Molecules with more than One Chiral Carbon

2,3-Dihydroxybutanoic acid

$CH_3\overset{3}{C}H(OH)\overset{2}{C}H(OH)C(=O)OH$

What are all the possible *R* and *S* combinations of the two chiral carbons in this molecule?

Carbon-2	*R*	*R*	*S*	*S*
Carbon-3	*R*	*S*	*R*	*S*

2,3-Dihydroxybutanoic acid

$CH_3\overset{3}{C}H(OH)\overset{2}{C}H(OH)C(=O)OH$

4 Combinations = 4 Stereoisomers

Carbon-2	*R*	*R*	*S*	*S*
Carbon-3	*R*	*S*	*R*	*S*

2,3-Dihydroxybutanoic acid

$CH_3\overset{3}{C}H(OH)\overset{2}{C}H(OH)C(=O)OH$

4 Combinations = 4 Stereoisomers

What is the relationship between these stereoisomers?

Carbon-2	*R*	*R*	*S*	*S*
Carbon-3	*R*	*S*	*R*	*S*

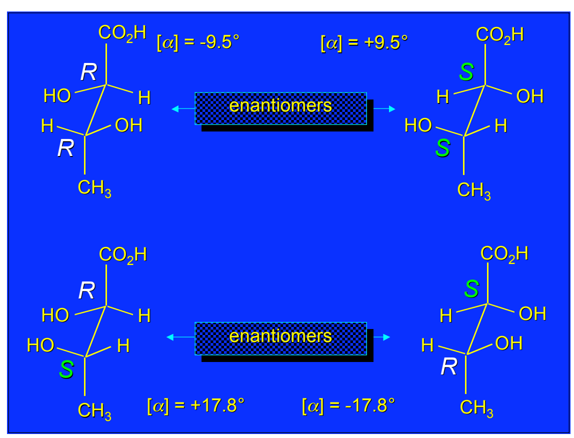
2,3-Dihydroxybutanoic acid

$CH_3\overset{3}{C}H(OH)\overset{2}{C}H(OH)C(=O)OH$

enantiomers: 2*R*,3*R* and 2*S*,3*S*
2*R*,3*S* and 2*S*,3*R*

They have the same physical properties.

Carbon-2	*R*	*R*	*S*	*S*
Carbon-3	*R*	*S*	*R*	*S*

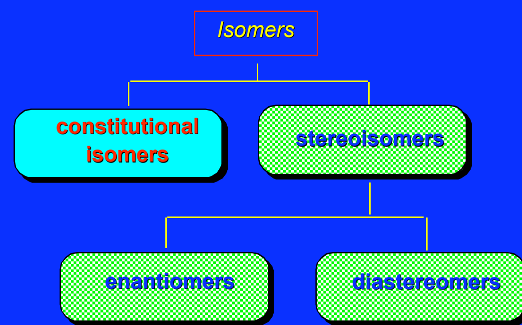


2,3-Dihydroxybutanoic acid

but not all relationships are enantiomeric

stereoisomers that are not enantiomers are diastereomers

Carbon-2	*R*	*R*	*S*	*S*
Carbon-3	*R*	*S*	*R*	*S*



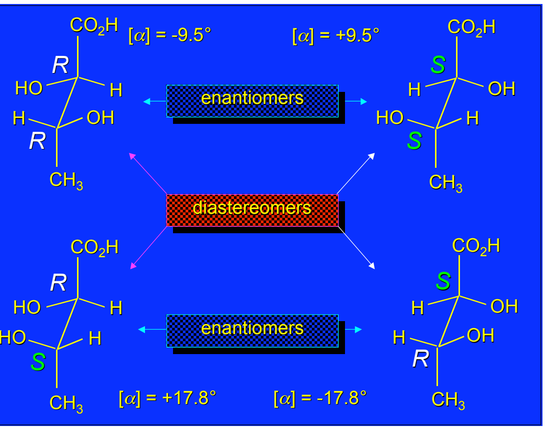
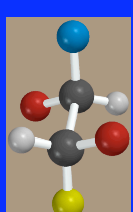


Table 5.1 Physical Properties of the Stereoisomers of Tartaric Acid

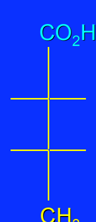
	Melting point, °C	$[\alpha]_D^{25\,°C}$	Solubility, g/100 g H_2O at 15 °C
(2*R*,3*R*)-(+)-Tartaric acid	170	+11.98°	139
(2*S*,3*S*)-(−)-Tartaric acid	170	−11.98°	139
(2*R*,3*S*)-Tartaric acid	140	0°	125
(±)-Tartaric acid	206	0°	139

