A Reminder…

isomers

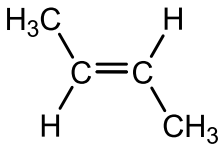
Same molecular formula, but not identical.

constitutional isomers

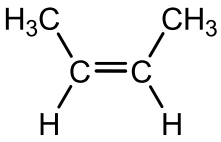
Different in the way their atoms are connected.

stereoisomers

Same connectivity, but different spatial arrangement.



and



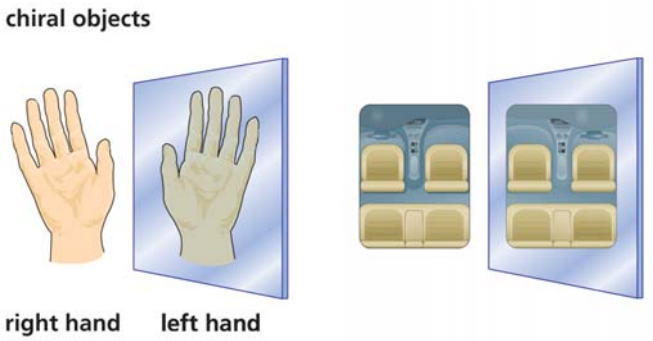
trans-2-butene

cis-2-butene

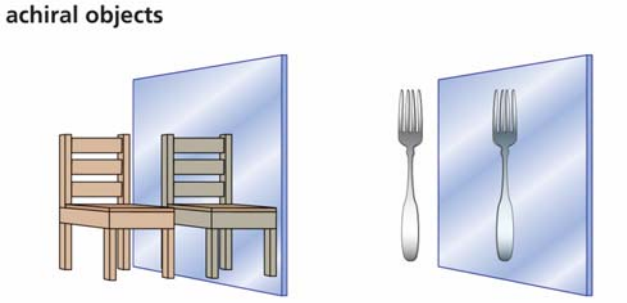
*are **stereoisomers**.*

Chirality: A Type of Stereoisomerism

Any object that *cannot* be superimposed on its mirror image is **chiral**.



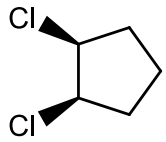
Any object that *can* be superimposed on its mirror image is **achiral**.



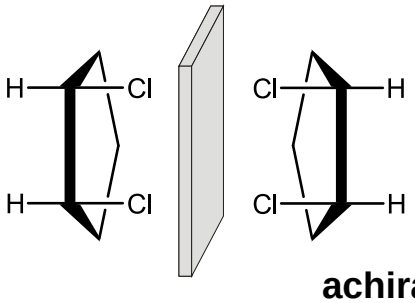
Chirality: A Type of Stereoisomerism

Molecules can also be **chiral** or **achiral**.
How do we know which?

Example #1:
Is this molecule chiral?



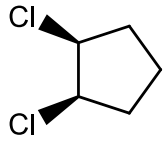
1. If a molecule can be superimposed on its mirror image, it is **achiral**.



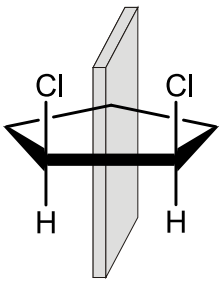
achiral.

Mirror Plane of Symmetry = Achiral

Example #1:
Is this molecule chiral?

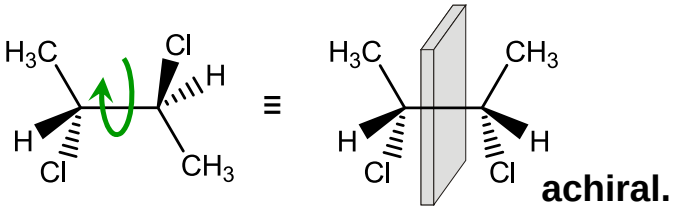


2. If you can find a mirror plane of symmetry in the molecule, in any conformation, it is **achiral**.



achiral.

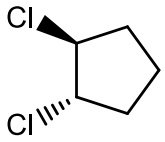
Can subject unstable conformations to this test.



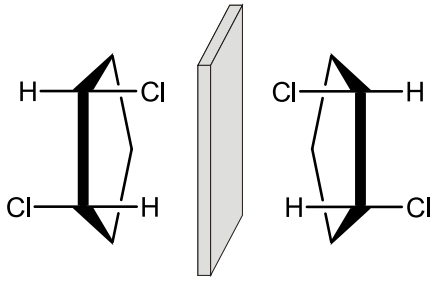
achiral.

Finding Chirality in Molecules

Example #2:
Is this molecule chiral?



1. If a molecule *cannot* be superimposed on its mirror image, it is **chiral**.

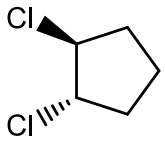


chiral.

The mirror image of a chiral molecule is called its **enantiomer**.

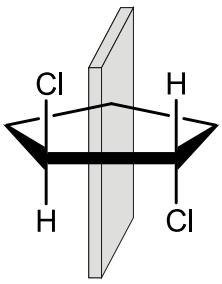
Finding Chirality in Molecules

Example #2:
Is this molecule chiral?



