SAPIENZA
UNIVERSITÀ DI ROMA

Corso di Laurea Magistrale in Ingegneria Biomedica

Complementi di Chimica e Biochimica per le Tecnologie Biomediche

Elementi di Stereochimica

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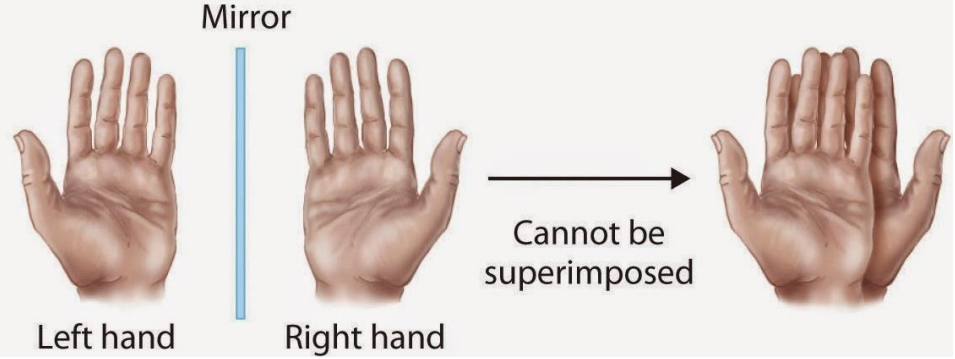
DIPARTIMENTO DI
SCIENZE DI BASE E APPLICATE PER L'INGEGNERIA

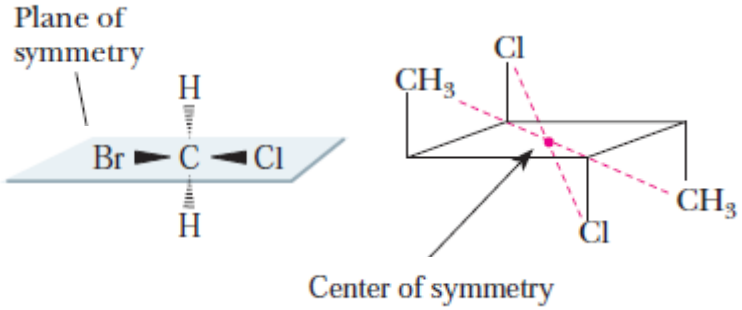
Definizione

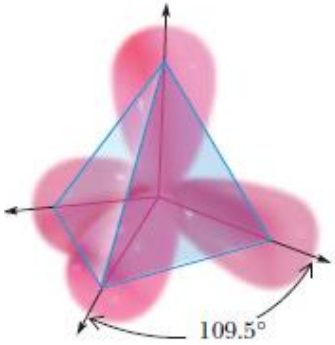
Stereochimica: studio della disposizione delle molecole nello spazio

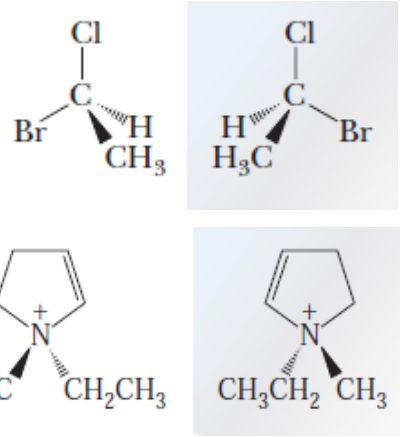
Composto chirale: composto che non presenta elementi di simmetria e, pertanto, non è sovrapponibile alla propria immagine speculare

Composto achirale: composto che manca di chiralità









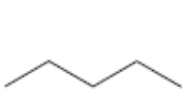
Centro (C) chirale: atomo (C) tetraedrico legato a 4 gruppi differenti

Stereoisomeri

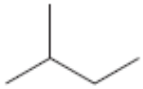
Isomers
Different compounds with the same molecular formula

Constitutional isomers
Different compounds with the same molecular formula but a different connectivity

Stereoisomers
Different compounds with the same molecular formula, the same connectivity, but a different orientation of their atoms in space



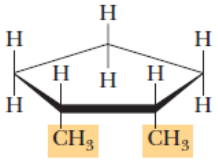
Pentane
(C_5H_{12})



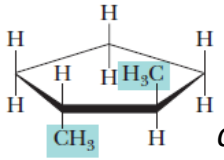
2-Methylbutane
(C_5H_{12})

1-Pentene
(C_5H_{10})

