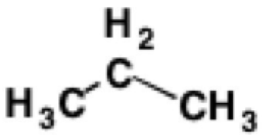
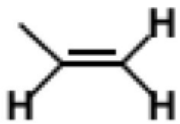
SAPIENZA

Chemistry and Introduction to Biochemistry

Functional Groups

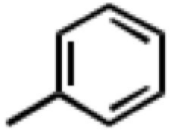


alkane



alkene

alkyne

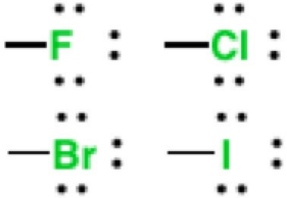


benzene ring (phenyl)

amine

alcohol

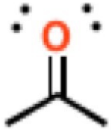
ether



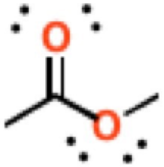
alkyl halide

thiol

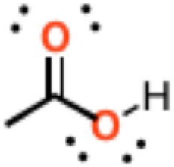
aldehyde



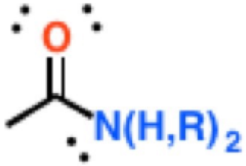
ketone



ester



carboxylic acid

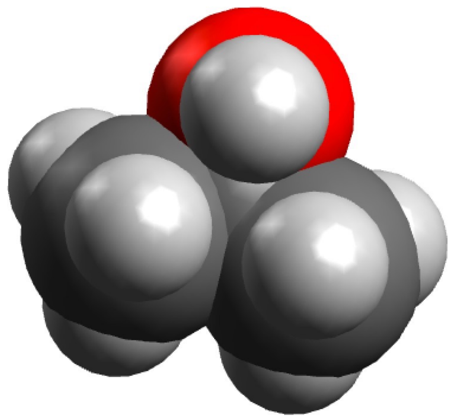


amide

Avogadro

Avogadro is an open source advanced molecule editor and visualizer designed for cross-platform use in *computational chemistry, molecular modeling, bioinformatics, materials science*, and related areas. It offers flexible high quality rendering and a powerful plugin architecture.

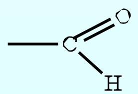
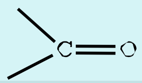
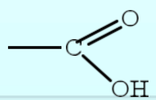
download it http://avogadro.cc/



Chemistry and Introduction to Biochemistry
Functional Groups

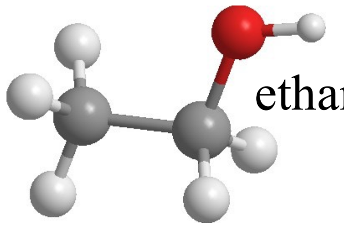
A functional group is defined as a part of the structure of a molecule characterized by specific elements, which gives the compound a typical reactivity similar to that of other compounds containing the same group.

In other words, the functional group constitutes the center of the chemical reactivity of the molecule.

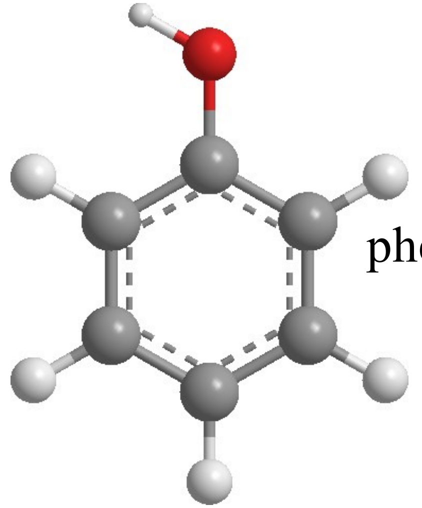
functional group		class of compounds	notes
C=C	carbon-carbon double bond	alkenes	
C≡C	carbon-carbon triple bond	alkynes	
—X	any halogen	• haloalkanes • acyl halides	• when it substitutes an H in an alkane • when it substitutes an OH in a carboxylic acid
—OH	hydroxy	• alcohols • enols • phenols	• when bound to sp^3 carbon • when bound to sp^2 carbon • when bound to an aromatic ring
—SH	sufyhydryl	thiols	when bound to sp^3 carbon
	aldehyde	aldehydes	
	carbonyl	ketones	
	carboxylic	carboxylic acids	
$—NH_2$	amine	• amines • aromatic amines • ammides	• when it substitutes an H in an alkane • when bound to an aromatic ring • when it substitutes an OH in a carboxylic acid

Functional groups of oxygen

1) alcohols & phenols

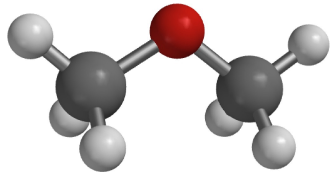


ethanol



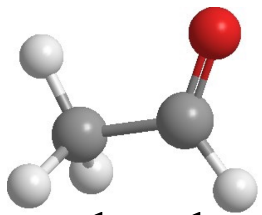
phenol

2) ethers

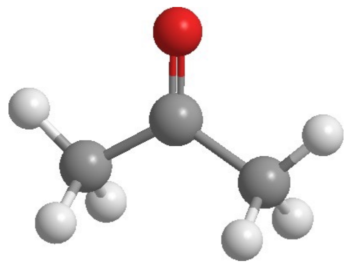


dimethyl ether

3) aldehydes & ketones

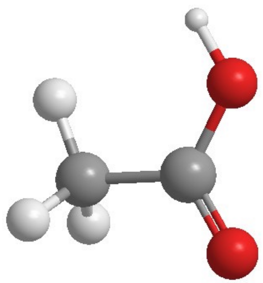


ethanal

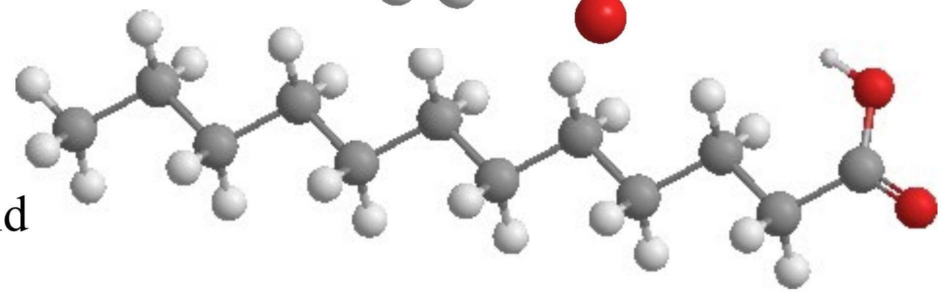


dimethyl ketone

4) carboxylic acids



ethanoic acid



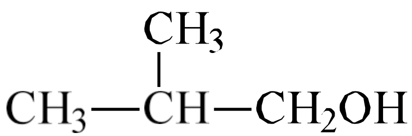
dodecanoic acid

Alcohols and phenols

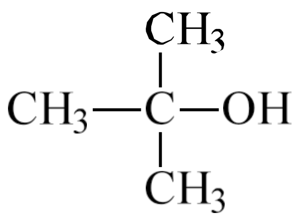
The functional groups of oxygen are numerous and important.
The simplest is the hydroxyl group:

−OH present in alcohols and phenols

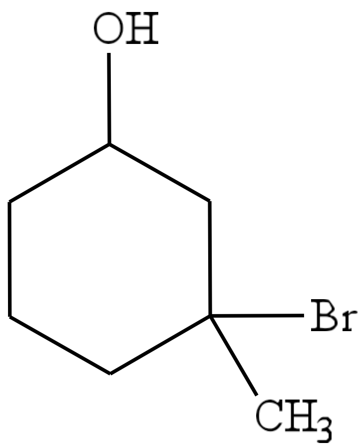
Nomenclature: the name of an alcohol is given by the name of the corresponding hydrocarbon, to which the ending -ol is added.
The longest hydrocarbon chain is identified, and is numbered by giving the lowest number to the C to which the OH is bound.



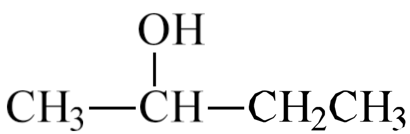
2-methyl-1-propanol



2-methyl-2-propanol



3-bromo-3-methylcyclohexanol

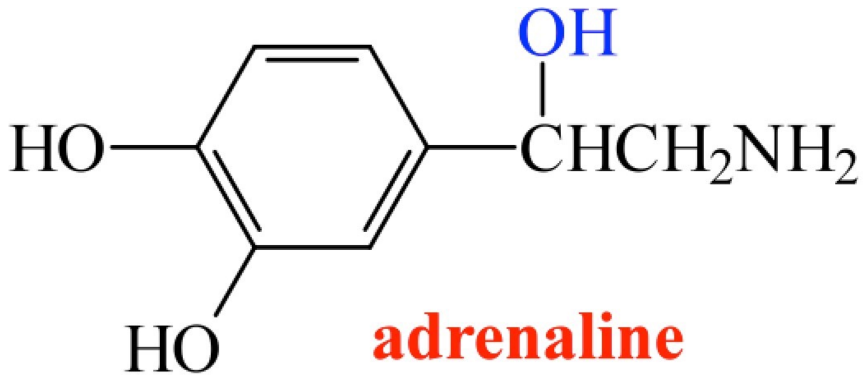


2-butanol

Some alcohols

CH_3CH_2OH

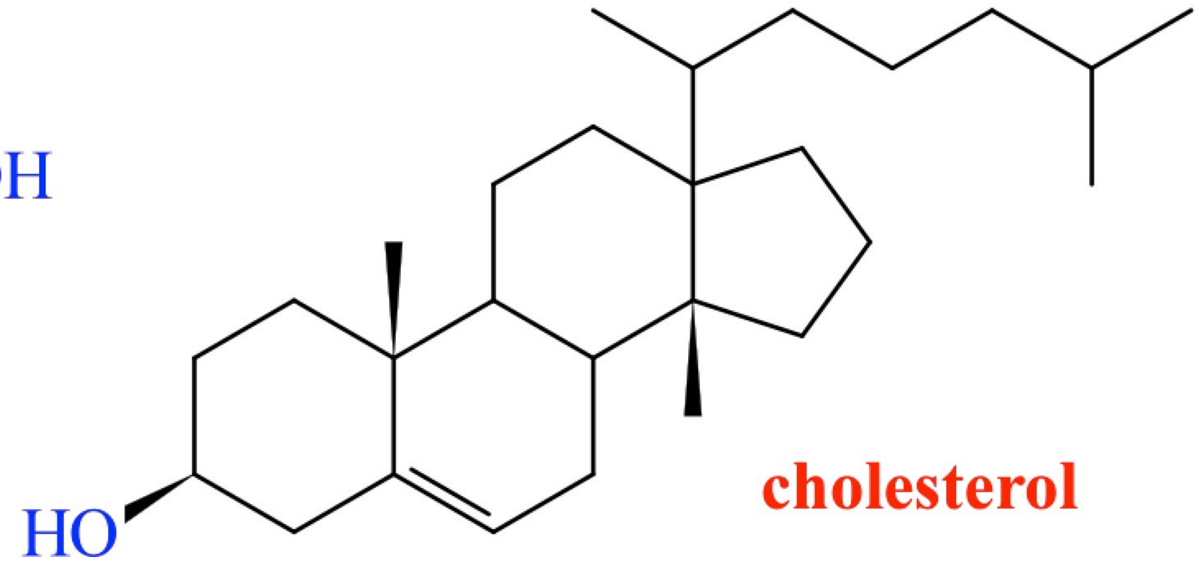
ethanol



adrenaline

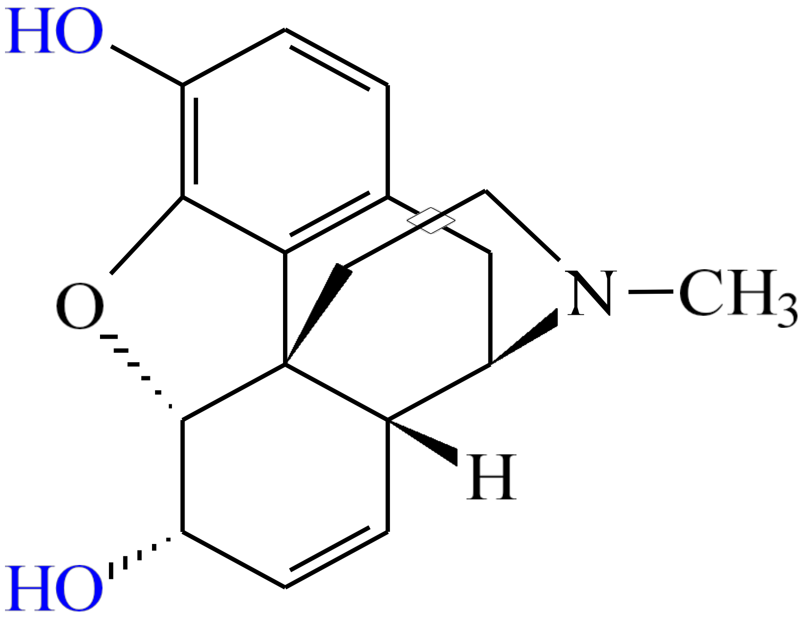
$HOCH_2CH(OH)CH_2OH$

glycerol



cholesterol

Alcohols are Found in Many Natural Products



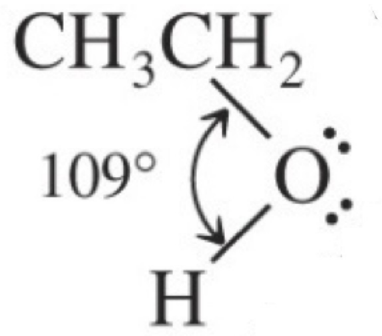
Morphine

most abundant of opium's alkaloid

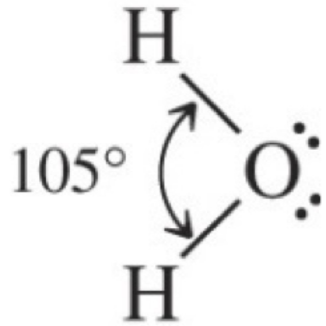
An alcohol can be viewed as either a hydroxyl derivative of an alkane or an alkyl derivative of water

