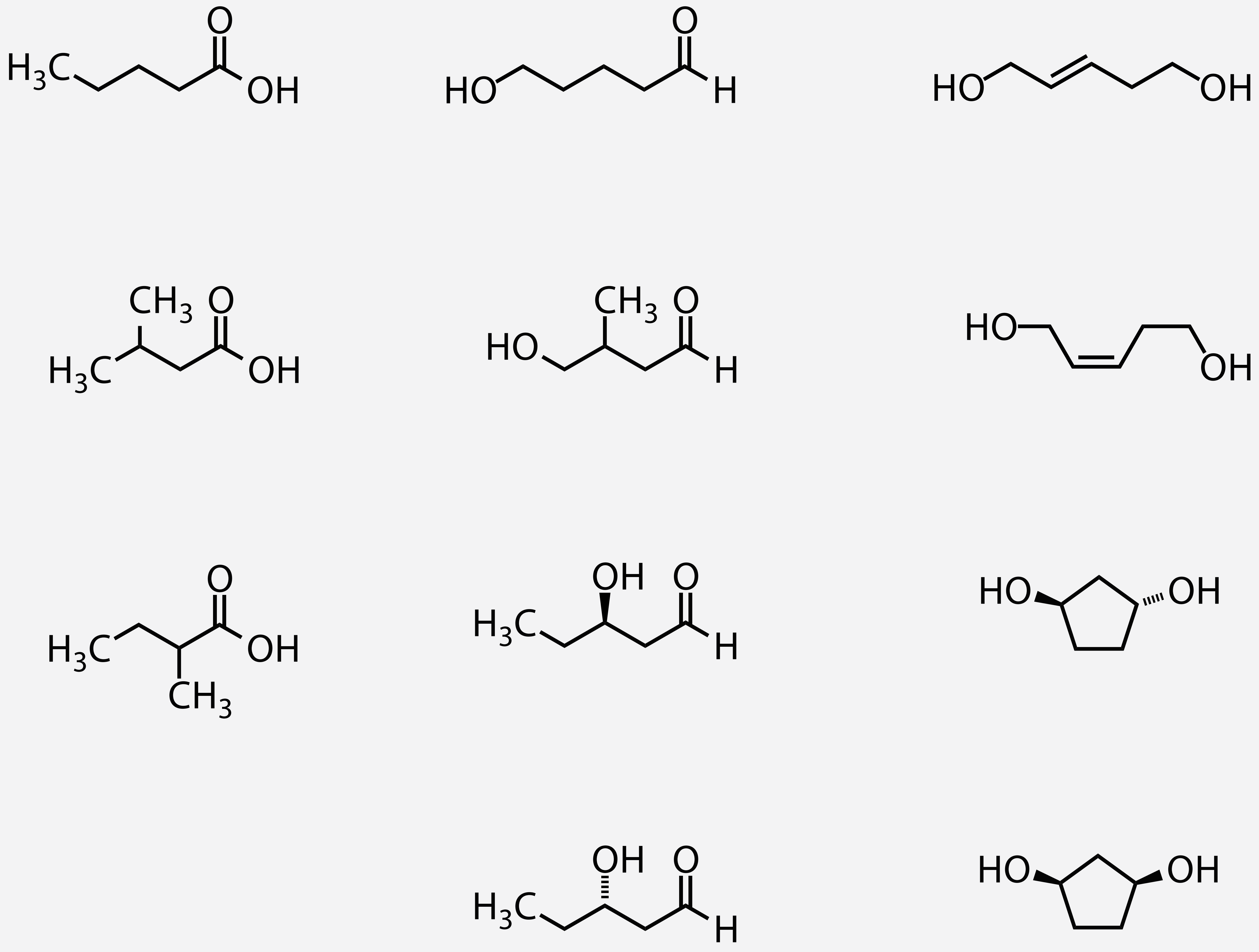
3.2. Isomerism

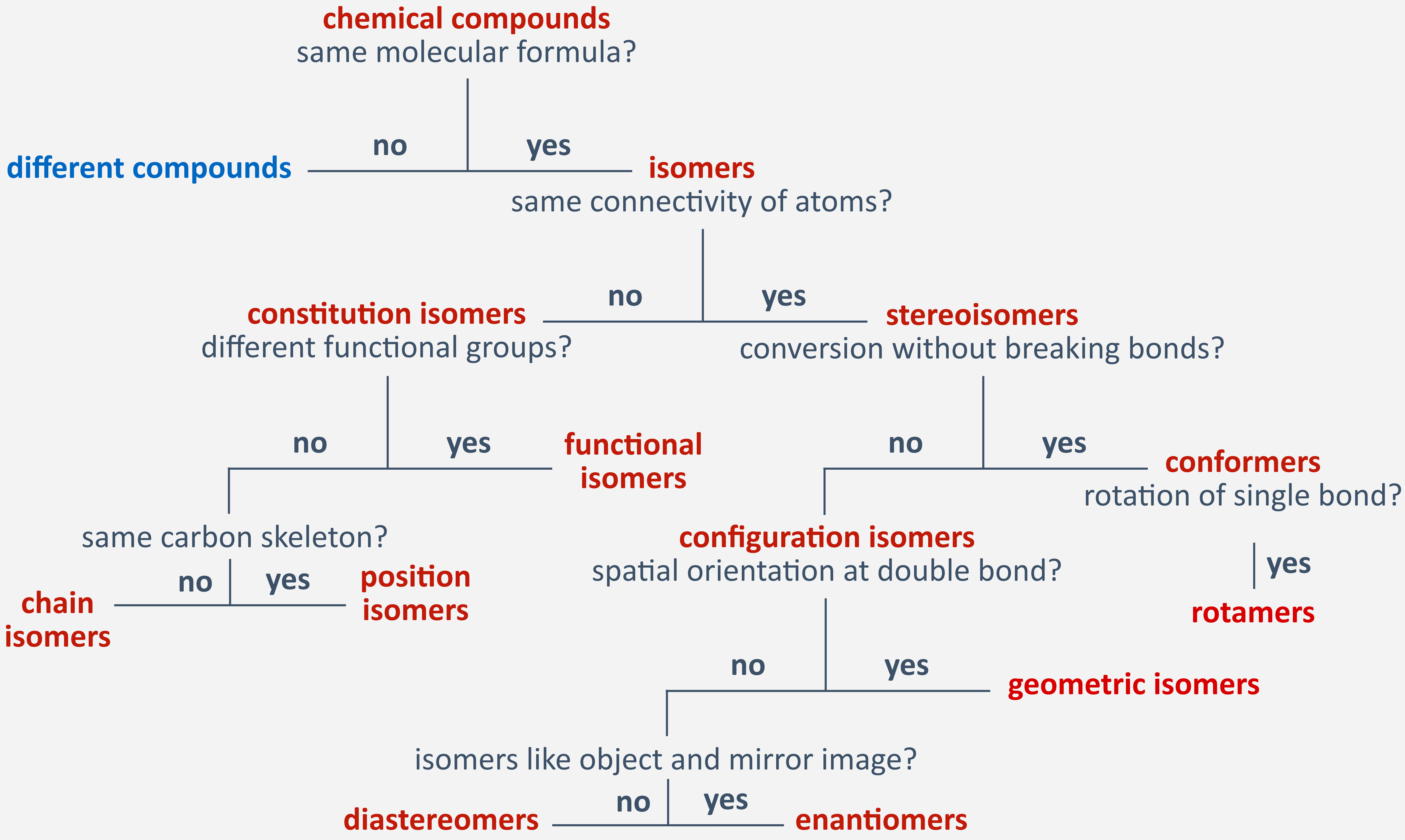
Isomers

- examples of a few isomers, that is, molecules with the molecular formula $C_5H_{10}O_2$



