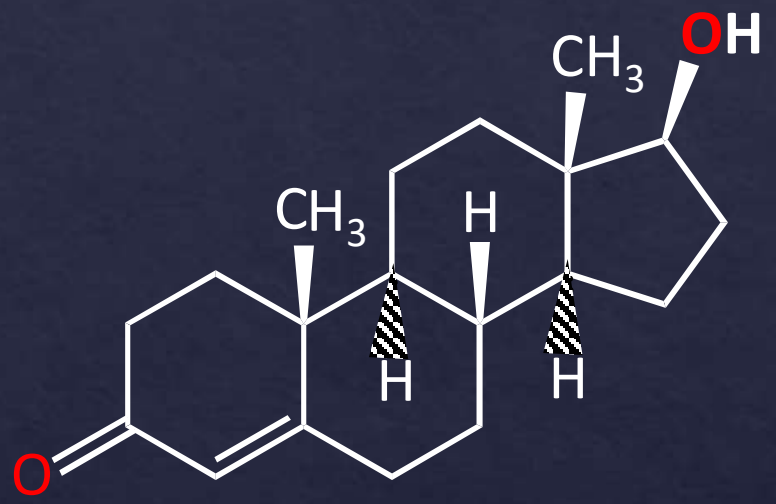
Antoine-Laurent Lavoisier

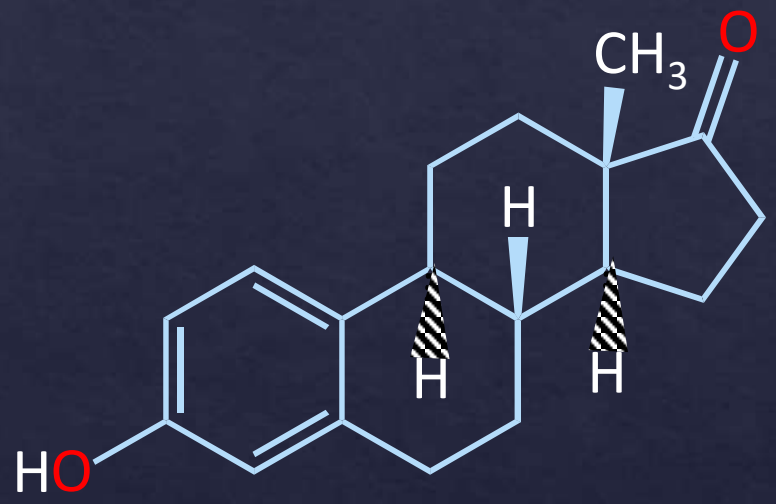
Cycloalkanes + *isomers

CYCLOALKANES

Abundant in nature, especially in polycyclic frames: the steroid sex hormones



Testosterone



Estrone

Regulate growth and function of reproductive organs; stimulate development of secondary sexual characteristics

Naming cycloalkanes

Molecular formula: $(CH_2)_n$ not C_nH_{2n+2}

Named as cycloalkanes: cyclopropane,  ,
cyclobutane,  , etc.

When substituents: Cycloalkyl.

Monosubstituted cycloalkanes: carbon of attachment is defined as "C1":

Ethylcyclobutane (no # needed)

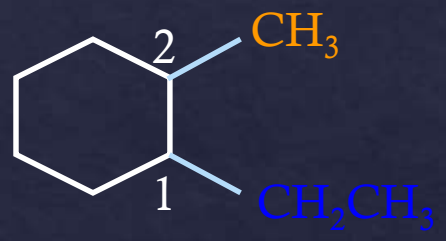
Larger stem controls:

1-Cyclopropylpentane

Disubstituted cycloalkanes:

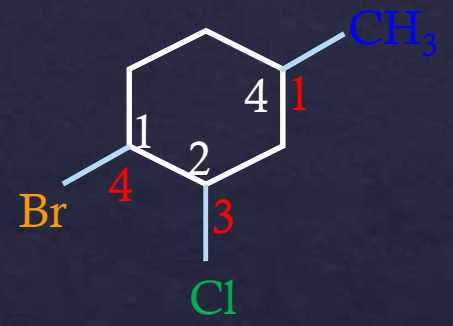
a. Lowest digit numbering

b. Substituents go in alphabetical order



1-Ethyl-2-methylcyclohexane

E before m



1,2,4 not 1,3,4

1-Bromo-2-chloro-4-methylcyclohexane

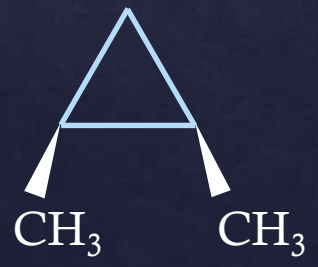
Let's look at stereoisomers in more detail

With two (or more) substituents, new type of isomerism:

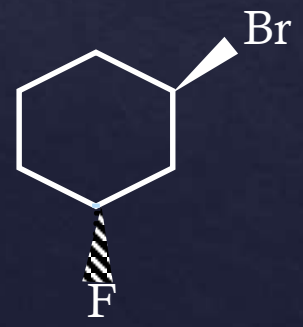
Same side: cis

Opposite sides: trans

} Stereoisomers



cis-1,2-Dimethyl-cyclopropane



trans-1-Bromo-3-fluorocyclohexane

Definition of Stereoisomers

Same connectivity (not constitutional isomers), but differing arrangement in space.

Note: This definition includes all rotamers (anti, gauche, etc.).

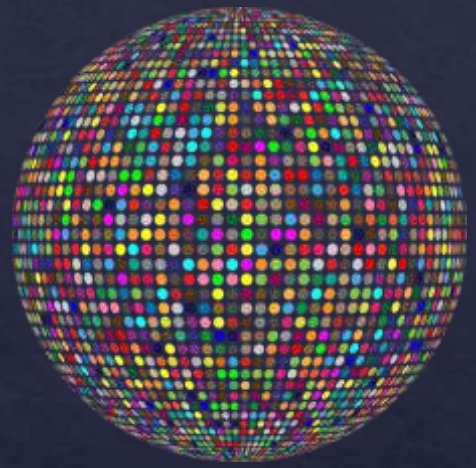
However

Stereoisomers should be stable at room temperature. Rotamers interconvert rapidly by rotation, whereas *cis*/*trans* isomerization requires bond breaking.

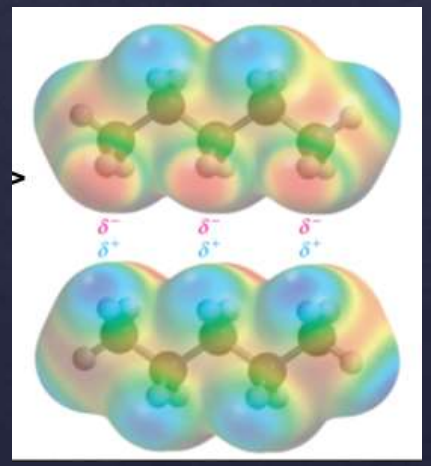

Quiz
Insert
Home
Delete
Ctrl

Physical properties

higher boiling
& melting points



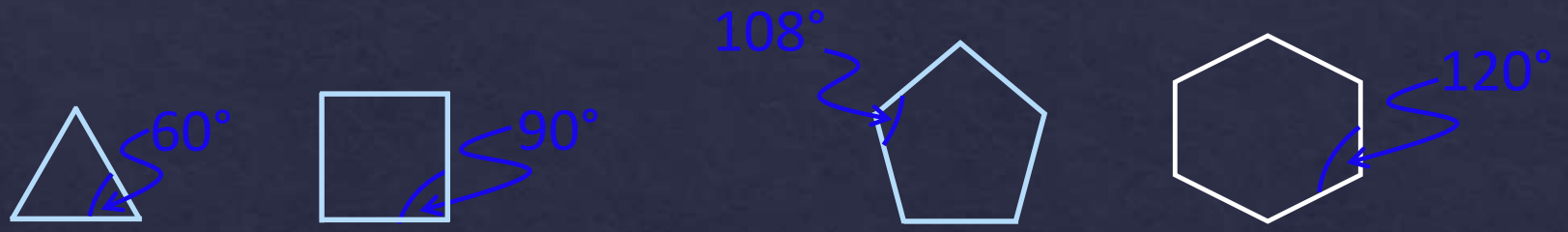
higher density



↑ London interactions more rigid & symmetric cyclic systems

Different melting & boiling T if odd or even # C

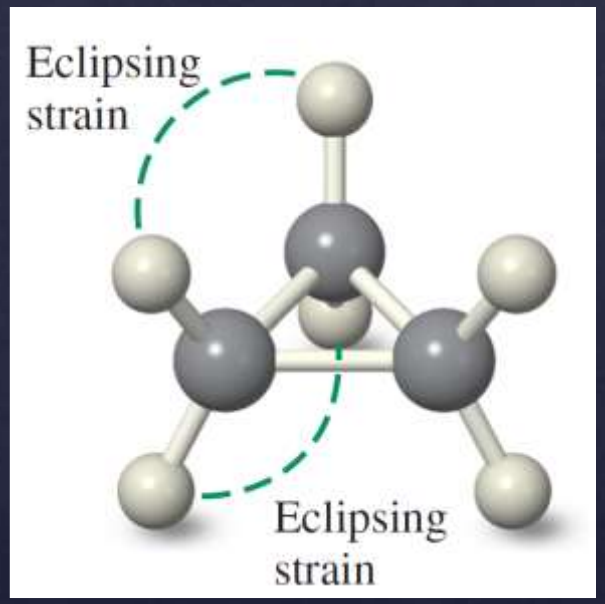
Ring Strain

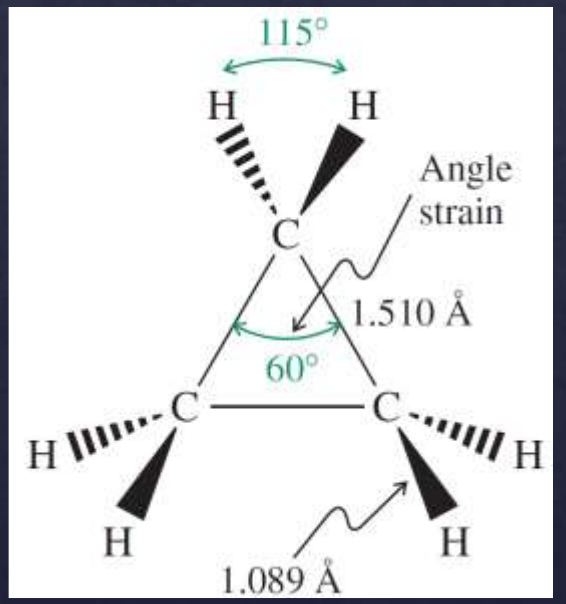


sp^3-Carbon wants 109.5°

1. Small rings (cyclopropane, cyclobutene)
2. Common rings (cyclo-pentane, -hexane, -heptane)
3. Medium rings (8-12 C)
4. Large rings (>12C)

