To name the enantiomers of a compound unambiguously, their names must include the "handedness" of the molecule. The method for this is formally known as R/S nomenclature.

**Introduction**

The method of unambiguously assigning the handedness of molecules was originated by three chemists: R.S. Cahn, C. Ingold, and V. Prelog and, as such, is also often called the Cahn-Ingold-Prelog rules. In addition to the Cahn-Ingold system, there are two ways of experimentally determining the absolute configuration of an enantiomer:

1. **X-ray diffraction** analysis. Note that there is no correlation between the sign of rotation and the structure of a particular enantiomer.
2. Chemical correlation with a molecule whose structure has already been determined via X-ray diffraction.

However, for non-laboratory purposes, it is beneficial to focus on the R/S system. The sign of optical rotation, although different for the two enantiomers of a chiral molecule, at the same temperature, cannot be used to establish the absolute configuration of an enantiomer; this is because the sign of optical rotation for a particular enantiomer may change when the temperature changes.

**Stereocenters are labeled R or S**

The "right hand" and "left hand" nomenclature is used to name the enantiomers of a chiral compound. The stereocenters are labeled as R or S.

Consider the first picture: a curved arrow is drawn from the highest priority (1) substituent to the lowest priority (4) substituent. If the arrow points in a counterclockwise direction (left when leaving the 12 o' clock position), the configuration at stereocenter is considered **S** ("Sinister" → Latin= "left"). If, however, the arrow points clockwise (right when leaving the 12 o' clock position) then the stereocenter is labeled **R** ("Rectus" → Latin= "right"). The **R** or **S** is then added as a prefix, in parenthesis, to the name of the enantiomer of interest.

**Example 1**

(R)-2-Bromobutane

(S)-2,3- Dihydroxypropanal
Sequence rules to assign priorities to substituents

Before applying the R and S nomenclature to a stereocenter, the substituents must be prioritized according to the following rules:

**Rule 1**

First, examine at the atoms directly attached to the stereocenter of the compound. A substituent with a higher atomic number takes precedence over a substituent with a lower atomic number. Hydrogen is the lowest possible priority substituent, because it has the lowest atomic number.

1. When dealing with isotopes, the atom with the higher atomic mass receives higher priority.
2. When visualizing the molecule, the lowest priority substituent should always point away from the viewer (a dashed line indicates this). To understand how this works or looks, imagine that a clock and a pole. Attach the pole to the back of the clock, so that when looking at the face of the clock the pole points away from the viewer in the same way the lowest priority substituent should point away.
3. Then, draw an arrow from the highest priority atom to the 2nd highest priority atom to the 3rd highest priority atom. Because the 4th highest priority atom is placed in the back, the arrow should appear like it is going across the face of a clock. If it is going clockwise, then it is an R-enantiomer; If it is going counterclockwise, it is an S-enantiomer.

When looking at a problem with wedges and dashes, if the lowest priority atom is not on the dashed line pointing away, the molecule must be rotated.

Remember that

- Wedges indicate coming towards the viewer.
- Dashes indicate pointing away from the viewer.

**Rule 2**

If there are two substituents with equal rank, proceed along the two substituent chains until there is a point of difference. First, determine which of the chains has the first connection to an atom with the highest priority (the highest atomic number). That chain has the higher priority.

If the chains are similar, proceed down the chain, until a point of difference.

**For example:** an ethyl substituent takes priority over a methyl substituent. At the connectivity of the stereocenter, both have a carbon atom, which are equal in rank. Going down the chains, a methyl has only has hydrogen atoms attached to it, whereas the ethyl has another carbon atom. The carbon atom on the ethyl is the first point of difference and has a higher atomic number than hydrogen; therefore the ethyl takes priority over the methyl.
Rule 3

If a chain is connected to the same kind of atom twice or three times, check to see if the atom it is connected to has a greater atomic number than any of the atoms that the competing chain is connected to.

- If none of the atoms connected to the competing chain(s) at the same point has a greater atomic number: the chain bonded to the same atom multiple times has the greater priority
- If however, one of the atoms connected to the competing chain has a higher atomic number: that chain has the higher priority.

Example 2

A 1-methylethyl substituent takes precedence over an ethyl substituent. Connected to the first carbon atom, ethyl only has one other carbon, whereas the 1-methylethyl has two carbon atoms attached to the first; this is the first point of difference. Therefore, 1-methylethyl ranks higher in priority than ethyl, as shown below:

However:
Remember that being double or triple bonded to an atom means that the atom is connected to the same atom twice. In such a case, follow the same method as above.

**Caution!!**
Keep in mind that priority is determined by the **first** point of difference along the two similar substituent chains. After the first point of difference, the rest of the chain is irrelevant.

When looking for the first point of difference on similar substituent chains, one may encounter branching. If there is branching, choose the branch that is higher in priority. If the two substituents have similar branches, rank the elements within the branches until a point of difference.
After all your substituents have been prioritized in the correct manner, you can now name/label the molecule \textbf{R} or \textbf{S}.

1. Put the lowest priority substituent in the back (dashed line).
2. Proceed from 1 to 2 to 3. (it is helpful to draw or imagine an arcing arrow that goes from 1--\(\rightarrow\) 2--\(\rightarrow\)3)
3. Determine if the direction from 1 to 2 to 3 clockwise or counterclockwise.

i) If it is \textit{clockwise} it is \textbf{R}.
ii) If it is \textit{counterclockwise} it is \textbf{S}.

\textbf{USE YOUR MODELING KIT:} Models assist in visualizing the structure. When using a model, make sure the lowest priority is pointing away from you. Then determine the direction from the highest priority substituent to the lowest: clockwise (R) or counterclockwise (S).

\textbf{IF YOU DO NOT HAVE A MODELING KIT:} remember that the dashes mean the bond is going into the screen and the wedges means that bond is coming out of the screen. If the lowest priority bond is not pointing to the back, mentally rotate it so that it is. However, it is very useful when learning organic chemistry to use models.

\textit{If you have a modeling kit use it to help you solve the following practice problems.}

\textbf{Problems}

Are the following \textbf{R} or \textbf{S}?
Solutions

1. **S**: \( \text{I} > \text{Br} > \text{F} > \text{H} \). The lowest priority substituent, \( \text{H} \), is already going towards the back. It turns left going from \( \text{I} \) to \( \text{Br} \) to \( \text{F} \), so it's a **S**.

2. **R**: \( \text{Br} > \text{Cl} > \text{CH}_3 > \text{H} \). You have to switch the \( \text{H} \) and \( \text{Br} \) in order to place the \( \text{H} \), the lowest priority, in the back. Then, going from \( \text{Br} \) to \( \text{Cl} \), \( \text{CH}_3 \) is turning to the right, giving you a **R**.

3. **Neither R or S**: This molecule is achiral. Only chiral molecules can be named R or S.

4. **R**: \( \text{OH} > \text{CN} > \text{CH}_2\text{NH}_2 > \text{H} \). The \( \text{H} \), the lowest priority, has to be switched to the back. Then, going from \( \text{OH} \) to \( \text{CN} \) to \( \text{CH}_2\text{NH}_2 \), you are turning right, giving you a **R**.

5. **(5) S**: \( \text{\{-COOH\}} > \text{\{-CH\_2OH\}} > \text{\{-C\#CH\}} > \text{\{-H\}} \). Then, going from \( \text{\{-COOH\}} \) to \( \text{\{-CH\_2OH\}} \) to \( \text{\{-C\#CH\}} \) you are turning left, giving you a **S** configuration.

References


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