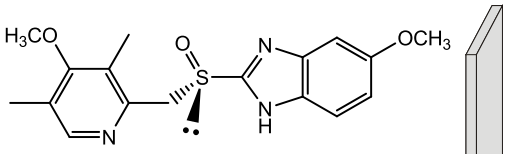
2. If you *cannot* find a mirror plane of symmetry in the molecule, in any conformation, it is **chiral**.

(Or maybe you haven't looked hard enough.)

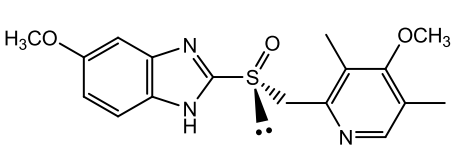


chiral.

Pharmacology of Enantiomers



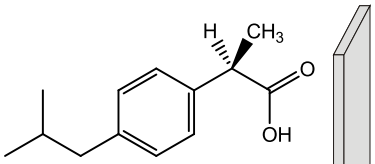
(+)-esomeprazole
proton pump inhibitor



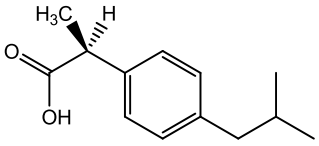
(-)-esomeprazole
inactive

Prilosec: Mixture of both enantiomers. Patent to AstraZeneca expired 2002.
Nexium: (+) enantiomer only. Process patent coverage to 2007.

More examples at http://z.umn.edu/2301drugs.

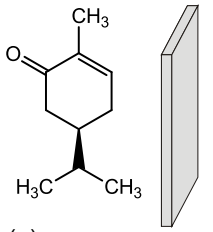


(+)-ibuprofen
analgesic

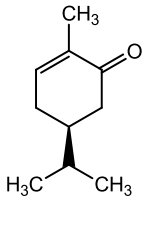


(-)-ibuprofen
inactive (but is converted to + enantiomer by an enzyme)

Advil (Wyeth) is a mixture of both enantiomers.



(+)-carvone
spearmint oil

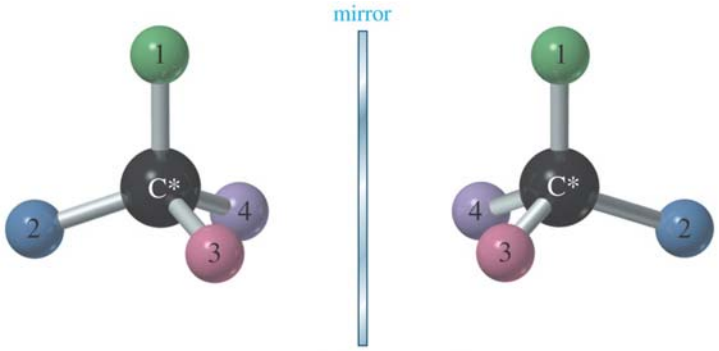


(-)-carvone
caraway oil

Each enantiomer is recognized by its own smell receptor.

Chirality Is Often Due to Chiral Centers

Chiral center: A tetrahedral atom with four different groups attached.

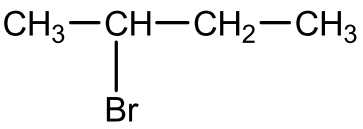


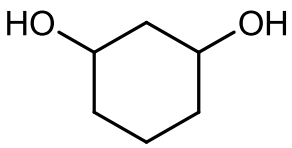
Cannot be superimposed on their mirror images. **Chiral.**

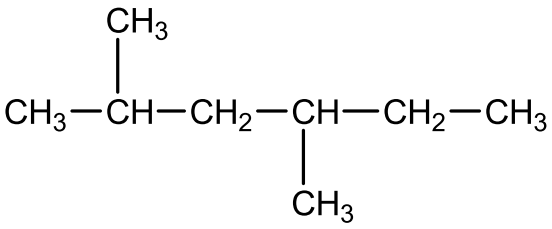
Stereocenter: Atom for which exchange of two groups leads to a stereoisomer. Includes alkene carbons.

Identifying Chiral Centers

Where are the chiral centers in the following molecules?

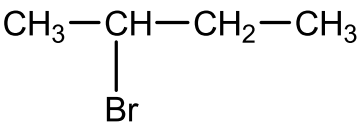


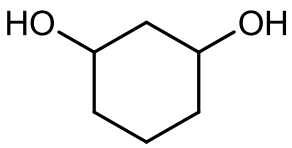




Chirality Is Often Due to Chiral Centers

- If a molecule contains **no** chiral centers, it is almost always *achiral* (with very few exceptions).
- If a molecule has **one** chiral center, or an **odd number** of chiral centers, it is *always chiral*.
- If a molecule has **two** chiral centers, or an **even number** of chiral centers, it may or may not be chiral.





Chiral or achiral?
If chiral, what do enantiomers look like?

Cahn-Ingold-Prelog Notation: (*R*) vs. (*S*) Configuration of Chiral Centers

1. Assign priority numbers (1 through 4) to each group attached to the chiral center, based on atomic number.

   In case of a tie, look at next atoms along the chain.

   - If one has a higher atomic number than others, it gets priority.
   - Then, if one has more copies of an atom, it gets priority. Multiple bonds count as multiple copies of the same atom.

2. Rotate the molecule so that the lowest-priority (#4) group is pointed to the back.

3. If groups 1 → 2 → 3 are organized clockwise, then configuration is (*R*); if groups 1 → 2 → 3 are organized counterclockwise, then configuration is (*S*).