CH_3CH_3

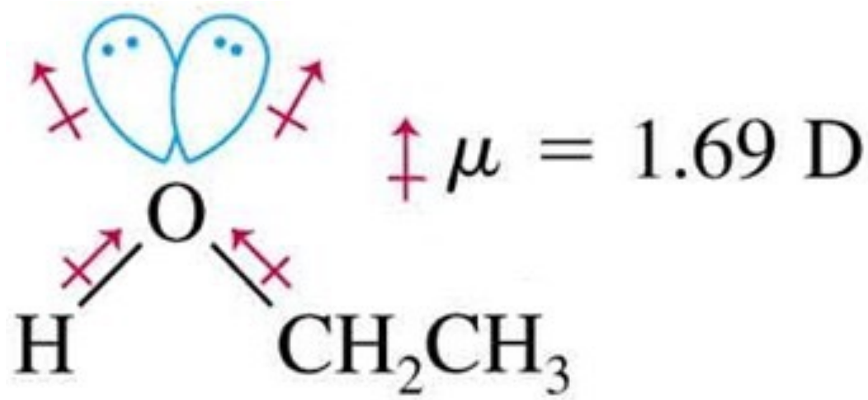
ethane

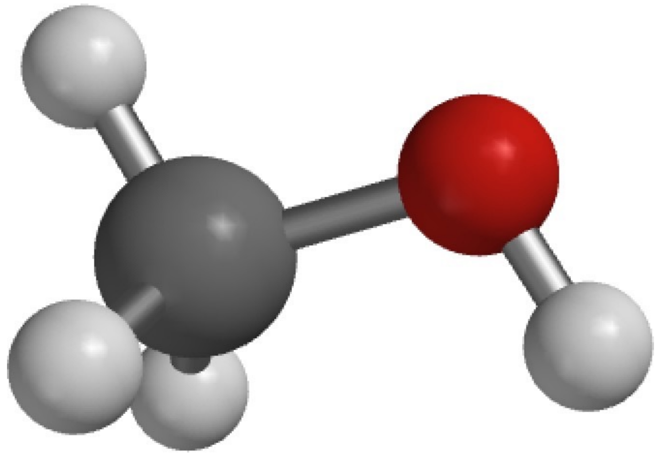


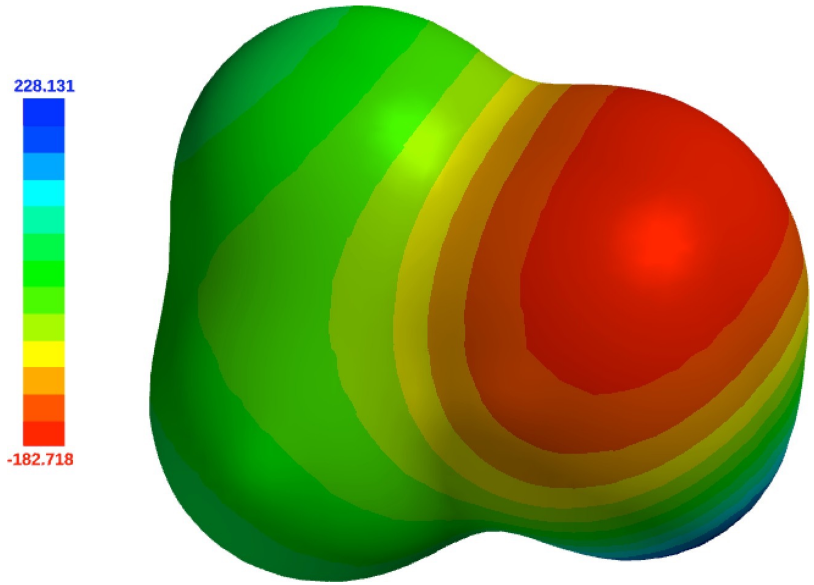
ethyl alcohol
(ethanol)

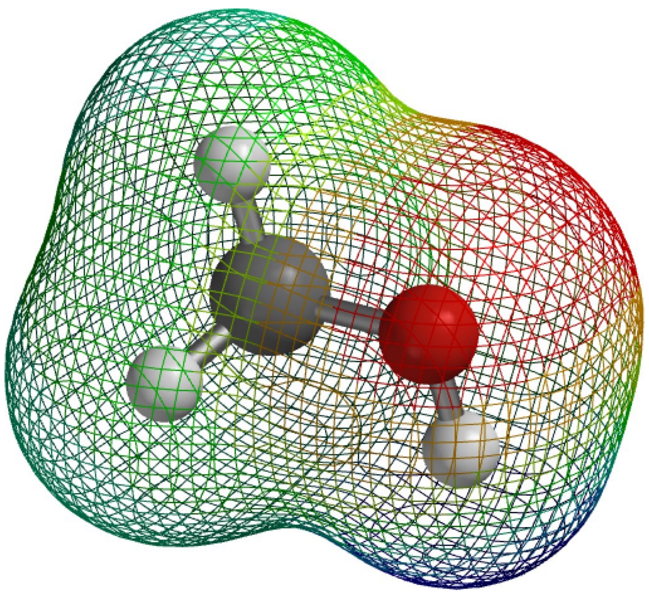


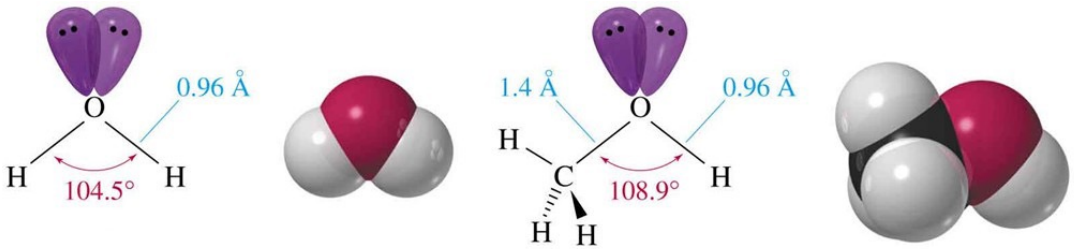
water

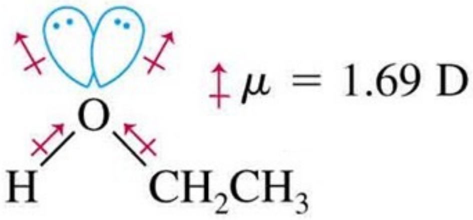

O
H
CH_2CH_3
$\mu = 1.69$ D




228.131
-182.718





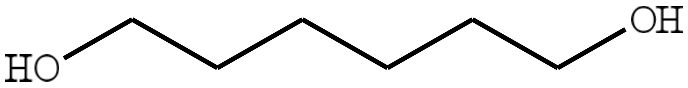


The presence of the OH group makes alcohols polar, therefore soluble in water, and it raises the boiling point with respect to the corresponding alkanes.

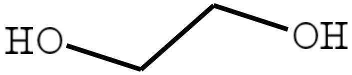
alkane	**T_{eb} (°C)**	**alcohol**	**T_{eb} (°C)**
CH_4	−161.6	CH_3OH	64.8
CH_3CH_3	−89.0	CH_3CH_2OH	78.3
$CH_3CH_2CH_3$	−42.1	$CH_3CH_2CH_2OH$	97.1

alcohol	solubility in H_2O at 25 °C
methanol	miscible
ethanol	miscible
1-propanol	miscible
2-methyl-2-propanol	miscible
2-methyl-1-propanol	10%
1-butanol	9.1%
1-pentanol	2.7%
cyclohexanol	3.6%
1-hexanol	0.6%
phenol	9.3%

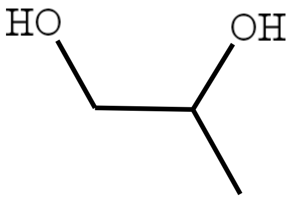
Compounds containing 2 (3) OH groups: diols (triols)



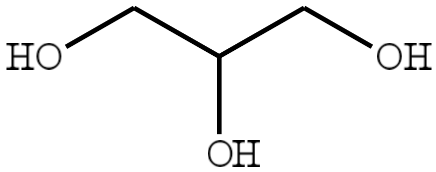
hexane-1,6-diol

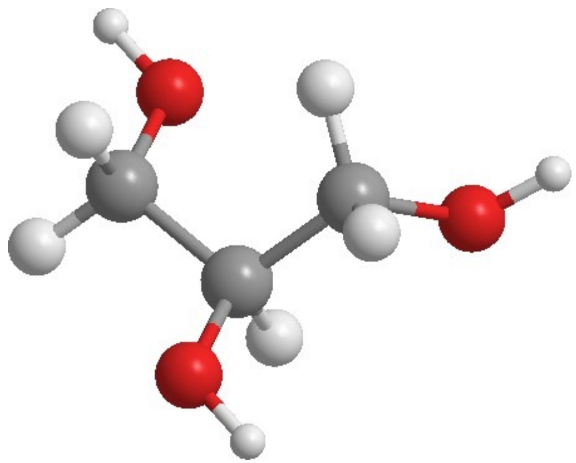


ethane-1,2-diol (glicole etilenico)



propane-1,2-diol (glicole propilenico)

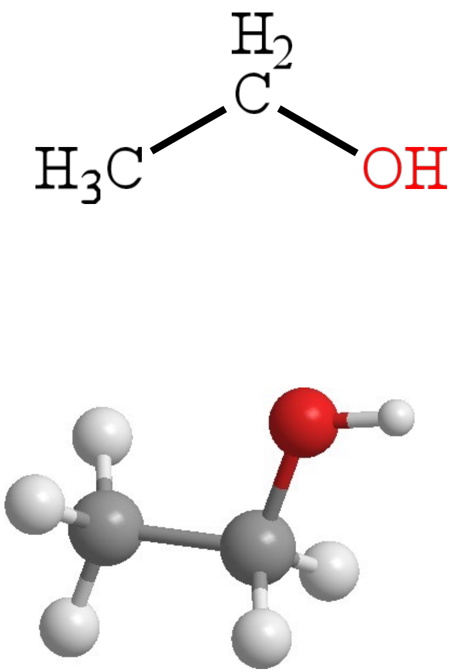




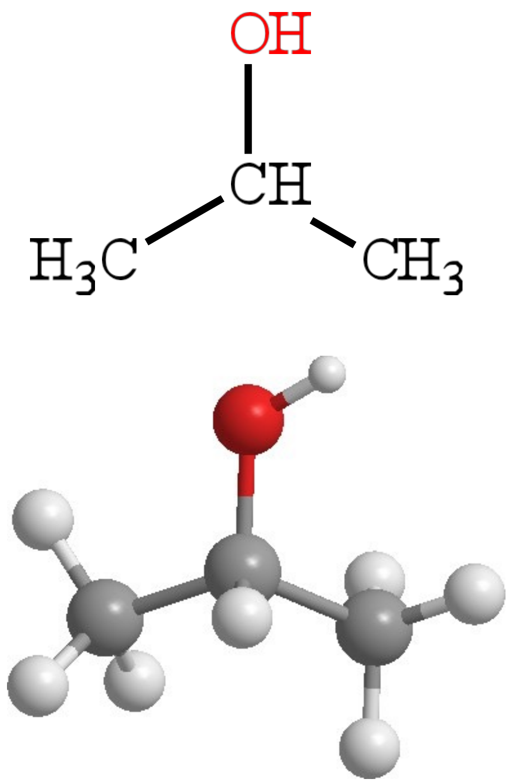
propane-1,2,3-triol (glycerol) → lipids

Alcohols are also classified according to the carbon the hydroxyl is directly attached to:

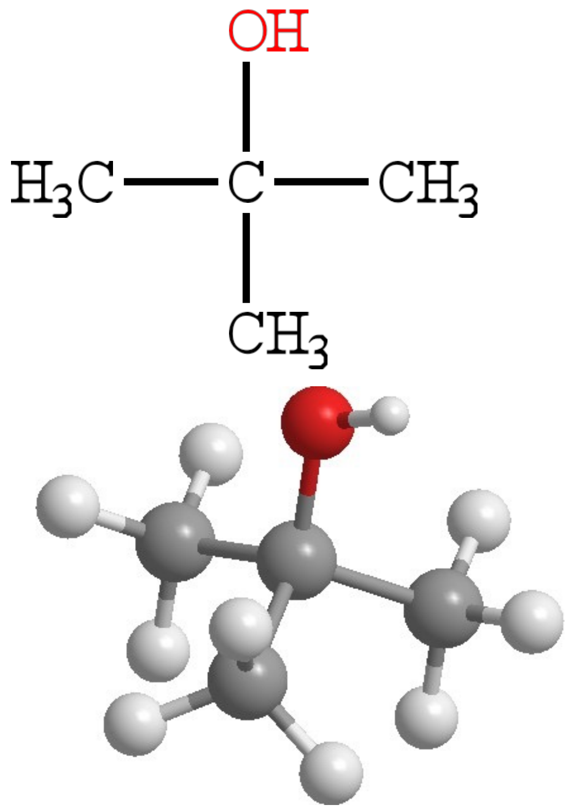
primary



secondary



tertiary



Acid-base reactions

Alcohols have only weak acidic character (methanol and ethanol about as water, others with longer chain even less) and do not react with weak bases. It is therefore necessary to use very strong bases (e.g. sodium hydride)

$$ROH + NaH \rightarrow RO^{-}Na^{+} + H_2$$

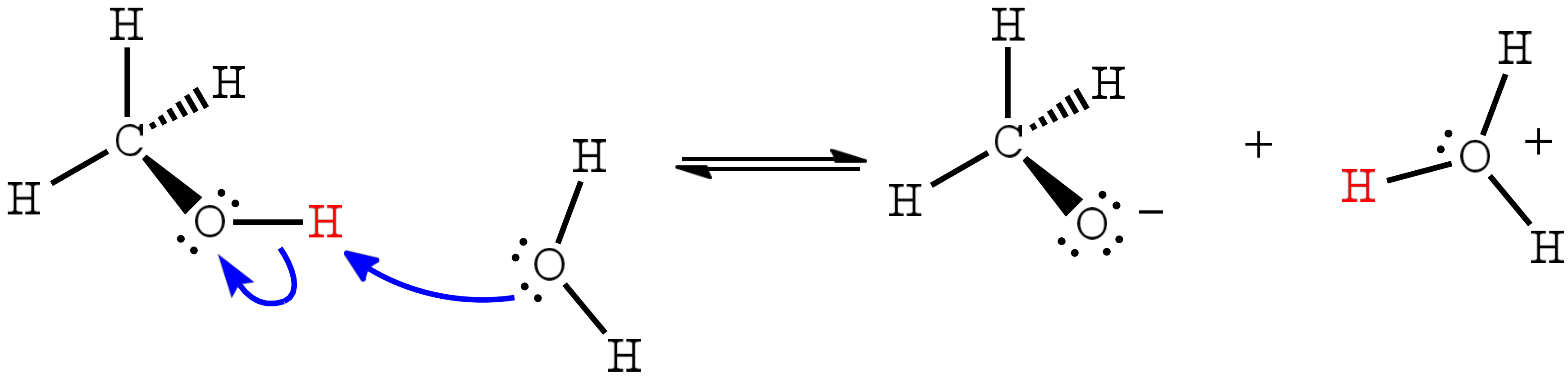
$$CH_3CH_2\,OH + NaH \rightarrow CH_3CH_2O^{-}Na^{+} + H_2$$

