7.9

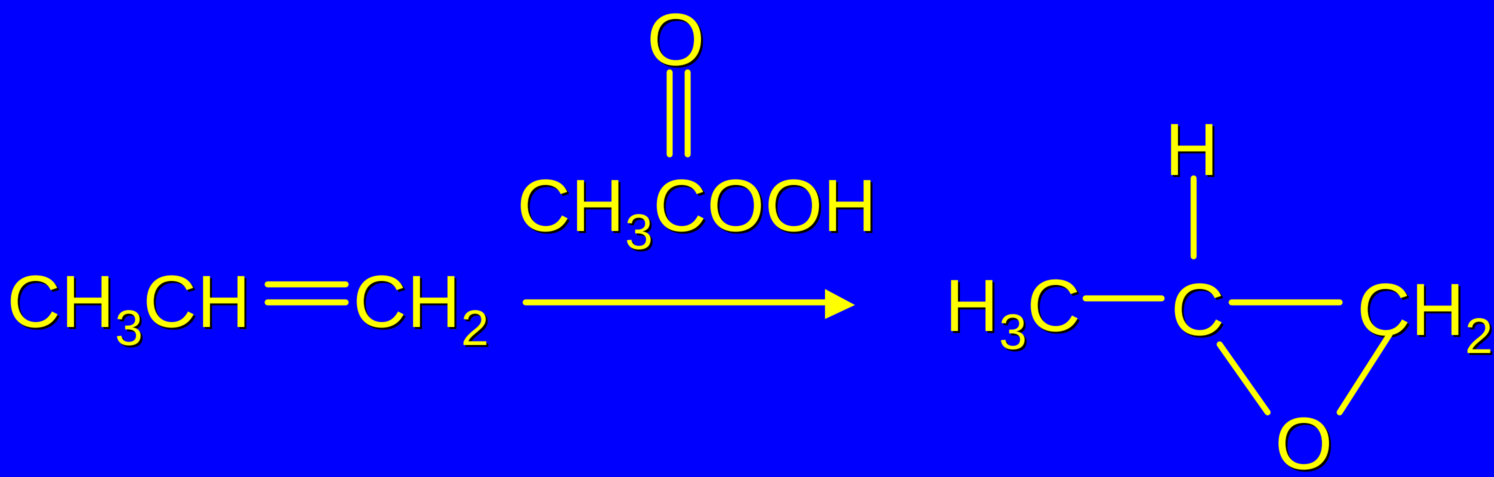
Reactions That Create A Stereogenic Center

Many reactions convert achiral reactants to chiral products.

It is important to recognize, however, that if all of the components of the starting state (reactants, catalysts, solvents, etc.) are achiral, any chiral product will be formed as a racemic mixture.

This generalization can be more simply stated as "Optically inactive starting materials can't give optically active products." (Remember: In order for a substance to be optically active, it must be chiral and one enantiomer must be present in greater amounts than the other.

