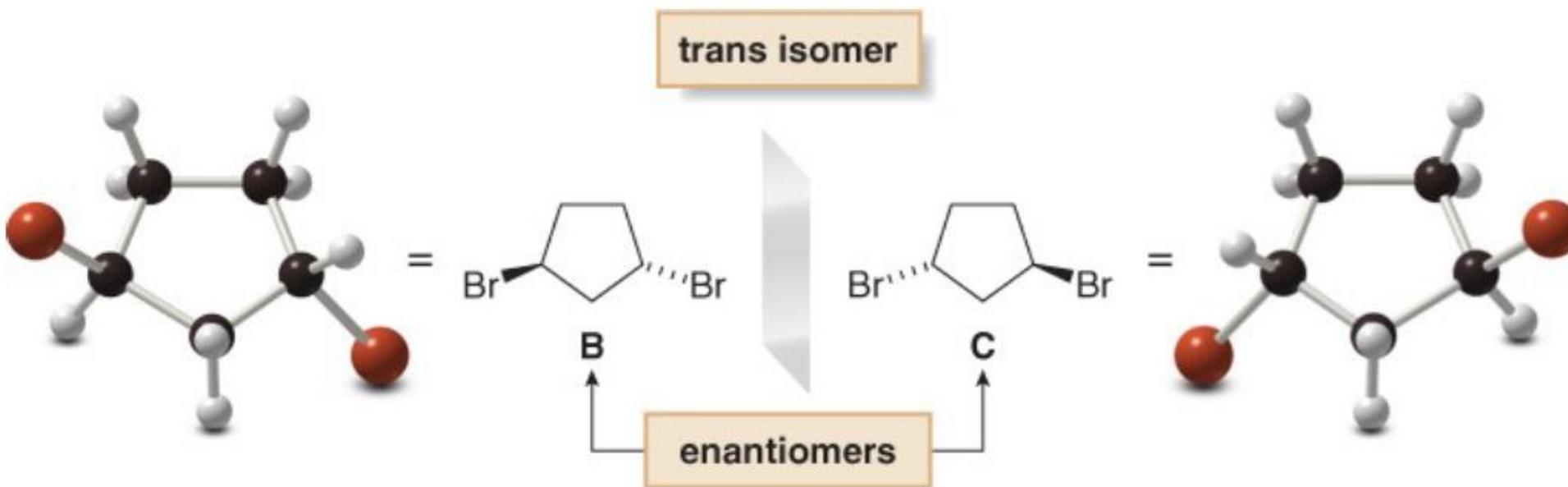


Composti ciclici



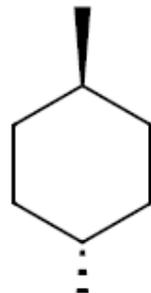
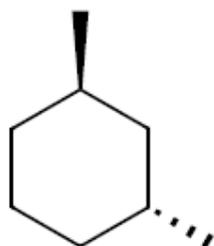
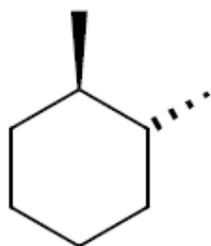
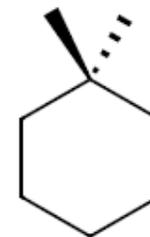
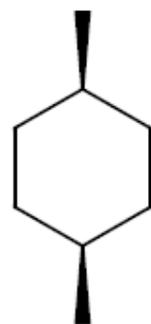
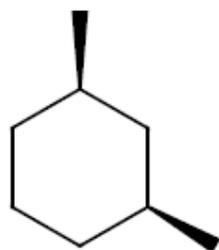
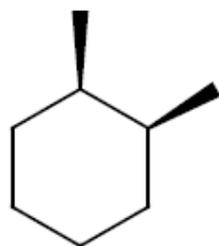
Le due immagini speculari sono identiche, l'isomero *cis* è un composto meso achirale

Composti ciclici

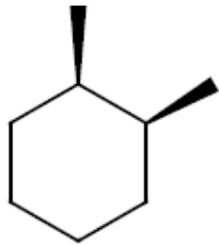


L'omero *trans* (B) non è sovrapponibile alla sua immagine speculare (C),
(B) e (C) sono enantiomeri