Alcohols are very weak acids

In the absence of electron-withdrawing groups (which increase their acidity) and electron-repelling groups (which reduce their acidity) the ionization constants are ca. $K_A = 1 \cdot 10^{-15}$ M

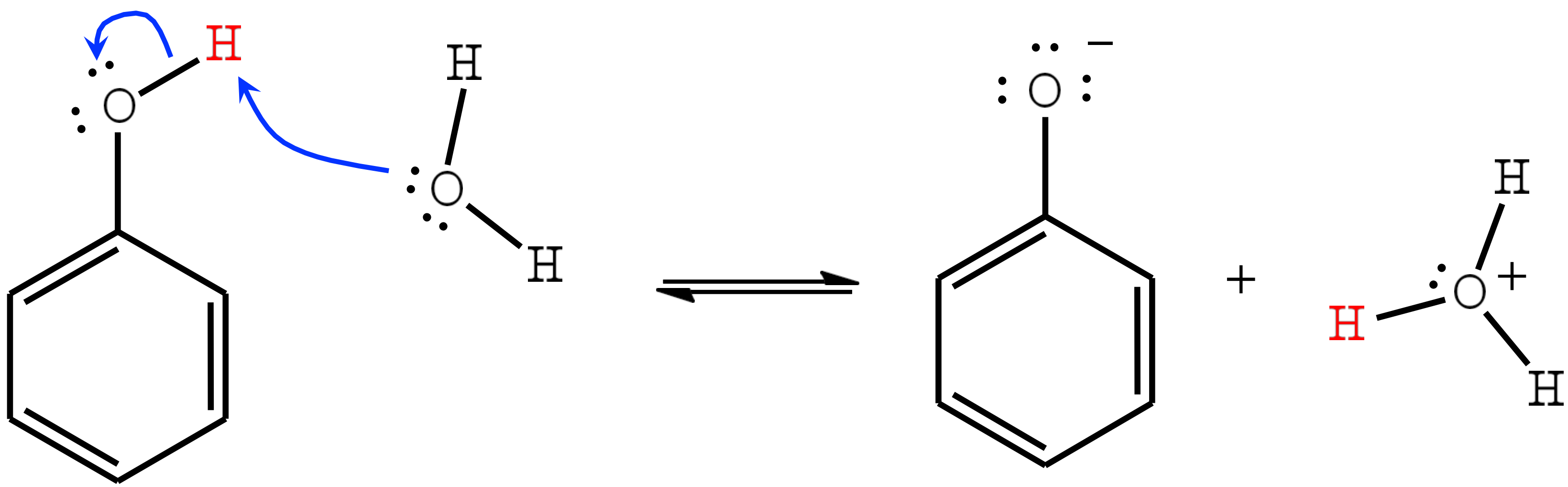
$$CH_3OH + H_2O \rightleftarrows CH_3O^- + H_3O^+$$

$$K_A = \frac{[CH_3O^-]\cdot[H_3O^+]}{[CH_3OH]} \cong 3.2 \cdot 10^{-16}\,M \qquad pK_A = 15.5$$



Although they have a hydroxyl group (-OH), the phenols do not behave like alcohols.

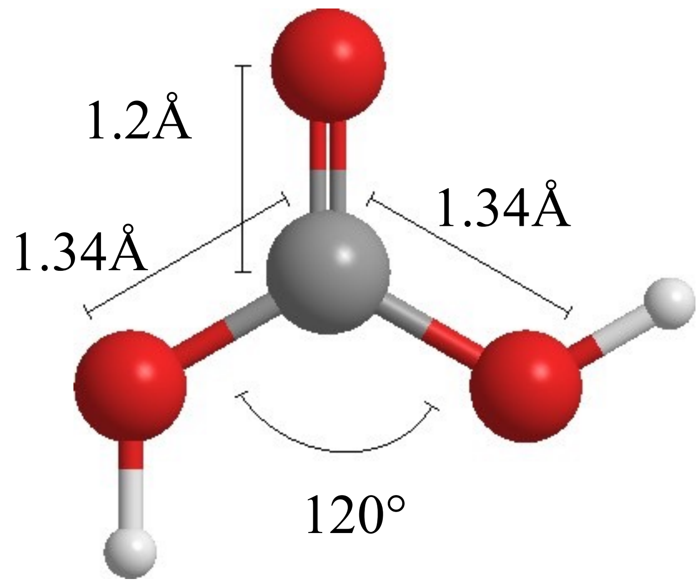
Phenol has a weak acidic character: $pK_A = 9.95$



This happens because the negative charge of the anion that is formed by the dissociation of the hydrogen of the hydroxyl group (phenate ion) is stabilized by resonance on the whole aromatic ring.

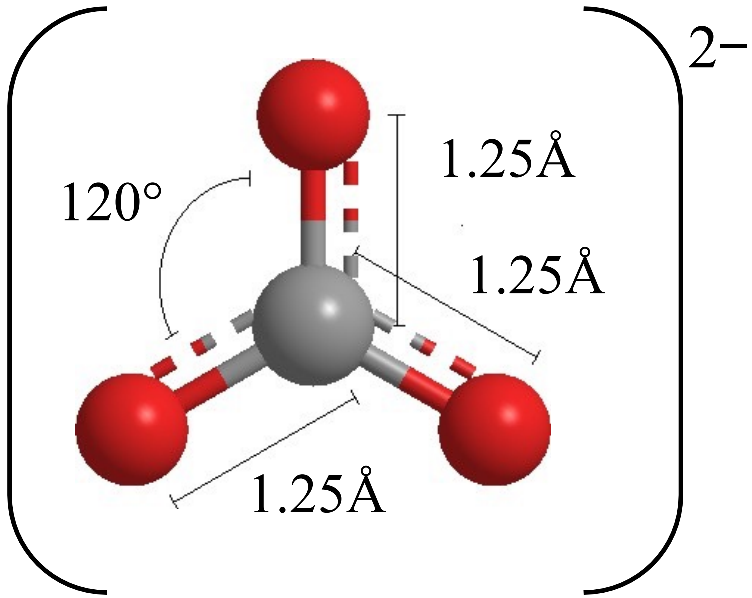
Resonance limit forms

carbonic acid H_2CO_3

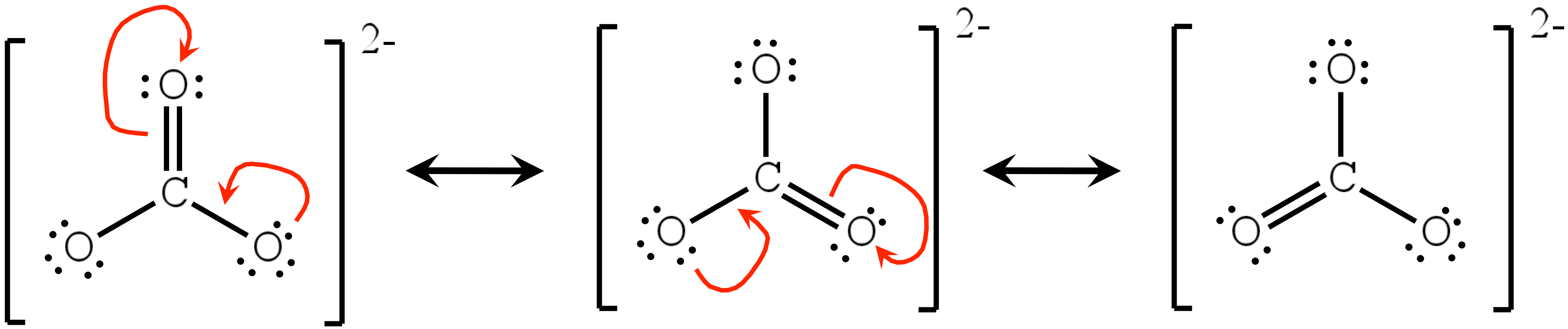


carbonate dianion CO_3^{2-}

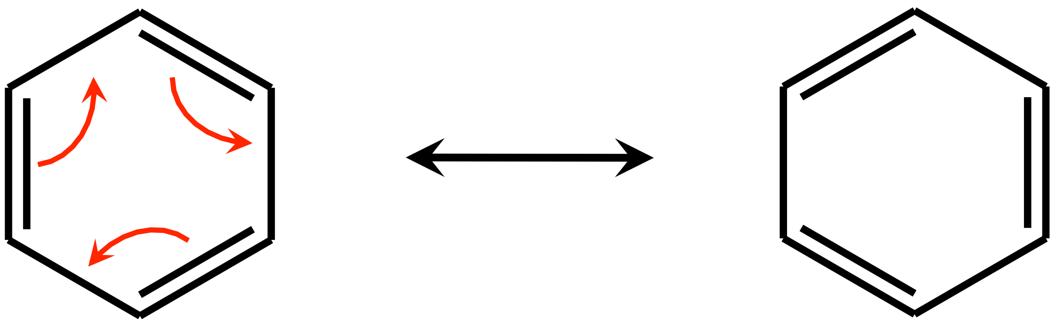
3 resonance limit forms



Resonance limit forms

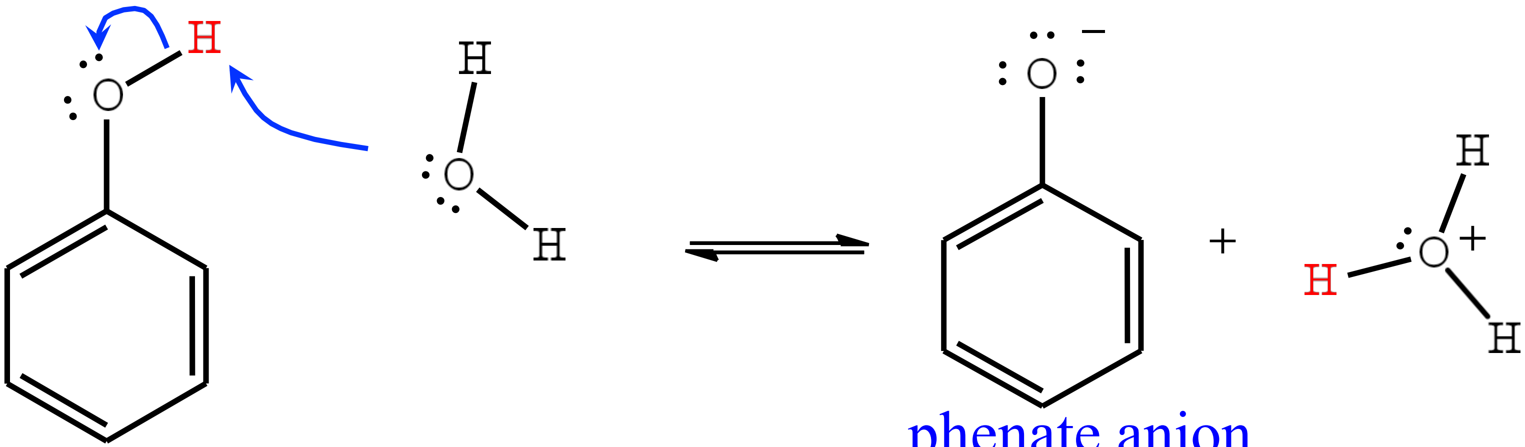


carbonate dianion



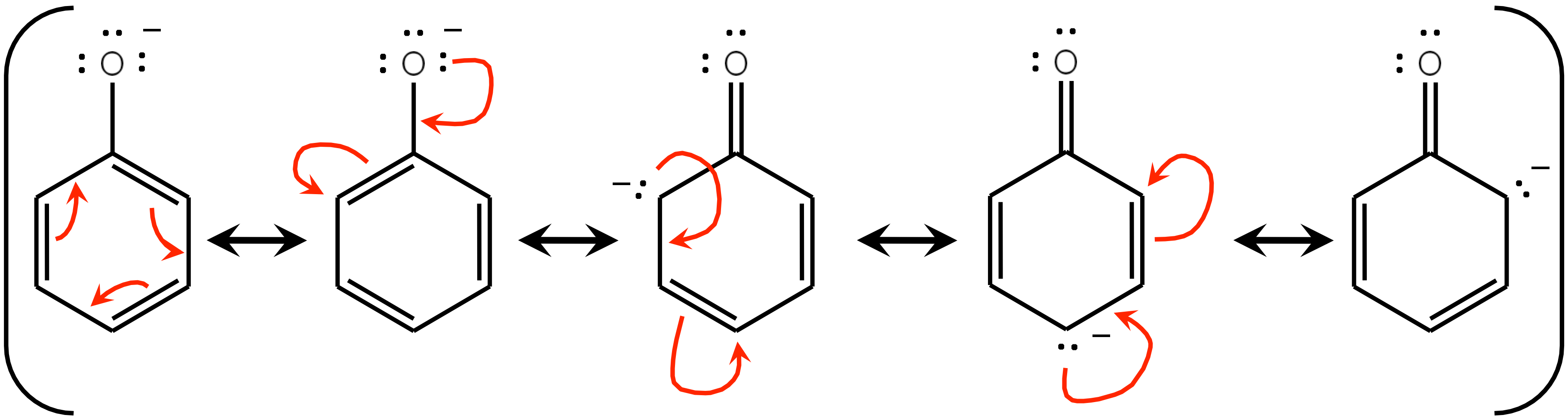
benzene

The phenate anion is stabilized by resonance among several limit forms. Phenols are stronger acids than alcohols.



