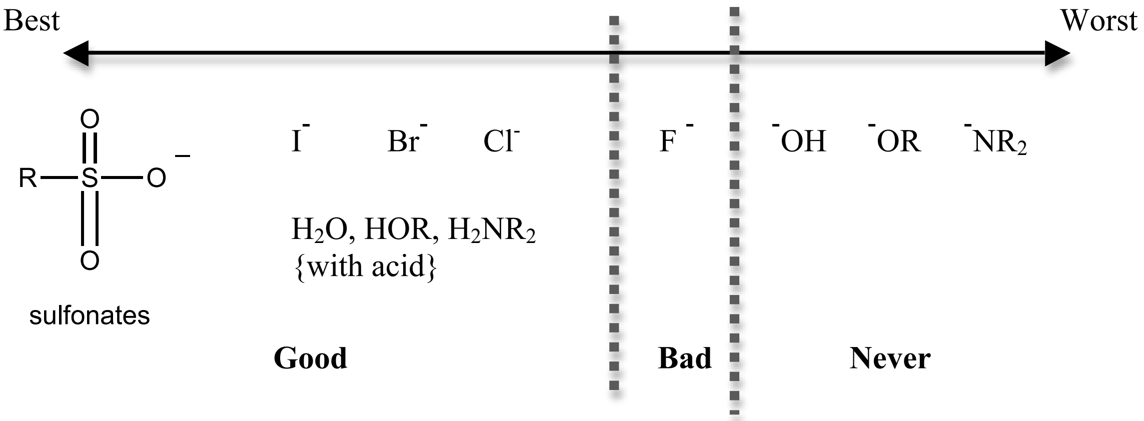
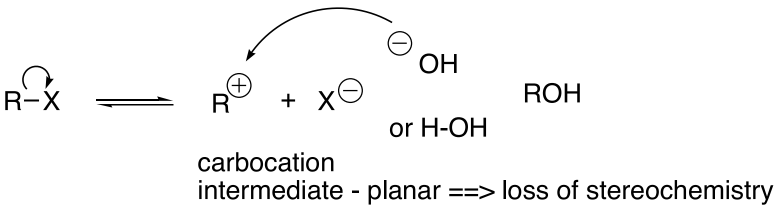
Alcohols and Ethers from Alkyl Halides

Nucleophilic Substitution (S_N1 and S_N2)

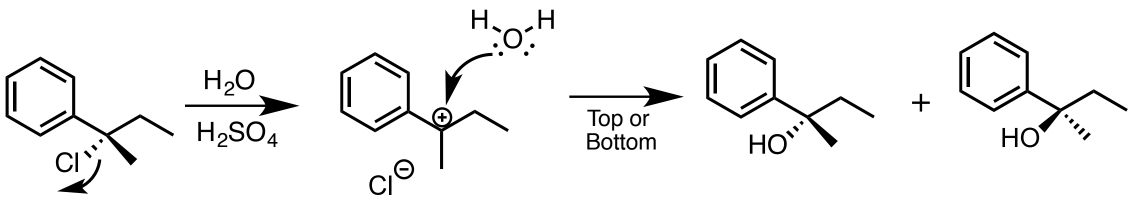
Leaving Groups:



S_N1

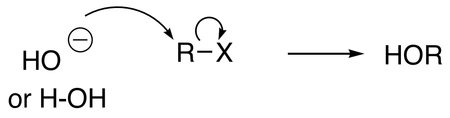


- Rate depends on 1 concentration - unimolecular
- Not stereospecific
- Not concerted (stepwise)
- Carbocation intermediate (planar - loses stereochemistry usually)
- Best substrates: 3°, allylic, and benzylic halides.