Fischer Projections

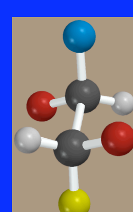


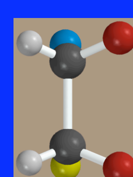
recall for Fischer projection: horizontal bonds point toward you; vertical bonds point away

staggered conformation does not have correct orientation of bonds for Fischer projection



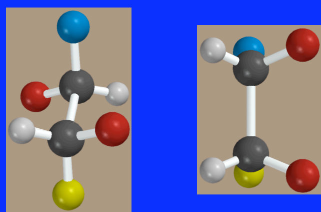
Fischer projections

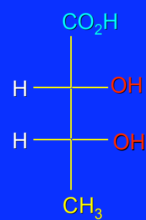




transform molecule to eclipsed conformation in order to construct Fischer projection

Fischer projections





Erythro and Threo

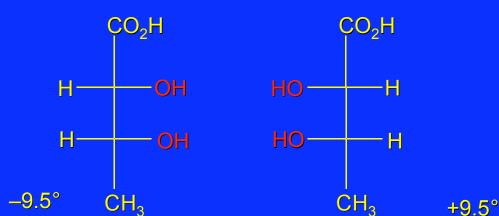
stereochemical prefixes used to specify relative configuration in molecules with two chiral carbons

easiest to apply using Fischer projections

orientation: vertical carbon chain

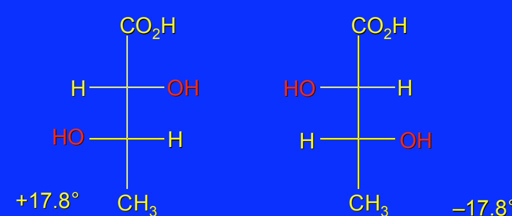
Erythro

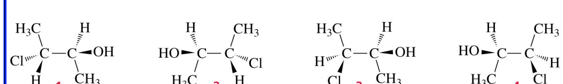
when carbon chain is vertical, same (or analogous) substituents on <u>same side</u> of Fischer projection



Threo

when carbon chain is vertical, same (or analogous) substituents on <u>opposite sides</u> of Fischer projection

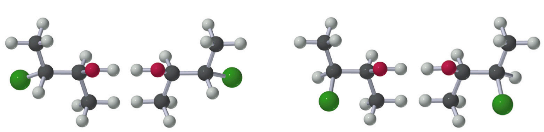




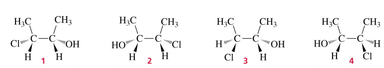
erythro enantiomers

threo enantiomers

perspective formulas of the stereoisomers of 3-chloro-2-butanol (staggered)



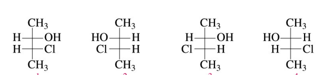
stereoisomers of 3-chloro-2-butanol



erythro enantiomers

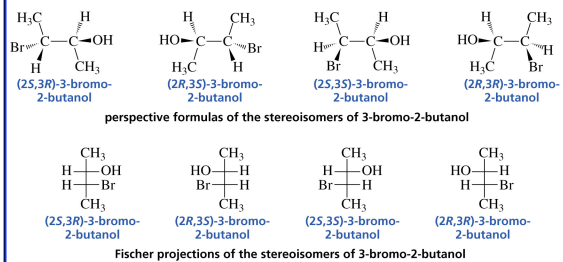
threo enantiomers

perspective formulas of the stereoisomers of 3-chloro-2-butanol (eclipsed)



erythro enantiomers

threo enantiomers



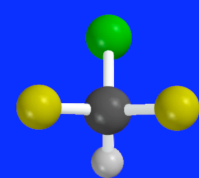
Achiral Molecules with Two Chiral Centers

It is possible for a molecule to have chiral carbons yet be achiral.

Symmetry Tests for Chirality

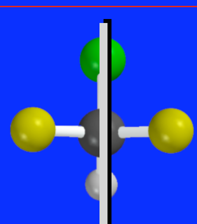
Any molecule with a plane of symmetry or a center of symmetry must be achiral.

Plane of symmetry



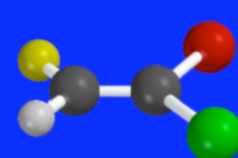
A plane of symmetry bisects a molecule into two mirror image halves. Chlorodifluoromethane has a plane of symmetry.

