

R/S Nomenclature of Stereogenic Centers - Review

To assign the configuration of a stereogenic center, a set of rules, the Cahn-Ingold-Prelog rules, were created. The configuration at a stereocenter is described as being R, from latin *rectus* (or right-handed), or S, from the latin *sinister* (or left-handed), depending on the order in which the different substituents are arranged around the stereocenter. The rules that are applied are as follows:

- 1) Each group attached to the stereocenter is assigned a priority, where the higher the atomic number, the higher the priority. For example:



For isotopes of the same atom, the one with the higher atomic weight takes priority. Tritium, an isotope of hydrogen, has an atomic weight of 3 and has a higher priority than deuterium which has an atomic weight of 2. Hydrogen with an atomic weight of 1 has the lowest priority.



- 2) If two identical atoms are attached to the stereocenter, the next atom in both chains are examined until a difference is found moving away from the stereocenter. A priority assignment is made at the first point at which the atoms of different priorities are found.

- 3) A double bond is counted as two single bonds for both atoms involved.

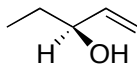


The same principle is extended to triple bonds.



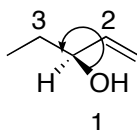
- 4) After priorities have been assigned, the molecule is viewed with the lowest priority away from the viewer. If you can trace a clockwise path from the group of highest priority to the one of second priority and then to the one of third priority, the stereocenter is assigned the R configuration. If the arrangement is in a counterclockwise path, the stereocenter is assigned the S configuration.

An example is the naming of the below chiral alcohol.



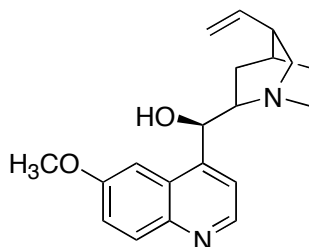
(S)-pent-1-en-3-ol

The first step in naming this compound is to find the parent name of the longest chain. In this case it is 5 carbons long and therefore is a pentane. There is also one terminal double bond present in the molecule at position 1. Replace *-ane* with *-ene* to give pent-1-ene. Since the molecule is an alcohol, you then drop the *-e* ending, replacing it with *-ol* for the name to become pent-1-en-3-ol. The stereochemical assignment is as shown below.



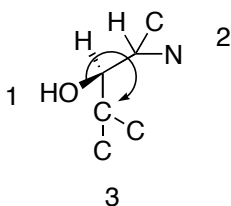
In pent-1-en-3-ol, the alcohol takes priority over the ethyl and vinyl groups. The vinyl group, with a carbon double bond takes a higher priority than the ethyl group in which only one carbon and one hydrogen is bonded to the carbon atom next to the stereogenic center. Thus, when the lowest priority group (hydrogen) is put away from the viewer, a counterclockwise path is found and is assigned the S configuration. Putting the overall name together gives (S)-pent-1-en-3-ol.

A more difficult example of assigning R or S configuration is in the molecule below, Quinine. Quinine is an anti-malarial compound from the *Cinchona officinalis*. It has five stereogenic centers and a wide range of different functional groups including an ether, alcohol, amines (2), aromatic rings (2), alkene



Quinine

The R/S configuration of the alcohol is shown to be an R center. The highest priority is given to the oxygen and the lowest given to the hydrogen. The carbon “next door” to the stereogenic center that is bonded to the nitrogen takes higher priority than the carbon in the aromatic ring since nitrogen has a higher atomic number than carbon. Thus, when the lowest priority group (hydrogen) is put away from the viewer, a clockwise path is found and is assigned the R configuration.



Aldehydes and Ketones: Nomenclature

A carbonyl group has a pi (π) bond between carbon and an oxygen atom. An oxo group is any atom with a double bond to oxygen. Compounds in which there is a carbonyl group are divided into different functional group classes depending on the other groups or atoms that are bonded to the carbon atom of the carbonyl group. In aldehydes, the carbonyl group is bonded to at least one hydrogen. In ketones, the carbonyl group is bonded to two carbon atoms.



carbonyl
group



oxo
group



aldehyde
when $y=C,H$



ketone

The carbon atom of the carbonyl group is bonded to three other groups, all in one plane, and therefore is trigonal planar. The bond angles between all the groups are approximately 120° and the carbon atom of the carbonyl group is sp^2 hybridized.

Aldehyde Nomenclature

Aldehydes are systematically named by changing the $-e$ ending of the parent hydrocarbon and replacing it with $-al$. The numbering of the parent hydrocarbon chain is such that it makes the aldehyde the first carbon of the chain. Other substituents are named using prefixes and numbered to indicate their positions relative to the aldehyde group. For complex examples, the aldehyde functionality can also be called a formyl group.



formyl group

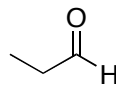
Some common names of simple aldehydes are given below along with their systematic names.