Cyclopentane
(C_5H_{10})

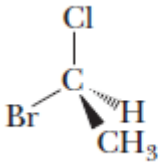


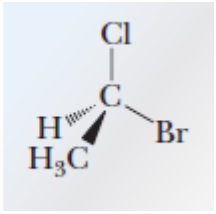
cis-1,2-Dimethyl-cyclopentane



trans-1,2-Dimethyl-cyclopentane

Isomeri configurazionali (non chirali)

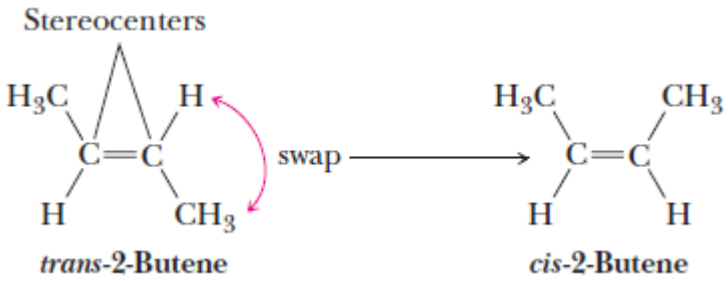


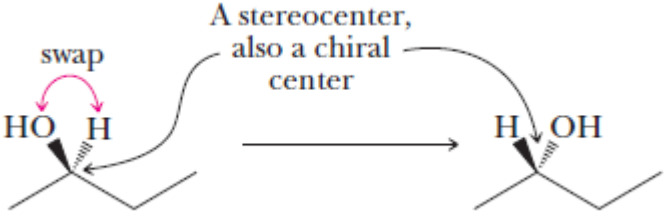


Isomeri configurazionali chirali o Enantiomeri

Stereoisomeri

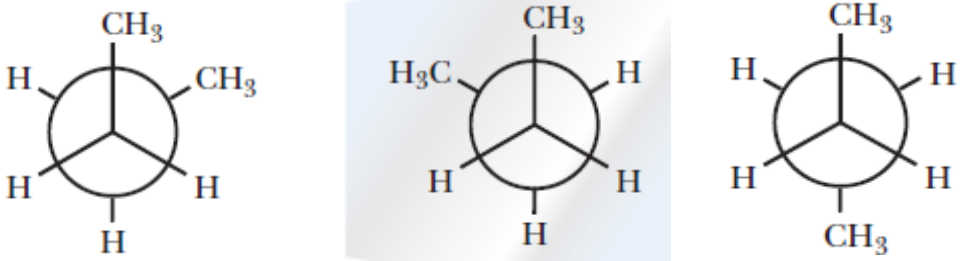
Centro stereogenico (stereocentro): atomo in cui lo scambio tra due sostituenti determina la formazione di stereoisomeri



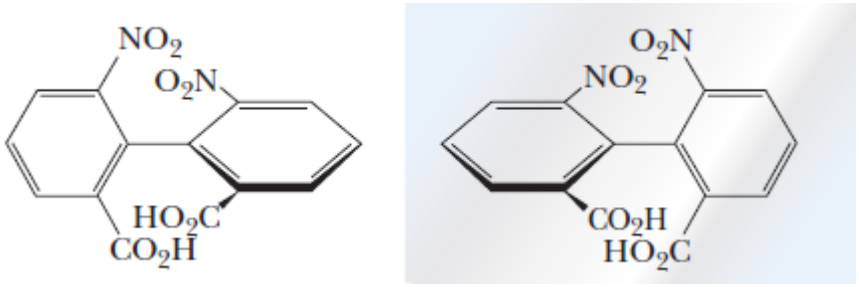


Diastereoisomeri (diastereomeri): stereoisomeri che non sono immagini speculari tra loro

Isomeri conformazionali: isomeri che possono essere ottenuti tramite rotazione intorno a un legame singolo



Atropoisomeri: enantiomeri che mancano di un centro chirale ma che non possono interconvertire facilmente a causa di un impedimento sterico