Plane of symmetry



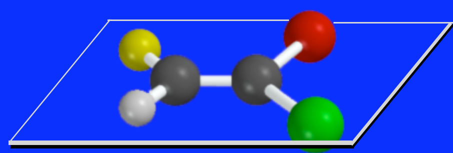
A plane of symmetry bisects a molecule into two mirror image halves. Chlorodifluoromethane has a plane of symmetry.

Plane of symmetry



A plane of symmetry bisects a molecule into two mirror image halves. 1-Bromo-1-chloro-2-fluoroethene has a plane of symmetry.

Plane of symmetry

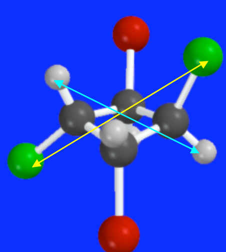


A plane of symmetry bisects a molecule into two mirror image halves.
1-Bromo-1-chloro-2-fluoroethene has a plane of symmetry.

Center of symmetry

A point in the center of the molecule is a center of symmetry if a line drawn from it to some element, when extended an equal distance in the opposite direction, encounters an identical element.

Center of symmetry



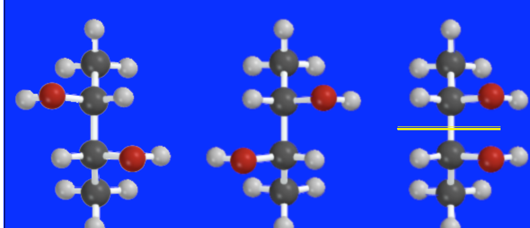
A point in the center of the molecule is a center of symmetry if a line drawn from it to any element, when extended an equal distance in the opposite direction, encounters an identical element.

2,3-Butanediol

```
     2   3
CH3CHCHCH3
    |    |
   HO   OH
```

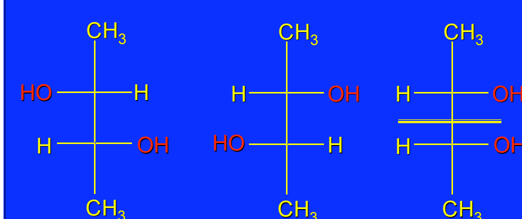
Consider a molecule with two equivalently substituted chiral carbons such as 2,3-butanediol.

Three stereoisomers of 2,3-butanediol

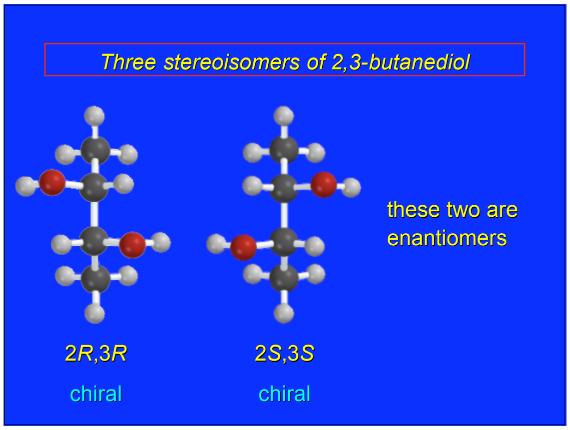


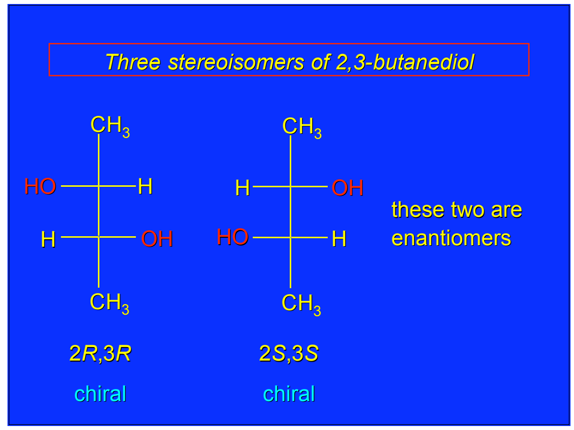
2*R*,3*R*	2*S*,3*S*	2*R*,3*S*
chiral	chiral	achiral