Example

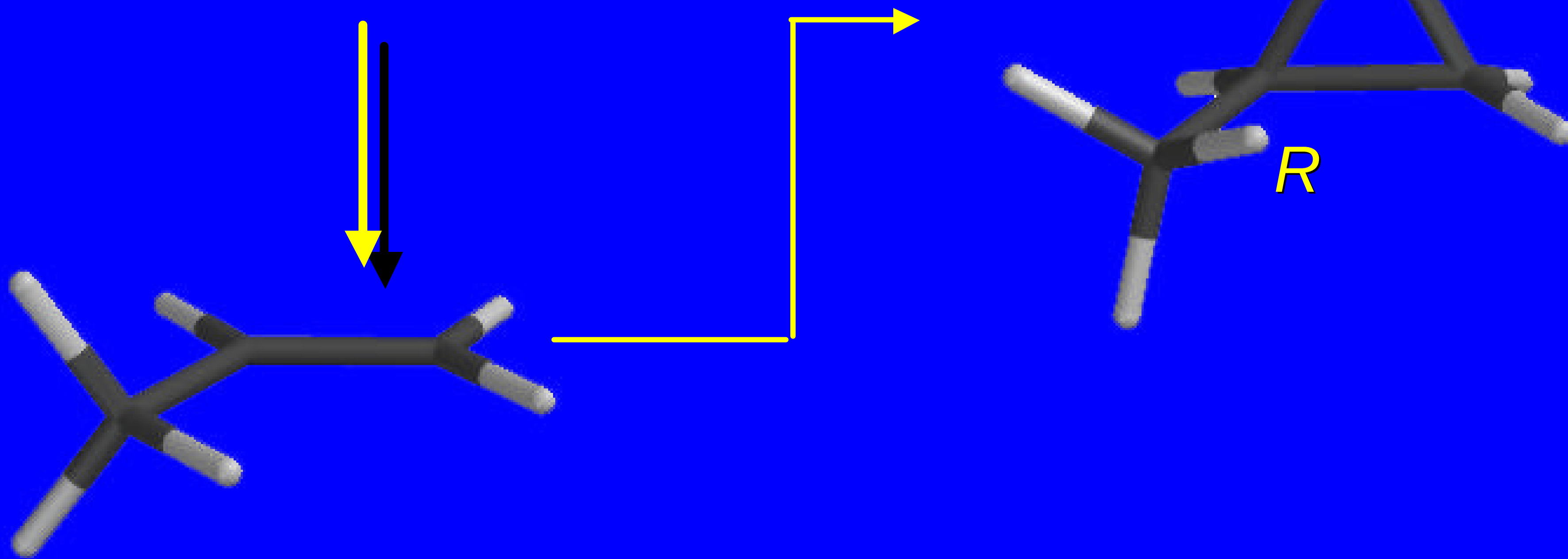


Achiral

Chiral, but racemic

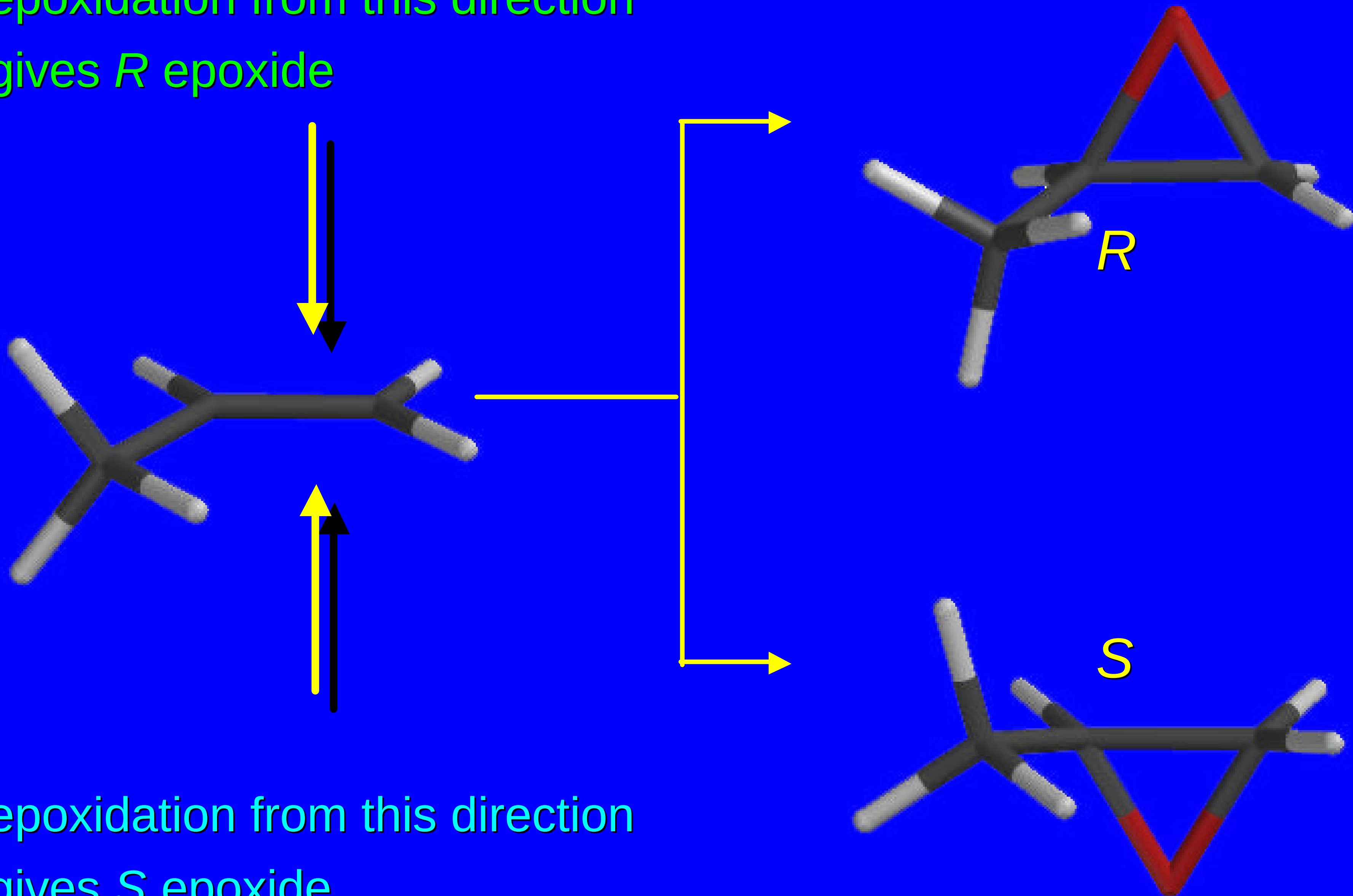
epoxidation from this direction

gives *R* epoxide



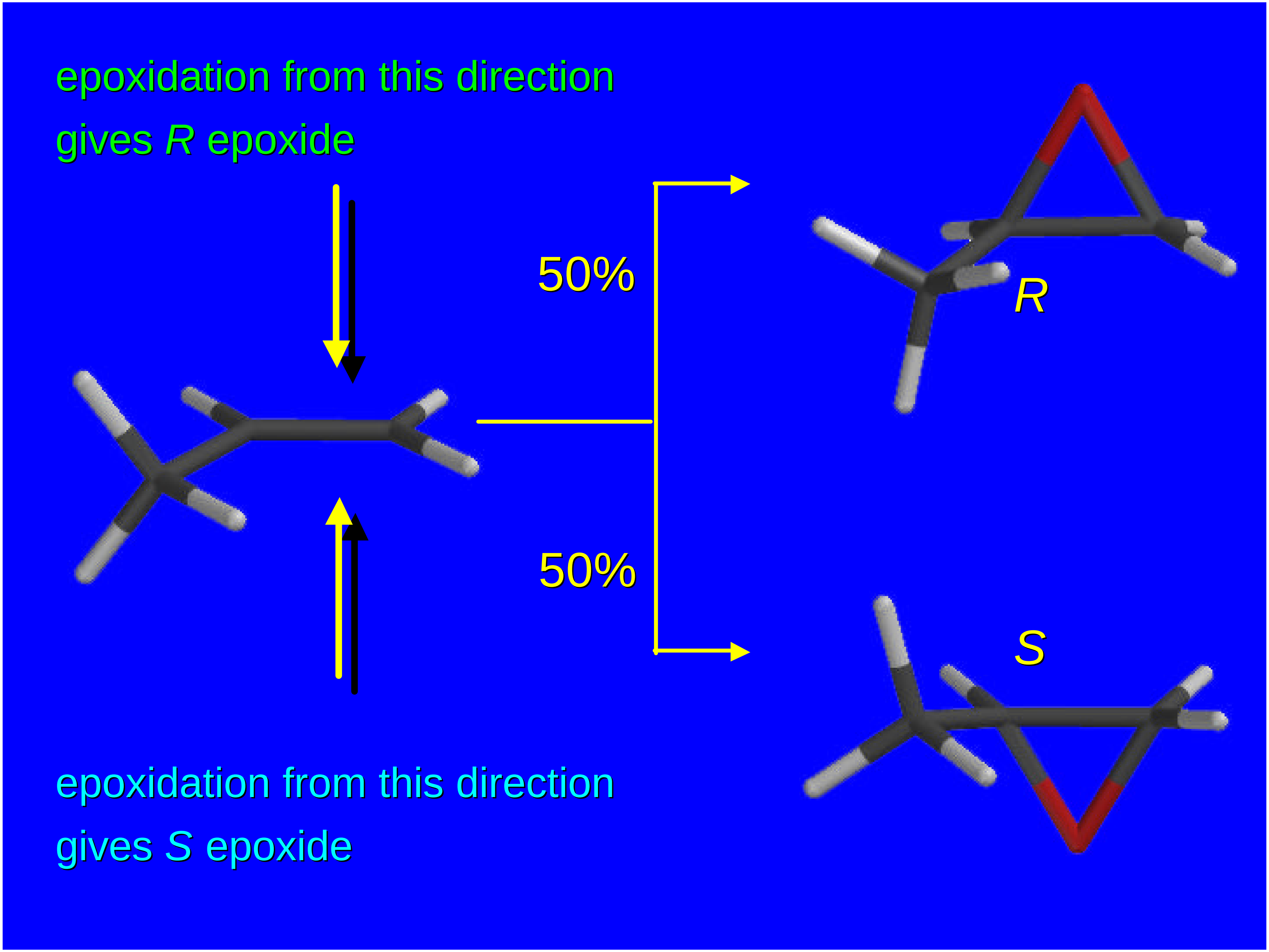
epoxidation from this direction

gives *R* epoxide

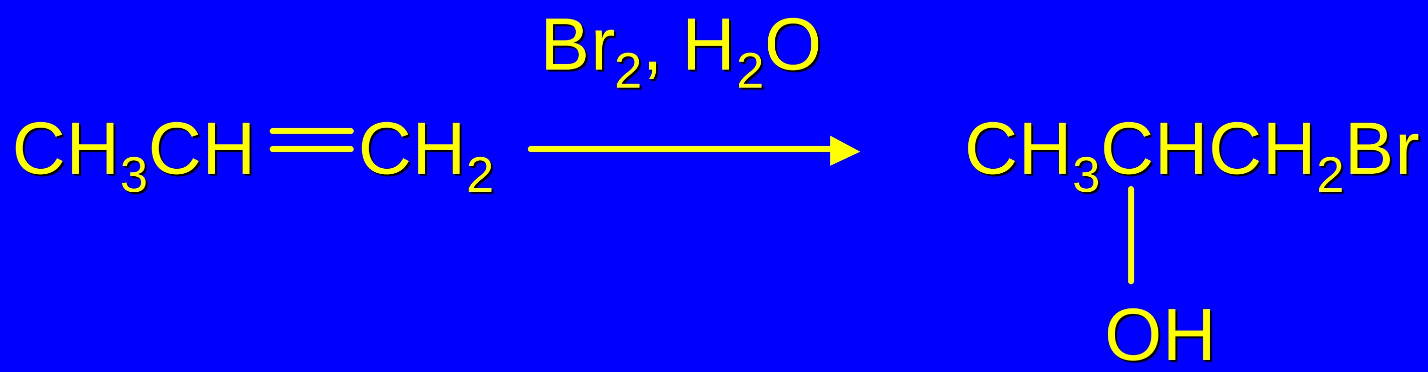


epoxidation from this direction

gives *S* epoxide


epoxidation from this direction
gives *R* epoxide
50%
R
50%
S
epoxidation from this direction
gives *S* epoxide

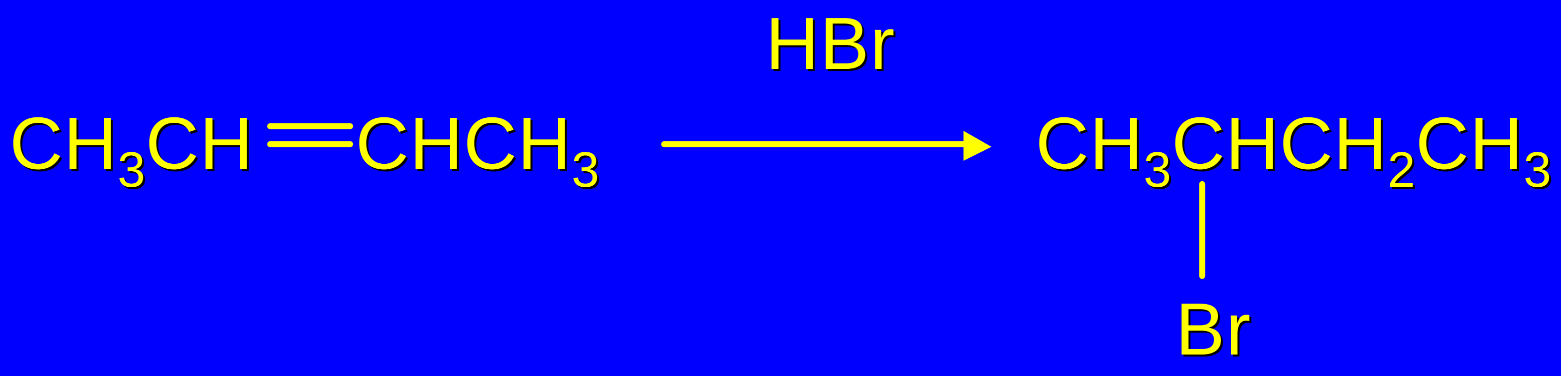
Example



Achiral

Chiral, but racemic

Example



Achiral

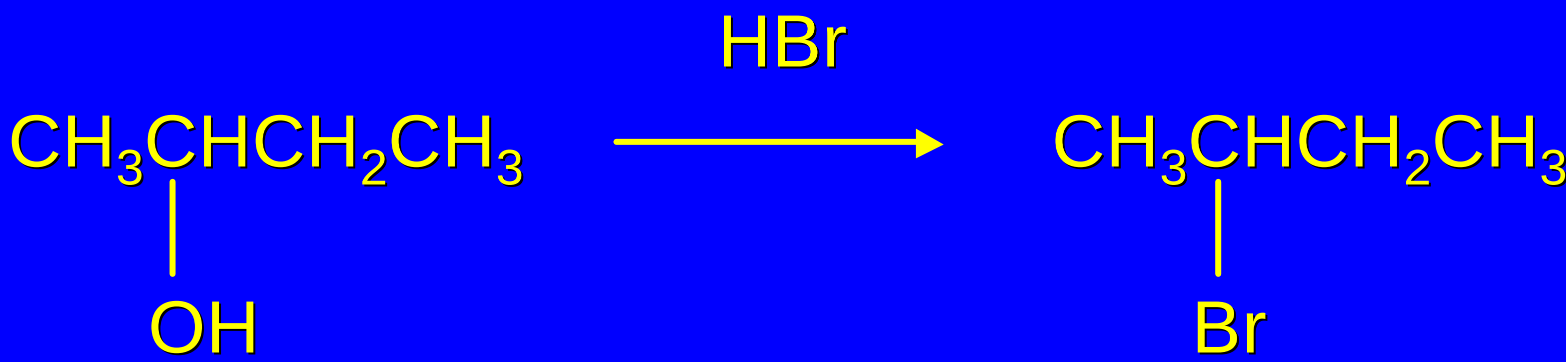
Chiral, but racemic

Many reactions convert chiral reactants to chiral products.

However, if the reactant is racemic, the product will be racemic also.

Remember: "Optically inactive starting materials can't give optically active products."

Example



Chiral, but racemic

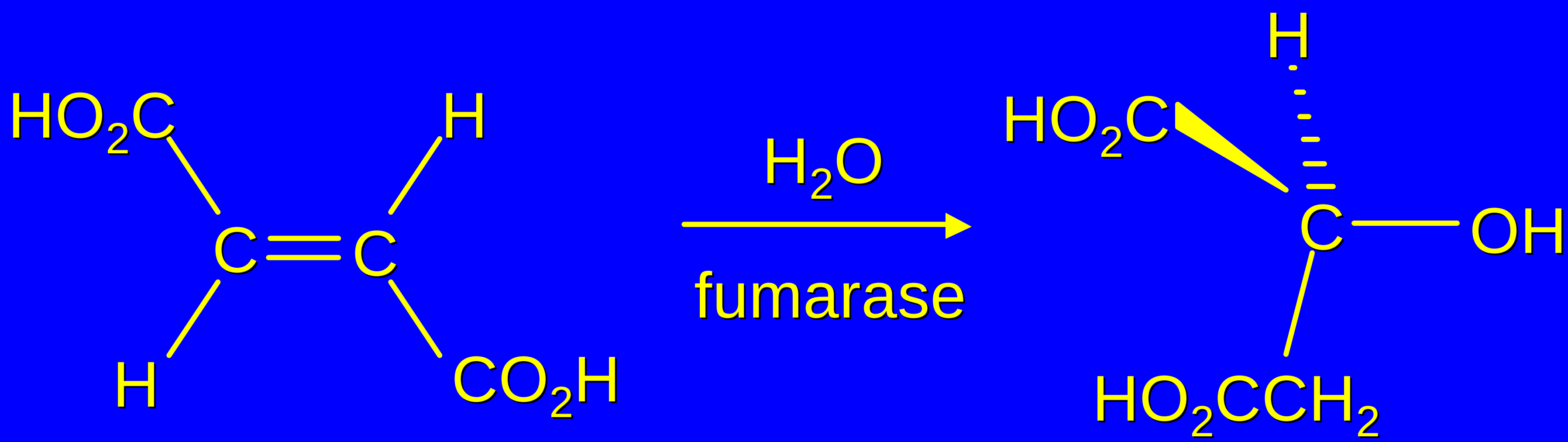
Chiral, but racemic

Many biochemical reactions convert an achiral reactant to a single enantiomer of a chiral product

Reactions in living systems are catalyzed by enzymes, which are enantiomerically homogeneous.

The enzyme (catalyst) is part of the reacting system, so such reactions don't violate the generalization that "Optically inactive starting materials can't give optically active products."

Example



Fumaric acid

(*S*)-(–)-Malic acid

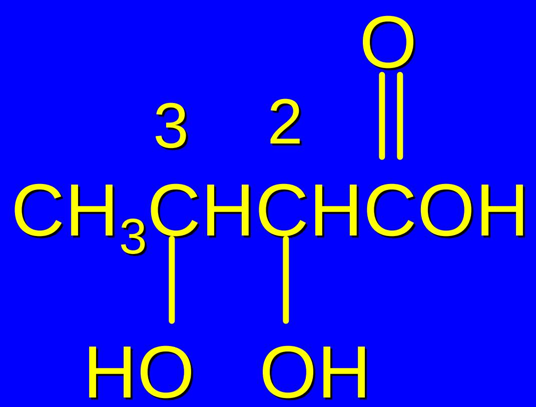
Achiral

Single enantiomer

7.10
Chiral Molecules
with
Two Stereogenic Centers

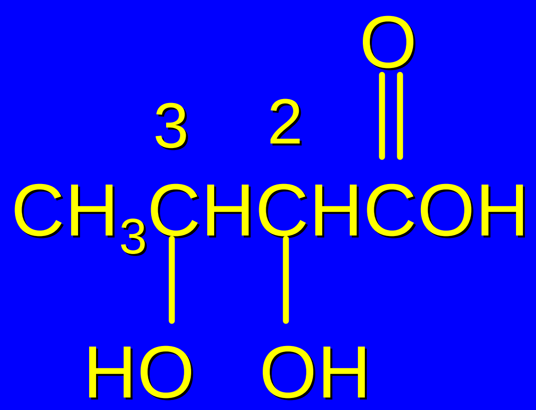
How many stereoisomers when a particular molecule contains two stereogenic centers?