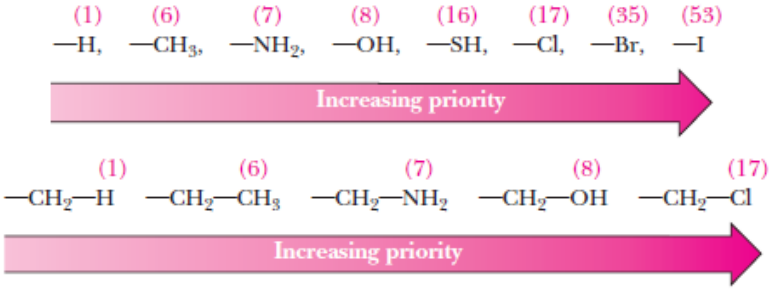
Nomenclatura dei centri chirali

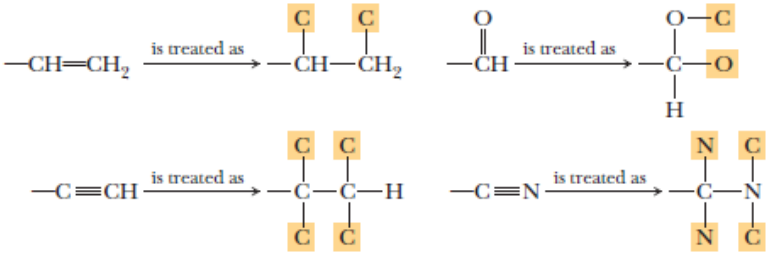
Configurazione assoluta: configurazione effettiva dell'enantiomero che si sta considerando

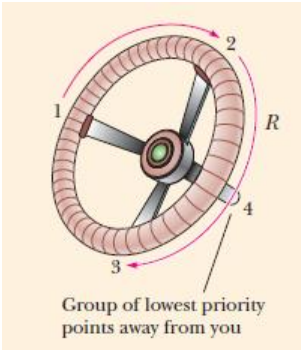
Sistema R,S: sistema di nomenclatura proposto da Cahn, Ingold e Prelog negli anni '50, accettato dalla IUPAC e basato su regole di priorità dei sostituenti

R = *rectus*; **S** = *sinister*

- Priorità basata sul numero atomico del sostituente
- A parità di atomo immediatamente legato al centro chirale, la priorità è assegnata al primo punto di differenza
- Doppi (tripli) legami si considerano come legami a due (tre) atomi dello stesso tipo



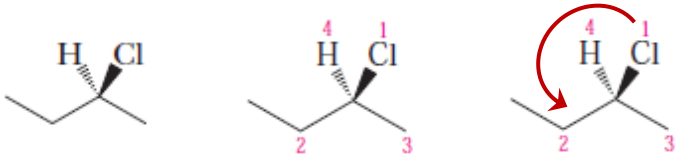




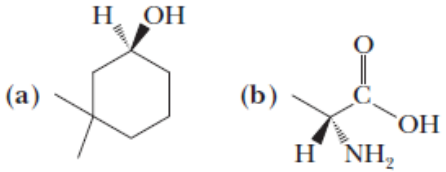
In pratica:

- Si individua il centro chirale
- Si scrive la molecola in modo da orientare il gruppo a priorità minore dal lato opposto rispetto al punto di osservazione
- Si assegnano le priorità ai sostituenti
- Si verifica il verso (orario o antiorario) dei sostituenti a partire da quello a priorità maggiore

Esempio:

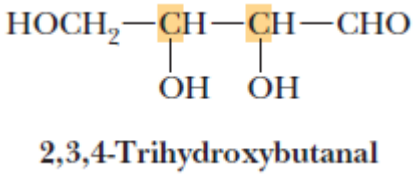


Esercizio: Assegnare la configurazione assoluta (R, S) a:

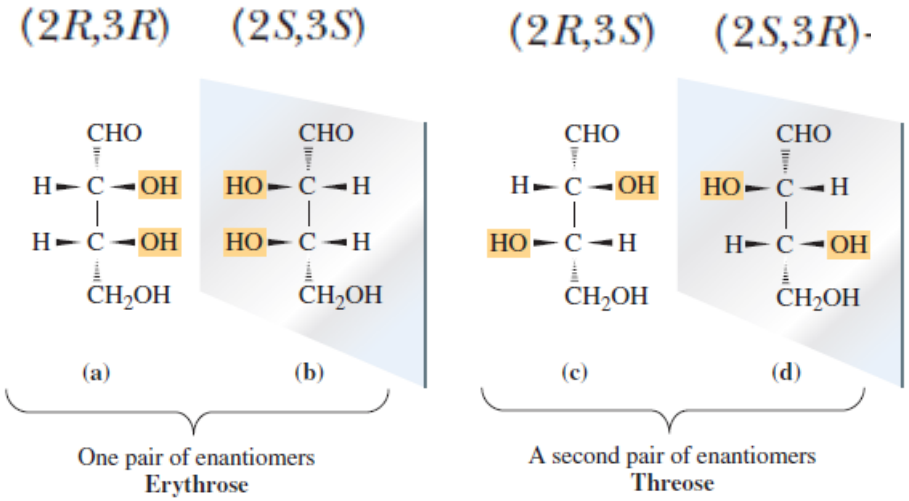


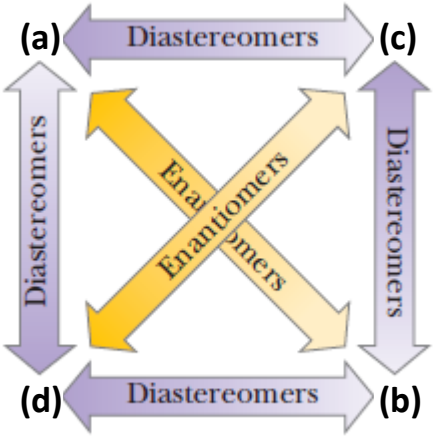
Molecole con più stereocentri

Dati ***n*** stereocentri, sono possibili $\mathbf{2^n}$ stereoisomeri

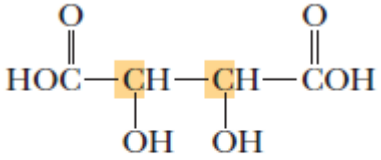


2,3,4-Trihydroxybutanal

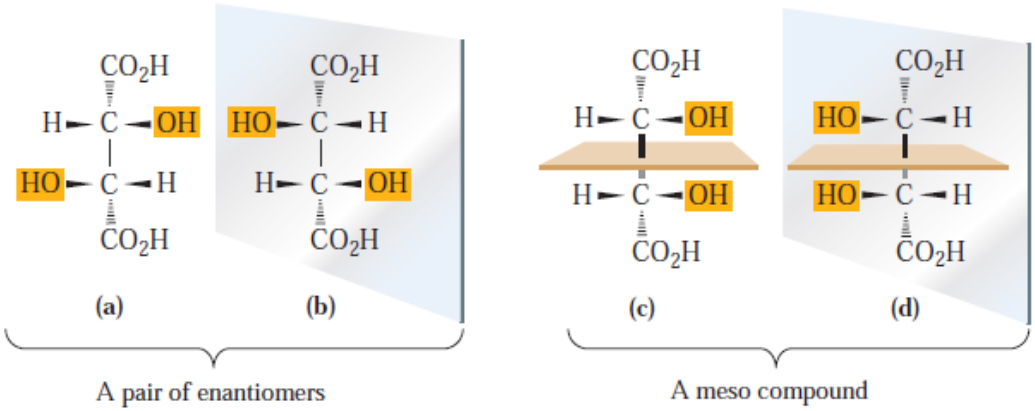




Composti meso



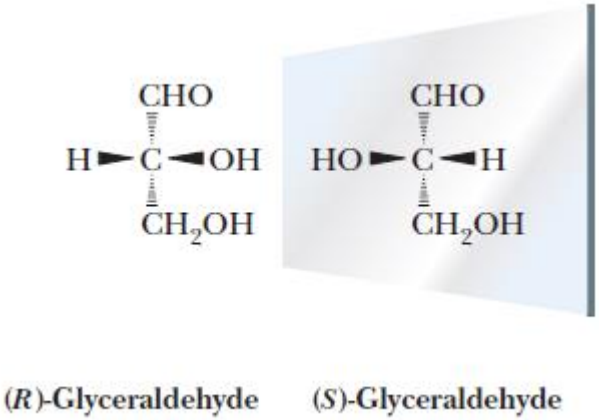
2,3-Dihydroxybutanedioic acid
(Tartaric acid)



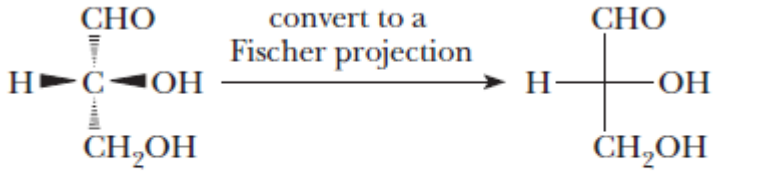
Composto meso: composto achirale avente 2 o più centri chirali e isomeri chirali