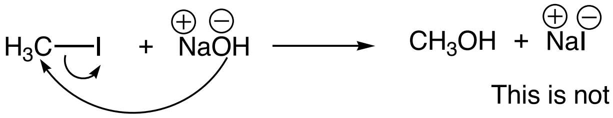
1:1 racemate

S_N2

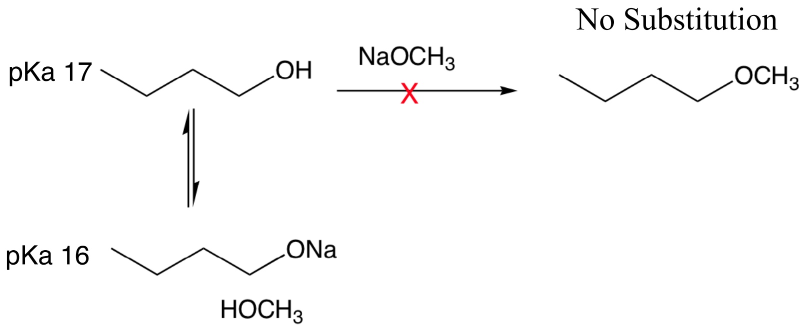


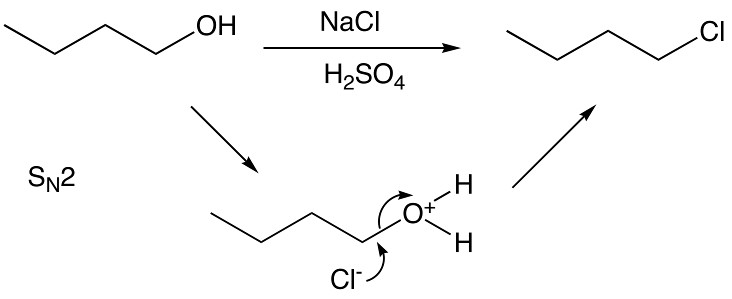
- Rate depends on 2 concentrations - bimolecular
- Stereospecific (the stereochemistry of the reactants determines the stereochemistry of the products)
- Inversion of configuration (Walden Inversion)
- Concerted (bonds are broken and formed at the same time)
- 1° halides work the best
- 2° halides work OK
- 3° halides don't work
- In general C=C-X (vinyl halides) also fail for this type of reaction

Examples:

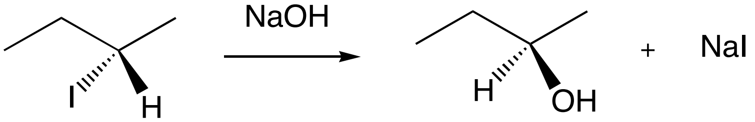


This is not reversible, because I- is more stable than OH-



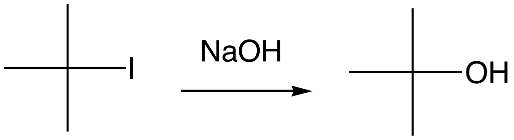


Walden inversion for S_N2:

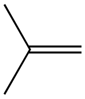


Limitations:

Would the following reaction occur?

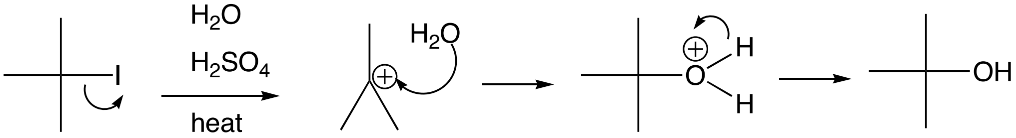


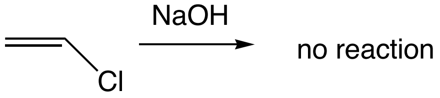
No, this involves a tertiary halide, which is too crowded. Elimination could occur though, to produce:



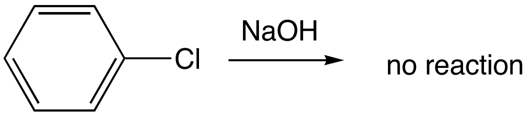
What reagents instead of NaOH could be used that would allow the above substitution reaction to occur?

Answer: H_2O, H_2SO_4 and heat would allow an S_N1 reaction to occur:

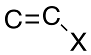




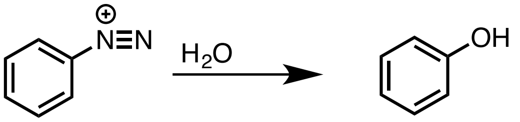
vinyl chloride

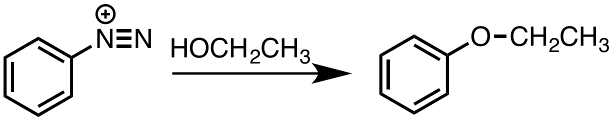


chlorobenzene

Note: No S_N reactions occur on 

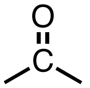
Exception – diazonium reactions





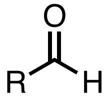
Aldehydes and Ketones: Nomenclature

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 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 is bonded to two carbon atoms.

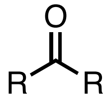


Carbonyl

Oxo



Aldehyde
where Y = C, H

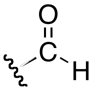


Ketone

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

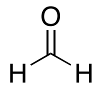
Aldehyde Nomenclature

Aldehydes are systematically named by changing the *–oic* ending of the parent carboxylic acid 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.
Aldehydes take higher priority in naming over ketones, alcohols, ethers, amines, alkenes, alkyl halides.