- **isomers have the same molecular formula but different structural formula**

A Decision Tree to Assign Types of Isomers

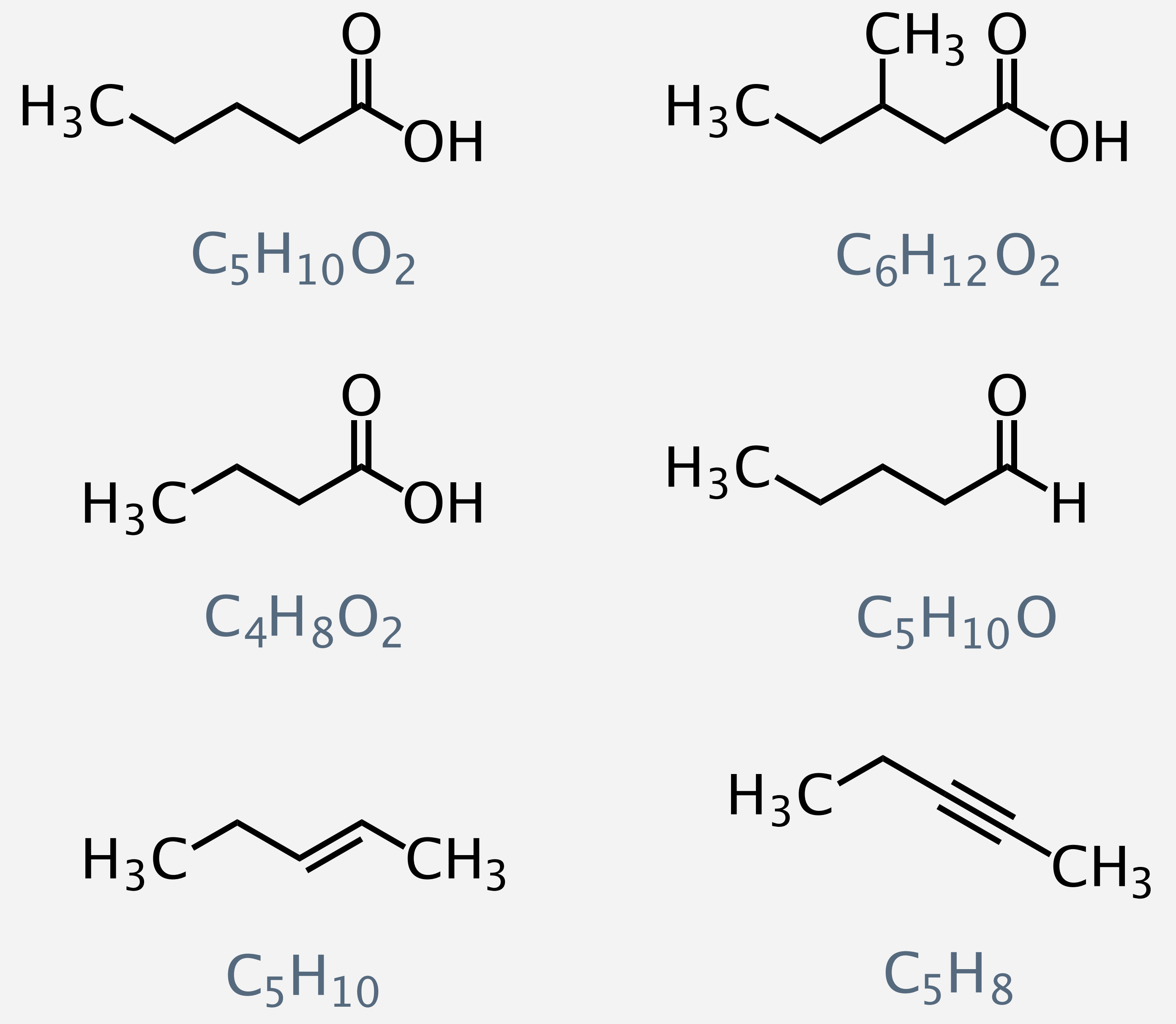


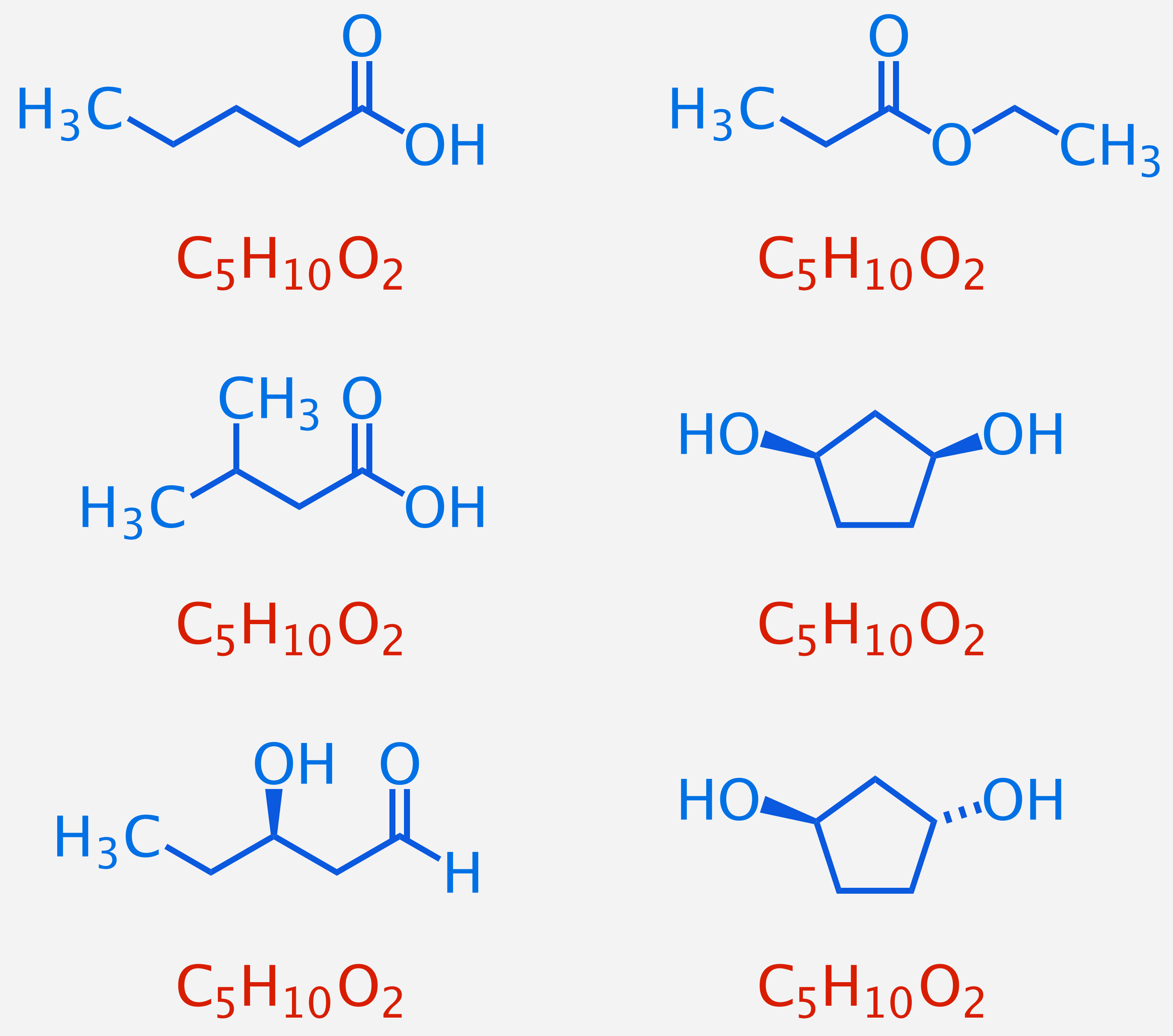
Different Compounds versus Isomers

chemical compounds
same molecular formula?

no → **different compounds**

yes → **isomers**





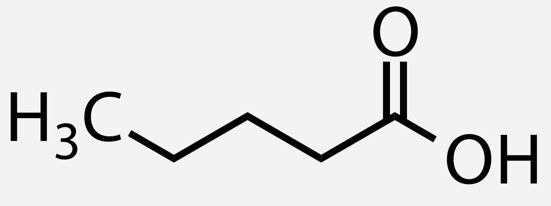
- **all types of isomers have the same molecular formula but different structural formula**

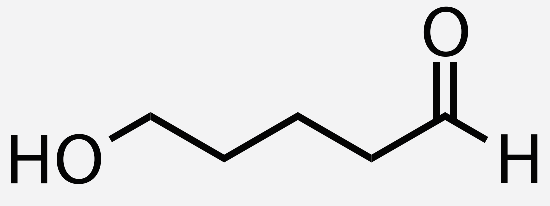
Constitution Isomers versus Stereoisomers

isomers
same connectivity of atoms?

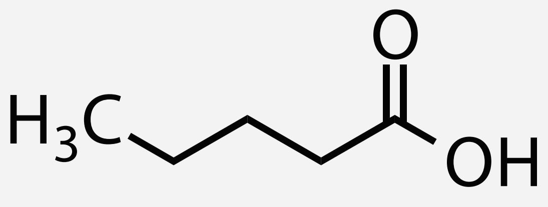
constitution isomers — **no** — **yes** — **stereoisomers**