2,3-Dihydroxybutanoic acid



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

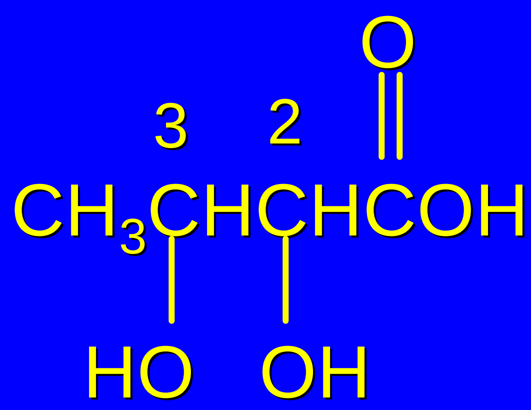
2,3-Dihydroxybutanoic acid



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

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

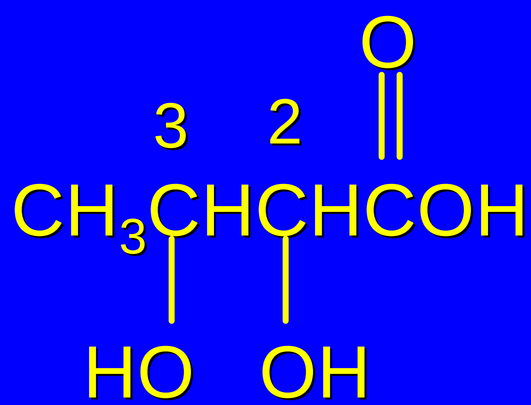
2,3-Dihydroxybutanoic acid



4 Combinations = 4 Stereoisomers

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

2,3-Dihydroxybutanoic acid

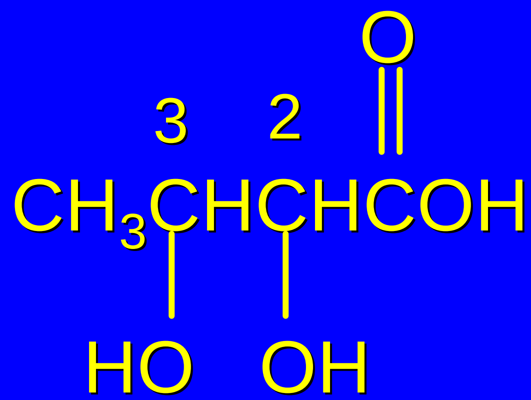


4 Combinations = 4 Stereoisomers

What is the relationship between these stereoisomers?

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

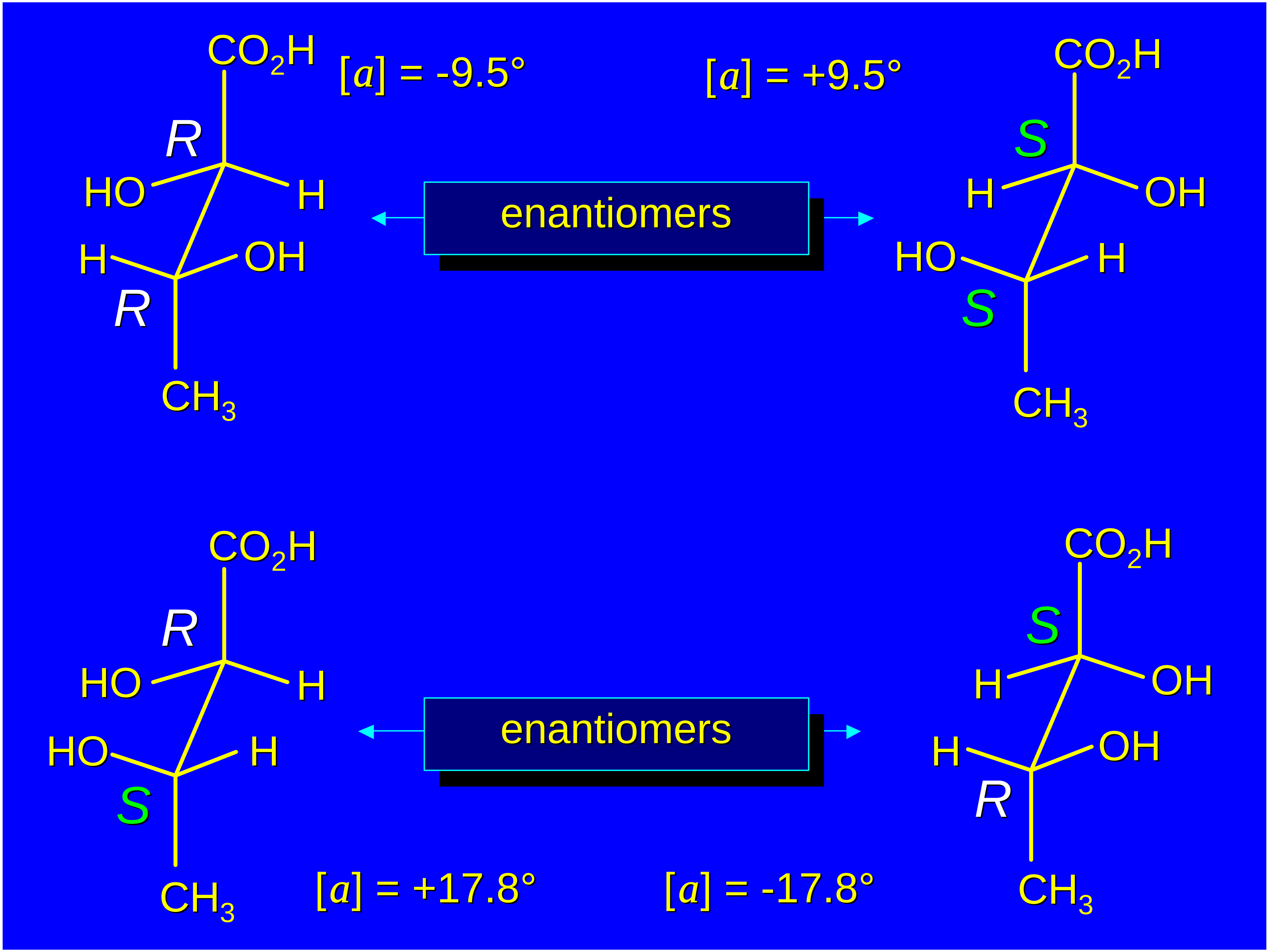
2,3-Dihydroxybutanoic acid



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

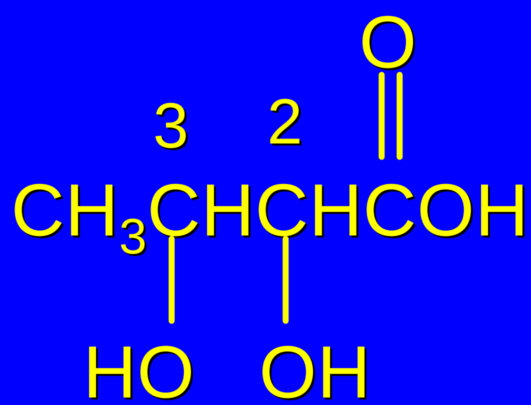
2*R*,3*S* and 2*S*,3*R*

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



CO2H
[a] = -9.5°
R
HO
H
H
OH
R
CH3
enantiomers
[a] = +9.5°
CO2H
S
H
OH
HO
H
S
CH3
CO2H
R
HO
H
HO
H
S
CH3
enantiomers
[a] = +17.8°
CO2H
S
H
OH
H
OH
R
CH3
[a] = -17.8°