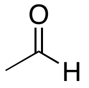


formyl group

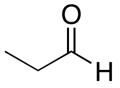
Some common simple aldehydes are given below along with their systematic names.



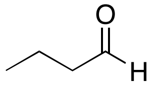
methanal
or formaldehyde



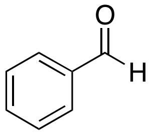
ethanal
or acetaldehyde



propanal
or propionaldehyde

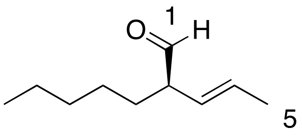


butanal
or butyraldehyde



Benzaldehyde

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

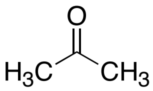


(2R,3E)-2-pentylpent-3-en-1-al

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 is also stereochemistry to take into account. The double bond is in the trans geometry and the aldehyde group is in the R configuration. Putting the overall name together gives (2R,3E)-2-pentylpent-3-en-1-al.

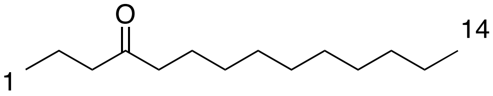
Ketone Nomenclature

Ketones are named by substituting the *–e* ending of the parent alkane and replacing it with *–one*. The numbering of the hydrocarbon starts from the end of the chain that 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 *or* propan-2-one

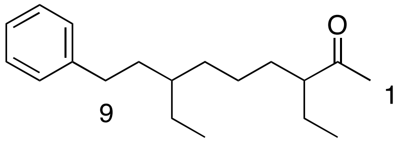
An example of naming ketones is given with the structure below:



4-tetradecanone
or tetradecan-4-one

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 to give the carbonyl the lowest number. You then drop the *–e* ending, replacing it with *–one* to give 4-tetradecanone.

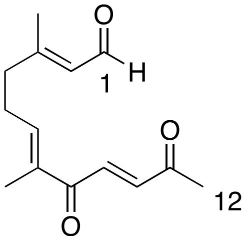
The below structure is a sex pheromone from the crocodile.



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 written 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) from the water boatman beetle (*Corixa* species), which is an anti-microbial agent and is toxic to fish and other predators.



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

The longest chain is 12 carbons and therefore a dodecane. This molecule is an aldehyde giving the parent name dodecanal.

Gyrinal has three trans double bonds at the 2,6 and 9 positions giving 2E,6E,9E-dodecatrienal.

Methyl groups are present at the 3 and 7 positions to give 3,7-dimethyl-2E,6E,9E-dodecatrienal.

Also present in gyrinal are two other carbonyl groups. Since this compound is being named as an aldehyde (which takes priority over ketones), the two carbonyl groups are 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.

Generally good solvents for organic compounds.

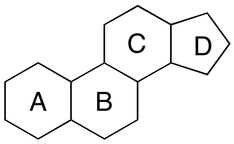
Aldehydes are generally insoluble in water (except small compounds such as acetone, formaldehyde, acetaldehyde, etc). They have dipoles and are hydrogen bond acceptors, but not hydrogen bond donors.

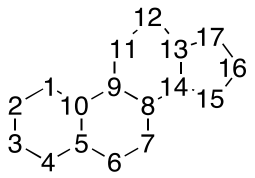
Steroids

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. Positions are numbered by the pattern shown below:





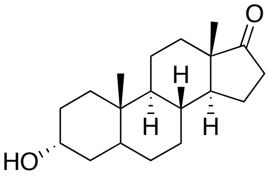
If groups attached to any of these four rings as drawn are pointing down, they are in the α position; if the groups are pointing up, they are in β position.

Many of the male and female steroidal hormones differ primarily by a methyl group at C-10 on the steroid skeleton.

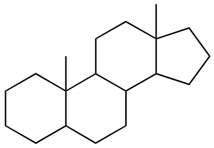
Androgens

Male steroidal hormones have the androstane skeleton.

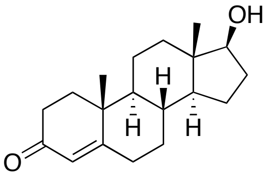
Androsterone was first isolated in 1931 by Adolf Butenandt from the extraction of 15,000 liters of urine. Approximately 15 milligrams of material was isolated and characterized as the below structure. The structure has two methyl groups at the 10 and 13 positions, a ketone functionality at the 17 position 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.



Androsterone



Androstane skeleton



Testosterone