Cyclopropane

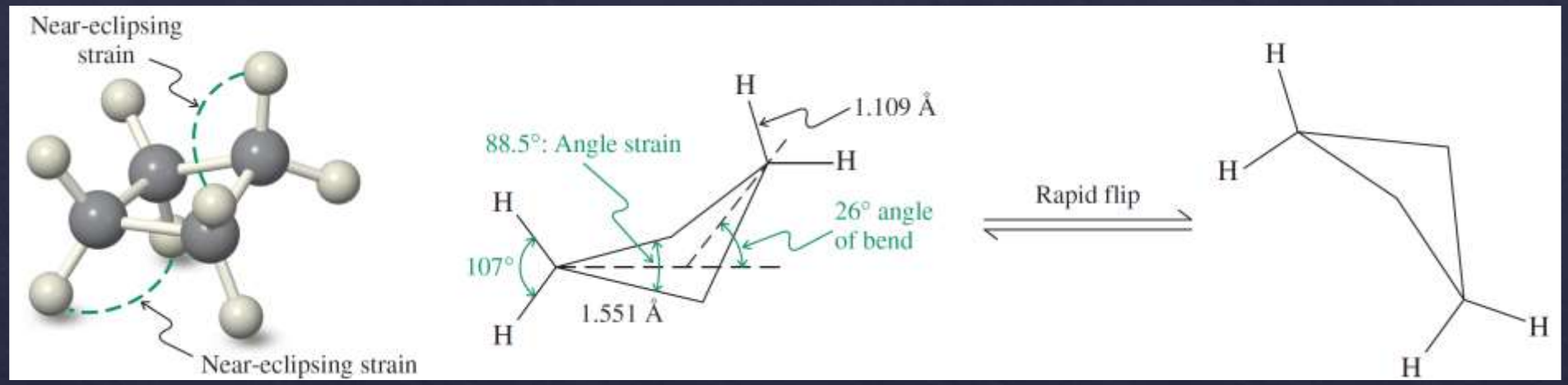




Torsional strain and bond-angle strain make so that the molecule is less stable than expected