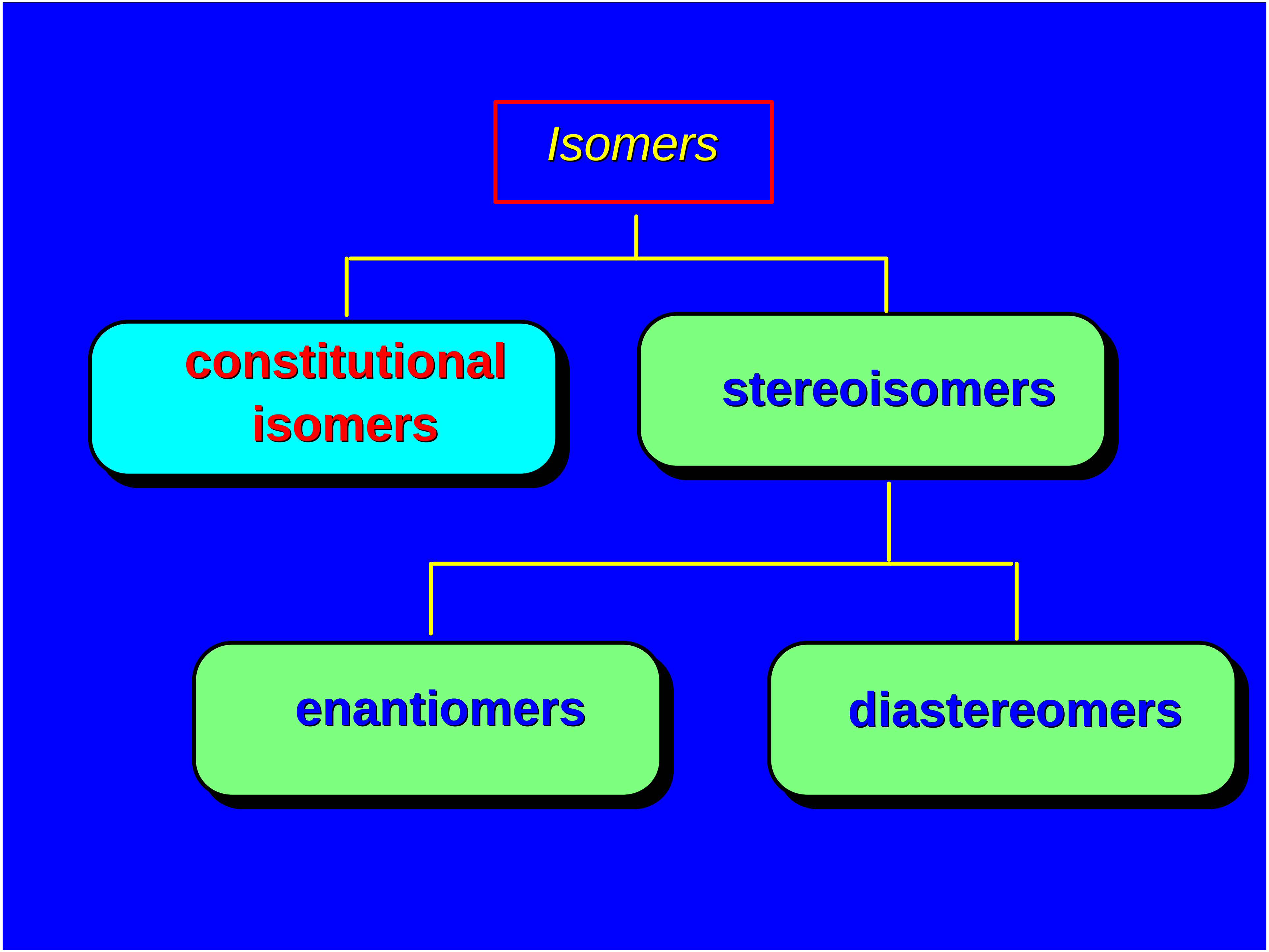
2,3-Dihydroxybutanoic acid

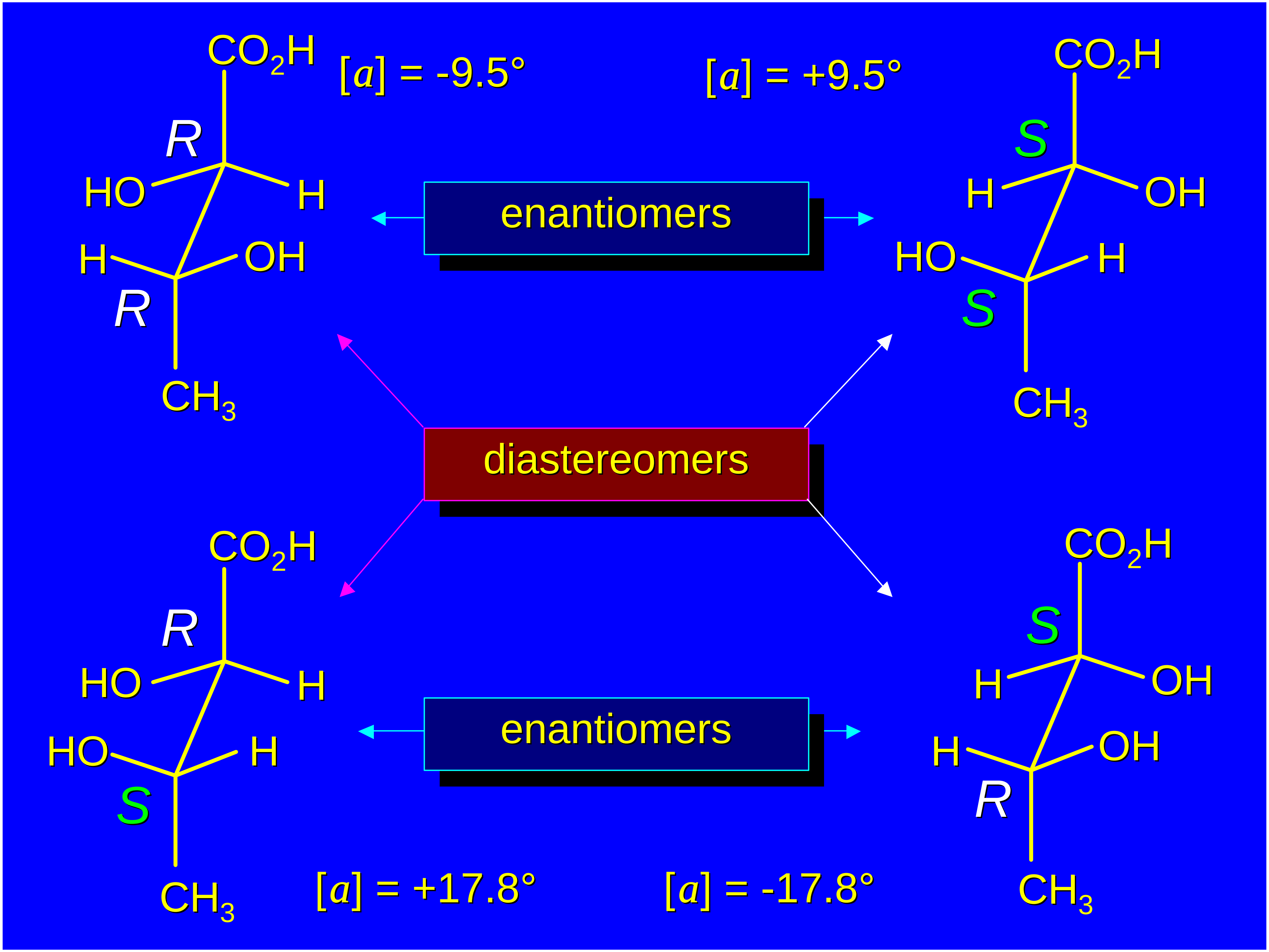


but not all relationships are enantiomeric

stereoisomers that are not enantiomers are diastereomers

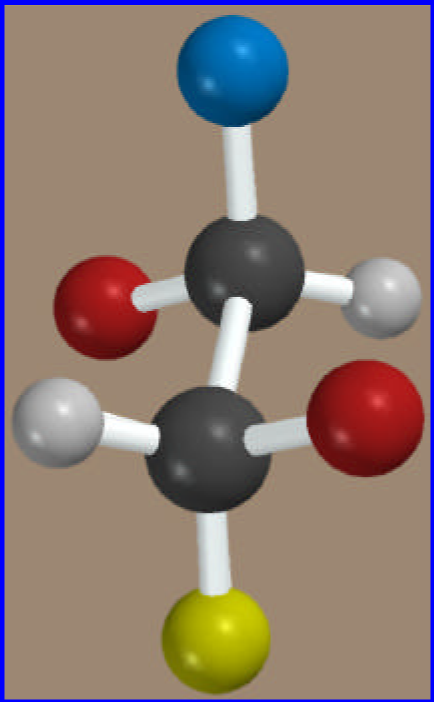
Carbon-2	*R*	*R*	*S*	*S*
Carbon-3	*R*	*S*	*R*	*S*


Isomers
constitutional isomers
stereoisomers
enantiomers
diastereomers

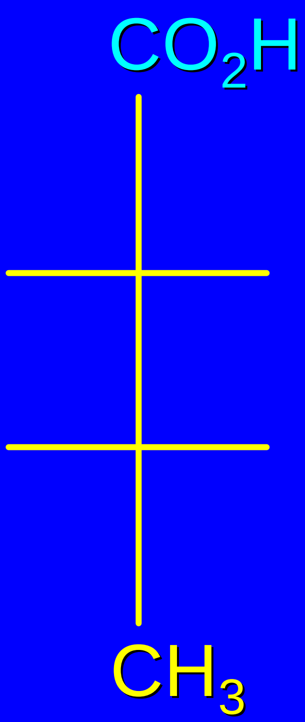


[a] = -9.5°
[a] = +9.5°
enantiomers
diastereomers
enantiomers
[a] = +17.8°
[a] = -17.8°
CO2H
R
HO
H
H
OH
R
CH3
CO2H
S
H
OH
HO
H
S
CH3
CO2H
R
HO
H
HO
H
S
CH3
CO2H
S
H
OH
H
OH
R
CH3

Fischer Projections

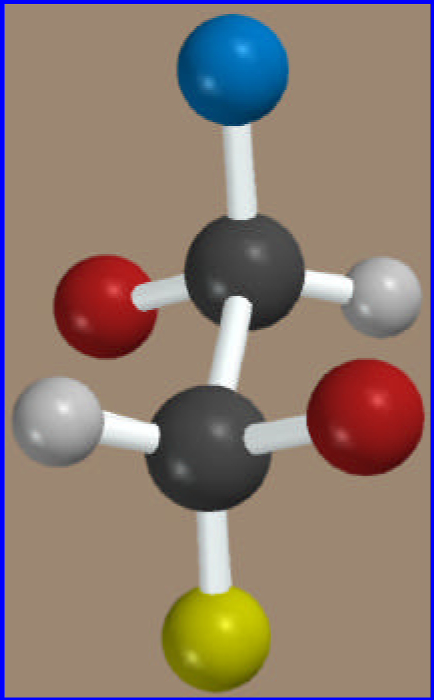


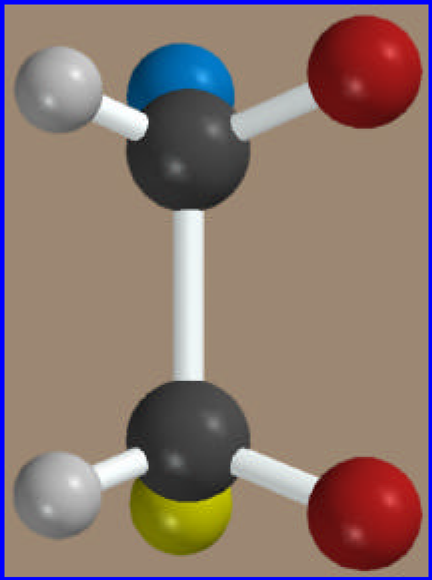
recall for Fischer projection: horizontal bonds point toward you; vertical bonds point away



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

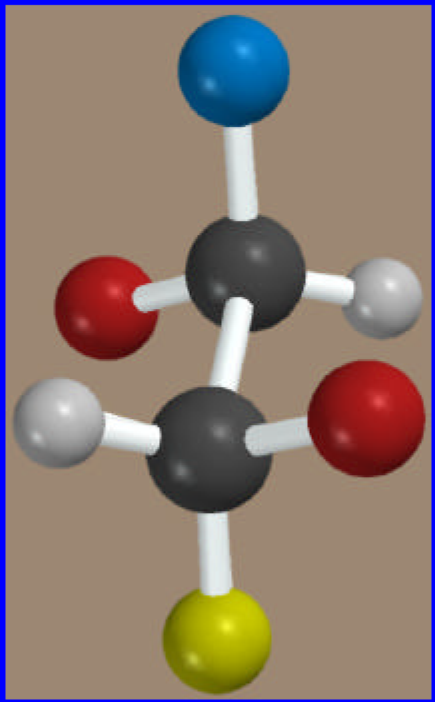
Fischer projections

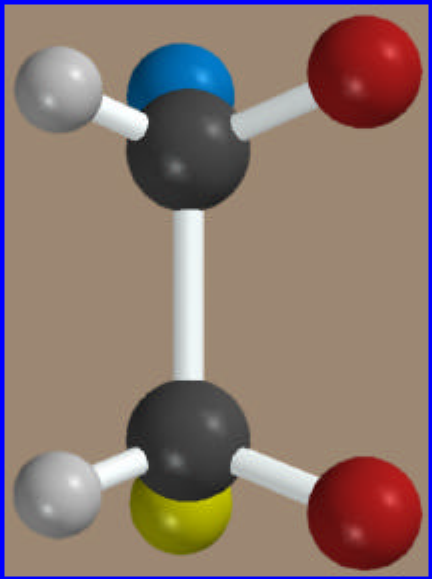


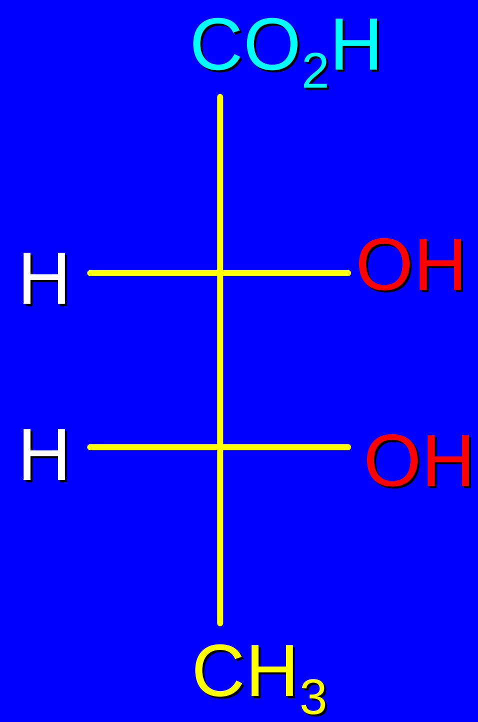


transform molecule to eclipsed conformation in order to construct Fischer projection