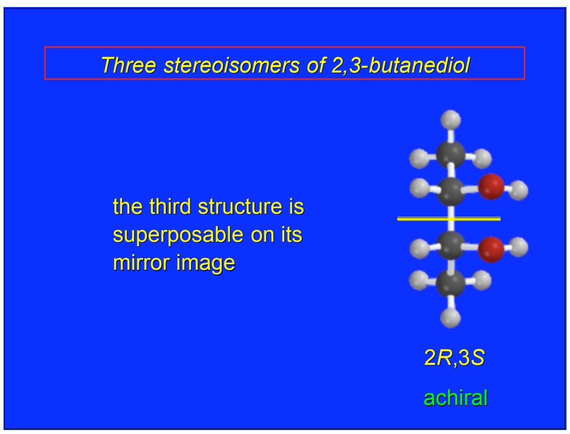
Three stereoisomers of 2,3-butanediol

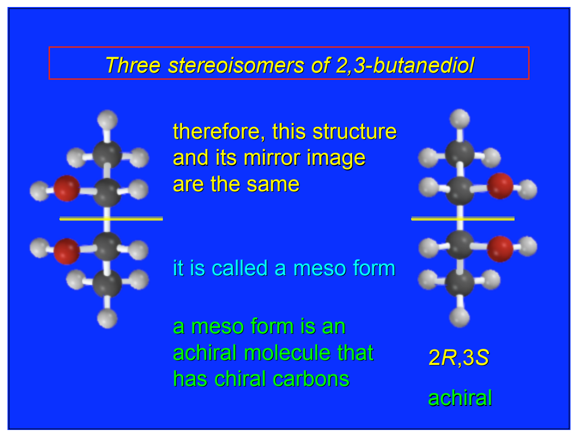


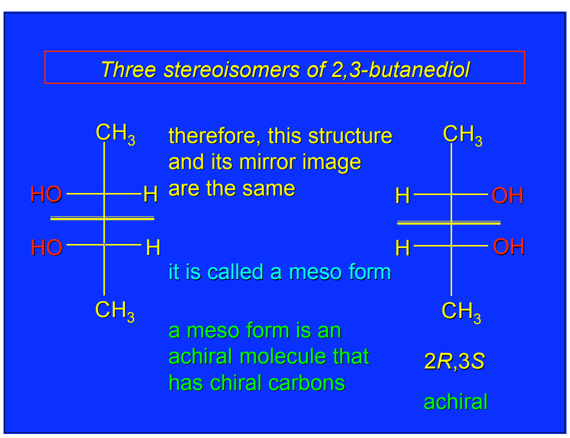
2*R*,3*R*	2*S*,3*S*	2*R*,3*S*
chiral	chiral	achiral

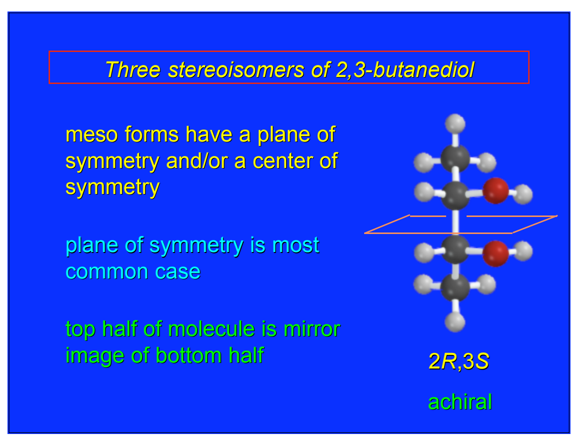

Three stereoisomers of 2,3-butanediol
these two are enantiomers
2R,3R
chiral
2S,3S
chiral


Three stereoisomers of 2,3-butanediol
CH3
HO
H
H
OH
CH3
CH3
H
OH
HO
H
CH3
these two are enantiomers
2R,3R
chiral
2S,3S
chiral

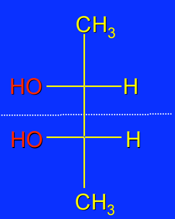

Three stereoisomers of 2,3-butanediol
the third structure is superposable on its mirror image
2R,3S
achiral


Three stereoisomers of 2,3-butanediol
therefore, this structure and its mirror image are the same
it is called a meso form
a meso form is an achiral molecule that has chiral carbons
2R,3S
achiral

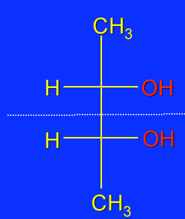

Three stereoisomers of 2,3-butanediol
CH3
HO
H
HO
H
CH3
therefore, this structure and its mirror image are the same
it is called a meso form
a meso form is an achiral molecule that has chiral carbons
CH3
H
OH
H
OH
CH3
2R,3S
achiral


Three stereoisomers of 2,3-butanediol
meso forms have a plane of symmetry and/or a center of symmetry
plane of symmetry is most common case
top half of molecule is mirror image of bottom half
2R,3S
achiral

Three stereoisomers of 2,3-butanediol



A line drawn the center of the Fischer projection of a meso form bisects it into two mirror-image halves.