Le proiezioni di Fisher

Proiezione di Fisher: proiezione bidimensionale di una molecola, in cui per convenzione i gruppi scritti orizzontalmente sono considerati in fuori e i gruppi scritti in verticale sono considerati rientranti nel piano



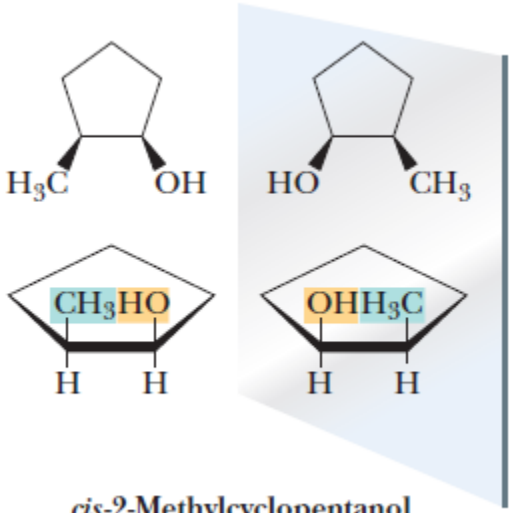
(*R*)-Glyceraldehyde (*S*)-Glyceraldehyde



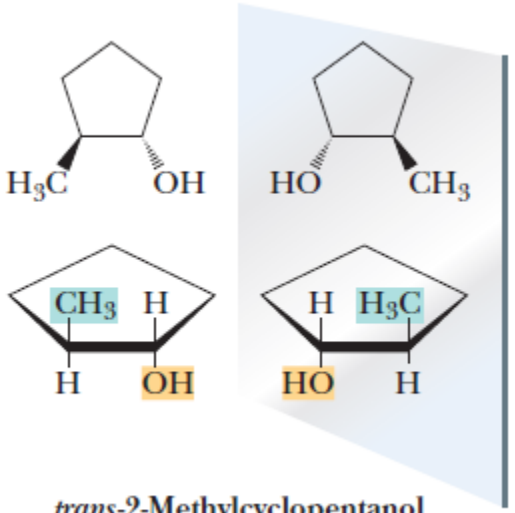
(*R*)-Glyceraldehyde (three-dimensional representation)

(*R*)-Glyceraldehyde (Fischer projection)

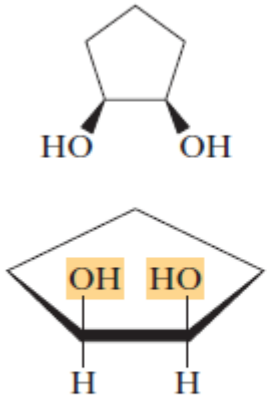
Molecole cicliche con più stereocentri



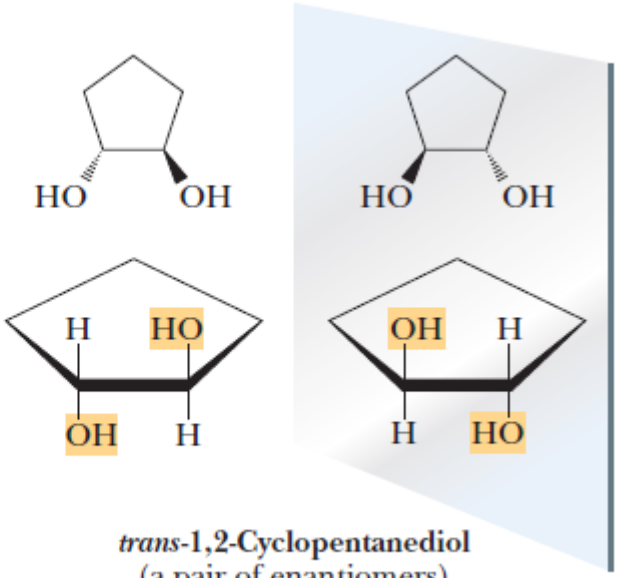
cis-2-Methylcyclopentanol
(a pair of enantiomers)



trans-2-Methylcyclopentanol
(a pair of enantiomers)

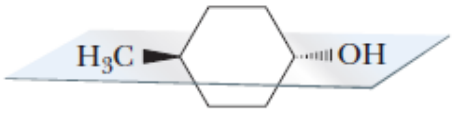


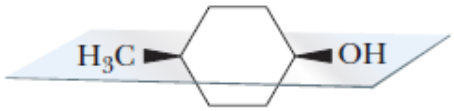
cis-1,2-Cyclopentanediol
(a meso compound)