phenate anion

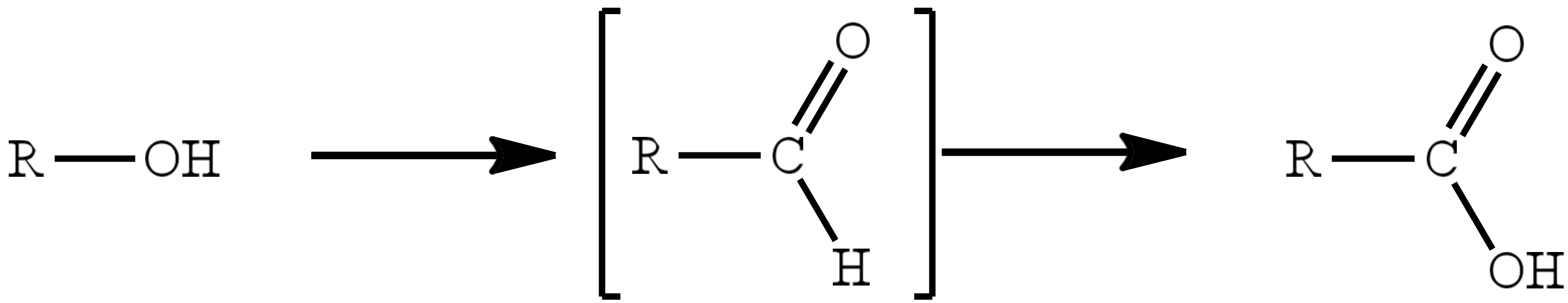
The charge is delocalized on the ring and the conjugate base is stabilized



ortho *para* *ortho*

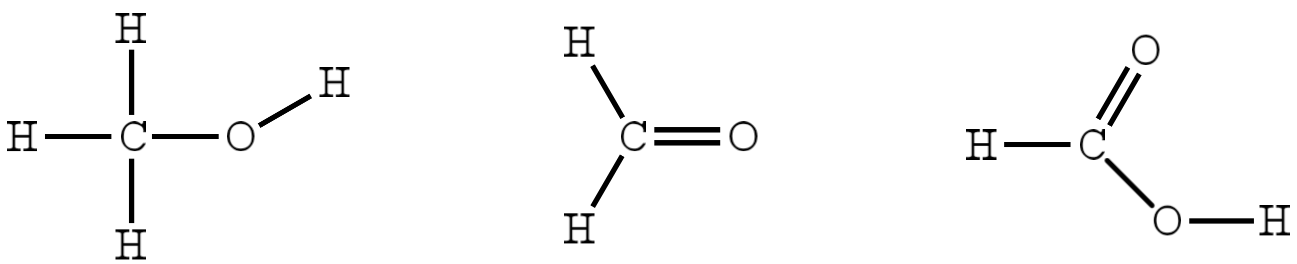
Alchol oxidation reactions

alcohol | carbonyl (aldehyde or ketone) | carboxyl



the O/H ratio increases

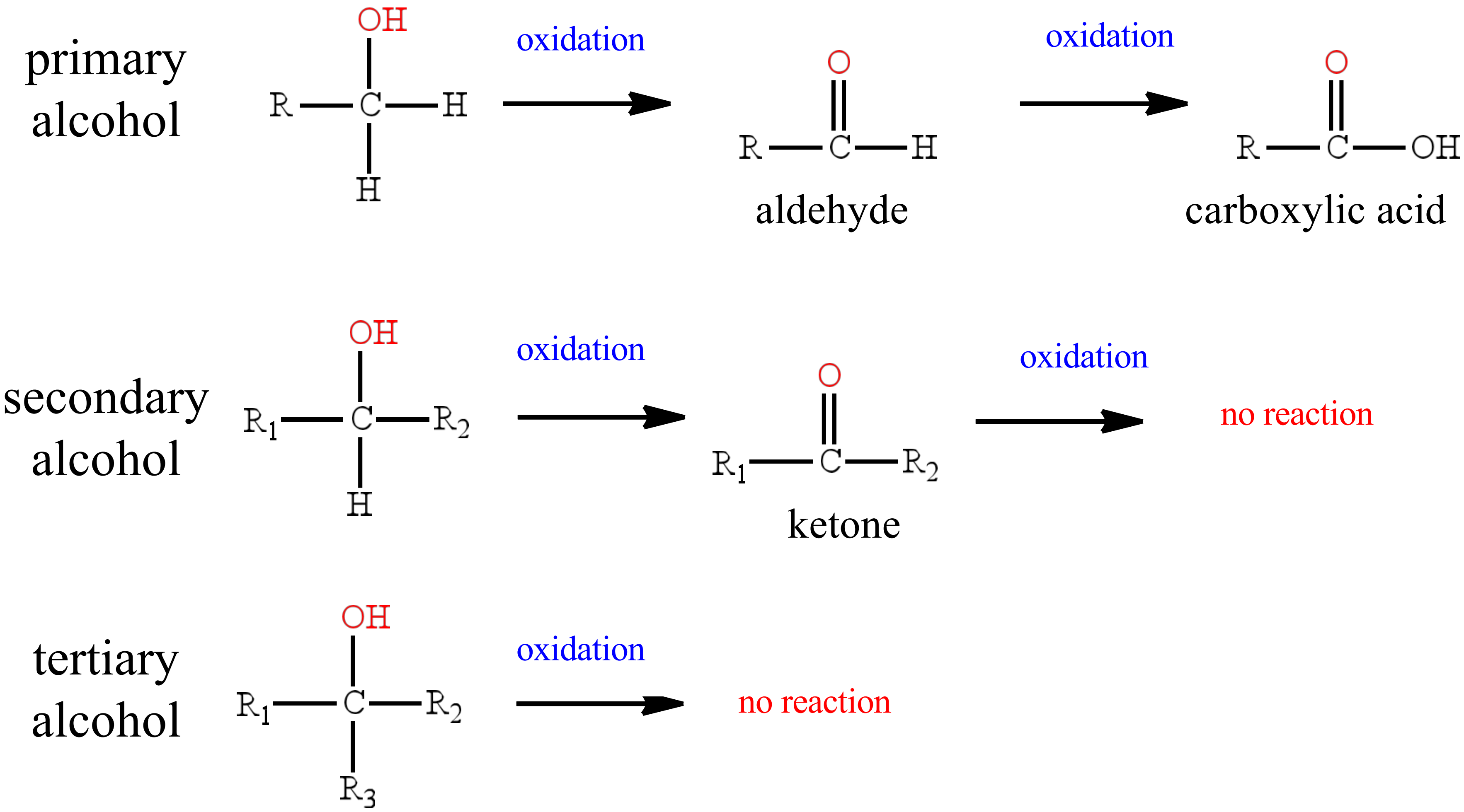
methanol | formaldehyde | formic acid



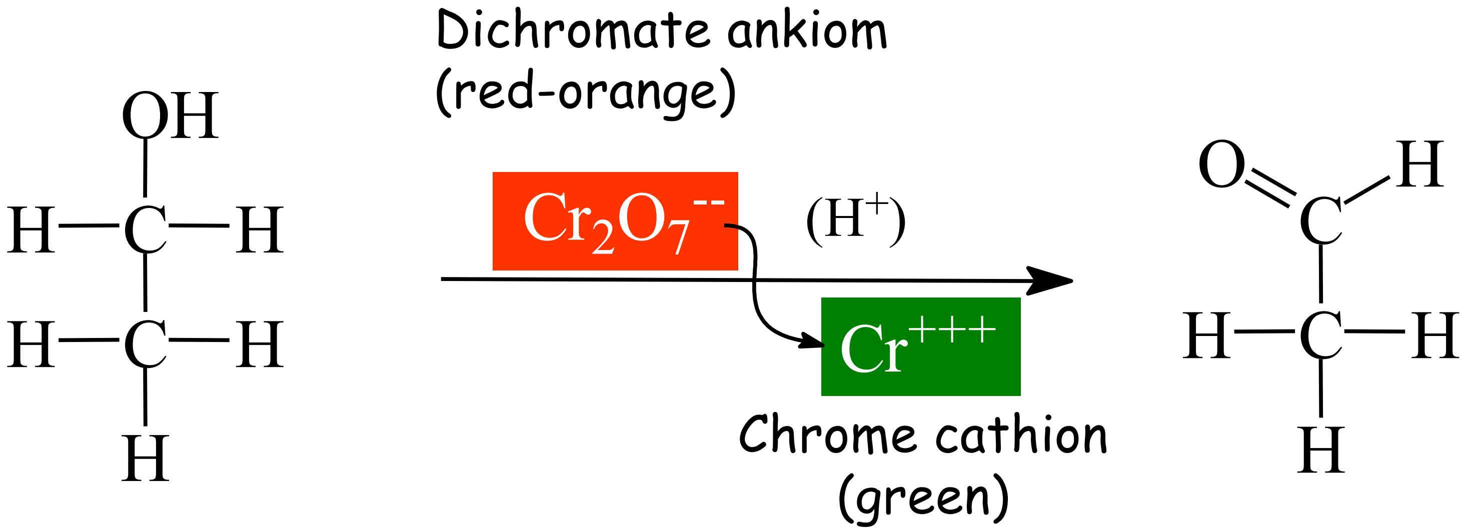
O/H 1/4 | 1/2 | 2/2

Alcohol oxidation reactions

The result of alcohol oxidation depends on the nature of the alcoholic C substituents and the presence of at least 1 H atom



The colour change of the dichromate ion in the oxidation reaction of alcohols (and aldehydes) is exploited in the rapid test of the level of ethanol in the breath

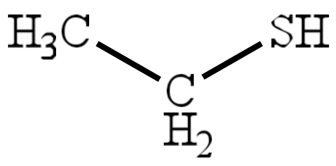


Ethanol

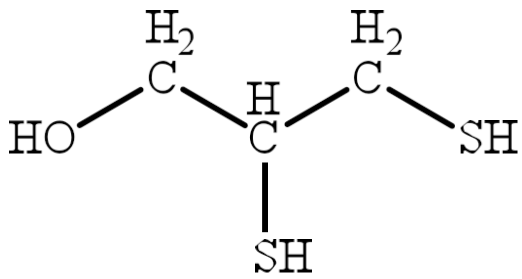
Ethanal

Functional groups of sulfur

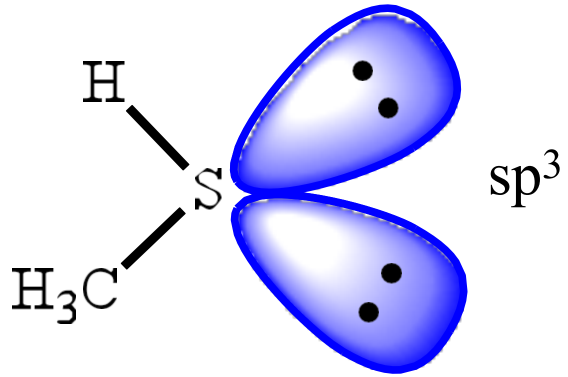
In practice the only important functional group of sulfur are thioalcohols or mercaptans (which resemble alcohols), which have the formula -SH



ethanethiol



dimercaptopropanol

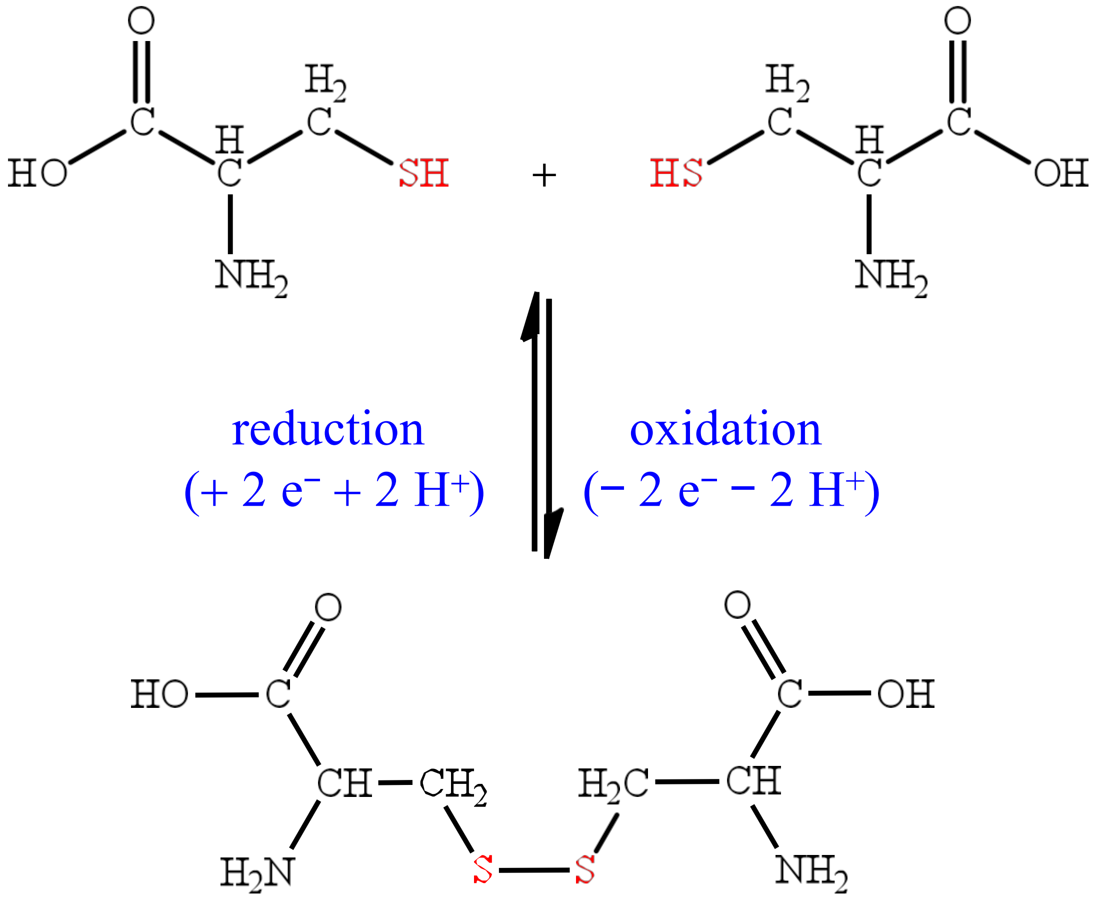


Sulfur is the homolog of oxygen and a thioalcohol has properties and geometry similar (not so really) to that of the corresponding alcohol, but unlike alcohols it behaves like weak acid with pK_A of about 9

$$CH_3CH_2SH\ (aq) + H_2O\ (l) \rightleftarrows CH_3CH_2S^-\ (aq) + H_3O^+\ (aq)$$