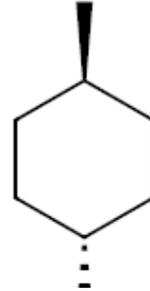
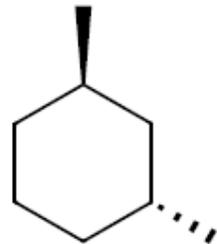
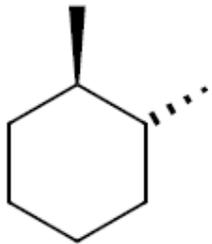
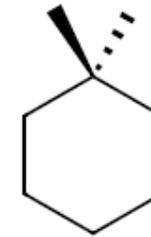
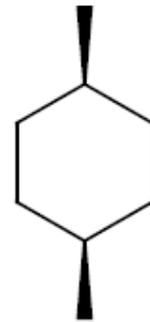
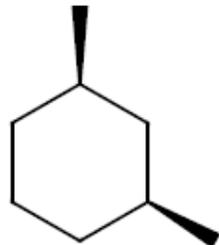
Indica se i seguenti dimetilcicloesani sono
chirali, achirali o meso



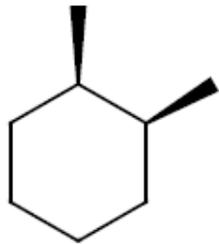
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chirali, achirali o meso



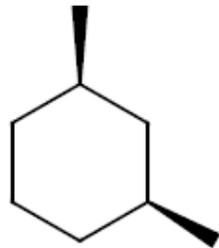
meso



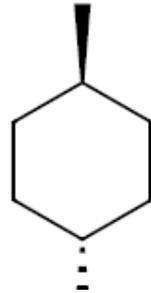
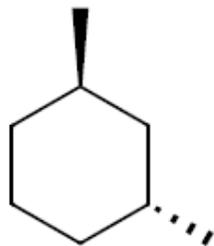
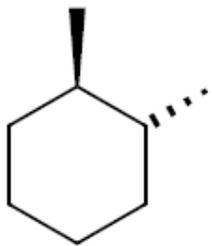
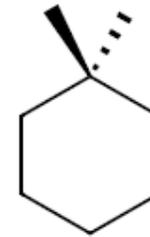
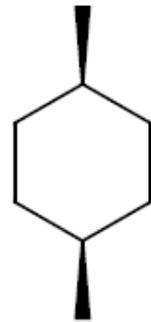
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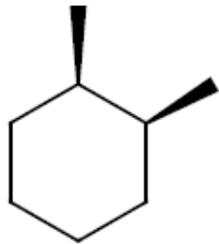
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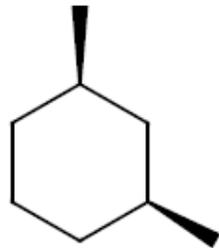
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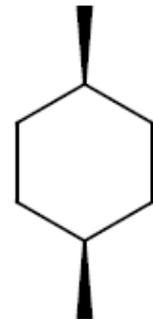
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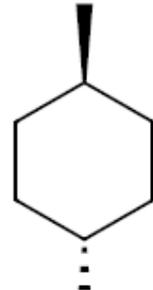
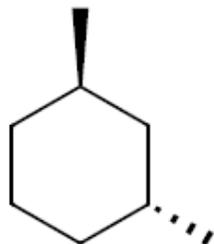
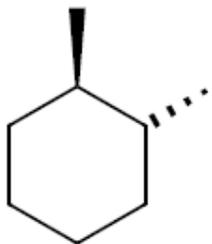
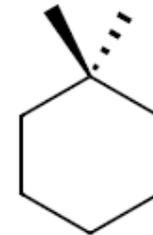
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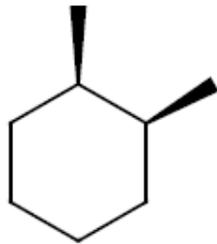
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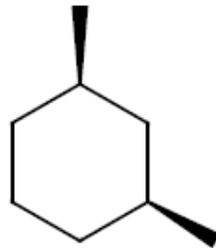
achirale