Fischer projections







Erythro and Threo

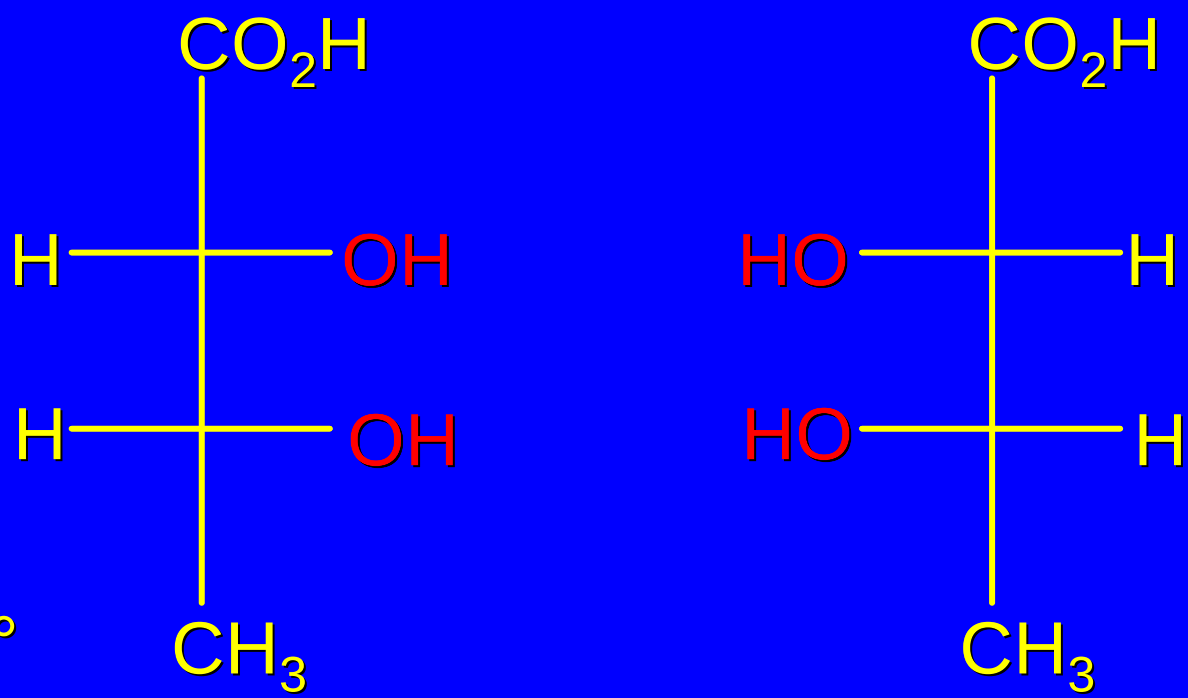
stereochemical prefixes used to specify relative configuration in molecules with two stereogenic centers