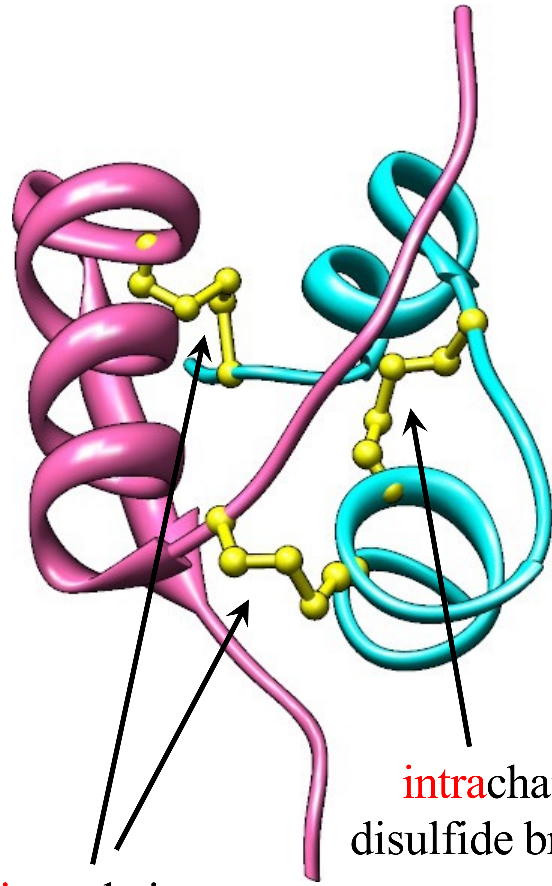
Thiols: oxidation reactions

cysteine (an aminoacid)



cystine
a dimer obtained
following oxidation
("disulfide bridge")

human insulin



intrachain
disulfide bridge

interchain
disulfide bridge

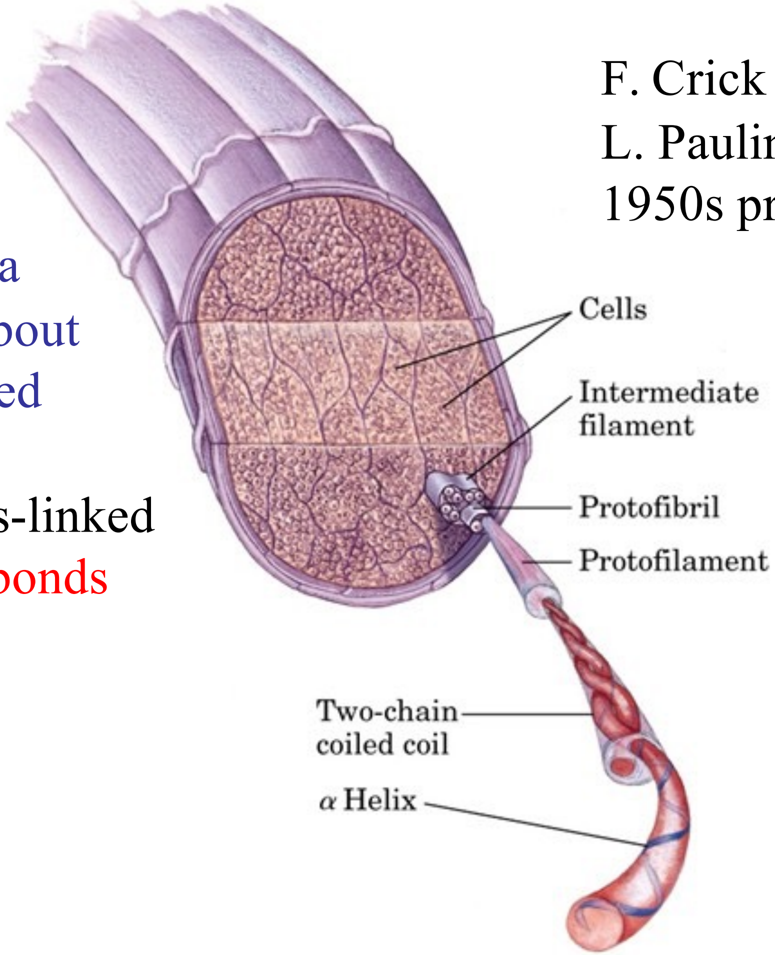
Keratin

most durable and less reactive protein of vertebrates.

- mammals: α-keratins
- birds & reptiles: β-keratins

Cross-section of a hair

F. Crick and
L. Pauling
1950s prediction

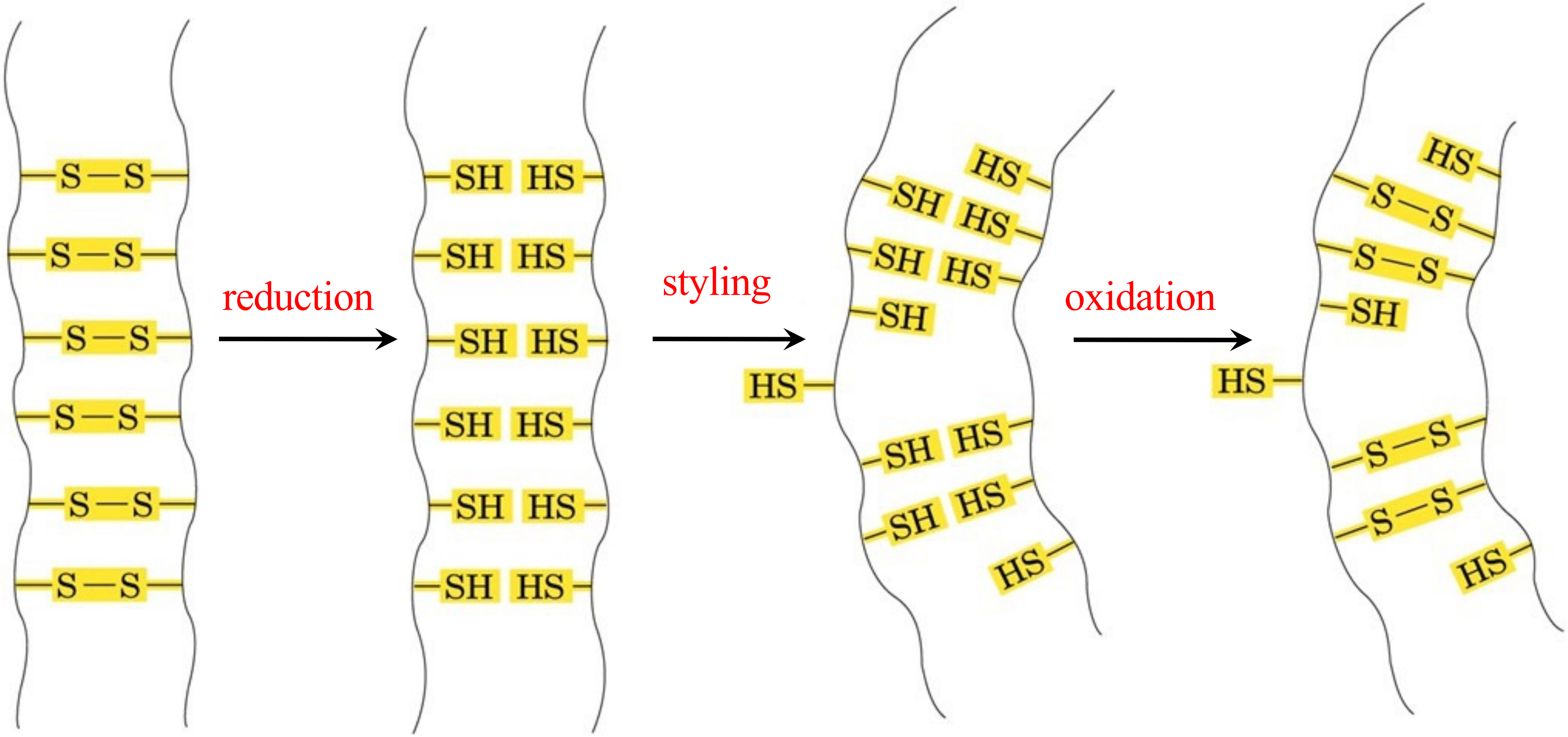


Keratin filaments are found in hair. In a single wool fiber with a diameter of about 20 μm, millions of filaments are bundled together within dead cells.
The individual keratin helices are cross-linked and stabilized by numerous disulfide bonds

The perm

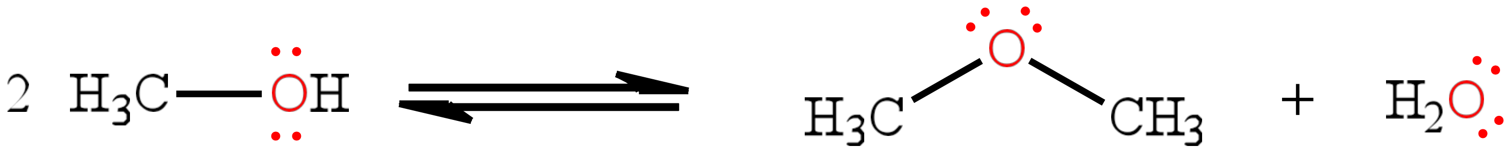
The perm is a biochemical engineering operation

keratin strands

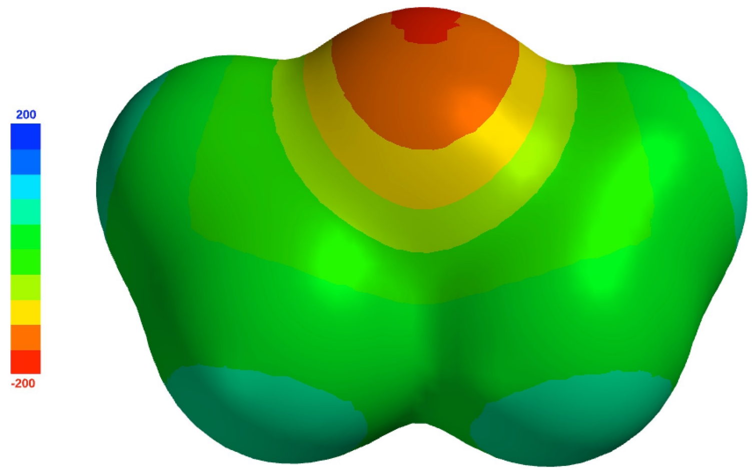


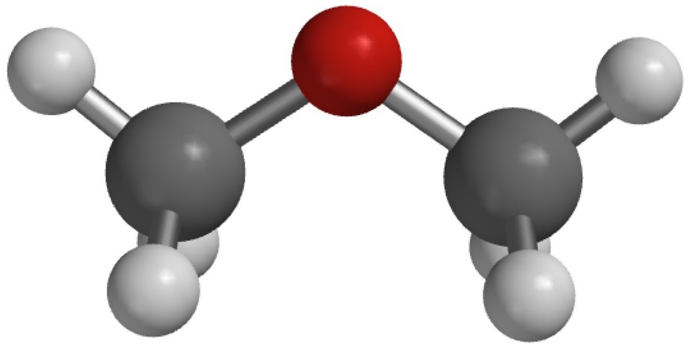
Ethers

Ether is the functional group deriving from the combination of two alcohols, with the elimination of a water molecule. These can be considered organic derivatives of water in which both hydrogens are replaced by organic groups. The bond angle at the oxygen is close to the tetrahedral angle



sp^3



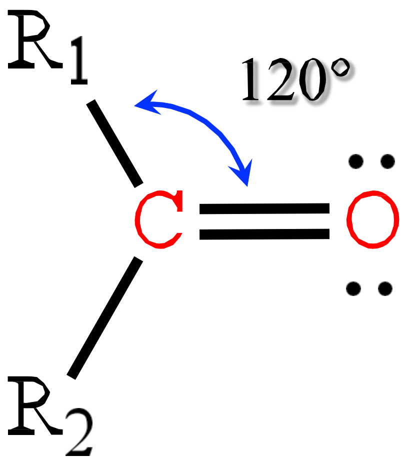


Ethers are molecules that behave like aprotic polar solvents, they lack hydrogen atoms available to form H-bonds. They are very volatile and have anesthetic properties.

Aldehydes and ketones

Can be considered oxidation products of primary and secondary alcohols. Consistently, the reduction of an aldehyde returns a primary alcohol and that of secondary alcohol a ketone.

They contain the carbonyl functional group (C = O)

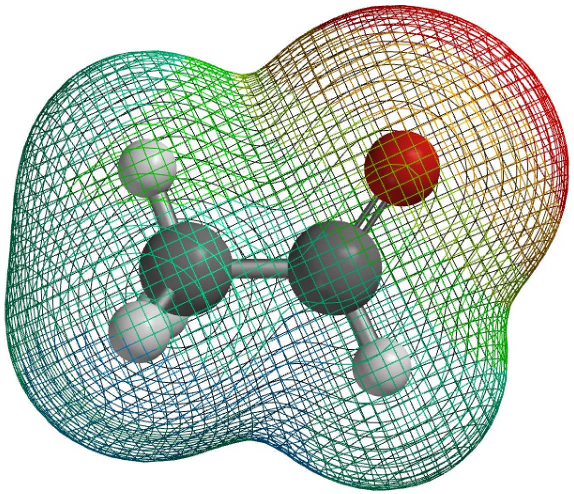


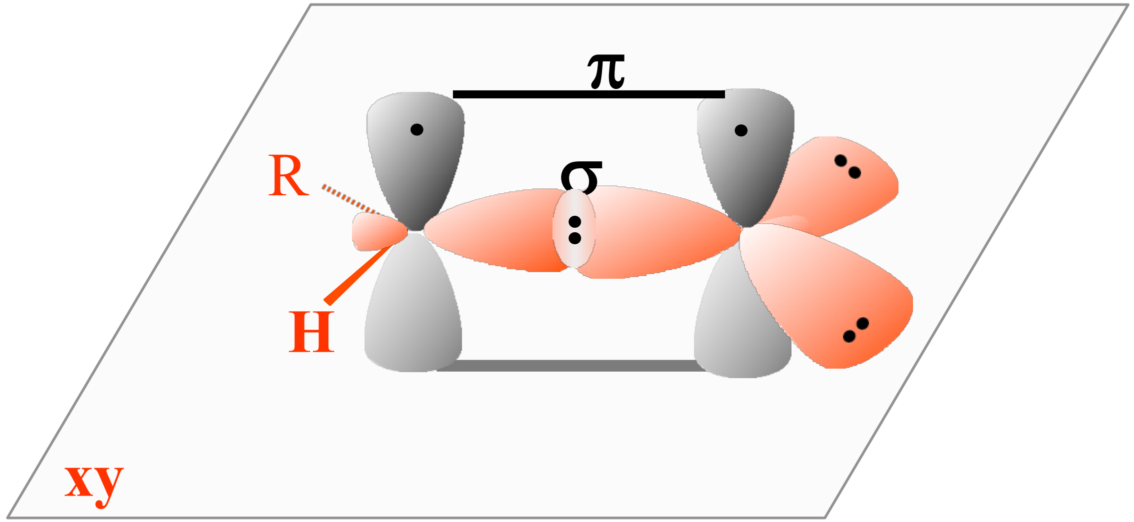
in the double bond between C and O we find a σ and π bond