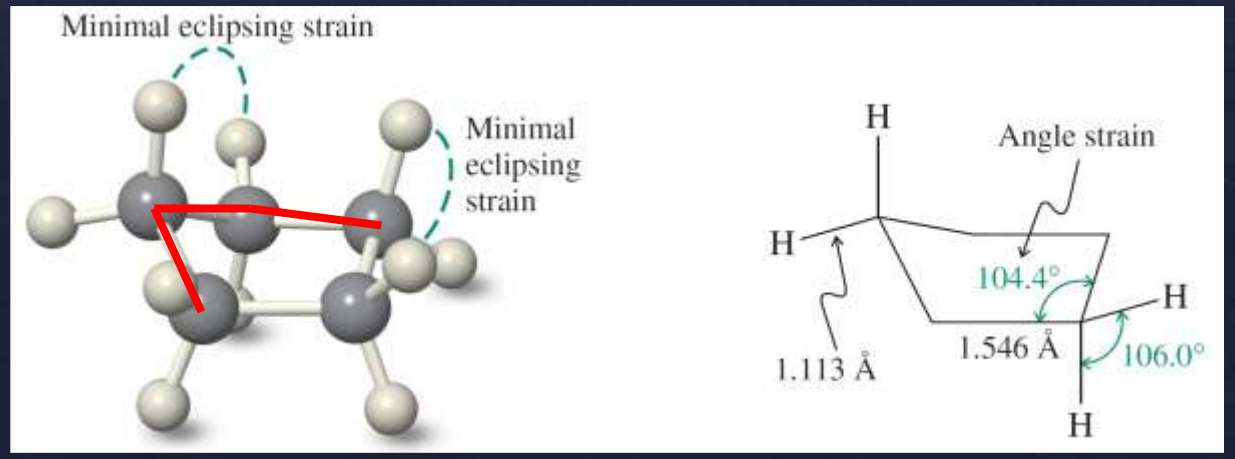
Pictures from Vollhardt & Schore

Cyclobutane: "Puckering" reduces eclipsing



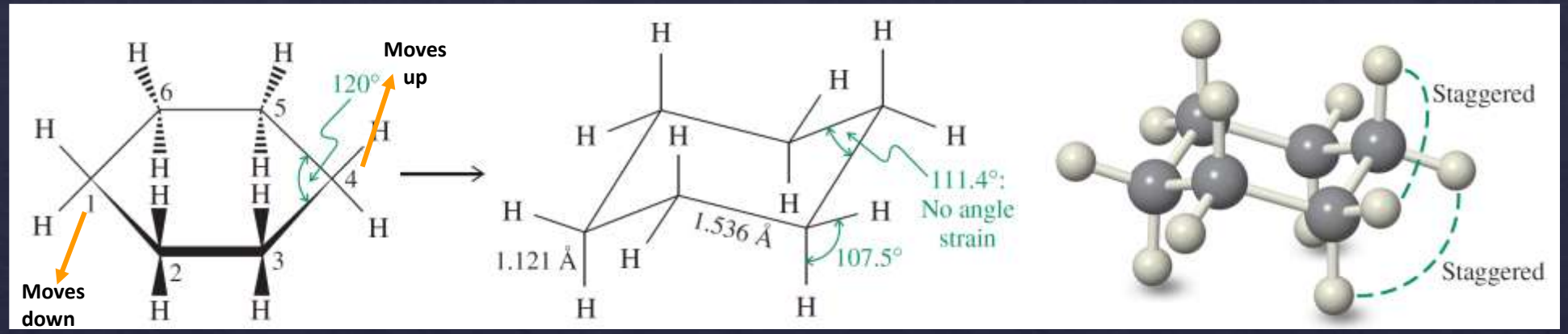
Cyclopentane: Envelope Conformation

Almost staggered

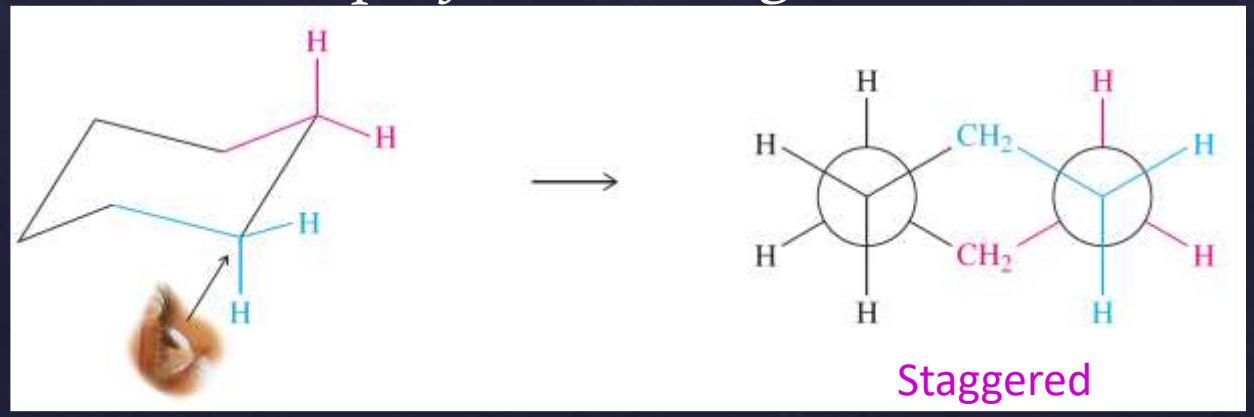


Pictures from Vollhardt & Schore

The (Almost) Unstrained Cyclohexane: A "Chair" Conformation



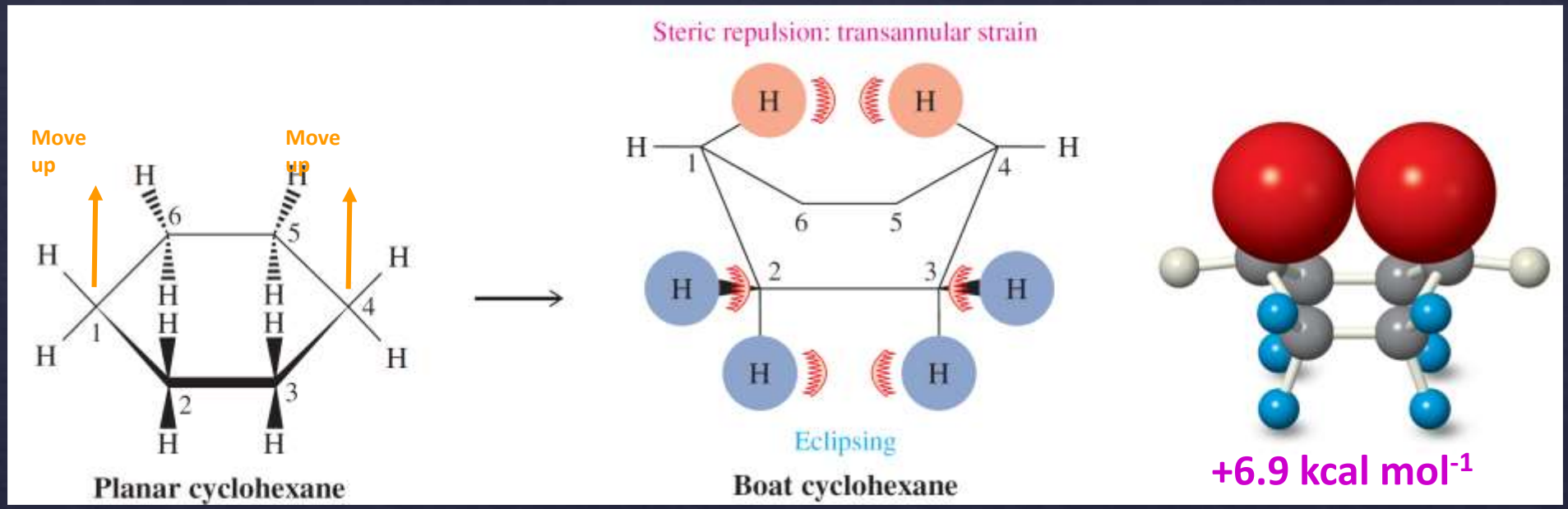
Newman projection along C-C bond



Chair

Pictures from Vollhardt & Schore

The cyclohexane alternative conformation (Boat) is strained

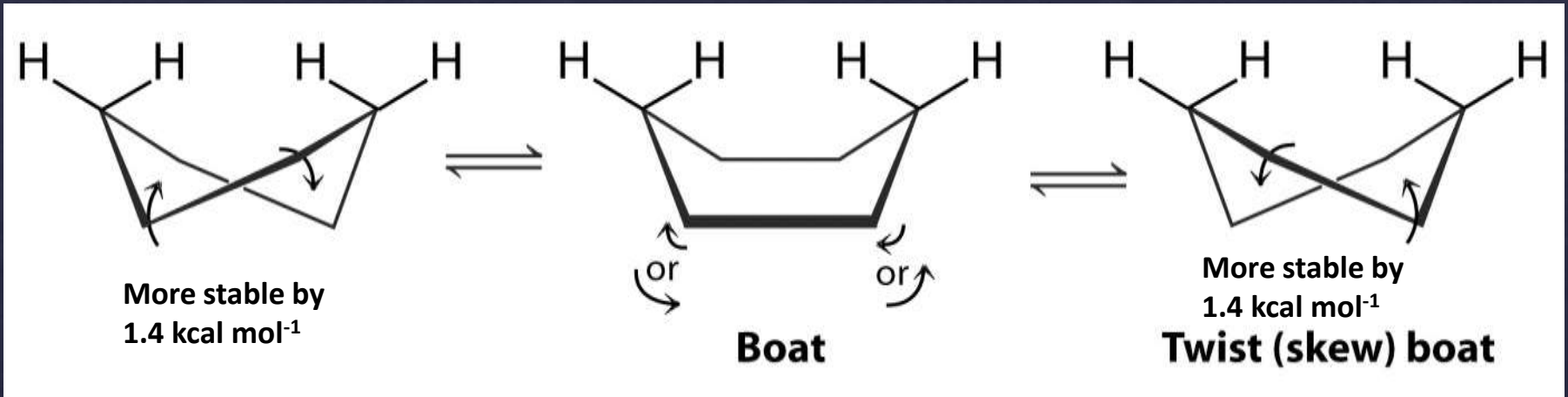


The boat form is a transition state in the dynamics of cyclohexane movement

Boat

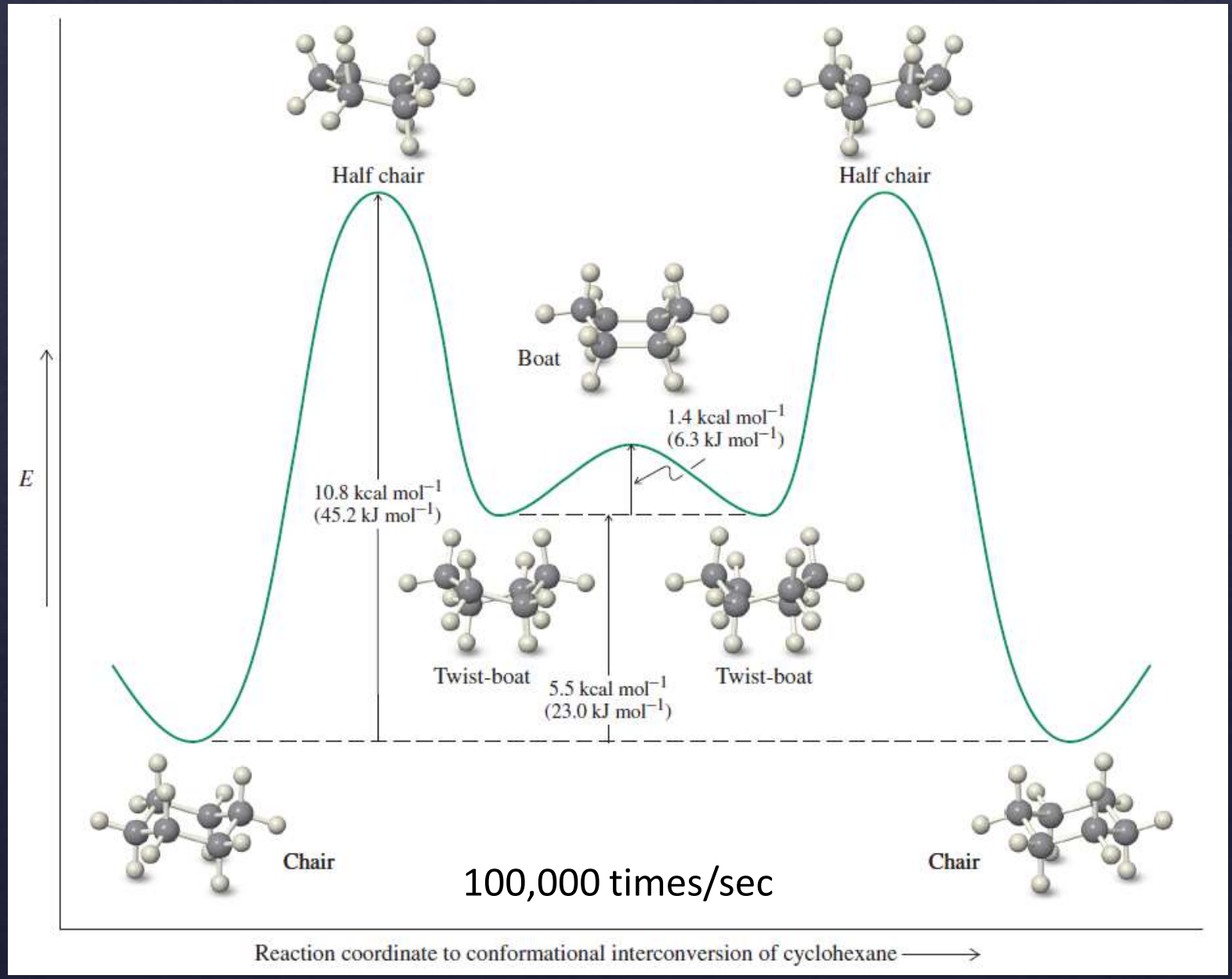
Picture from Vollhardt & Schore

…So it twists



But this is only part of its mobility.
The most important movement is a "flip" from one chair form to another.