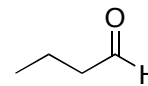
methanal
or formaldehyde



ethanal
or acetaldehyde

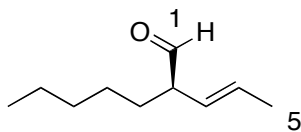


propanal
or propionaldehyde



butanal
or butyraldehyde

An example of naming aldehydes is given with the below structure.

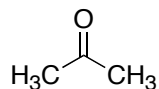


(2R,3E)-2-pentylpent-3-en-1-al

The first step in naming this compound is to find the parent name of the longest, most functionalized chain. In this case it is 5 carbons long and therefore is a pentane. There is a trans double bond present in the molecule at position 3. You then drop the *-ane* ending, replacing it with *-ene* to give pent-3-ene. Since the molecule is an aldehyde, you then drop the *-e* ending, replacing it with *-al* for the name to become pent-3-en-1-al. There is also a pentyl group at position 2, making the molecule 2-pentylpent-3-en-1-al. There are also stereochemical considerations to take into account. The double bond is in the trans geometry and the aldehyde is in the R configuration as discussed before. Putting the overall name together gives (2R,3E)-2-pentylpent-3-en-1-al.

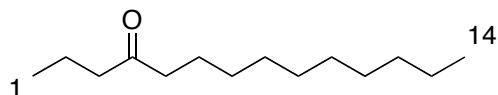
Ketone Nomenclature

Ketones are named by substituting the *-e* ending of the parent hydrocarbon and replacing it with *-one*. The numbering of the hydrocarbon starts from the end of the chain which gives the carbonyl group the lowest number. Other substituents are named using prefixes and numbered to indicate their position relative to the start of the chain. A common name for the simplest ketone (acetone) is given below along with its systematic name.



acetone
or 2-propanone

An example of naming ketones is given with the below structure.

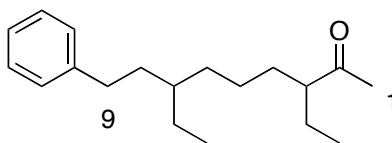


4-tetradecanone

The first step in naming this compound is to find the parent name of the longest chain, which in this case is 14 and therefore is a tetradecane. When numbering this compound, you start from the left hand side, giving the carbonyl the lowest number. You then drop the *-e* ending, replacing it with *-one* to give 4-tetradecanone.

Ketone Naming Example

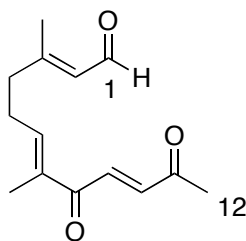
The below structure is a sex pheromone from the crocodile.



3,7-diethyl-9-phenyl-2-nonanone

The first step in naming this structure is to identify the longest chain, which is 9 and therefore is a nonane. Since the carbonyl group is at the 2 position, you then drop the *-e* ending, replacing it with *-one* to give 2-nonanone. At the 3 and 7 positions are ethyl groups which are given as prefixes to give 3,7-diethyl-2-nonanone. Also present is a phenyl group at the 9 position to give the final name as 3,7-diethyl-9-phenyl-2-nonanone. In this molecule there are also two stereogenic centers at the 3 and 7 positions but no information is given on the configuration of these centers. There are four possible stereoisomers for this compound, but only one is likely to be biologically active.

Another naming example involves Gyrinal (shown below) which is an anti-microbial agent from the water boatman beetle (*Corixa* species), and is toxic to fish and other predators.



Gyrinal or
3,7-dimethyl-8,11-dioxo-2E,6E,9E-dodecantrienal

The first step to naming this aldehyde is to identify the longest chain, which is 12 and therefore a dodecane. This molecule is an aldehyde giving the parent name dodecanal. Gyrinal also has three trans double bonds at the 2,6 and 9 positions giving 2E,6E,9E-dodecatrienal. Two methyl groups are also present at the 3 and 7 positions to give 3,7-dimethyl-2E,6E,9E-dodecatrienal. Also present in Gyrinal are two carbonyl groups. Since this compound is being named as an aldehyde, the two carbonyl groups will be named as oxo groups. Since the carbonyl groups are at the 8 and 11 positions the final name for Gyrinal is 3,7-dimethyl-8,11-dioxo-2E,6E,9E-dodecantrienal.

Physical Properties of Carbonyl Containing compounds

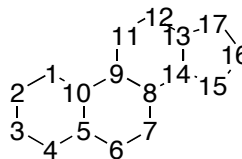
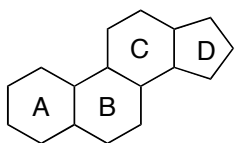
Carbonyl containing compounds are more polar than alkanes but less polar than alcohols. They are also generally insoluble in water (except small compounds such as acetone, formaldehyde, acetaldehyde etc). They are hydrogen bond acceptors.