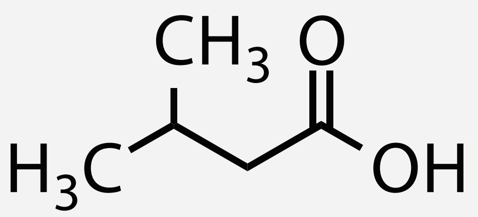
functional isomers


acid

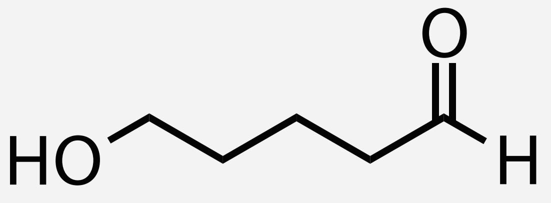

alcohol aldehyde

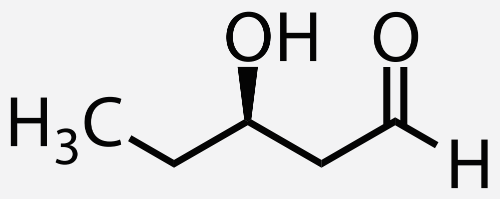
chain isomers


pentanoic acid

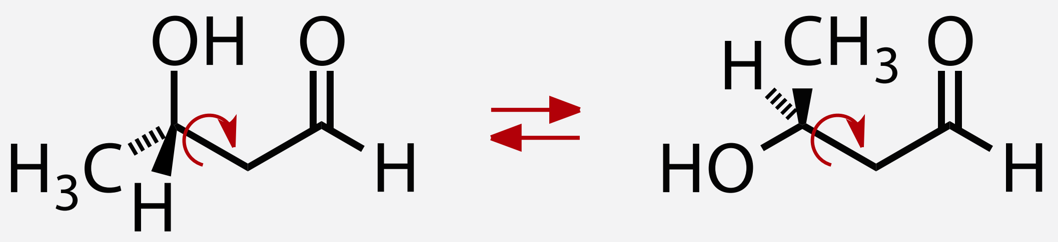

methylbutanoic acid

position isomers

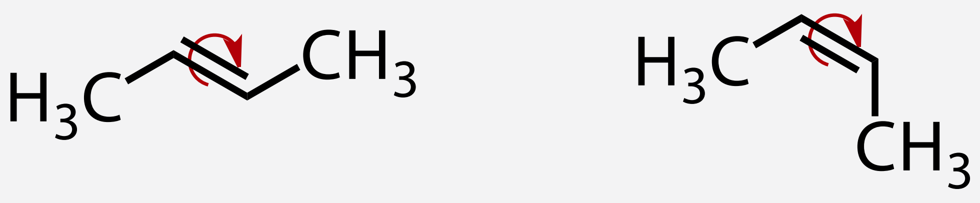

5-hydroxypentanal


3-hydroxypentanal

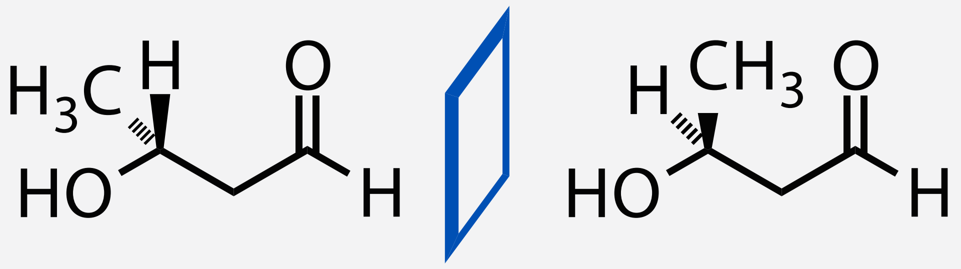
conformers


interconversion without breaking bonds

geometric isomers


interconversion by rotation at double bond

diastereomers or enantiomers


no interconversion by bond rotation

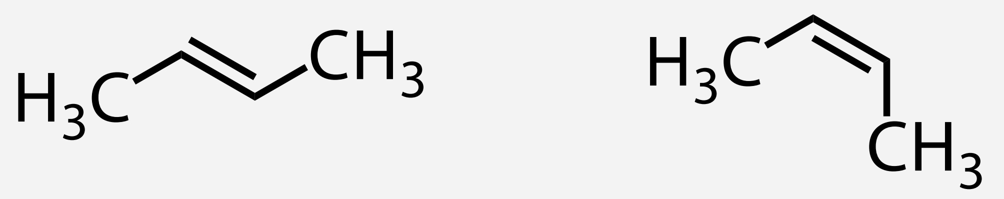
- **constitution refers to the connectivity of atoms, stereoisomers have the same constitution**

Configuration Isomers versus Conformers

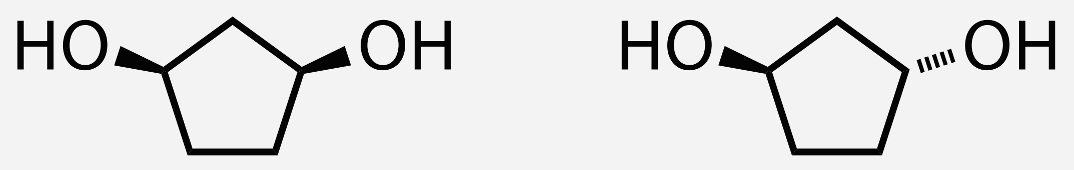
stereoisomers
interconversion without breaking bonds?