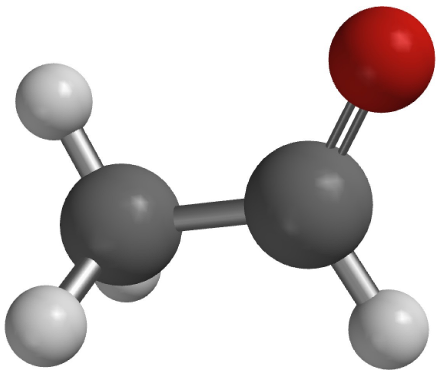
C and O have sp^2 hybridization and the carbonyl group is planar with angles of 120 °

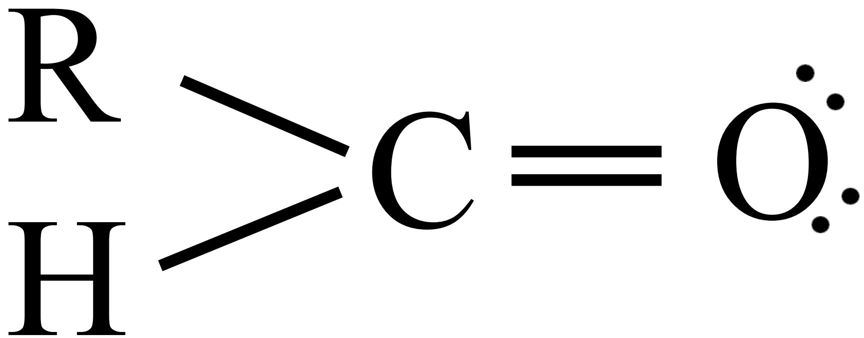
R_1 and R_2 can be two different groups and give rise to various functional groups containing the carbonyl group

Aldehydes contain a carbonyl group

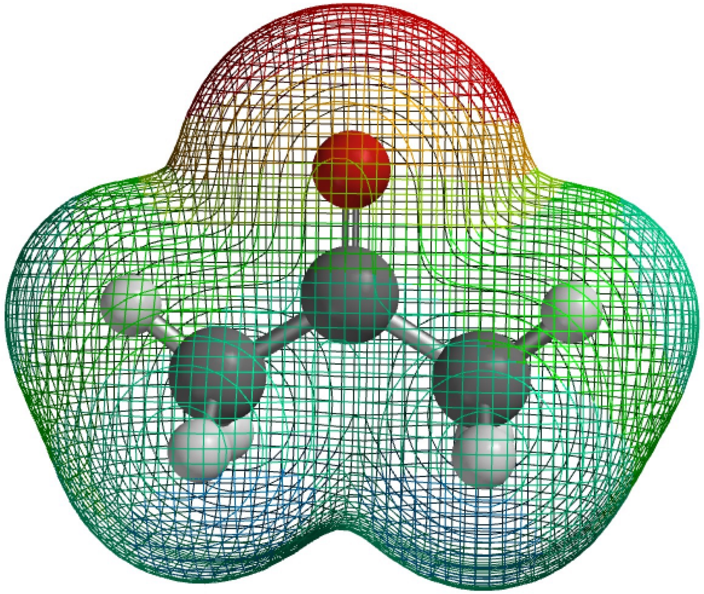


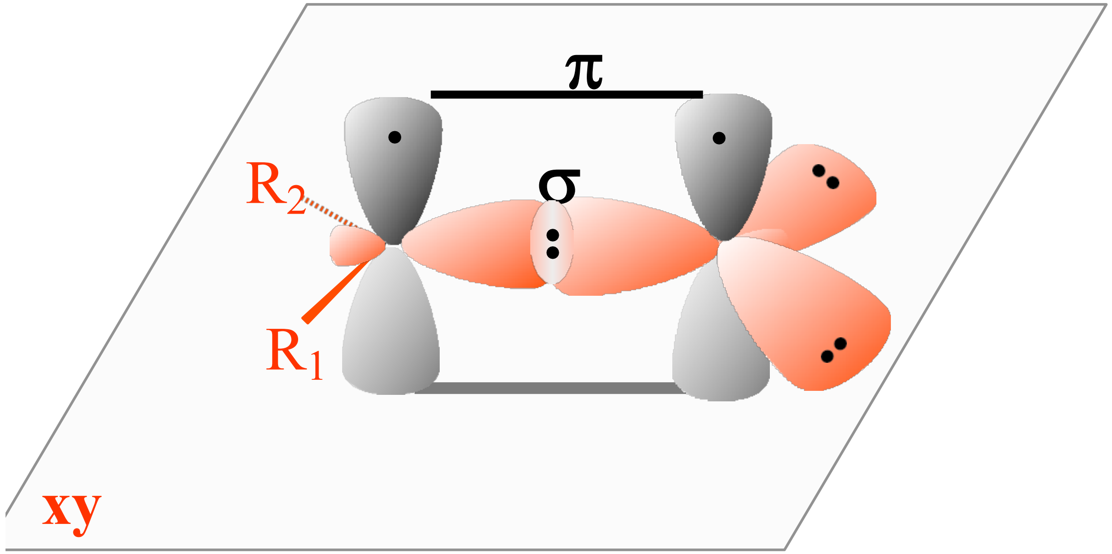


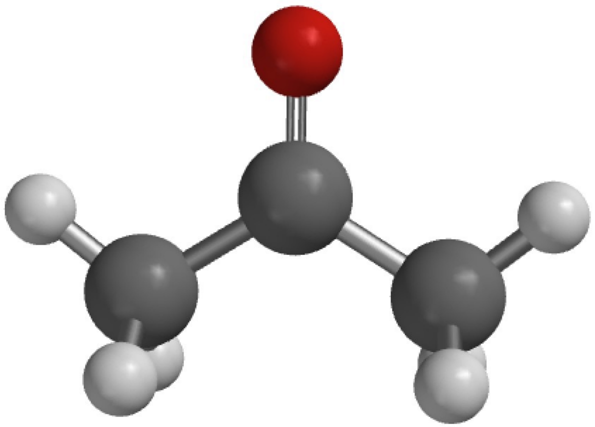


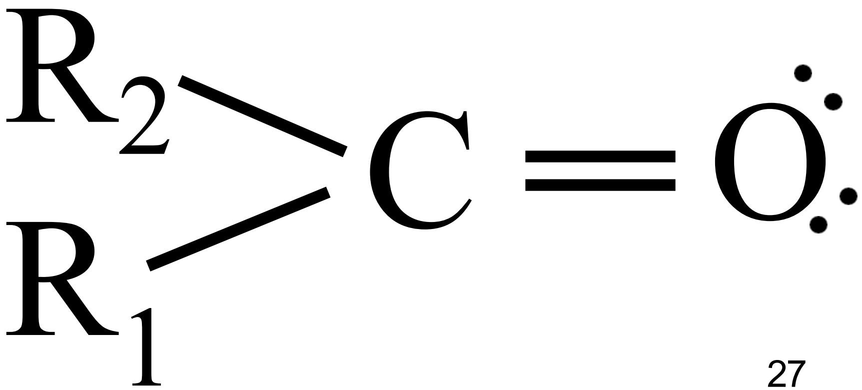


Ketones also contain a carbonyl group





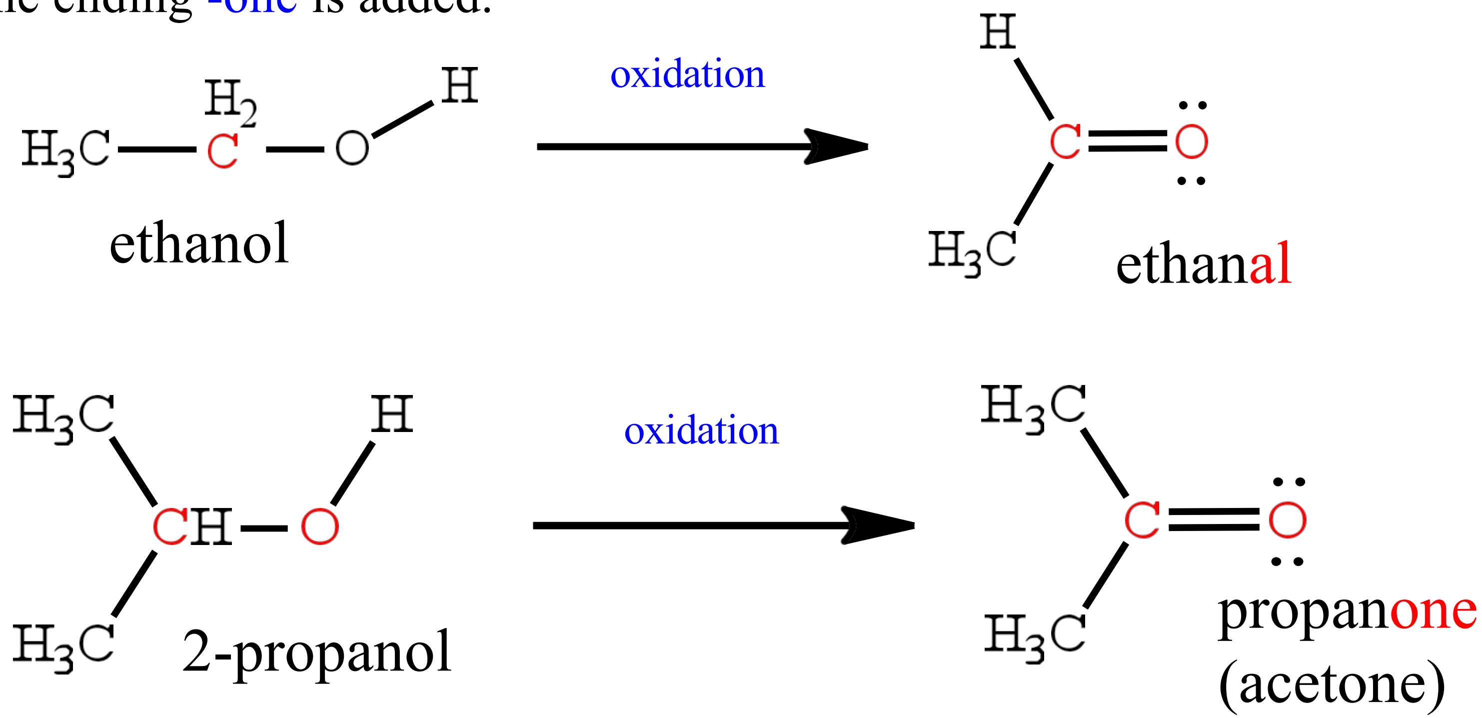




Nomenclature

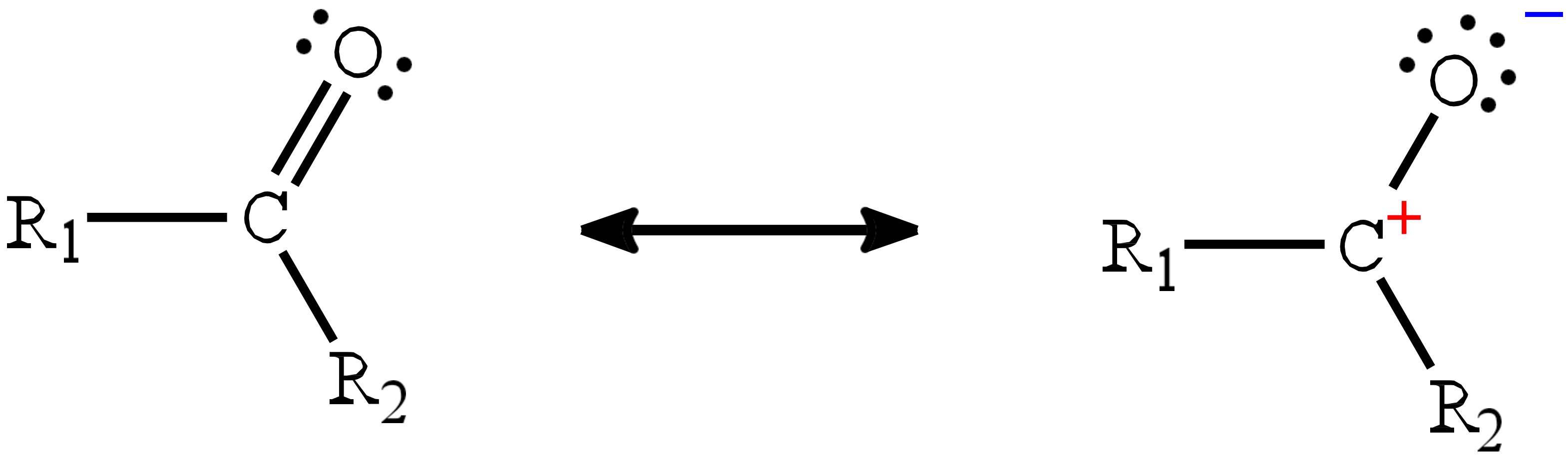
The name of aldehydes is given by the name of the corresponding hydrocarbon to which the ending -al is added

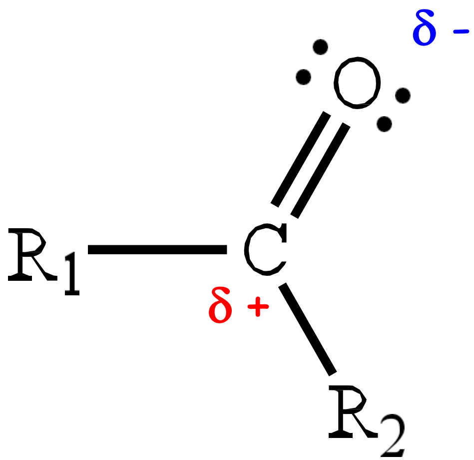
The name of ketones is given by the name of the corresponding hydrocarbon to which the ending -one is added.



The C = O group presents a planar trigonal geometry, therefore in the oxidation from alcohol to aldehyde or from alcohol to ketone, there is also a change of the corresponding hybridization of carbon from sp^3 to sp^2.