The Chair-Chair Flip Manifold



100,000 times/sec

Resources from
Vollhardt & Schore

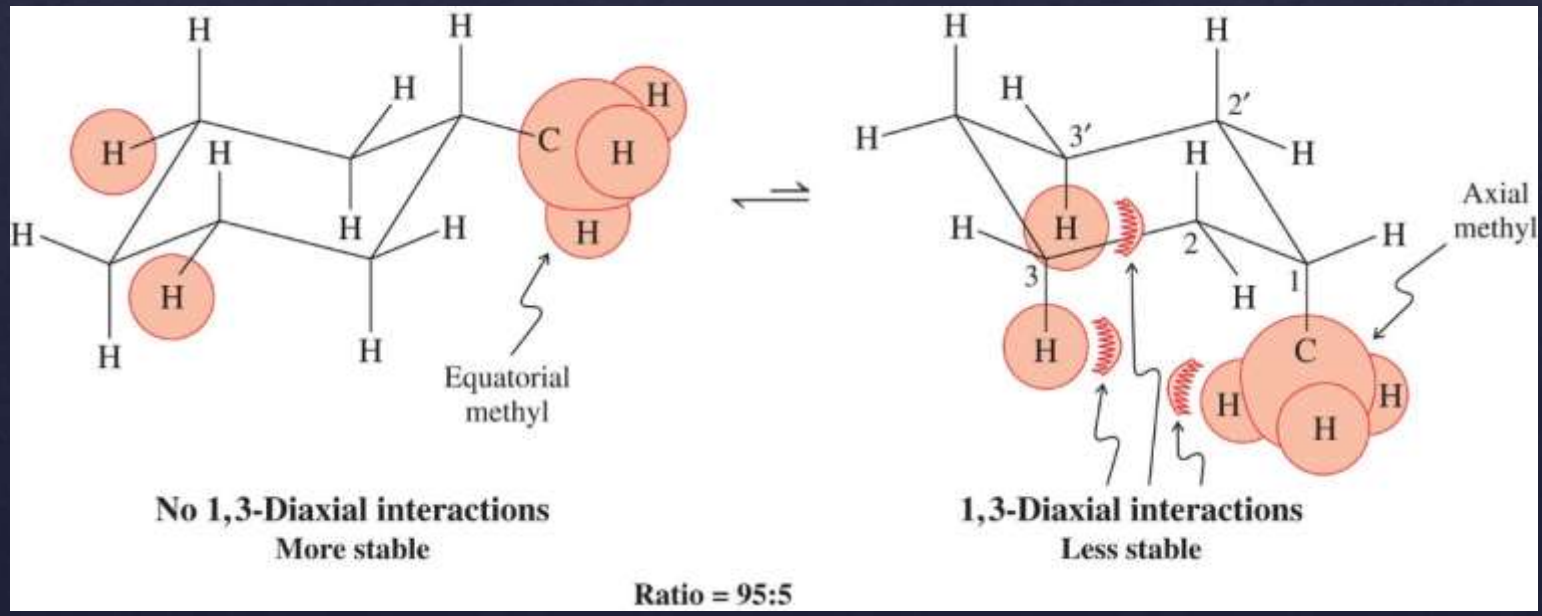
Monosubstituted Cyclohexanes

$\Delta G^\circ \neq 0$

Conformational Analysis: the energetics of axial-equatorial substituents

Example: methylcyclohexane

Anti
More stable

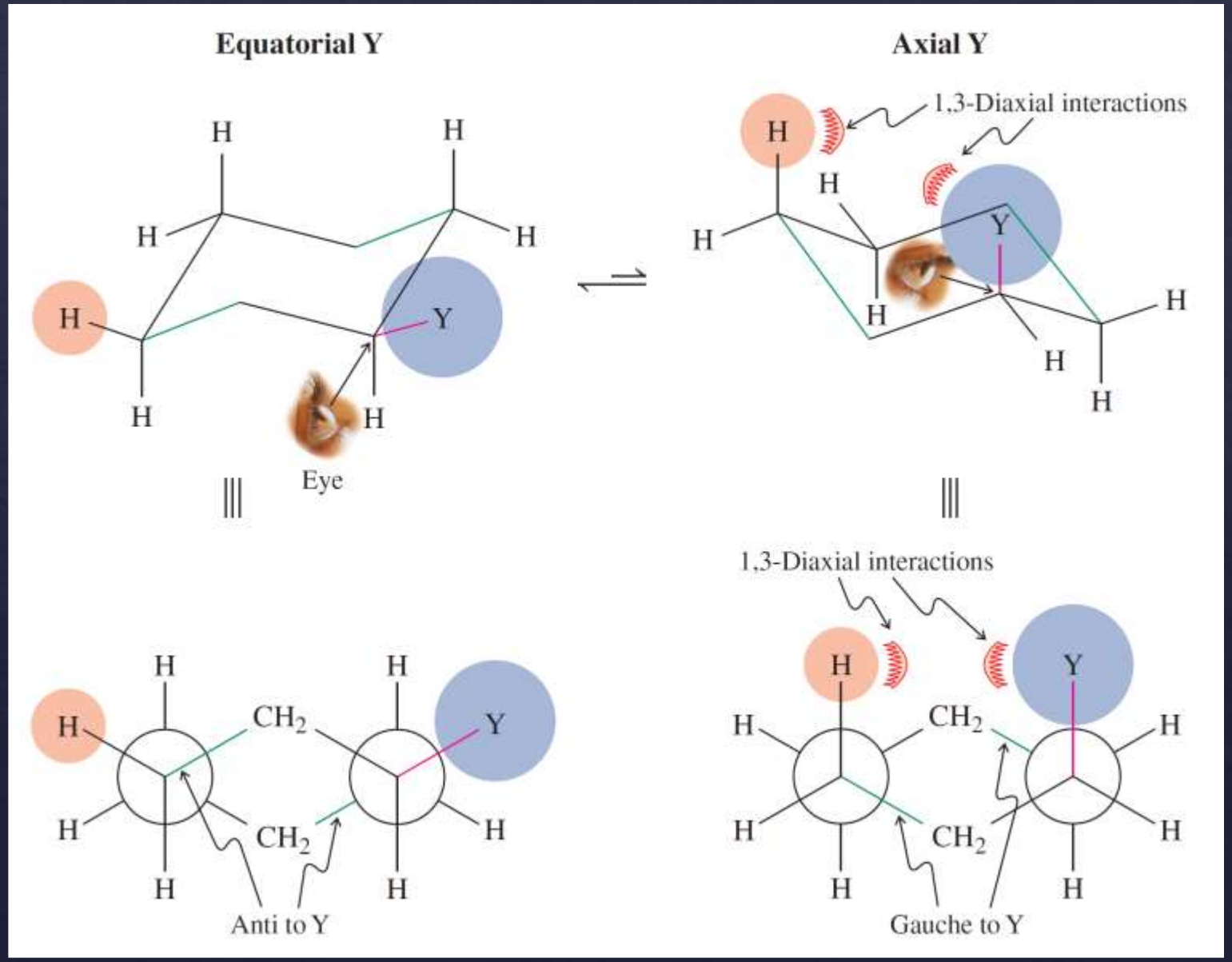


Gauche
Less stable

Transannular strain

Picture from Vollhardt & Schore

Axial-Equatorial Conformers

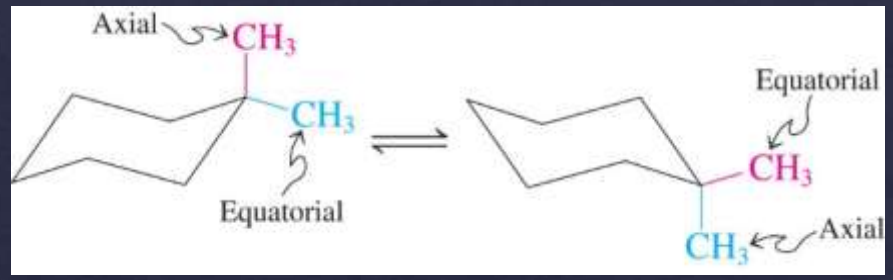


Picture from Vollhardt & Schore

$\Delta G°$ may be additive

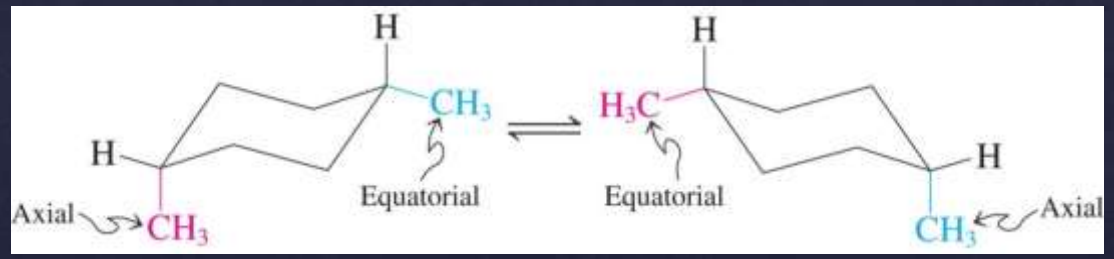
Consider the dimethylcyclohexanes:

$\Delta G° = 0$ kcal mol^{-1}



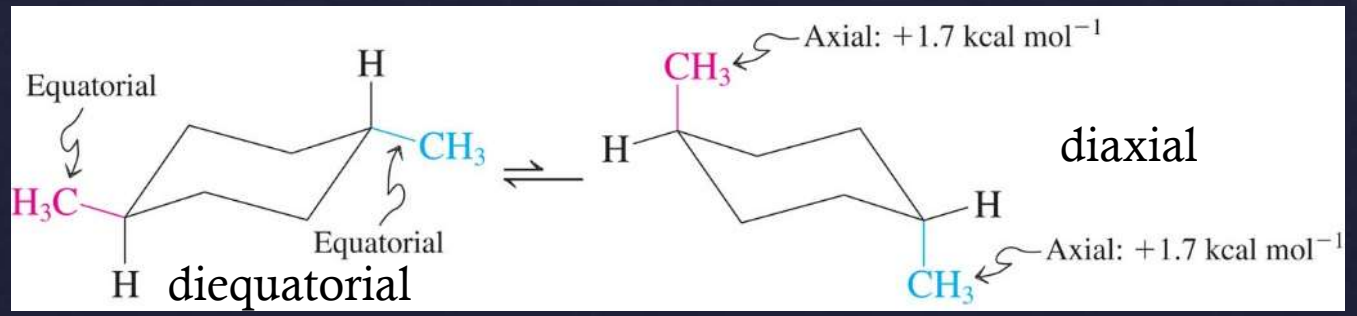
1,1-Dimethylcyclohexane

$\Delta G° = 0$ kcal mol^{-1}



cis-1,4-Dimethylcyclohexane

But:

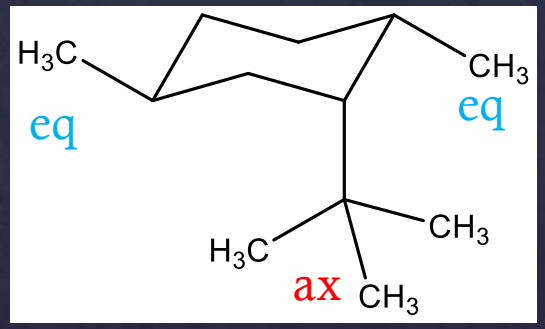


trans-1,4-Dimethylcyclohexane

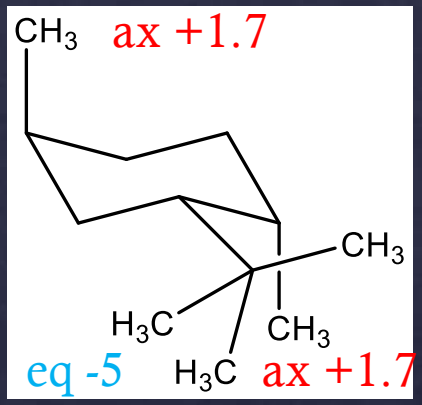
$\Delta G° = +3.4$ kcal mol^{-1} (I.e. 2x1.7 kcal mol^{-1})

Pictures from Vollhardt & Schore

The largest group often wins



$\Delta G° = 3.4–5 = -1.6$ kcal mol^{-1}

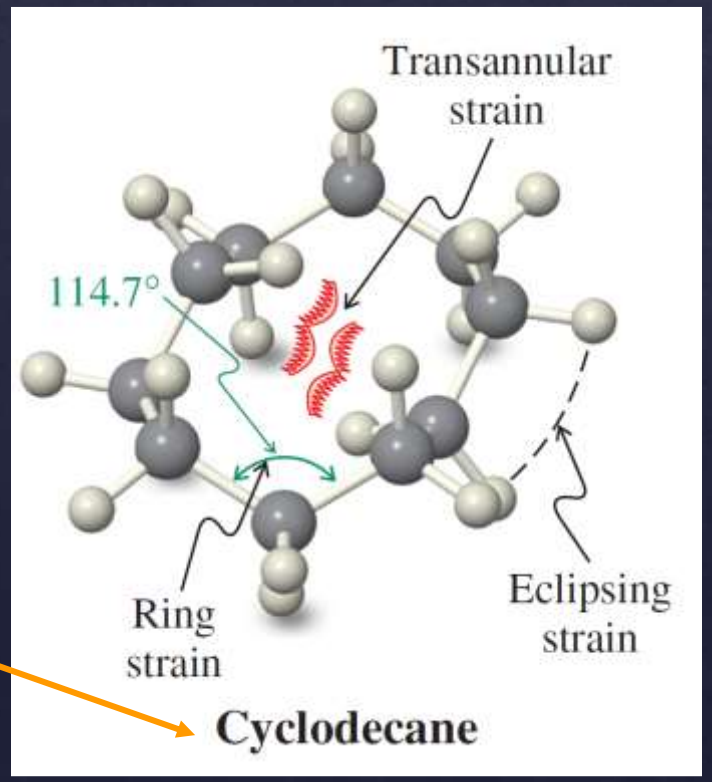


Large substituents, such as *tert*-Bu, are said to "lock" a conformation.