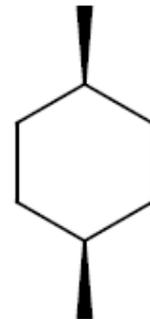
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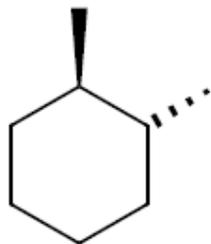
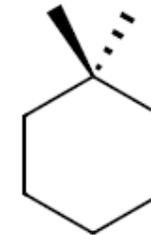
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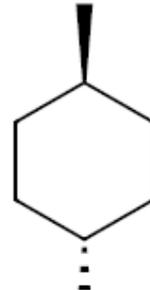
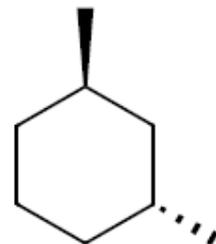
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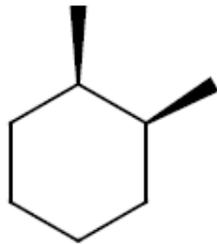
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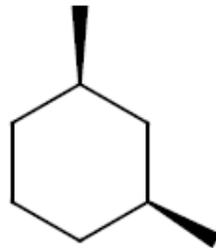
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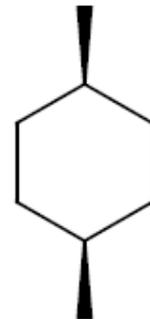
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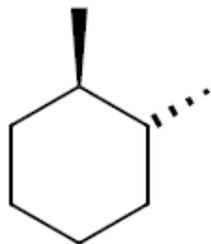
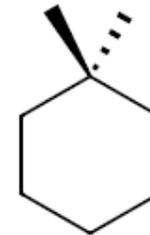
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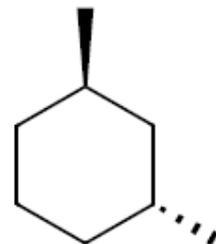
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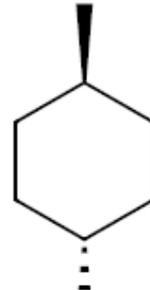
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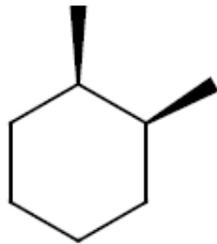
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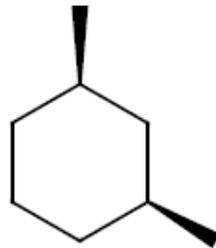
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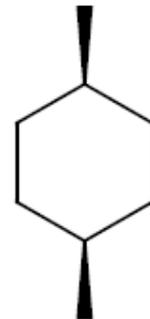
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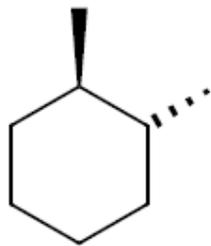
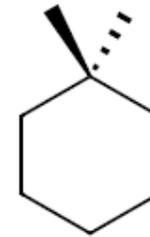
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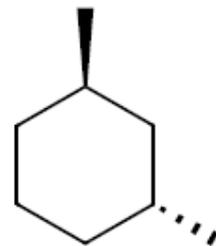
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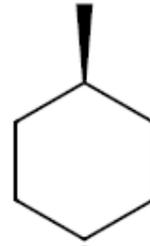
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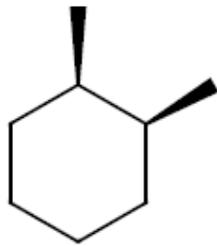


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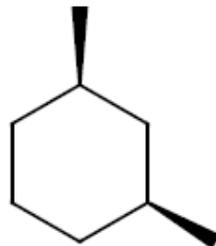


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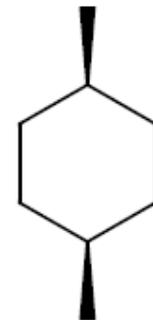
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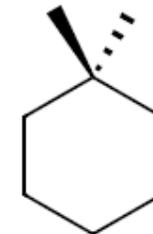
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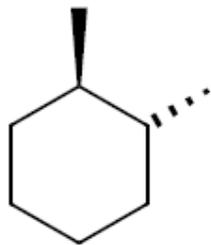
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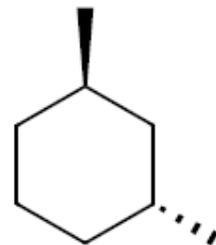
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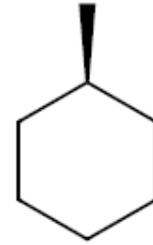
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