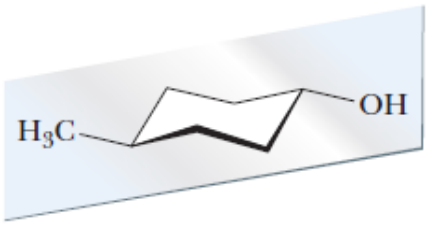
trans-1,2-Cyclopentanediol
(a pair of enantiomers)

Molecole cicliche con più stereocentri

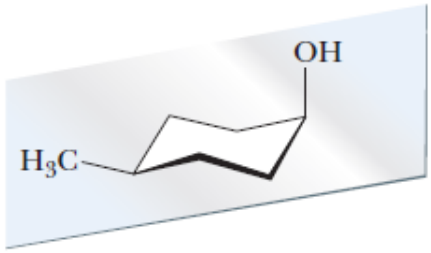




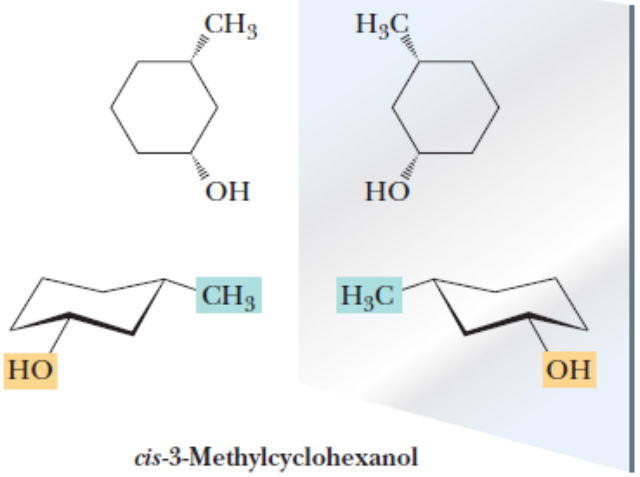
2 stereocentri che **non** sono centri chirali



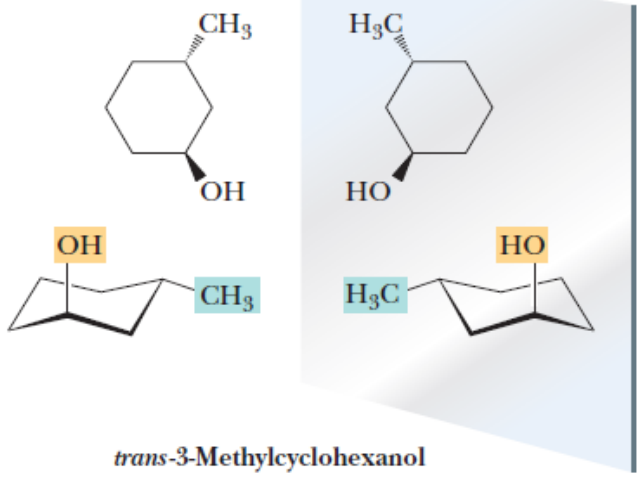
***trans*-4-Methylcyclohexanol**
(achiral, plane of symmetry)