Pictures from Vollhardt & Schore

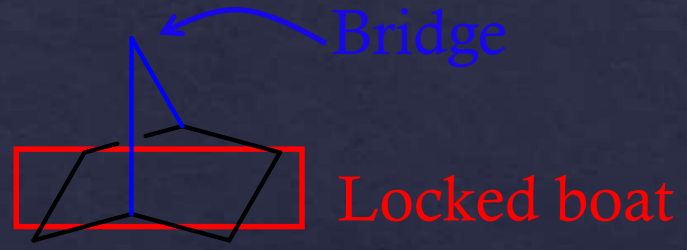
Medium Rings (8-12-Membered) Suffer Transannular Strain

Ring size (C_n)	Total strain	
3	27.6	(115)
4	26.3	(110)
5	6.5	(27)
6	0.1	(0.4)
7	6.4	(27)
8	10.0	(42)
9	12.9	(54)
10	14.0	(59)
11	11.0	(46)
12	2.4	(10)
14	0.0	(0.0)

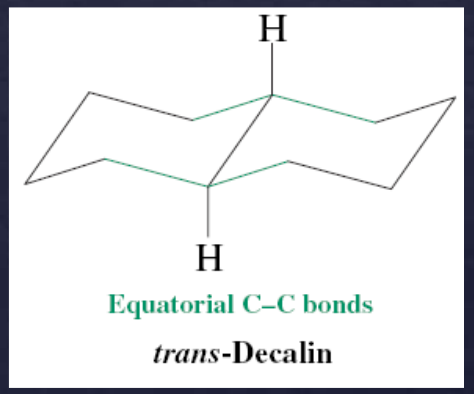


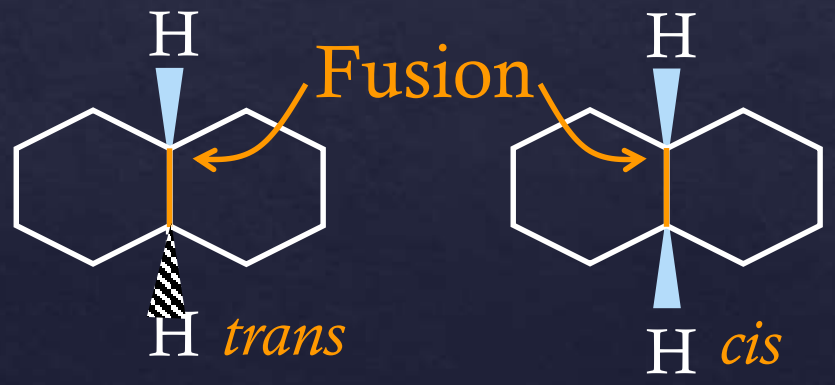
Pictures from Vollhardt & Schore

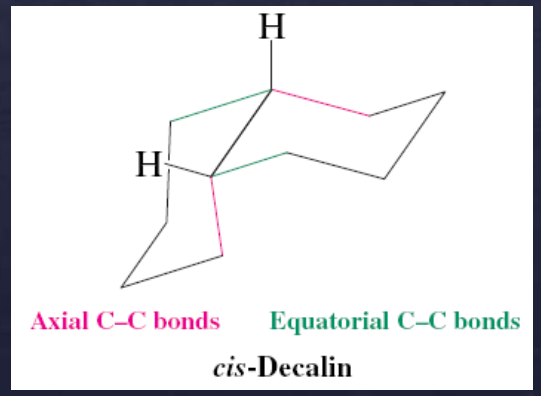
Bicyclic, fused, polycyclic, polyhedral alkanes



Bicyclo[2.2.1]heptane
(norbornane)







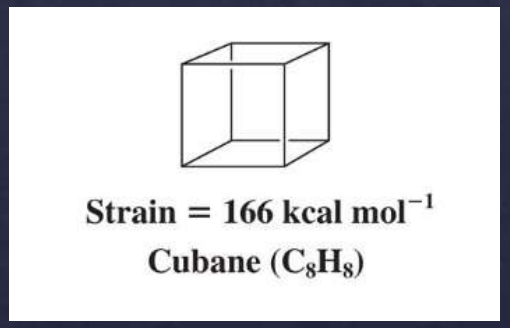
Bicyclo[4.4.0]decane
(decalin), trans and cis

Pictures from Vollhardt & Schore

Strained Hydrocarbons: What Is The Limit?

Exotic polyhedra: The five Platonic or Cosmic solids (Plato 350 BC)

Tetrahedron
(4 faces, fire)

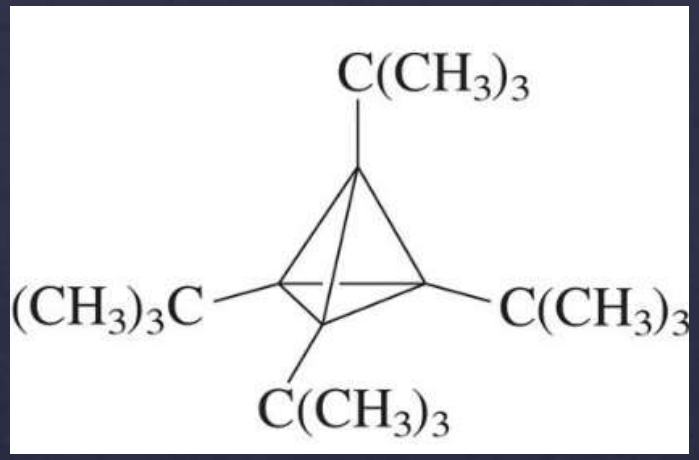


Cube
(6 faces, earth)

Dodecahedron
(12 faces, “ether”)

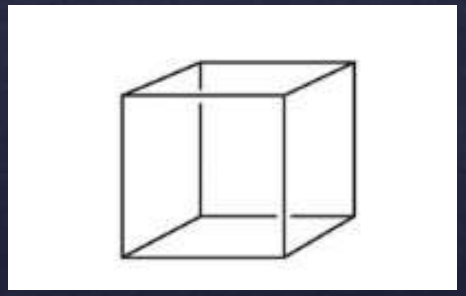
There are two more: icosahedron (20 faces, water) and octahedron (8 faces, air)

Pictures from Vollhardt & Schore



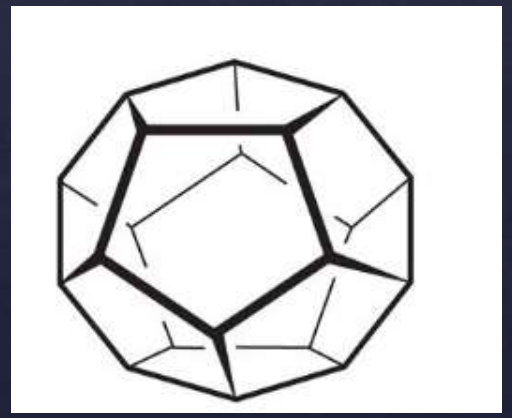
Maier, 1978,
tetra-*t*-Bu-tetrahedrane.
Substituted C_4H_4

m.p. 135°C Strain:
130 kcal mol^{-1}



Eaton, 1964,
cubane, C_8H_8

m.p. 126°C
Strain: 166 kcal mol^{-1}



Paquette, 1982,
dodecahedrane, $C_{20}H_{20}$,
12 cyclopentane faces

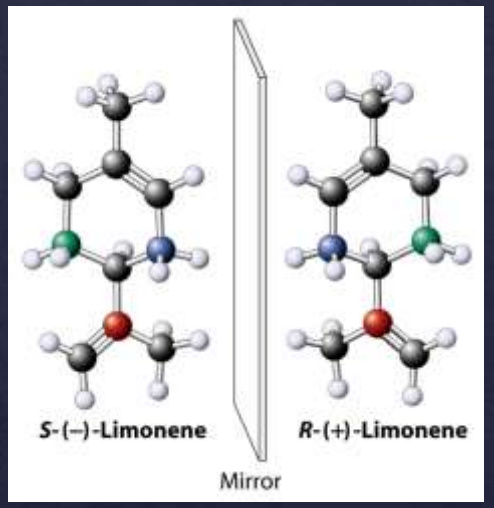
m.p. 430°C
Strain: 60 kcal mol^{-1}

Pictures from Vollhardt & Schore

STEREOISOMERS

Image and mirror image of limonene

Spruce tree



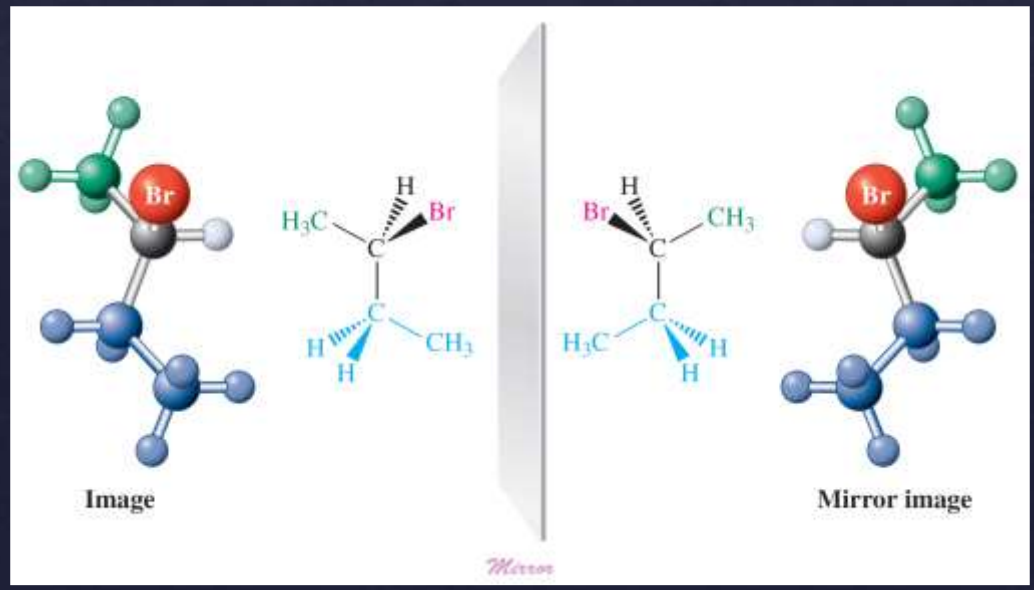
Orange

"Handedness"

Pictures from Vollhardt & Schore

And now…

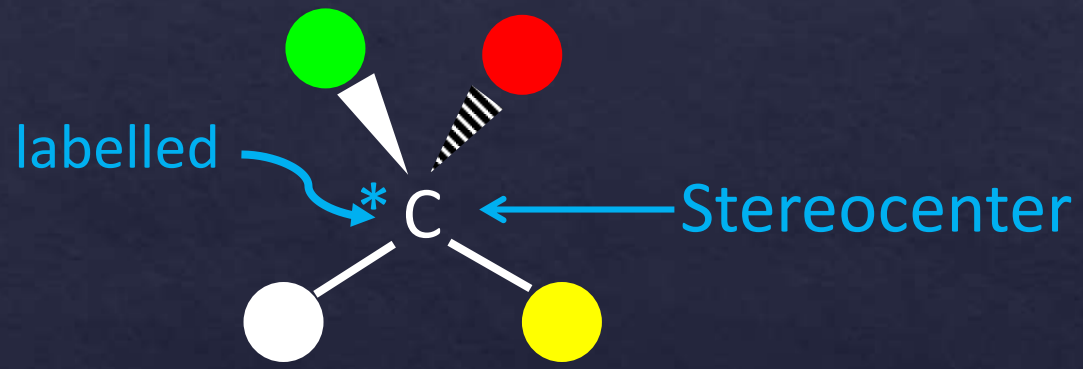
Enantiomers!!