Steroids

Steroids are triterpenoids, a group of compounds produced in plants and animals. They are very widespread in nature and have many important biological functions including regulating sexual characteristics of males and females.

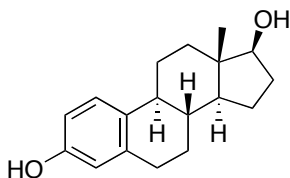
Steroids are characterized by a tetracyclic structure. A typical steroid ring structure consists of three six-membered rings and one 5-membered ring fused together. Depending on the biological function of the steroid, they have a variety of functional groups substituted on the skeleton.

The rings in a steroid skeleton are designated as the A, B, C and D rings with the numbering pattern as shown below. Groups pointing into the paper are considered alpha (α) and groups pointing out of the paper are considered beta (β).

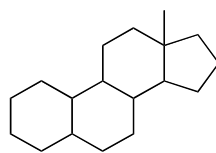


Steroids determine many of the secondary sexual characteristics in both plants and animals. Many of the male and female steroidal hormones differ primarily by a methyl group at C-10 on the steroid skeleton.

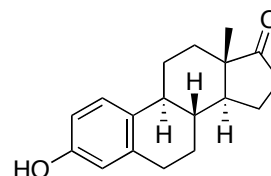
Estradiol was first isolated in 1929 from the extraction of 4 tons of hog ovaries. Approximately 15 milligrams of material was isolated and characterized as the below structure. The structure consists of an aromatized A ring, alcohol functionalities at positions 3 and 17 and an alpha methyl group at position 13. This is characteristic of an estrane skeleton, which has an beta (β) methyl group at the 13 position. Female steroidal hormones have the estrane skeleton. Another example of this type of skeleton is estrone, in which the alcohol at position 17 is oxidized to a ketone.



Estradiol

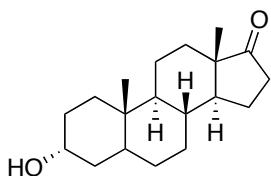


Estrane skeleton

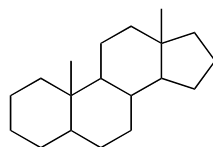


Estrone

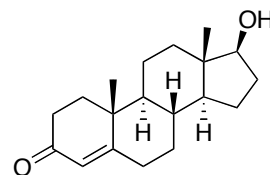
Androsterone was first isolated in 1931 from the extraction of 15,000 liters of urine. Approximately 15 milligrams of material was isolated and characterized as the below structure. The structure has two methyl groups at the 10 and 13 positions, a ketone functionality at the 17 position and an alpha (α) hydroxyl group at the 3 position. This type of structure is characteristic of an androstane skeleton, which has two beta (β) methyl groups at the 10 and 13 positions. Another example of this type of skeleton is testosterone. Testosterone differs from androsterone by a double bond between positions 4 and 5, a ketone at position 3 and an alcohol at position 17. Male steroidal hormones have the androstane skeleton.



Androsterone

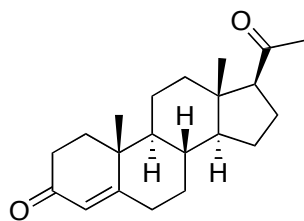


Androstane skeleton

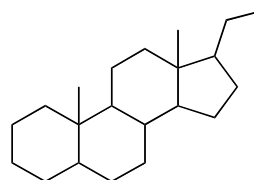


Testosterone

Progesterone is a hormone whose levels are elevated during pregnancy in females. Its structure has the pregnane skeleton, which has two methyl groups at positions 10 and 13 and a two carbon chain at position 17. Progesterone differs from testosterone by having the side chain at position 17.

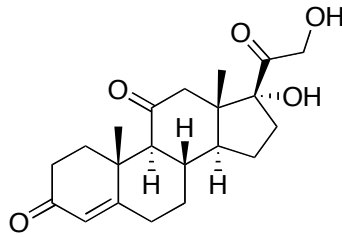


Progesterone



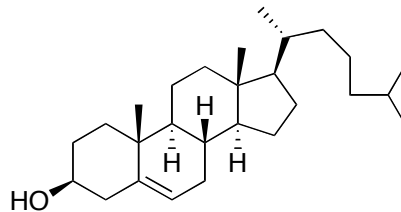
Pregnane skeleton

Cortisone is a hormone of the adrenal glands that is used medically to relieve inflammation. Cortisone is a highly oxidized steroid, containing a variety of functional groups including ketones, double bonds and alcohols.



Cortisone

Cholesterol is a major steroid found in membranes of animals, and is a precursor to a variety of other steroid structures. Cholesterol has an alcohol at the 3 position and double bond between the 4 and 5 positions and a functionalized side chain as shown below.



Cholesterol