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

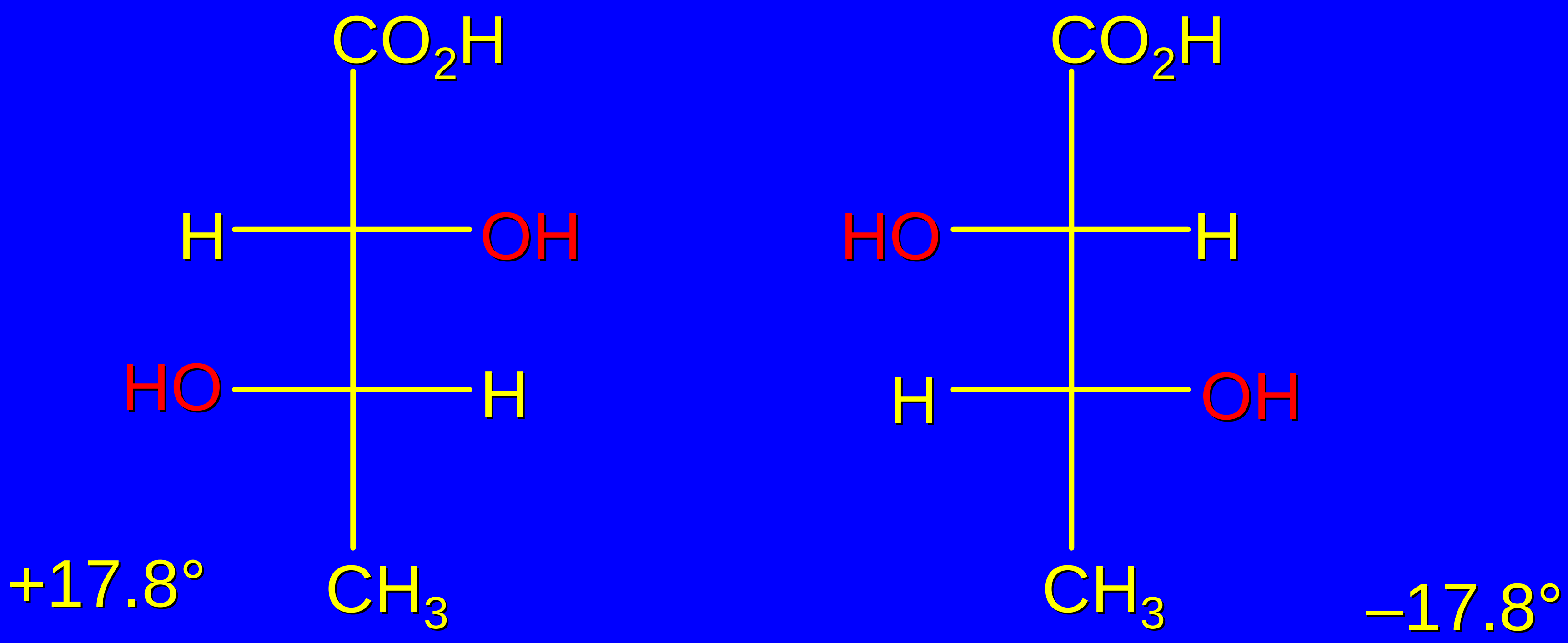


–9.5°

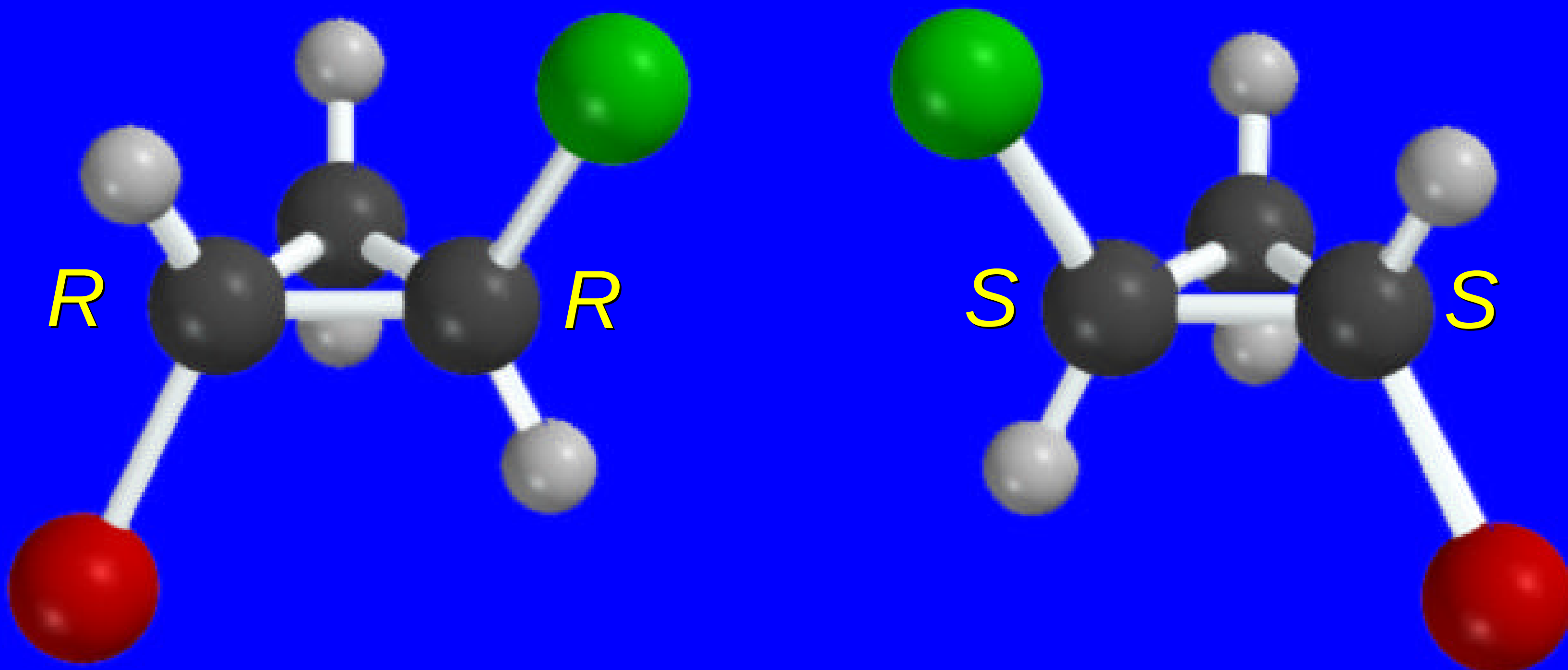
+9.5°

Threo

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



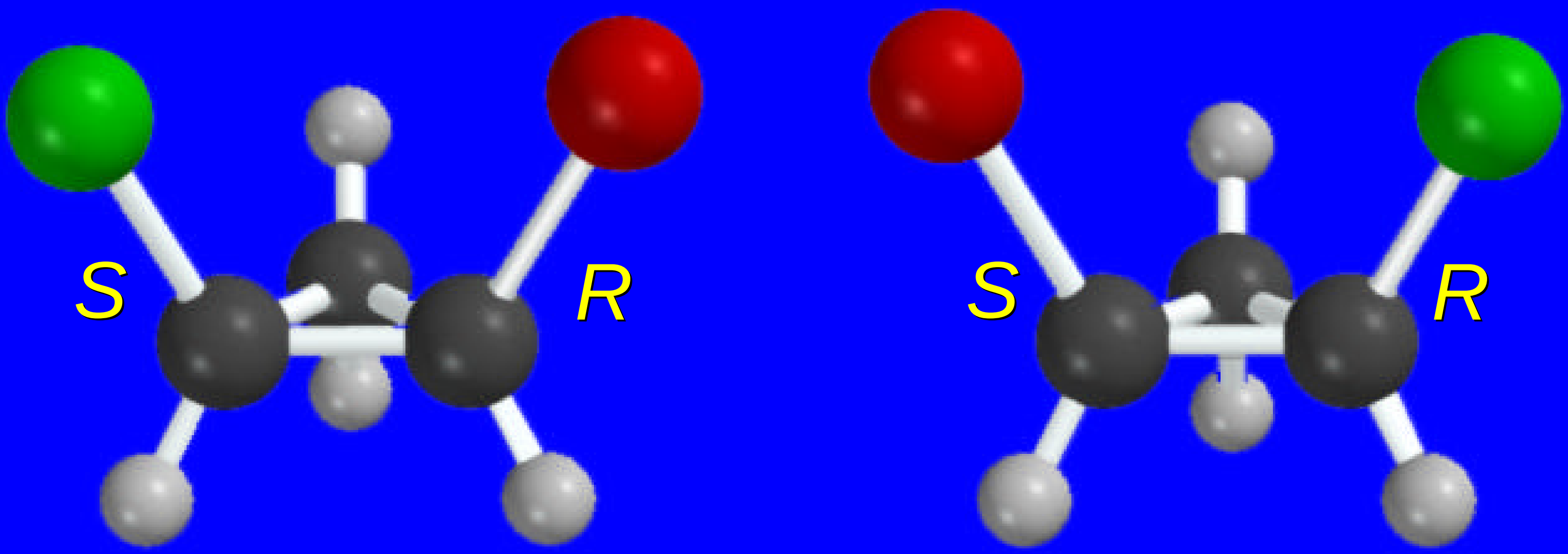
Two stereogenic centers in a ring



trans-1-Bromo-1-chlorocyclopropane

nonsuperposable mirror images; enantiomers

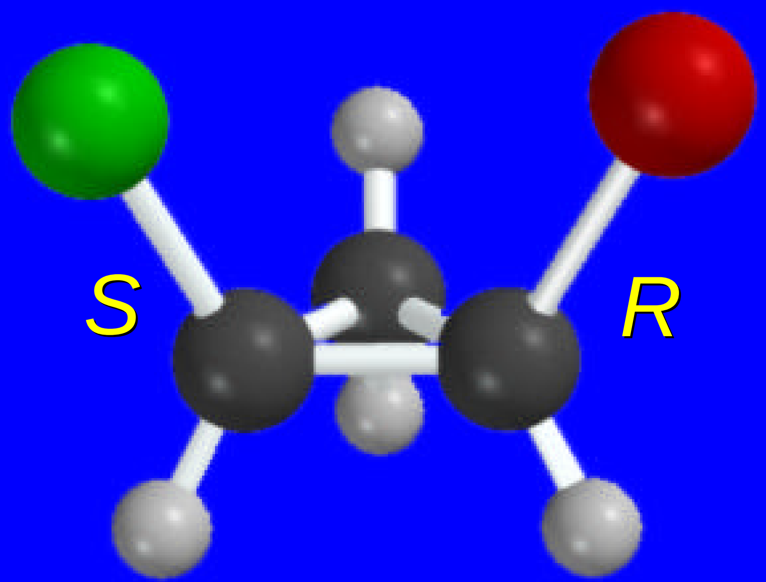
Two stereogenic centers in a ring

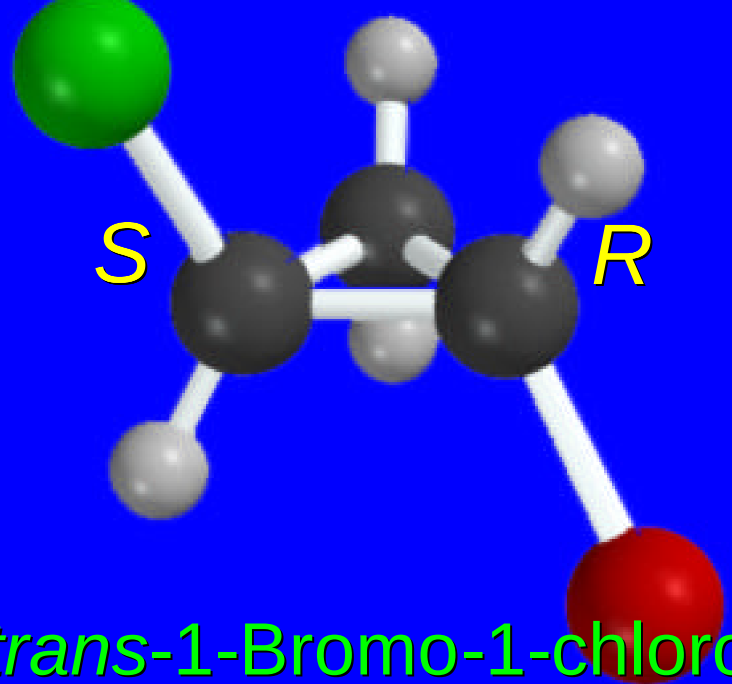


cis-1-Bromo-1-chlorocyclopropane

nonsuperposable mirror images; enantiomers

Two stereogenic centers in a ring





cis-1-Bromo-1-chloro-cyclopropane

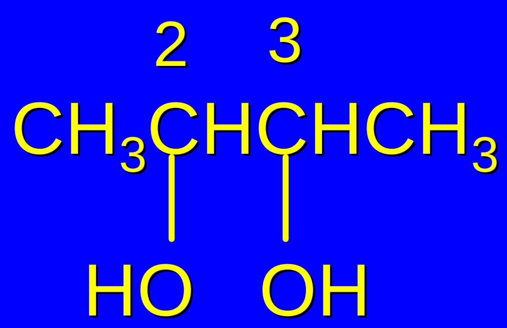
trans-1-Bromo-1-chloro-cyclopropane

stereoisomers that are not enantiomers; diastereomers

7.11
Achiral Molecules
with
Two Stereogenic Centers

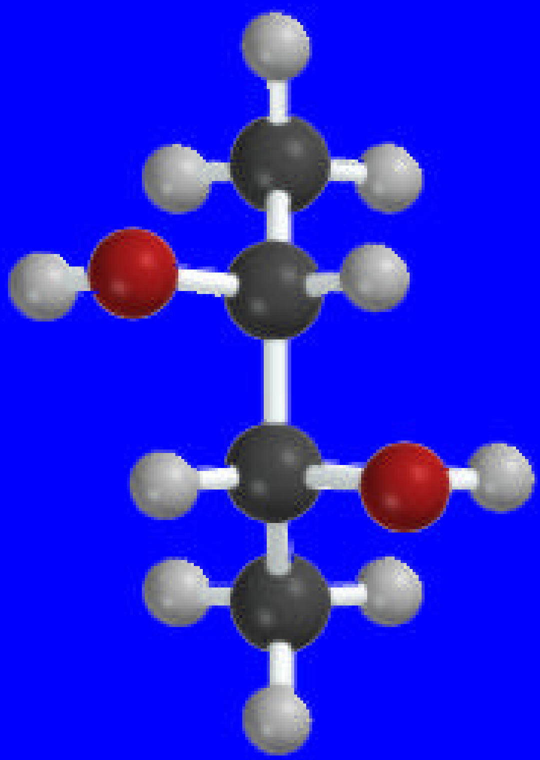
It is possible for a molecule to have stereogenic centers yet be achiral.

2,3-Butanediol



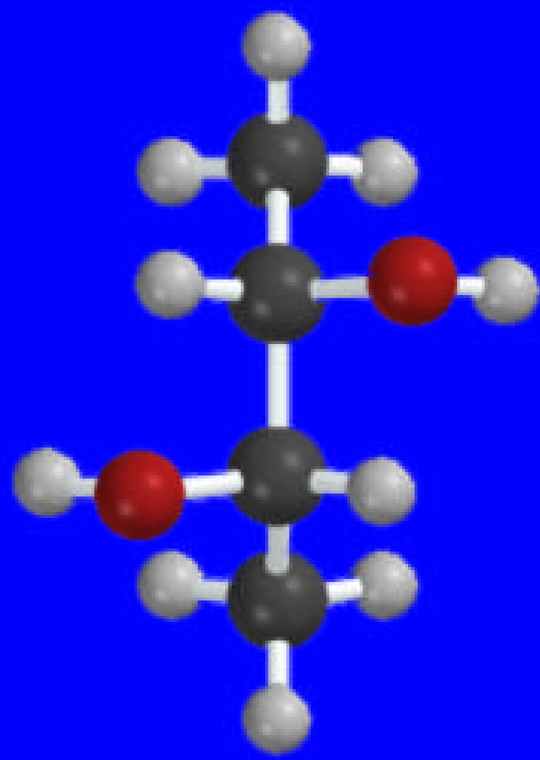
Consider a molecule with two equivalently substituted stereogenic centers such as 2,3-butanediol.