Picture from Vollhardt & Schore

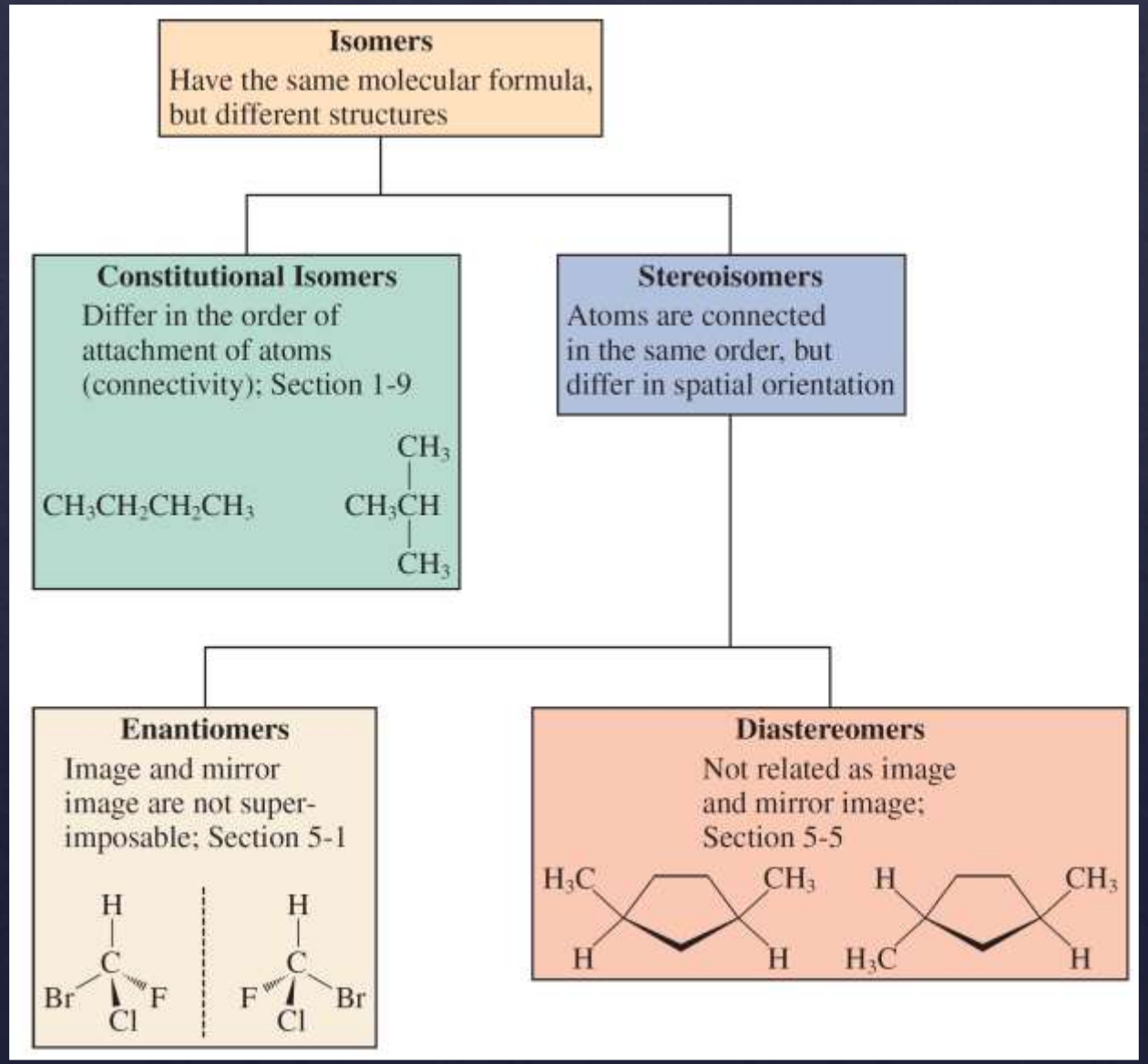
Stereocenters

Most organic molecules owe their chirality to the presence of a stereocenter, usually a carbon with 4 different substituents: an asymmetric carbon.



If image and mirror image of a molecule are superimposable it is achiral. Quick test: presence of a mirror plane. Chiral molecules lack a mirror plane.

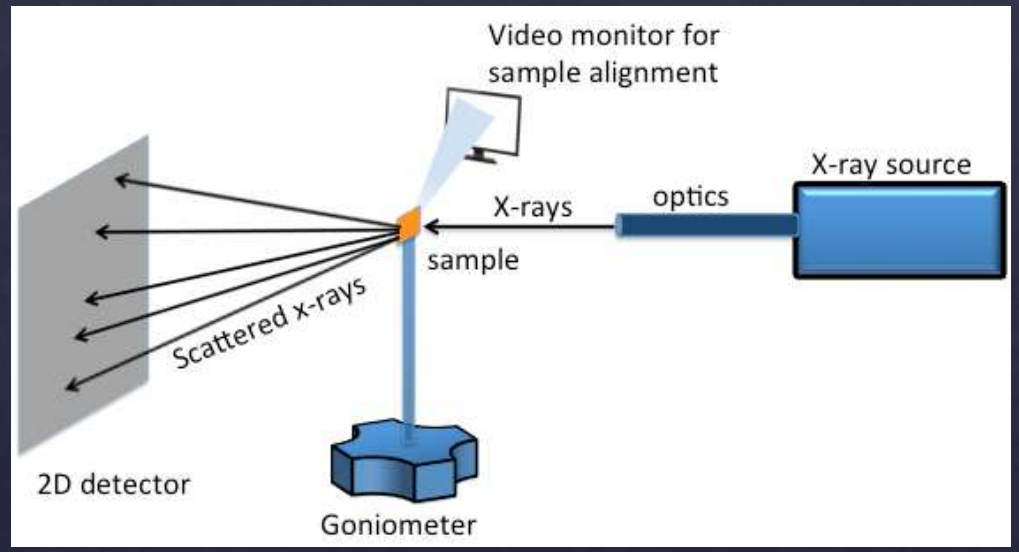
The various kinds of isomers



Picture from Vollhardt & Schore

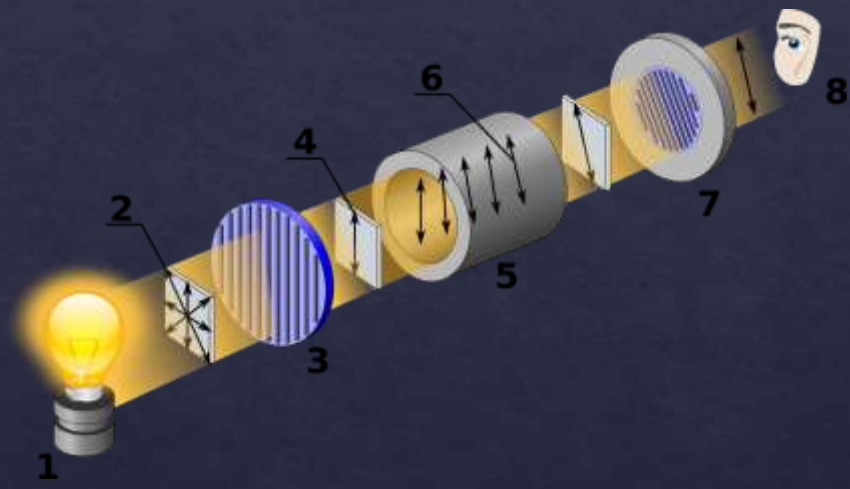
Enantiomers

X-ray crystallography



Picture from libretext

Polarimeter

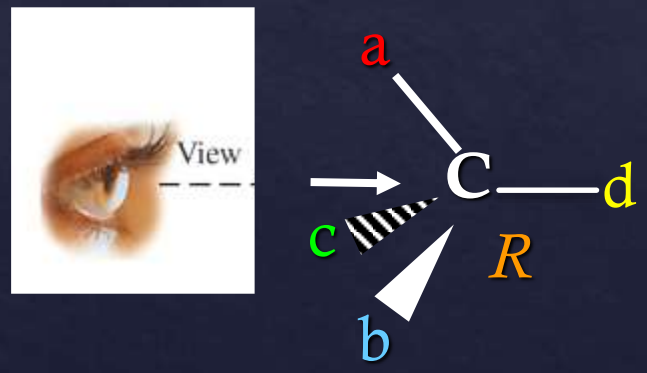


Picture from Vollhardt & Schore

Naming Enantiomers

Cahn-Ingold-Prelog *R,S*-Nomenclature

Label all substituents at stereocenter, starting at point of attachment, according to the sequence rules in order of decreasing priority: a, b, c, d (note color scheme). Face the molecule, looking down C-d bond:

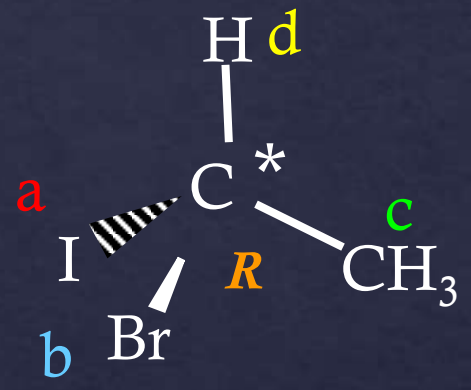


a, b, c clockwise: *R*

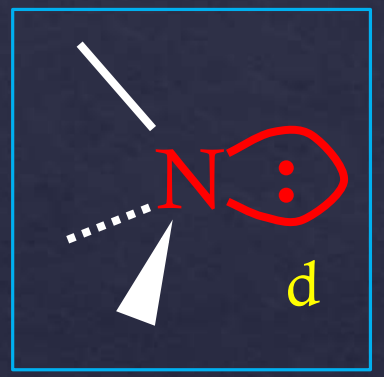
a, b, c counterclockwise: *S*

The Sequence Rules

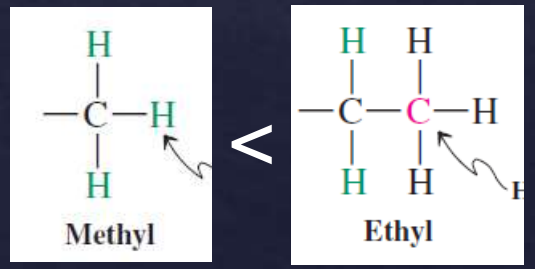
1. Order by atomic number, i.e. H = 1, lowest.