***cis*-4-Methylcyclohexanol**
(achiral, plane of symmetry)

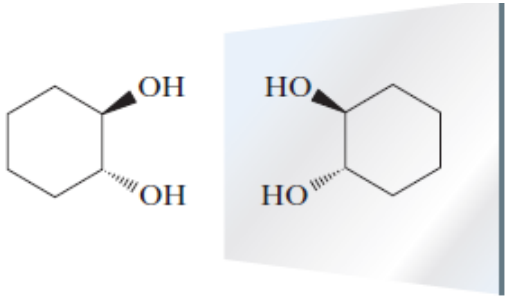


***cis*-3-Methylcyclohexanol**
(a pair of enantiomers)

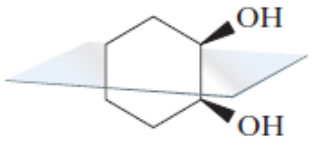


***trans*-3-Methylcyclohexanol**
(a pair of enantiomers)

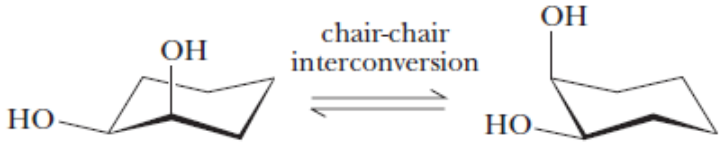
2 centri chirali
4 stereoisomeri



***trans*-1,2-Cyclohexanediol**
(a pair of enantiomers)



***cis*-1,2-Cyclohexanediol**
(achiral, plane of symmetry)



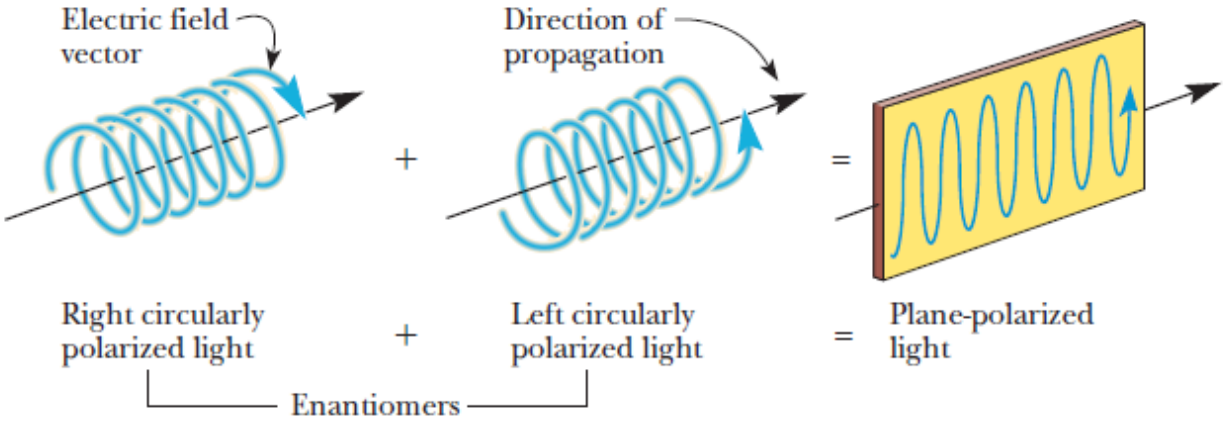
***cis*-1,2-Cyclohexanediol**
chair conformations

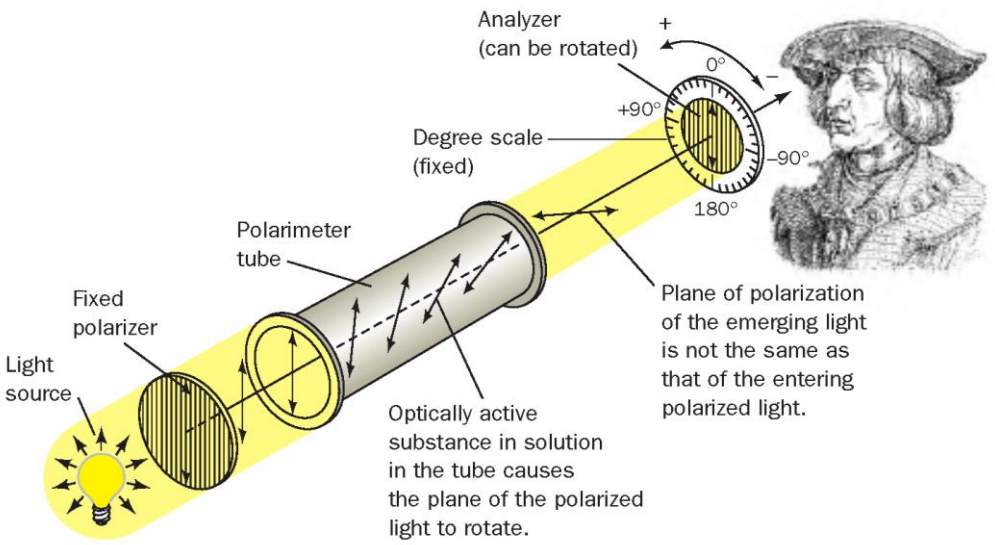
2 enantiomeri e una forma meso

Riassumendo

La chiralità in laboratorio

Le molecole chirali sono otticamente attive (ruotano il piano della luce polarizzata)