Three stereoisomers of 2,3-butanediol



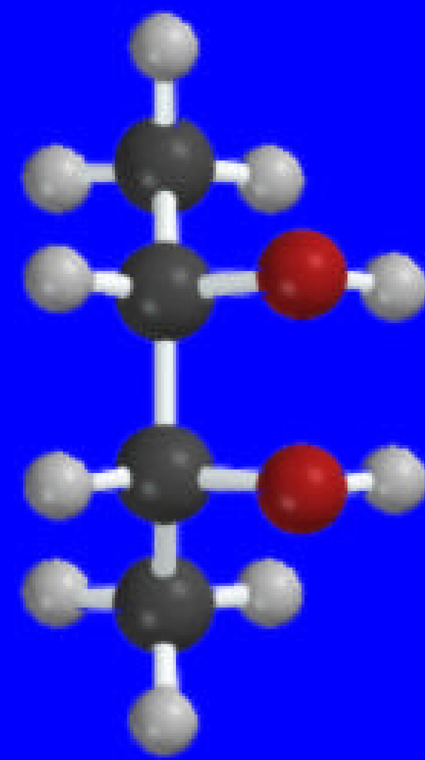
2*R*,3*R*

chiral



2*S*,3*S*

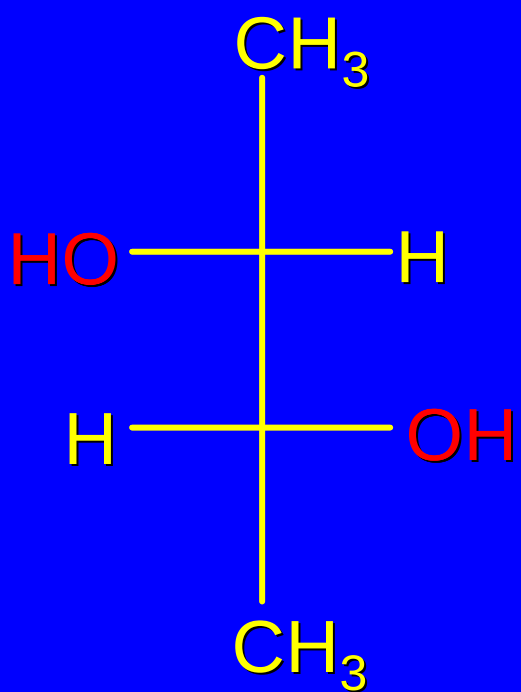
chiral



2*R*,3*S*

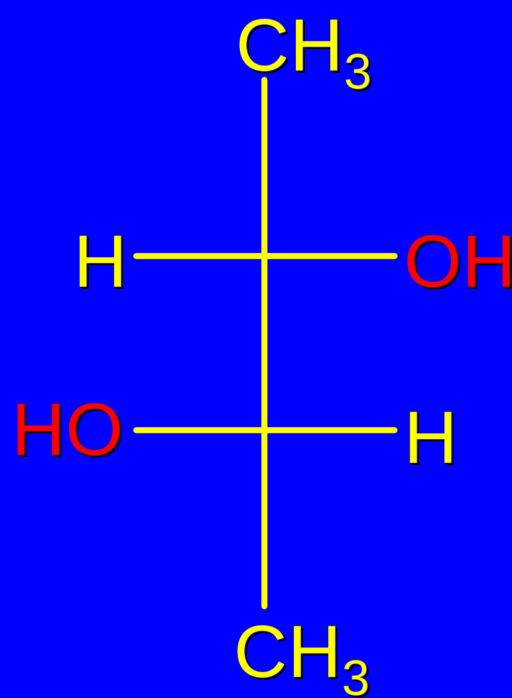
achiral

Three stereoisomers of 2,3-butanediol



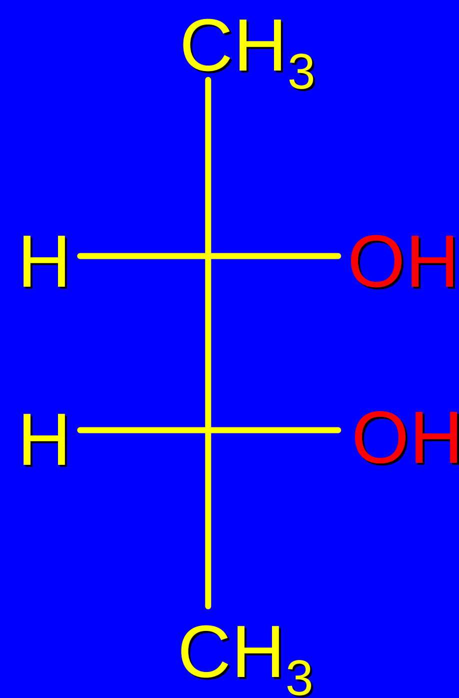
2*R*,3*R*

chiral



2*S*,3*S*

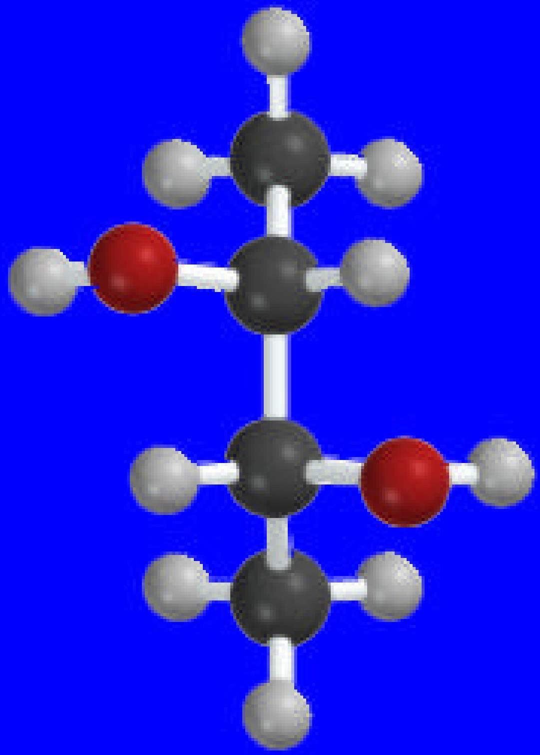
chiral



2*R*,3*S*

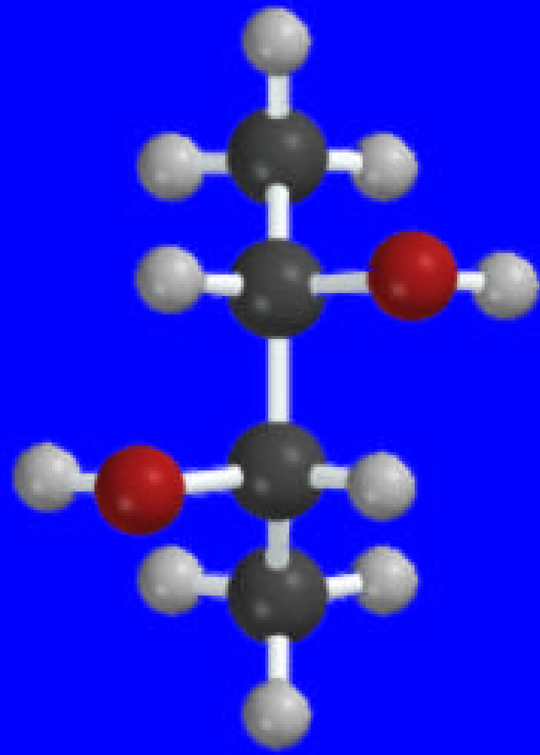
achiral

Three stereoisomers of 2,3-butanediol



2*R*,3*R*

chiral

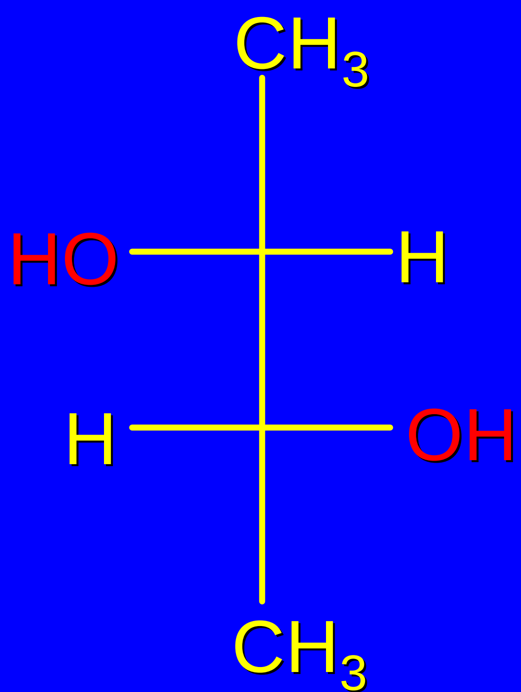


2*S*,3*S*

chiral

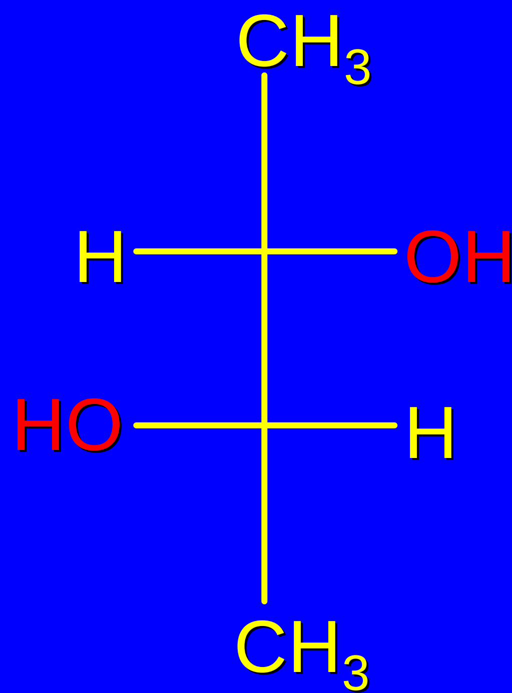
these two are enantiomers

Three stereoisomers of 2,3-butanediol



2*R*,3*R*

chiral



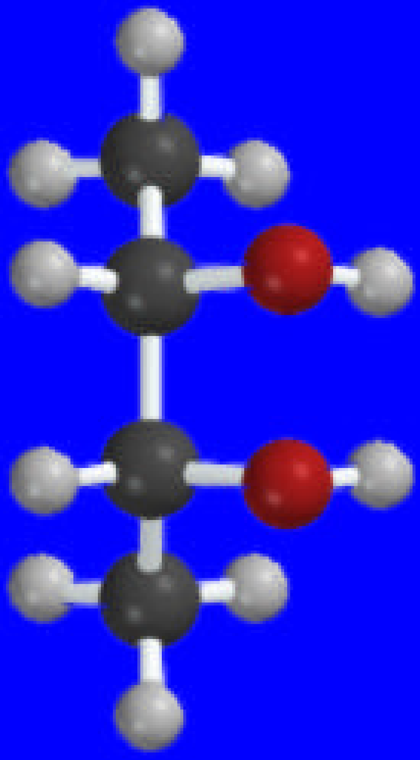
2*S*,3*S*

chiral

these two are enantiomers

Three stereoisomers of 2,3-butanediol

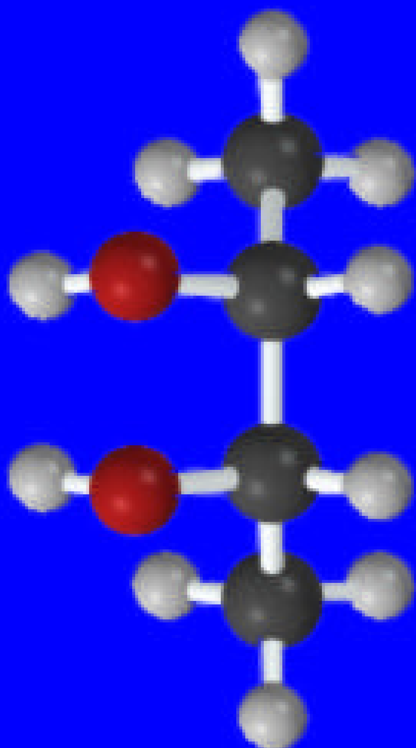
the third structure is superposable on its mirror image



2*R*,3*S*

achiral

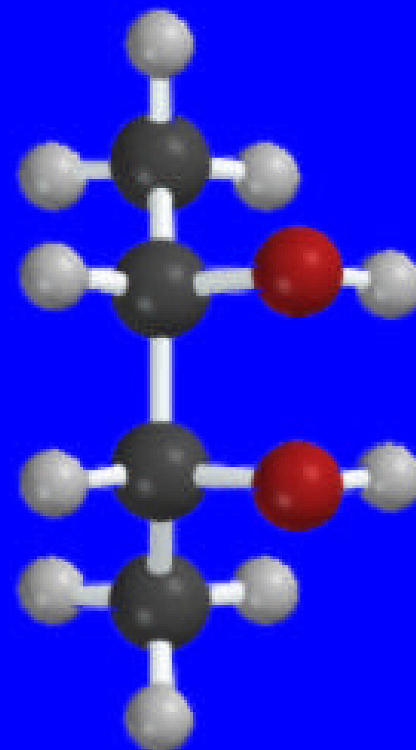
Three stereoisomers of 2,3-butanediol



therefore, this structure and its mirror image are the same

it is called a meso form

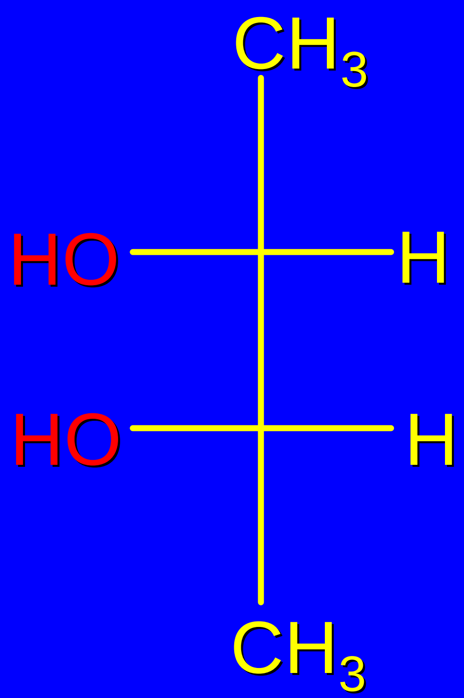
a meso form is an achiral molecule that has stereogenic centers



2*R*,3*S*

achiral

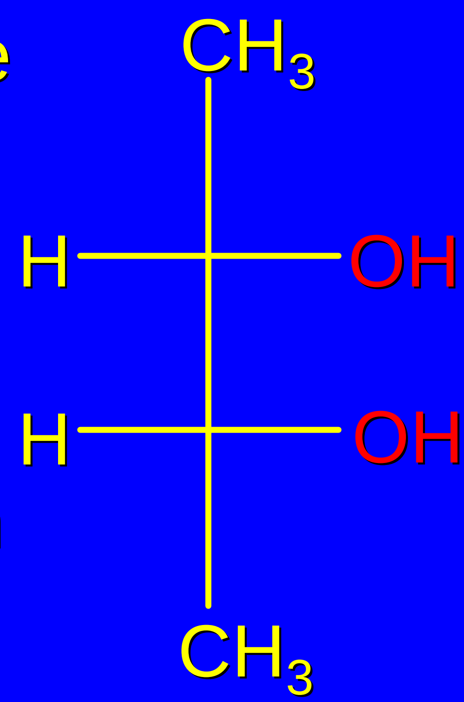
Three stereoisomers of 2,3-butanediol



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 stereogenic centers



2*R*,3*S*

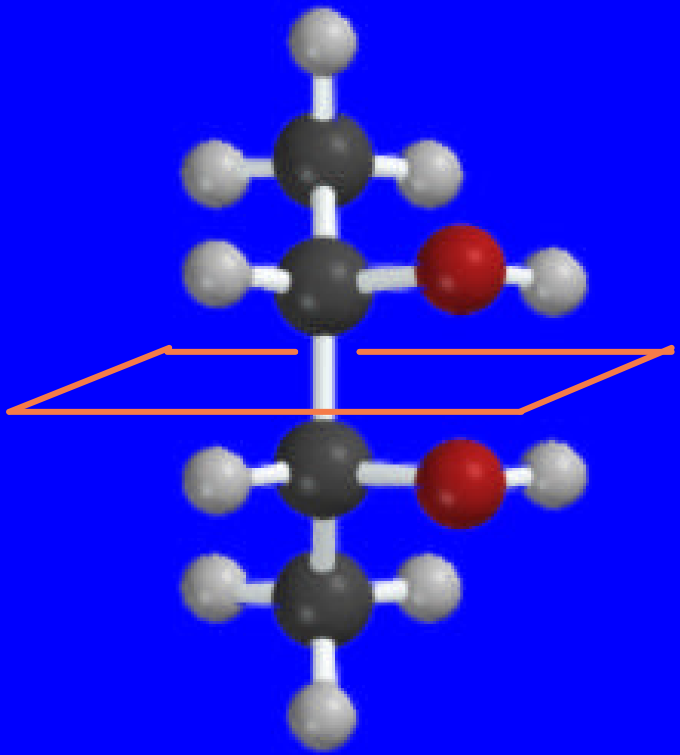
achiral

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

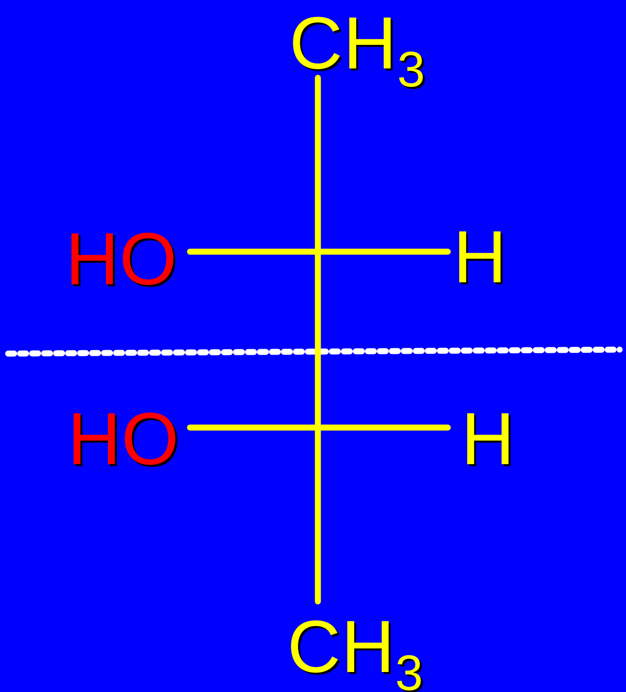
top half of molecule is mirror image of bottom half