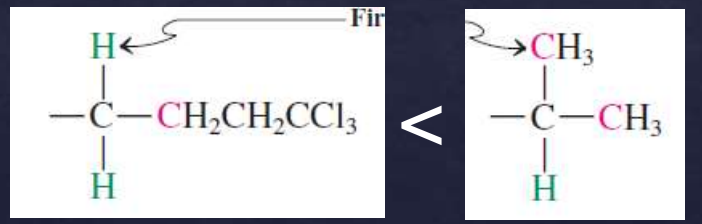


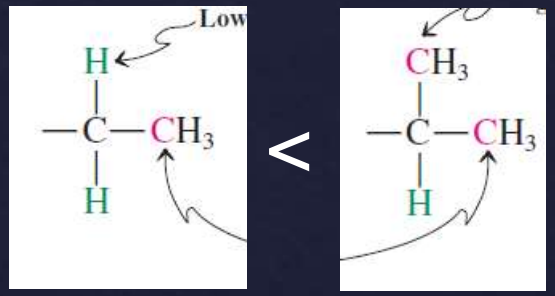
Exception: lone pair,
"zero". E.g., amines:



2. If same priority at first atom: Go to first point of difference.

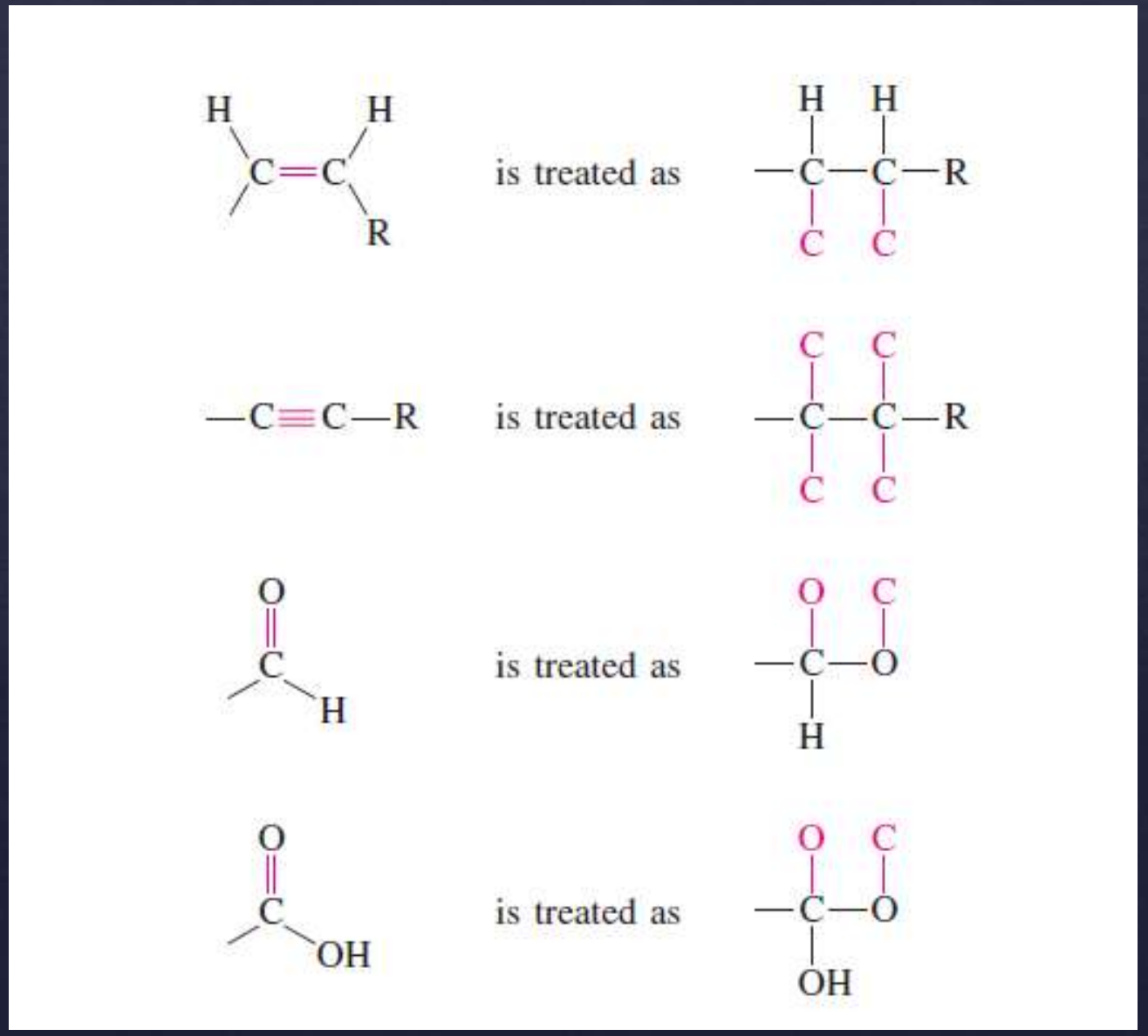






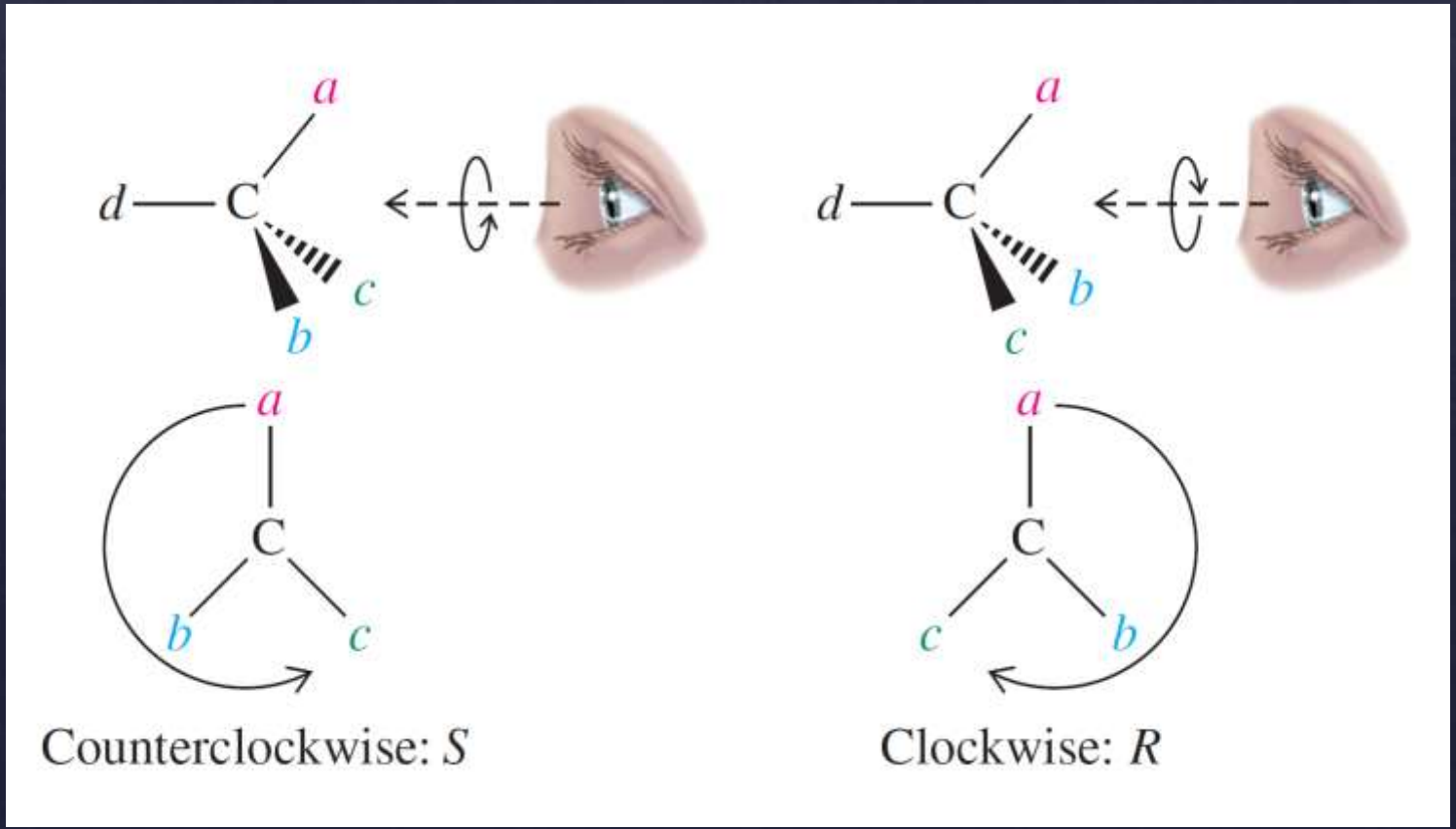
Pictures from Vollhardt & Schore

3. Multiple bonds: Add double or triple representations of atoms at the respective other end of the multiple bond.



Picture from Vollhardt & Schore

How do we name them now?



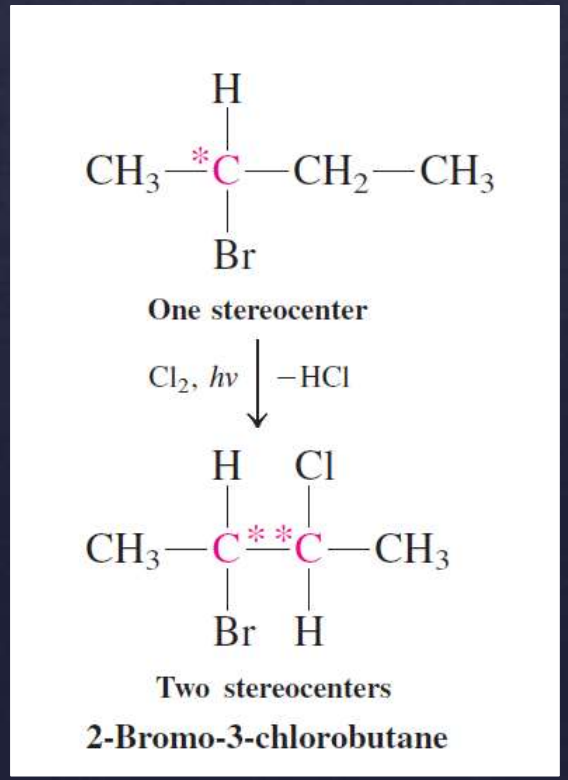
Picture from Vollhardt & Schore

Enough?