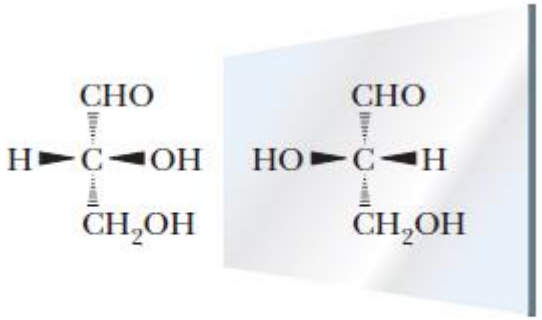


$$\text{Specific rotation} = [\alpha]_\lambda^T = \frac{\text{Observed rotation (degrees)}}{\text{Length (dm)} \times \text{Concentration}}$$

$$\text{Percent optical purity} = \frac{[\alpha]_{\text{sample}}}{[\alpha]_{\text{pure enantiomers}}} \times 100$$

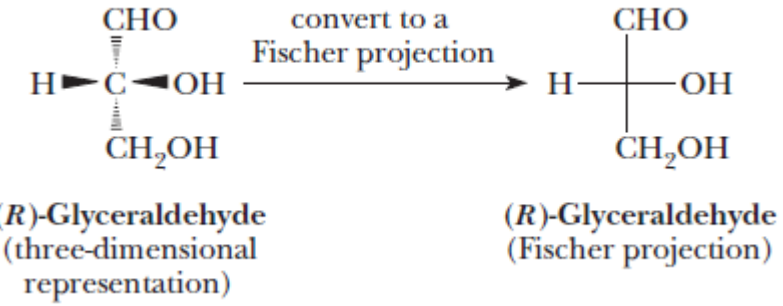
$$\text{Enantiomeric excess (ee)} = \%\text{R} - \%\text{S}$$

La chiralità in laboratorio



(*R*)-Glyceraldehyde (*S*)-Glyceraldehyde

D-gliceraldeide L-gliceraldeide

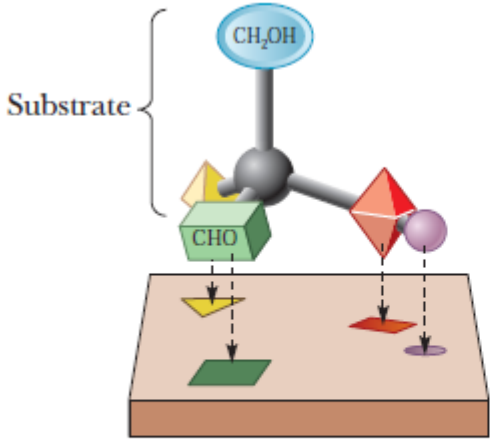


(*R*)-Glyceraldehyde (three-dimensional representation)

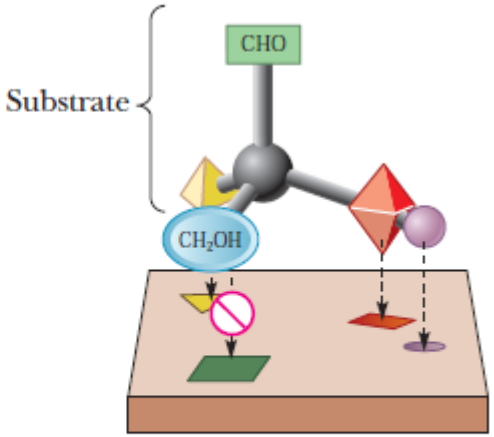
(*R*)-Glyceraldehyde (Fischer projection)

- Diffrazione di raggi X
- Dicroismo circolare
- NMR

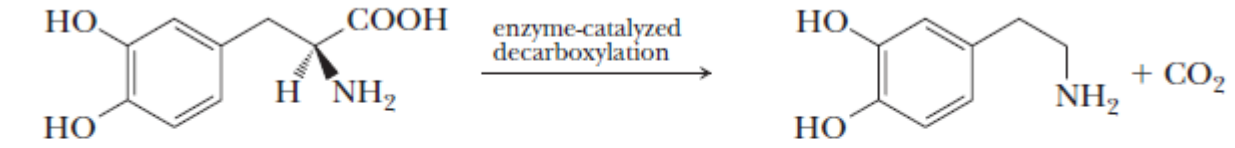
La chiralità in biochimica



This enantiomer of glyceraldehyde fits the three specific binding sites on the enzyme surface.



This enantiomer of glyceraldehyde does not fit the same binding sites.



(*S*)-(−)-3,4-Dihydroxyphenylalanine
(L-DOPA)
$[\alpha]_D^{13} -13.1$

Dopamine

Risoluzione di miscele racemiche

- Derivatizzazione con sali diastereomerici
- Separazione su colonna chirale