configuration isomers	no	yes	**conformers**

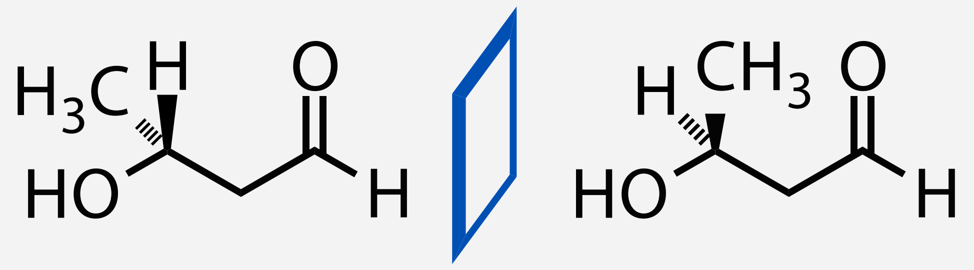
geometric isomers



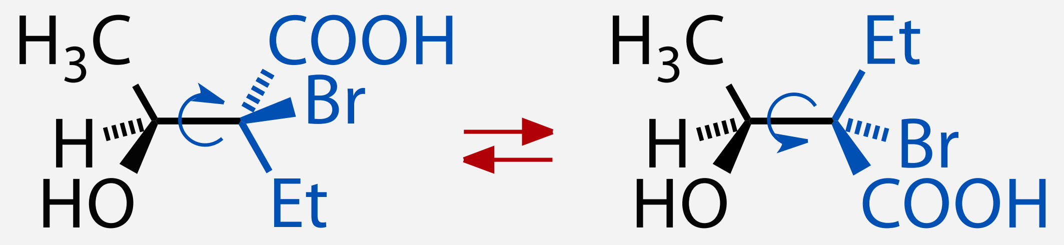
diastereomers



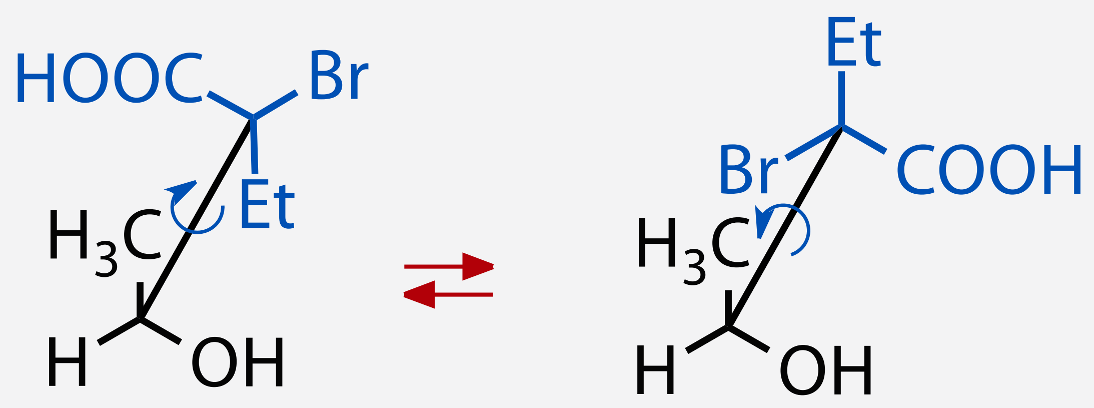
enantiomers



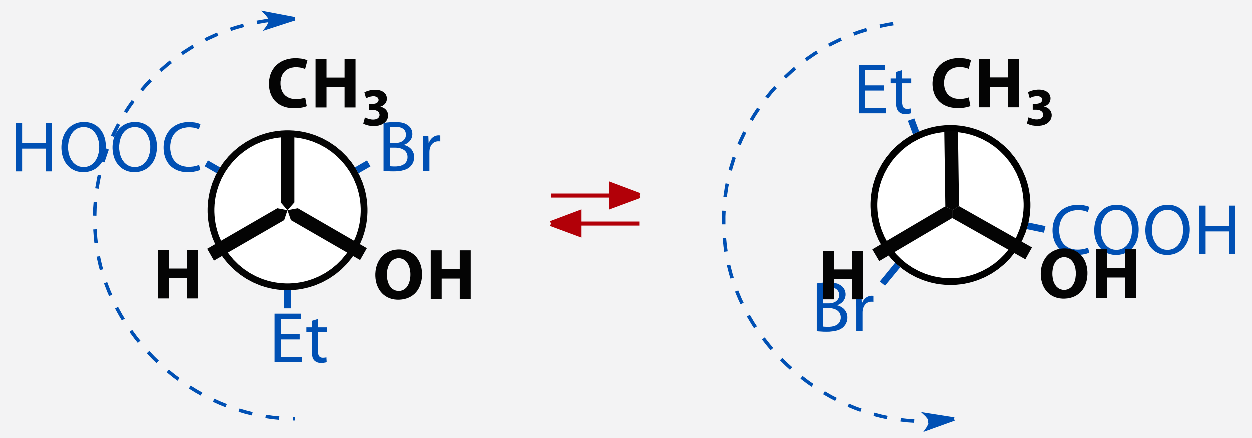
Natta projection



Sawhorse projection

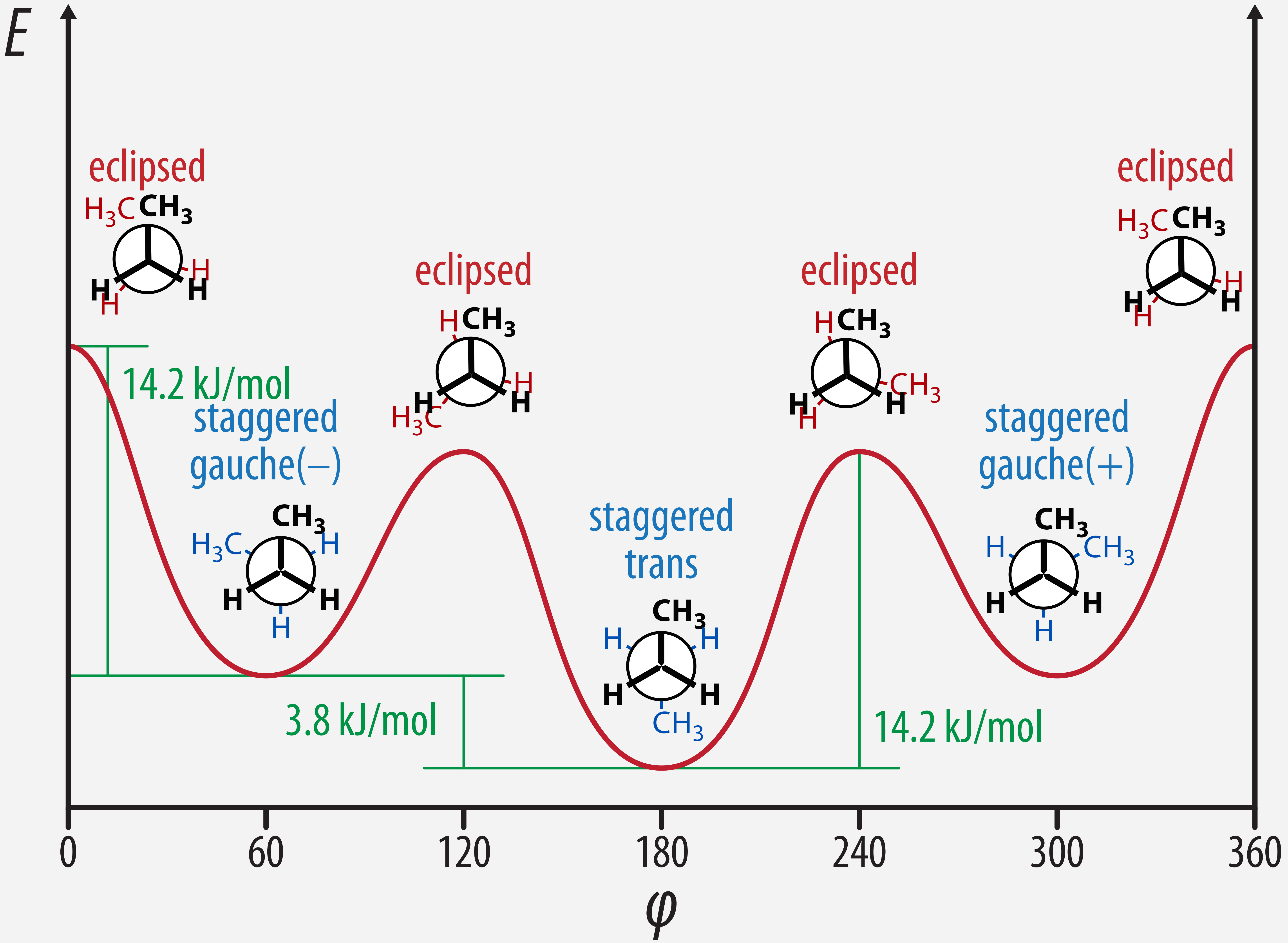


Newman projection



- **configuration** refers to **fixed shape in space**, **conformers have the the same configuration**

Conformations of Alkanes



- **fast rotation around single bonds at room temperature, conformers are identical compounds**

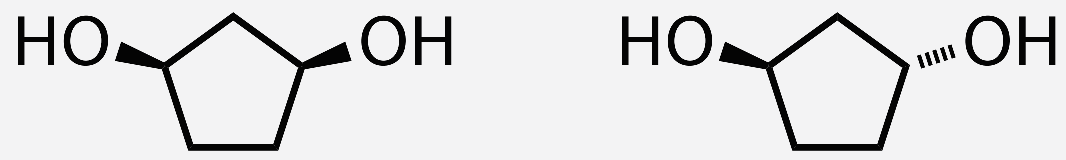
Stereoisomers versus Diastereomers and Enantiomers

configuration isomers
difference in spatial orientation at double bond?