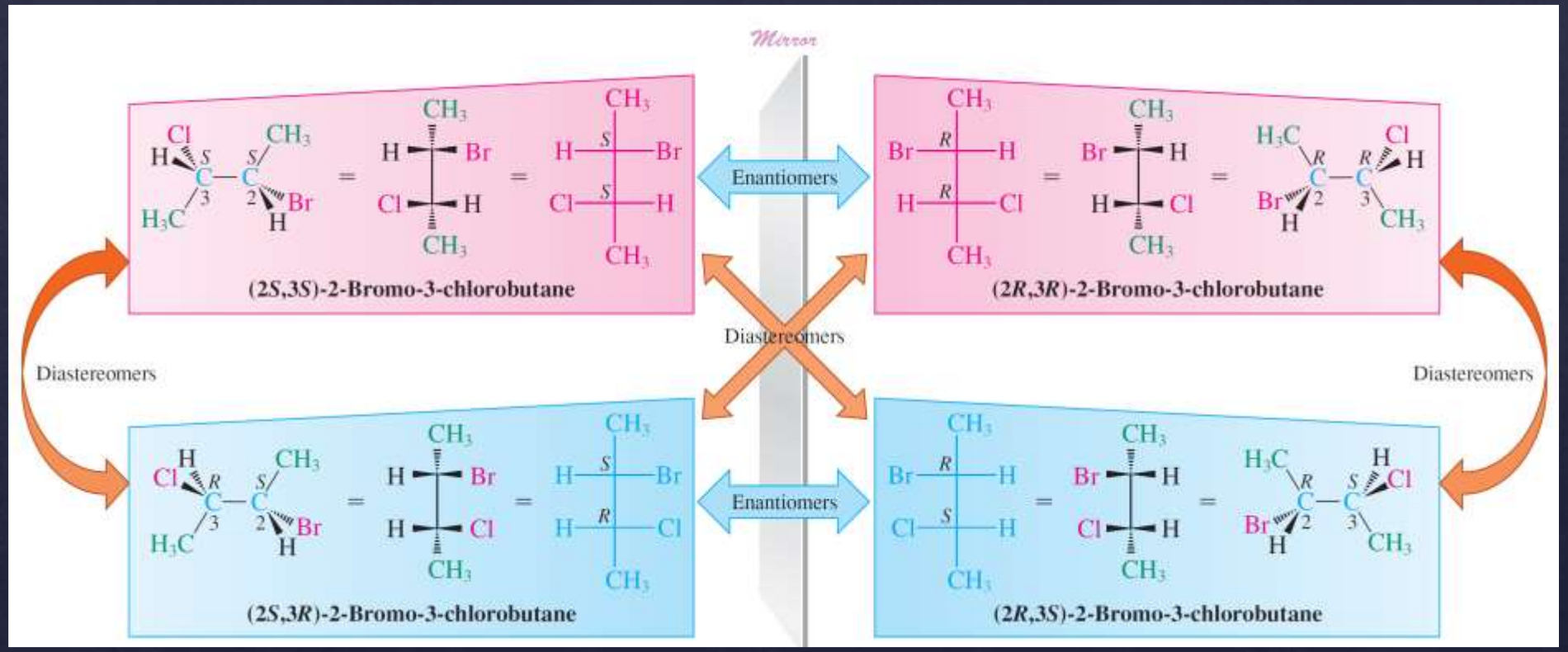
Diastereoisomers

Diastereomers are stereoisomers that are not related as image & mirror-image and they have 2 stereocenters

This creates 2 enantiomers pairs
RR | SS and RS | SR
For a total of 4 diastereoisomers



Picture from Vollhardt & Schore



Picture from Vollhardt & Schore

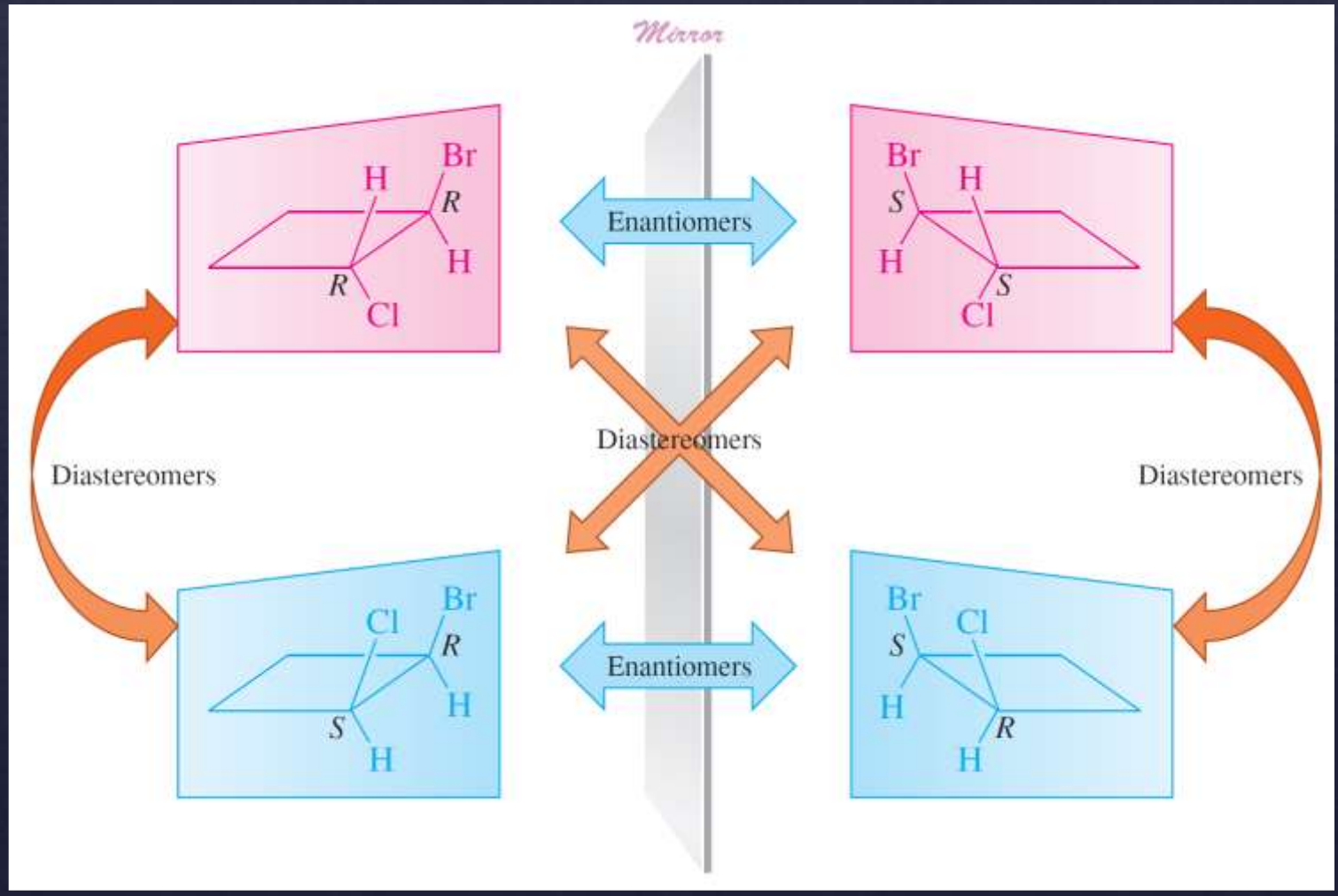
Diastereoisomers

Since they are not related as image & mirror-image, they have different:

- physical and chemical properties
- steric interactions and energies
- melting and boiling points
- densities
- specific rotations

They can be separated by fractional distillation, crystallization, or chromatography.

Cyclic Cis And Trans Isomers Are Diastereomers!



R,R (and *S,S*) = trans

R,S (and *S,R*) = cis

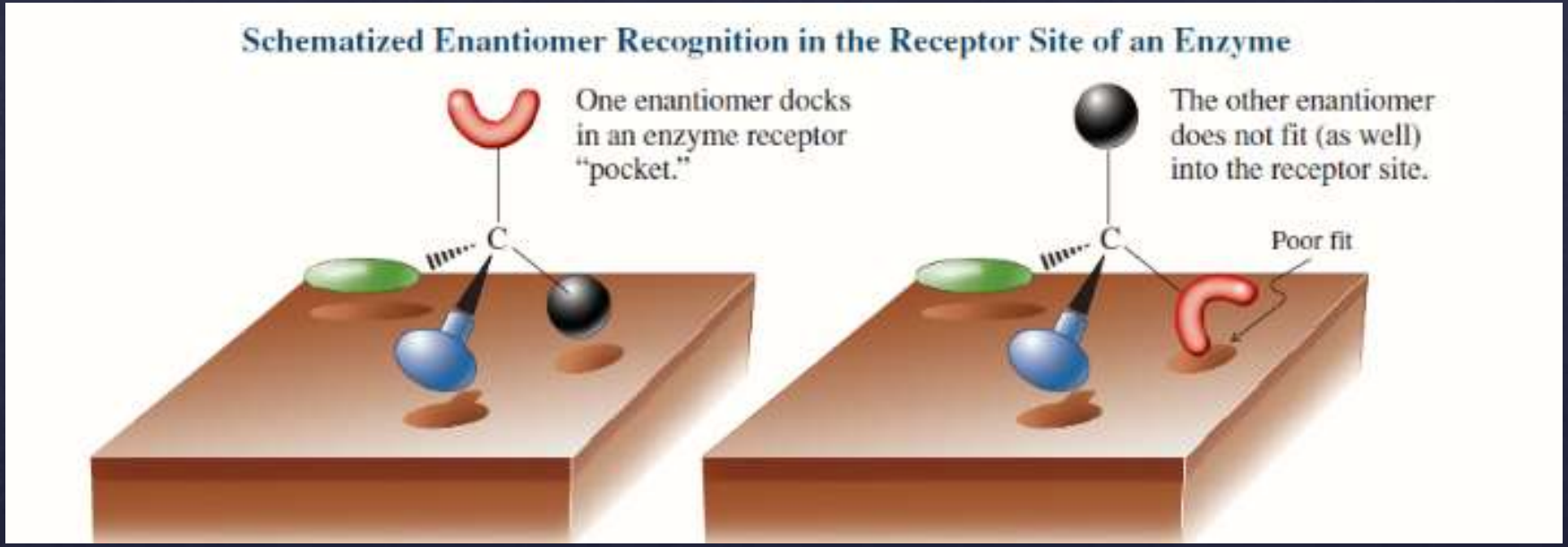
Picture from Vollhardt & Schore

What about 3 stereocenters?

Generally, a compound with *n* stereocenters can have a maximum of 2^n stereoisomers.

Enantiomer recognition in nature

Receptor sites in enzymes: the “active site”



Picture from Vollhardt & Schore