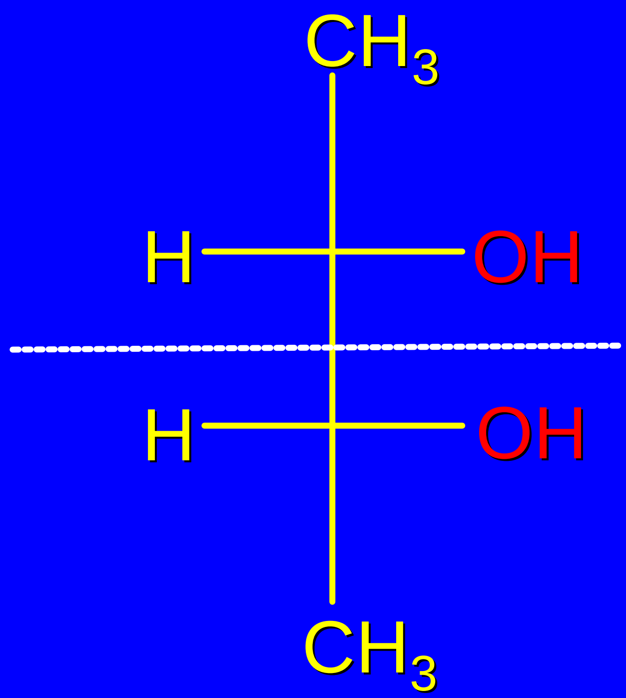
2*R*,3*S*

achiral

Three stereoisomers of 2,3-butanediol



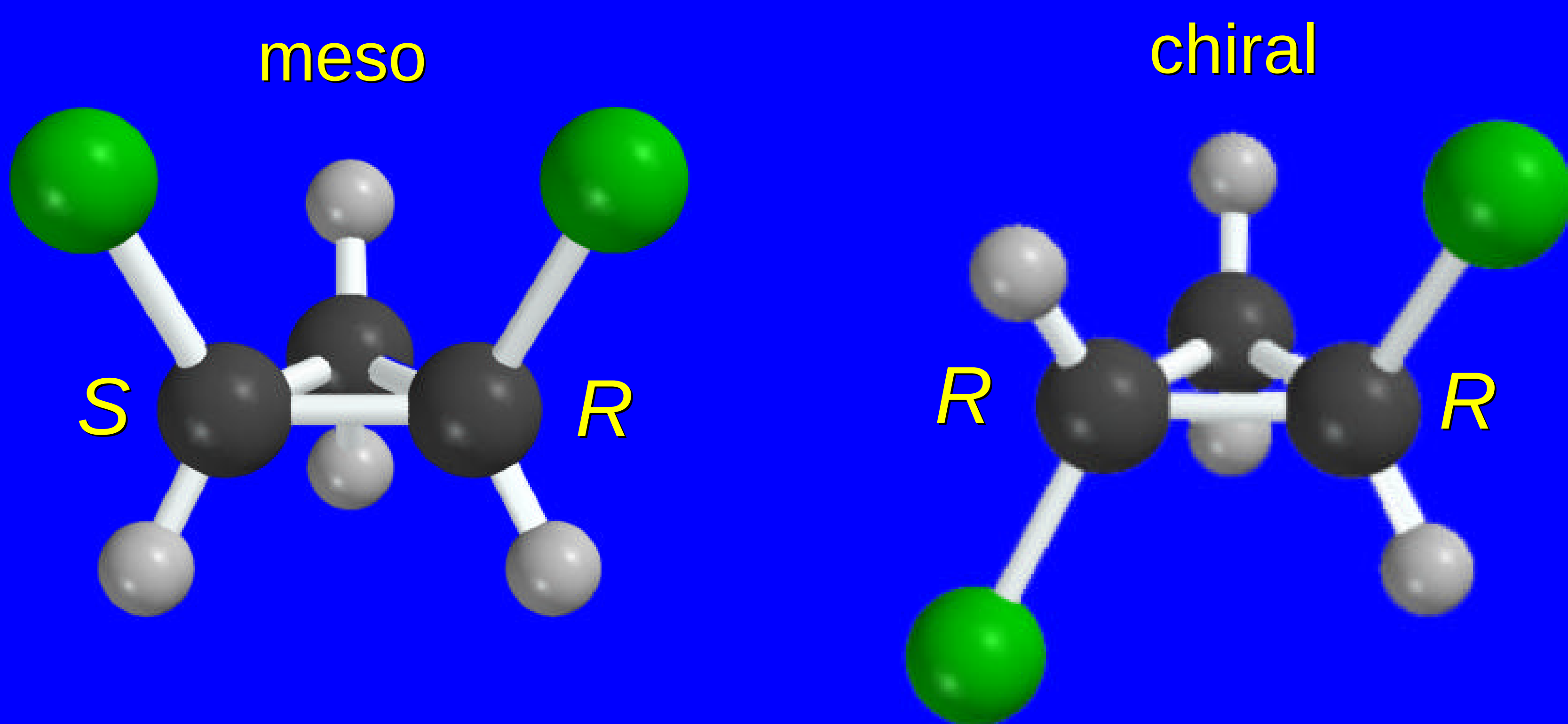
A line drawn the center of the Fischer projection of a meso form bisects it into two mirror-image halves.



2*R*,3*S*

achiral

Cyclic compounds



There are three stereoisomers of 1,2-dichloro-
cyclopropane; the achiral (meso) cis isomer

7.12 Molecules with Multiple Stereogenic Centers

How many stereoisomers?

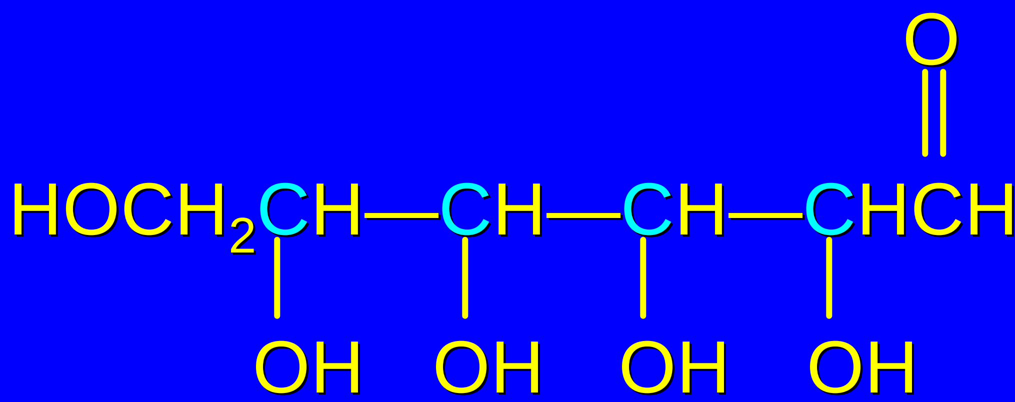
maximum number of stereoisomers = 2^n

where n = number of structural units capable of stereochemical variation

structural units include stereogenic centers and cis and/or trans double bonds

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

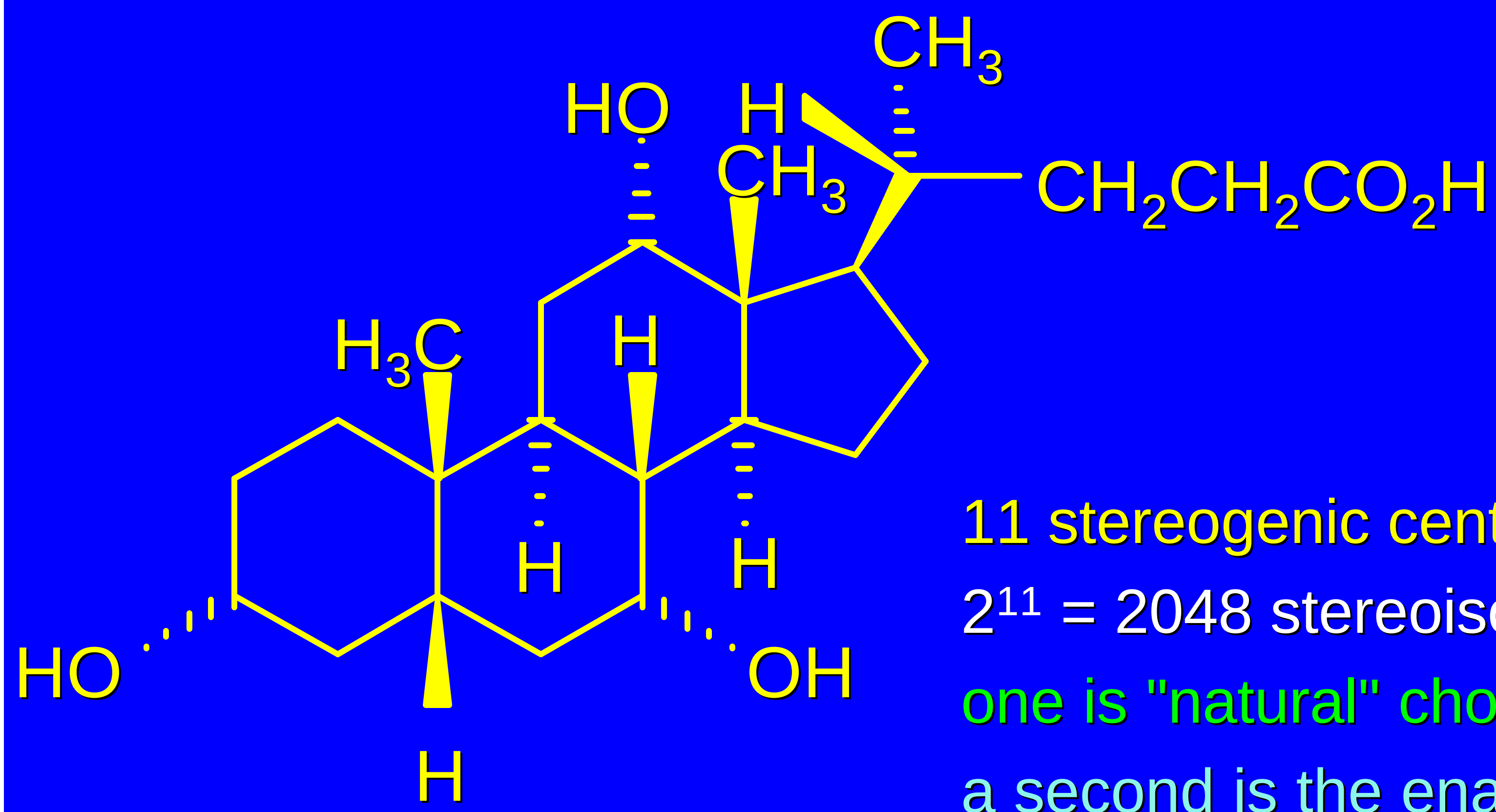
Example



4 stereogenic centers

16 stereoisomers

Cholic acid (Figure 7.13)



11 stereogenic centers

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 stereogenic centers 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