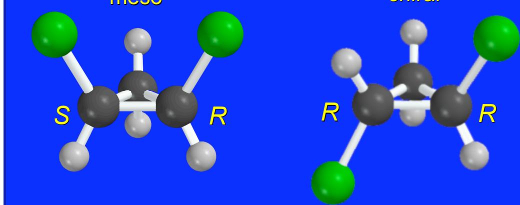
2*R*,3*S*

achiral

Cyclic compounds

meso

chiral



There are three stereoisomers of 1,2-dichloro-cyclopropane; the achiral (meso) cis isomer and two enantiomers of the trans isomer.

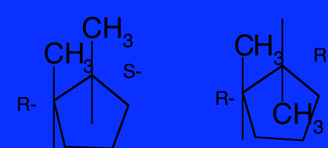
Chirality:

di-substituted cyclopentanes

and

cylcohexanes

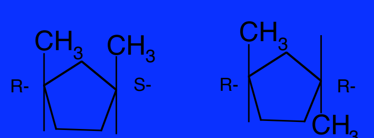
1,2-Disubstituted Cyclopentanes



meso

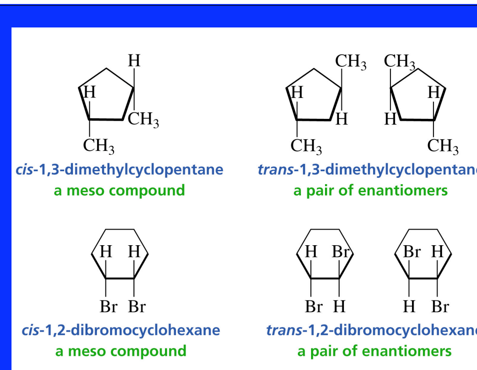
No plane of symmetry

1,3-Disubstituted Cylcopentanes

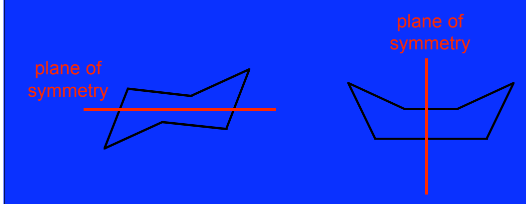


meso

No plane of symmetry

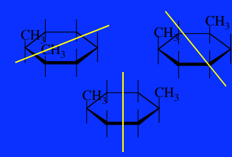


As long as any one conformer of a compound has a plane of symmetry, the compound will be achiral

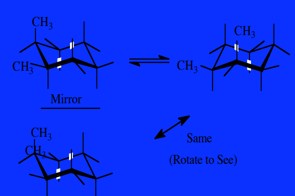


Cyclohexane Stereochemistry

Cis isomers

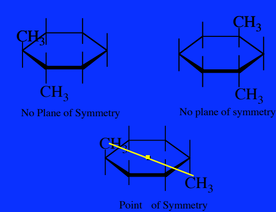


1,2-disubstituted-cis-cyclohexane Stereochemistry



Cyclohexane Stereochemistry

Trans isomers



Molecules
with
Multiple chiral carbons

How many stereoisomers?

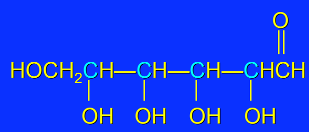
maximum number of stereoisomers = 2^n

where n = number of structural units capable of stereochemical variation

structural units include chiral carbons and cis and/or trans double bonds

number is reduced to less than 2^n if meso forms are possible

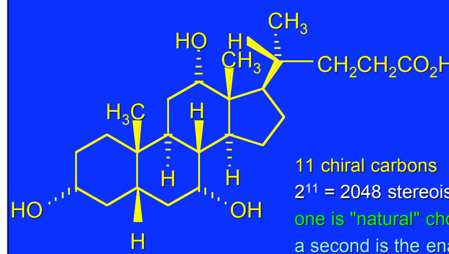
Example *Hexaldose sugar*



4 chiral carbons

16 stereoisomers

Cholic acid



11 chiral carbons

2^{11} = 2048 stereoisomers

one is "natural" cholic acid

a second is the enantiomer of natural cholic acid

2046 are diastereomers of cholic acid

How many stereoisomers?

maximum number of stereoisomers = 2^n

where n = number of structural units capable of stereochemical variation

structural units include chiral carbons and cis and/or trans double bonds

number is reduced to less than 2^n if meso forms are possible

How many stereoisomers?

3-Penten-2-ol