no → **diastereomers** or **enantiomers**

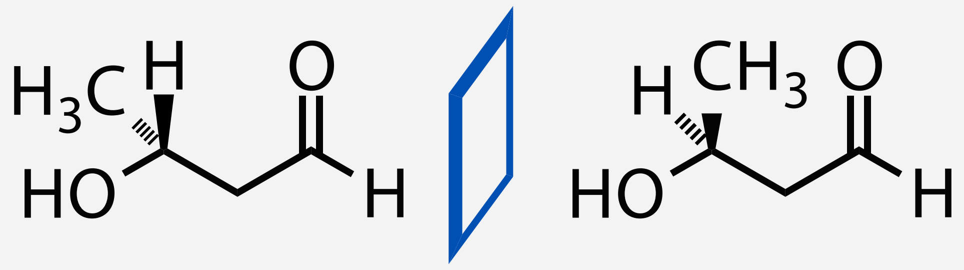
yes → **geometric isomers**

diastereomers

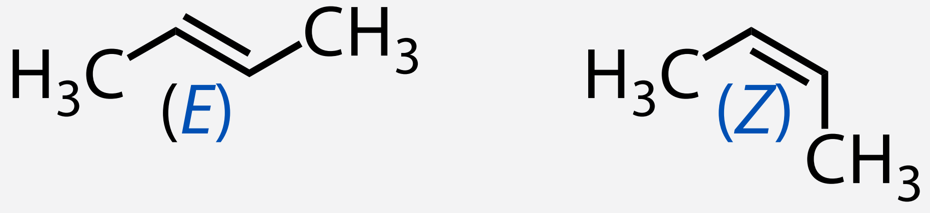


no mirror images

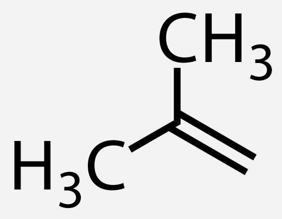
enantiomers



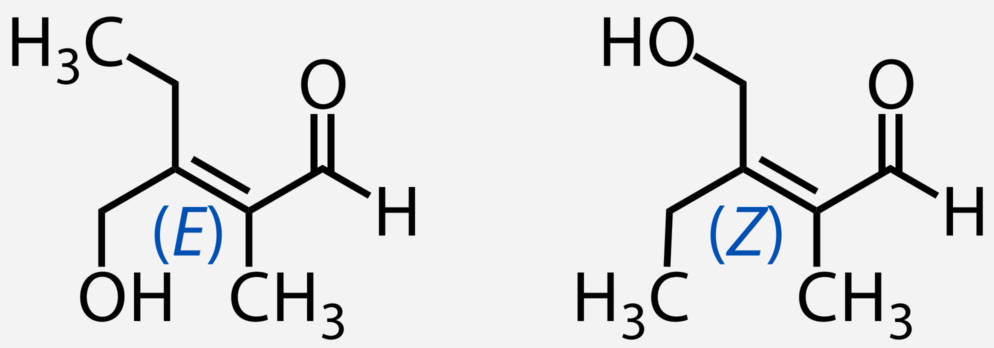
mirror images



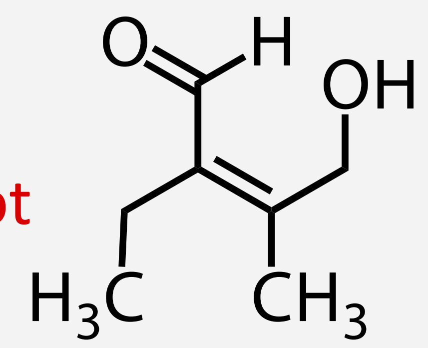
but not



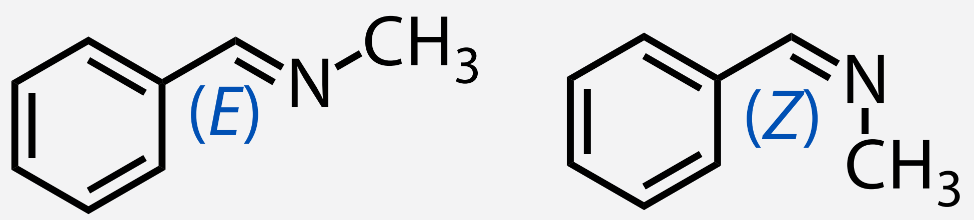
constitution!



but not



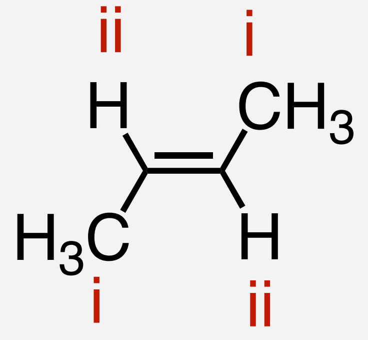
constitution!



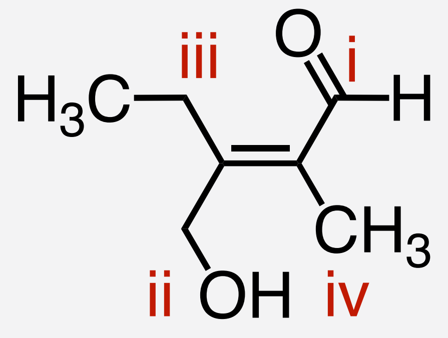
- geometric isomers exist due to lack of rotation around double bond (at room temperature)

Cahn-Ingold-Prelog Nomenclature of Geometric Isomers

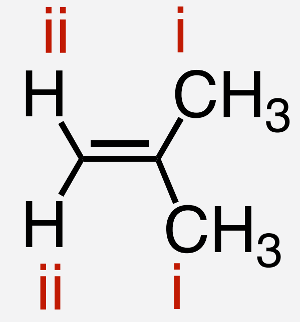
- an additional label is necessary to distinguish geometric isomers



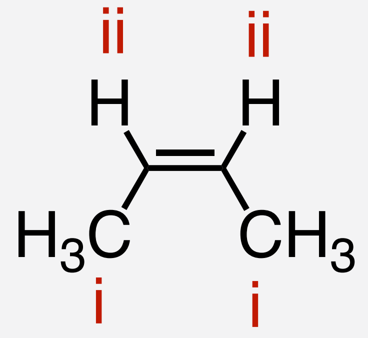
but-2*E*-ene



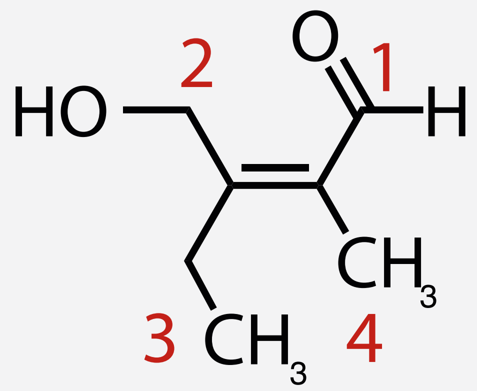
3-ethyl-4-hydroxy-2-methylbut-2*E*-enal



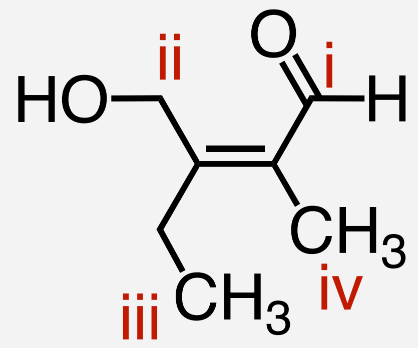
2-methylprop-1-ene
(no isomers)



but-2*Z*-ene



3-ethyl-4-hydroxy-2-methylbut-2*Z*-enal

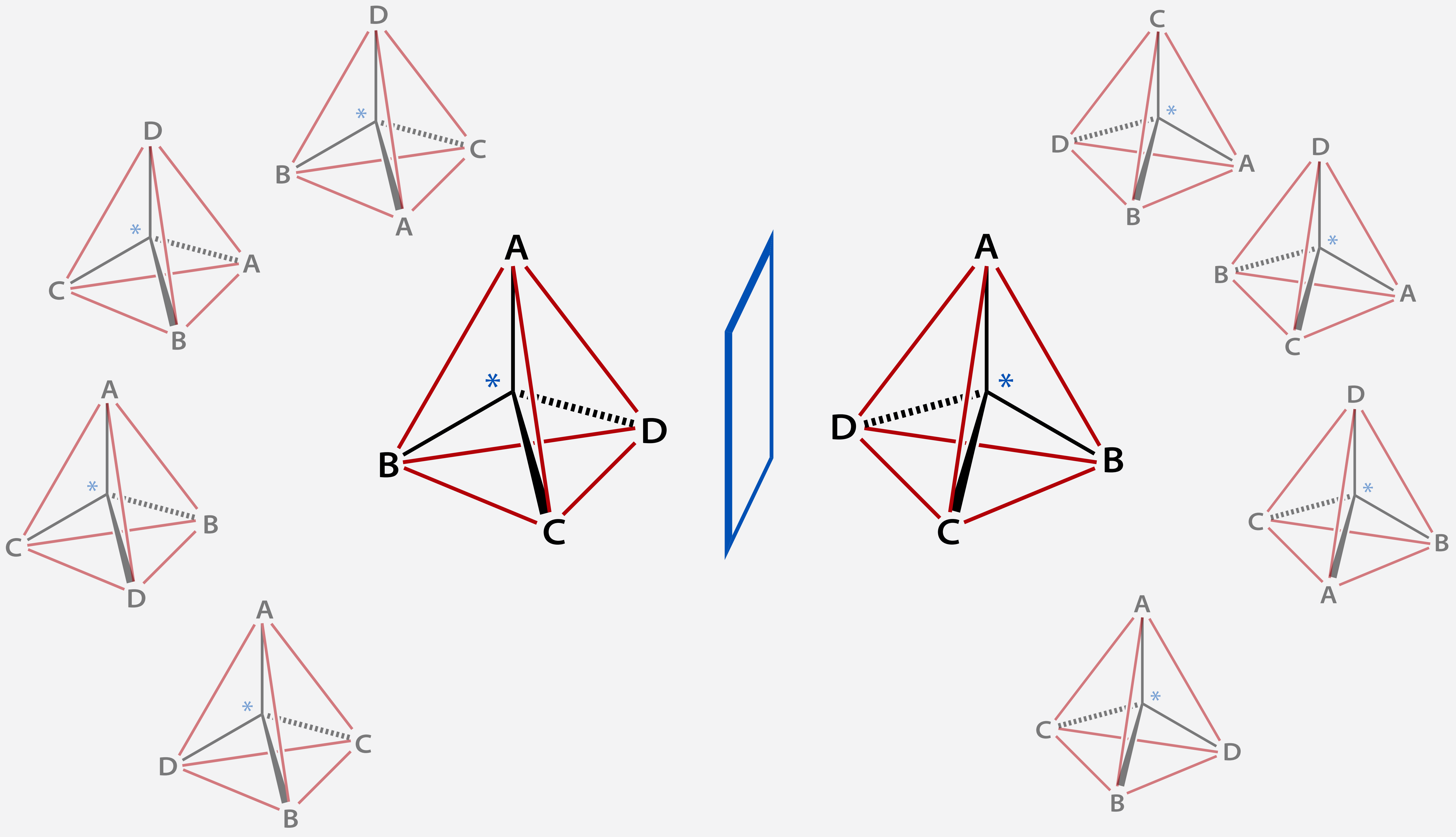


3-methylbut-2-en-1-ol
(no isomers)

- **IUPAC nomenclature, following the "Cahn-Ingold-Prelog" rules**
  - assign priorities to substituents according to increasing atomic weight of connecting atom
  - if the first connecting atom is the same, proceed to next connected atoms (highest wins)
  - (Z) if the two higher priority substituents on each carbon are on same side of double bond
  - (E) if the two higher priority substituents on each carbon are on opposite sides
  - labels used as prefix or added to the number prefixes in the compound names

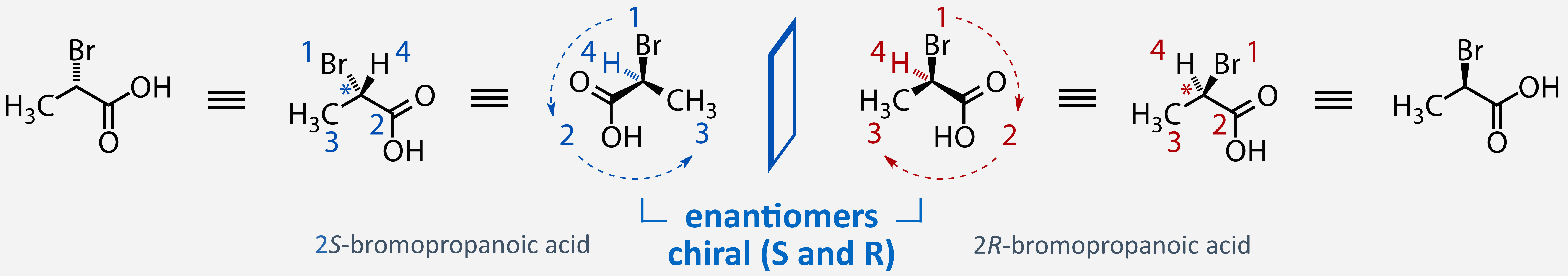
Stereocenters and Chirality

- **tetrahedral carbon atoms with four different residues are called “stereocenters”**



- **the presence of stereocenters implies the *possibility* to observe chirality (“handedness”)**
    - definition: chirality requires absence of intramolecular mirror plane / inversion center
    - chiral molecules exist as two “enantiomers”, i. e., non-superimposable mirror images
    - molecules with a single stereocenter **must** be chiral
    - molecules with more than one stereocenter **can** be chiral (see next slide)

Nomenclature of Stereocenters

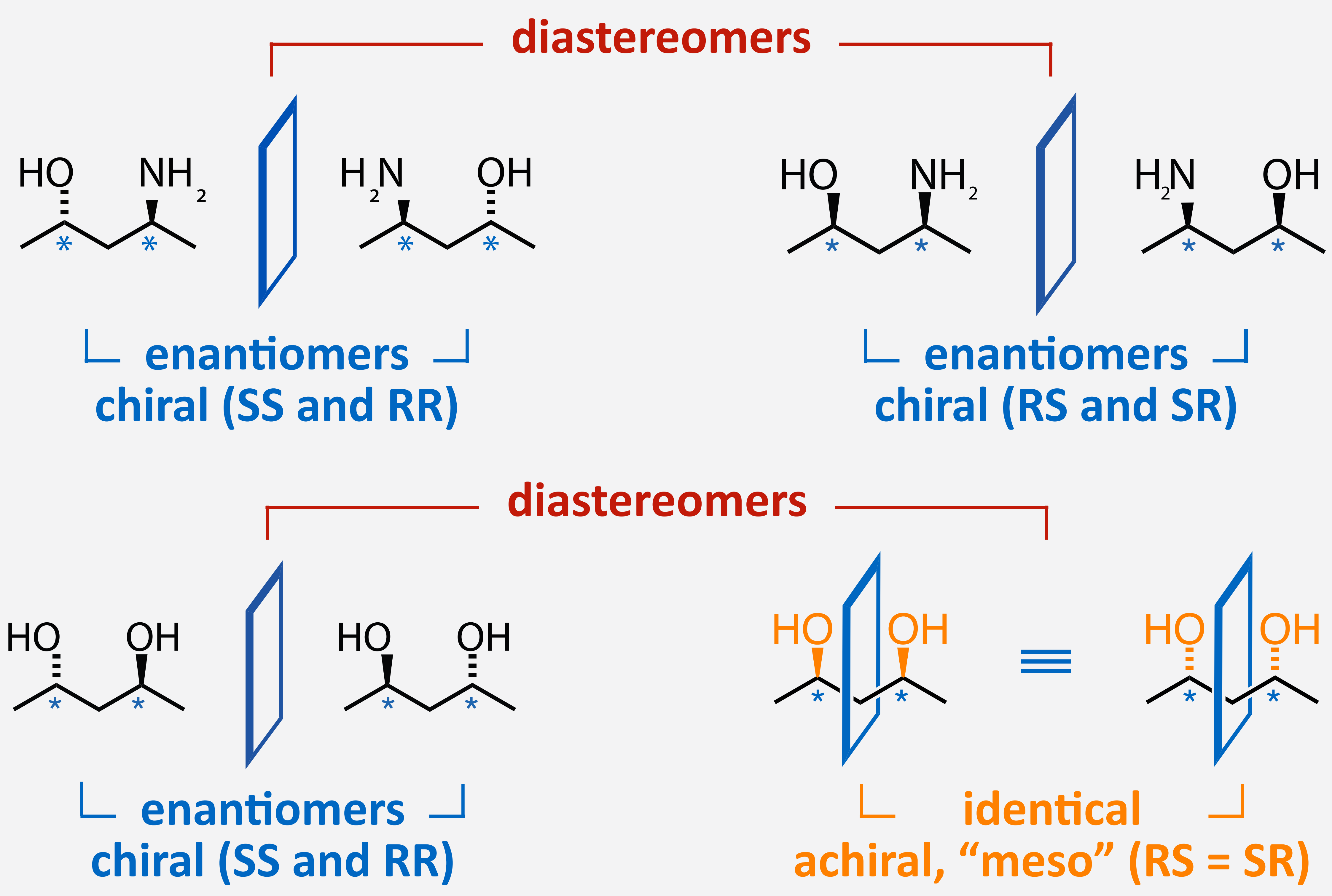


2*S*-bromopropanoic acid

2*R*-bromopropanoic acid

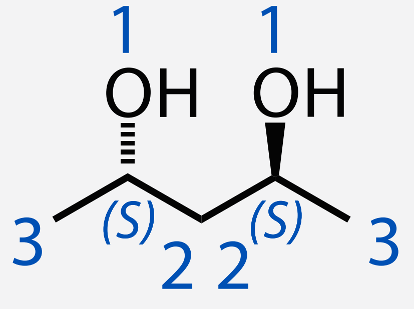
- **IUPAC nomenclature, following the "Cahn-Ingold-Prelog" rules**
  - assign priorities to substituents according to increasing atomic weight of connecting atom
  - if the first connecting atom is the same, proceed to the next connected atoms (highest priority wins)
  - turn the molecule such that the lowest priority substituent is pointing away from you
  - if substituents 1→ 2→ 3 are arranged clockwise, the configuration is *R* (for rectus/right)
  - if substituents 1→ 2→ 3 are arranged counter-clockwise, the configuration is *S* (for sinister/left)
- **stereochemical notation is used as prefix or added to the number prefixes**

Molecules with Multiple Stereocenters

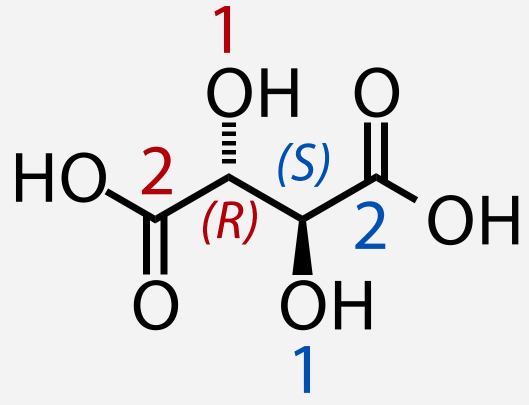


- **molecules with multiple stereocenters can be chiral or achiral, depending on symmetry**
  - chirality requires absence of an intramolecular mirror plane or inversion center
  - chiral molecules with *n* stereocenters exist as 2^{n-1} pairs of enantiomers (2^n stereoisomers)
  - stereoisomers with multiple stereocenters that are not enantiomers are diastereomers
  - molecules with multiple stereocenters but internal mirror plane are achiral

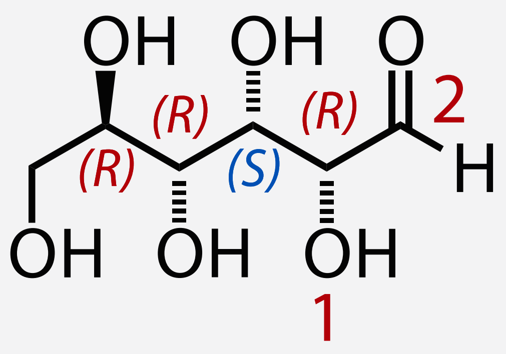
Examples of Molecules with Single and Multiple Stereocenters



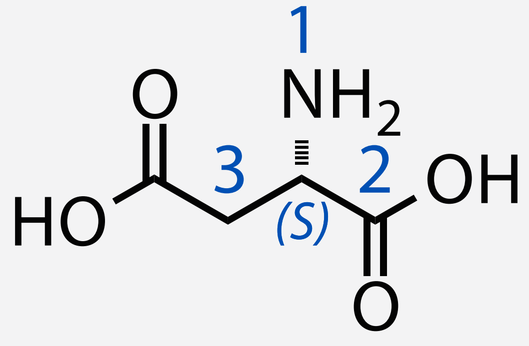
2*S*,4*S*-pentandiol



2*S*,3*R*-dihydroxypentandioic acid
D,L-tartric acid



2*R*,3*S*,4*R*,5*R*,6-pentahydroxyhexanal
D-glucose



2*S*-aminobutandioic acid
L-glutamic acid

Learning Outcomes

- differentiate different compounds, isomers, and identical compounds
- assign the type of isomer relationship between two molecules
- understand stereochemical notation in structure formulae
- name different conformers (using different stereochemical projections)
- assign stereochemistry of geometric isomers (E/Z, Cahn-Ingold-Prelog)
- find stereocenters and identify chirality
- differentiate enantiomers / diasteromers
- assign stereoconfiguration (R/S, Cahn-Ingold-Prelog)