Two resonant limit structures





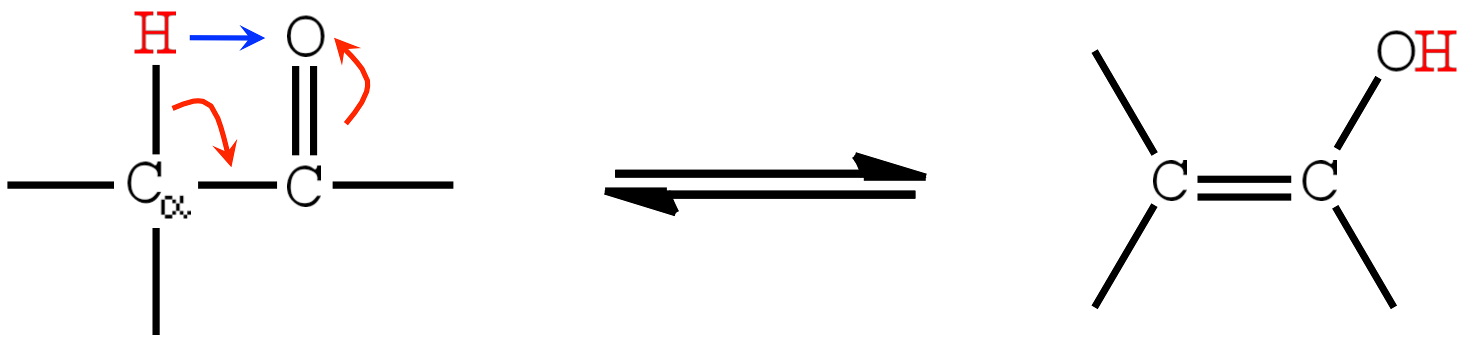
The carbonyl CO bond is polarized and this determines its reactivity

Keto-enol tautomerism

- Aldehydes and ketones can exist at equilibrium in the two keto and enol forms, which differ in the position of a proton and a double bond.

- This isomerism is called tautomerism, the forms are called tautomers and are two particular isomers that are in equilibrium.

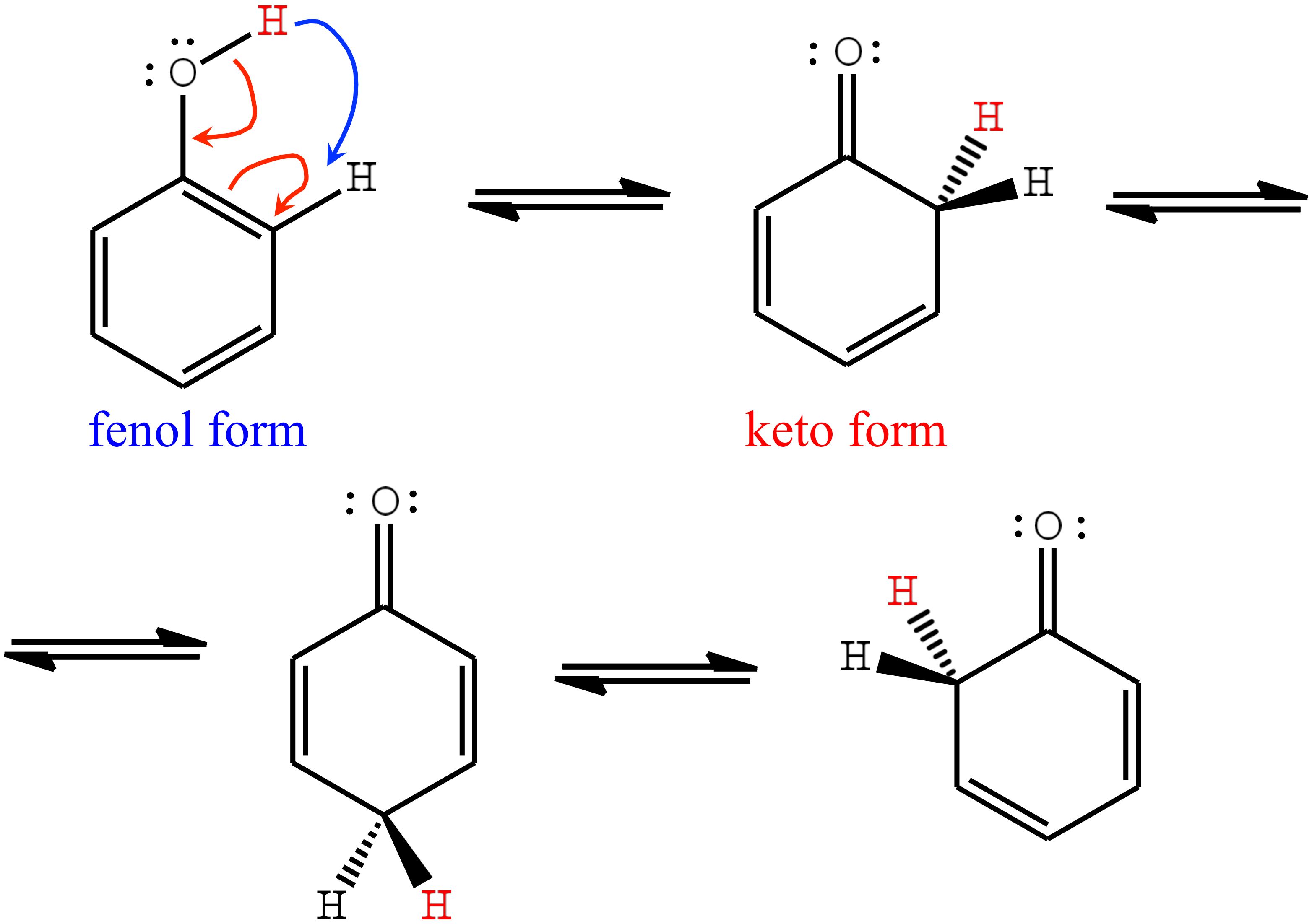
- A carbonyl compound, in order to exist in the enol form, must have a hydrogen atom linked to the carbon atom adjacent to the carbonyl (α carbon).



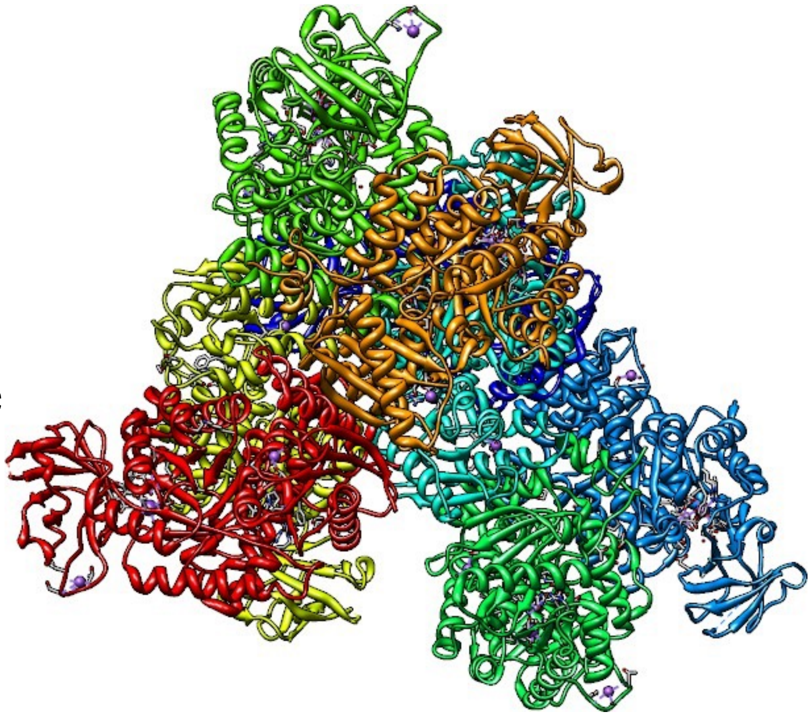
keto form

enol form

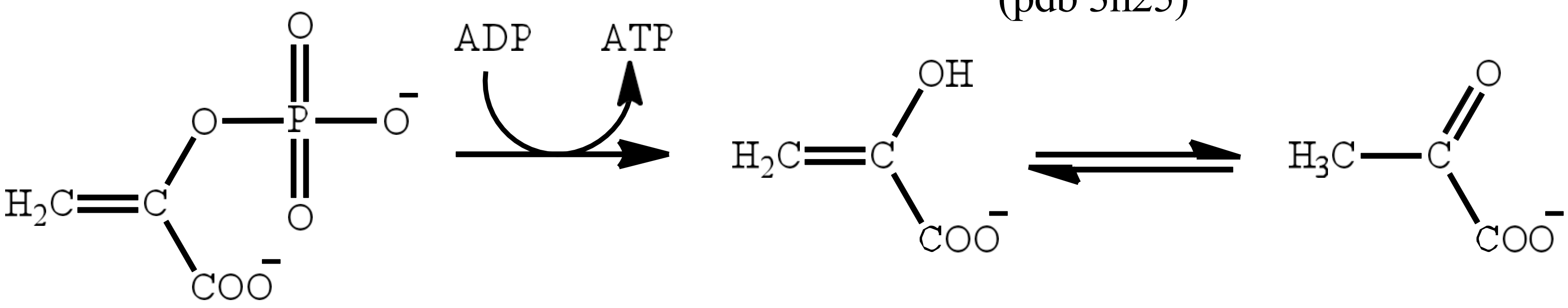
Keto-enol tautomerism in phenol



In the last stage of glycolysis, pyruvate kinase catalyzes the phosphorylation of ADP with the formation of enolpyruvate which spontaneously tautomerizes to the more stable keto form, pyruvate.



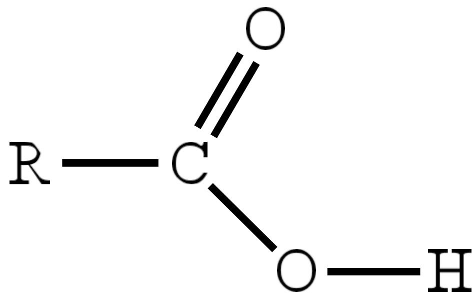
rabbit muscle piruvate kinase (pdb 3n25)



phosphoenolpyruvate enolpyruvate pyruvate

Carboxylic acids

functional group: carboxyl

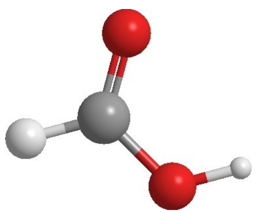


$R - COOH$

$R - CO_2H$

Nomenclature:

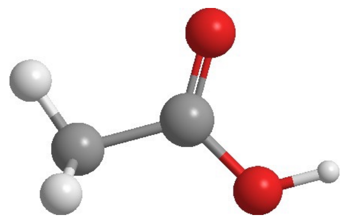
carboxylic acids are named by adding the -oic ending to the theme of the corresponding hydrocarbon name



$H{-}COOH$

methanoic acid

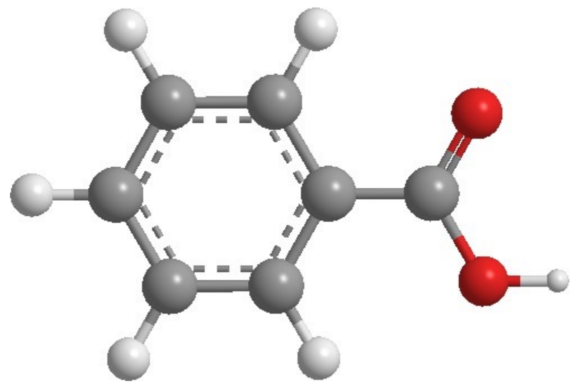
formic acid



$CH_3{-}COOH$

ethanoic acid

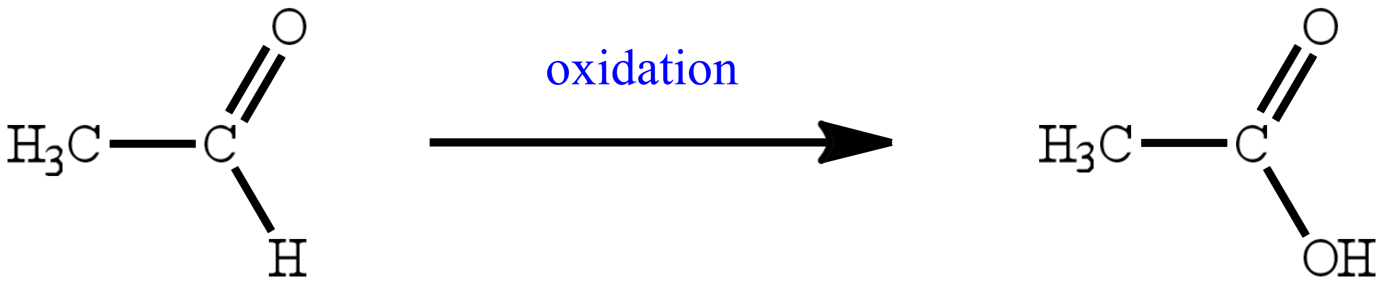
acetic acid



$C_6H_5{-}COOH$

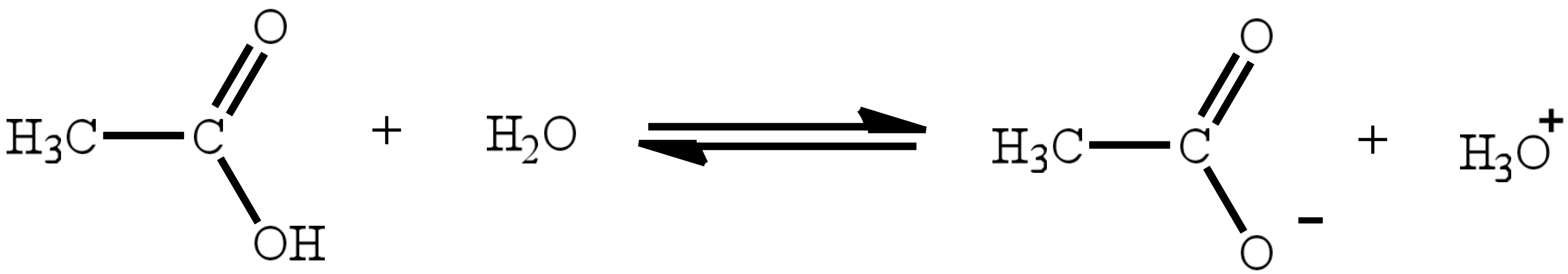
benzoic acid

Carboxylic acids are produced from the corresponding aldehydes:

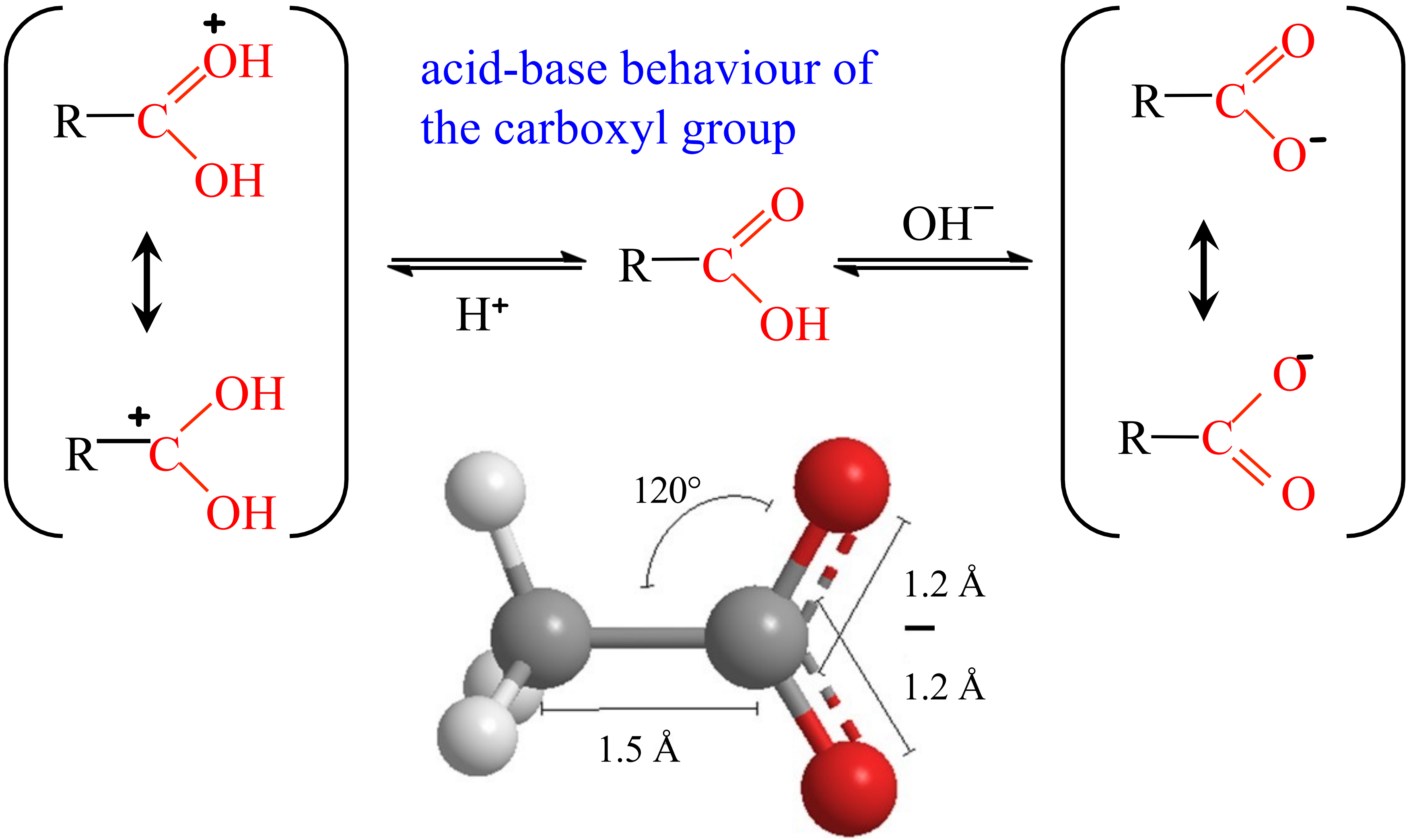


ethanal ethanoic acid

Carboxylic acids are weak acids, with pK_A values between 3 & 6

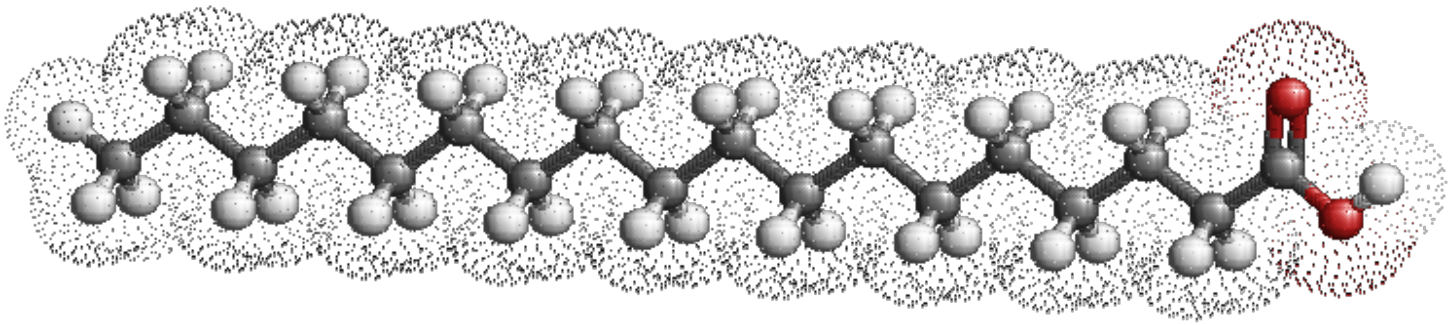


Resonance increases the acidity of the carboxyl group

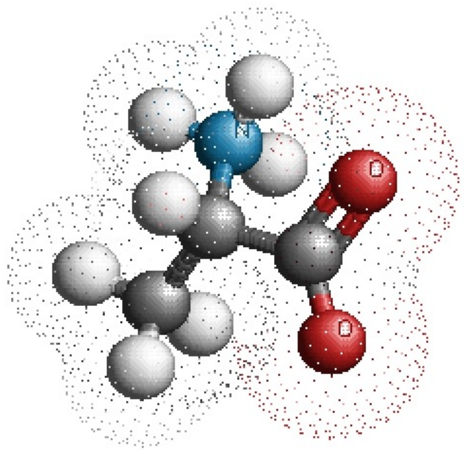


Carboxylic groups are present in (and characterize the chemical properties of) many important bio-molecules

palmitic acid (fatty acid)

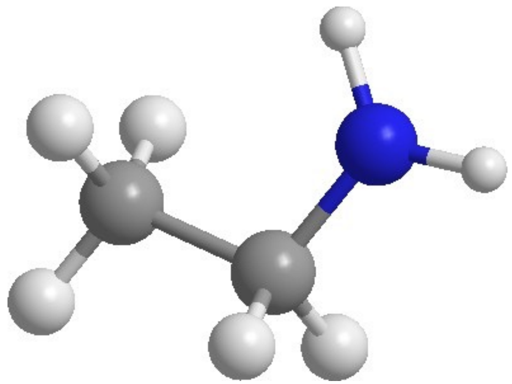


alanine (aminoacid)

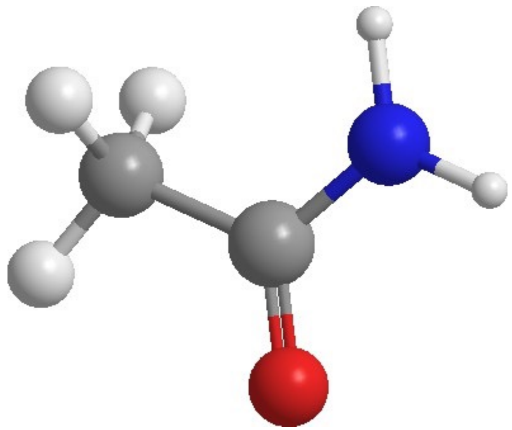


Functional groups of nitrogen

Amines

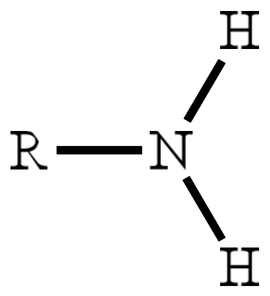


Amides

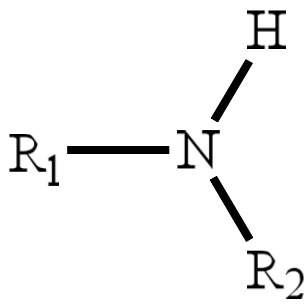


Amines

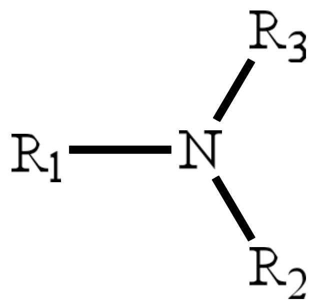
The amines having only one alkyl or aromatic group linked to nitrogen are called primary. The amines having the nitrogen atom bound to 2, 3 and 4 aromatic, aliphatic or alicyclic groups are termed secondary, tertiary and quaternary, respectively



primary

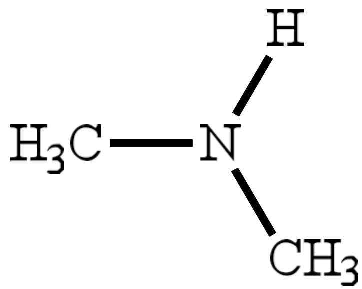


secondary

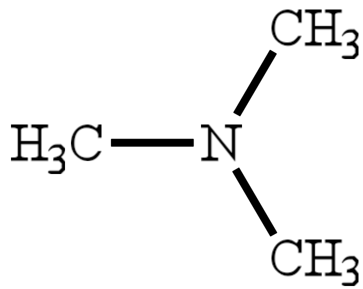


tertiary

methylamine

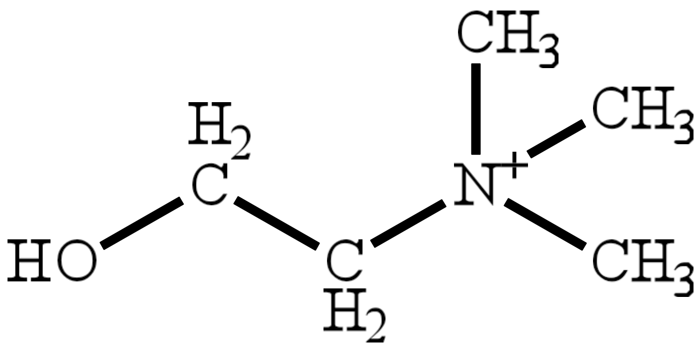


dimethylamine

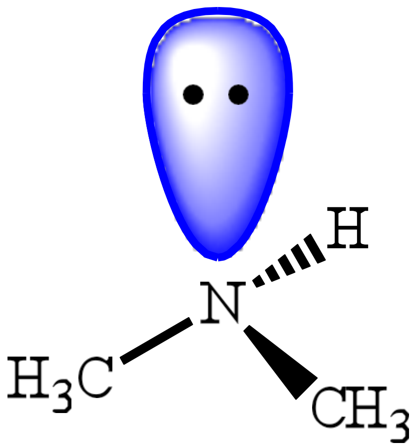


trimethylamine

The quaternary amines contain an ammonium ion bound to four organic compounds. A very important quaternary amine for the physiology is the choline (trimethyl-ethanol-ammonium ion)



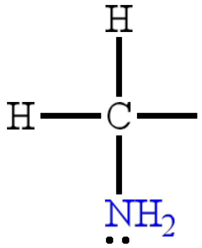
Amines are derivatives of ammonia with nitrogen having sp^3 hybridization and tetrahedral geometry, as in ammonia.



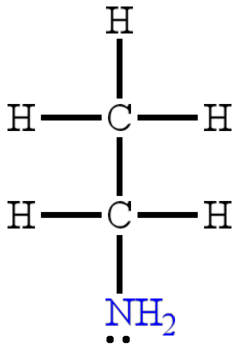
The lone pair in one of the 4 orbitals confers a basic character to the amines. All the amines are indeed weak bases with pK_B values between 4 and 6.

$$CH_3NH_2\,(aq) + H_2O\,(l) \rightleftarrows OH^-\,(aq) + CH_3NH_3^+(aq)$$

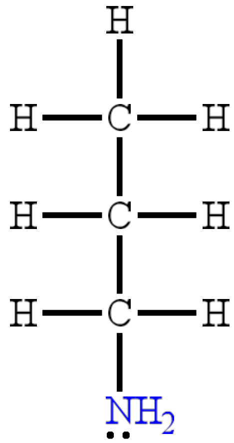
Aliphatic amines



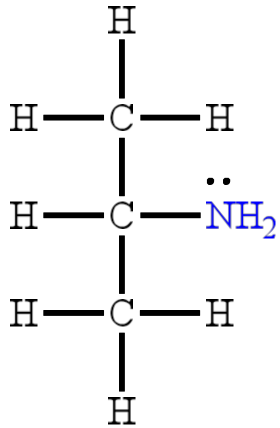
aminomethane
methylamine



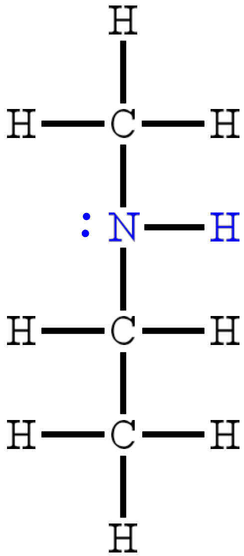
aminoethane
etilammina



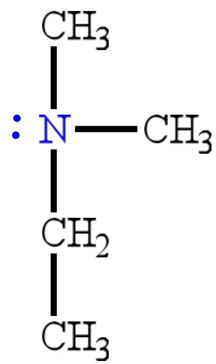
1-aminopropane
1-propylamine



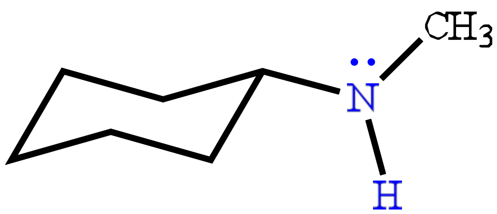
2-aminopropane
2-propylamine



N-methyl-aminoethane
methyl ethyl amine

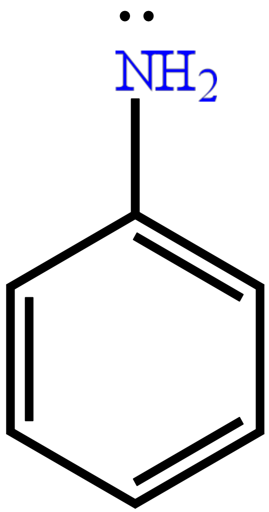


N,N-dimethyl-aminoethane
dimethyl-ethyl-amine

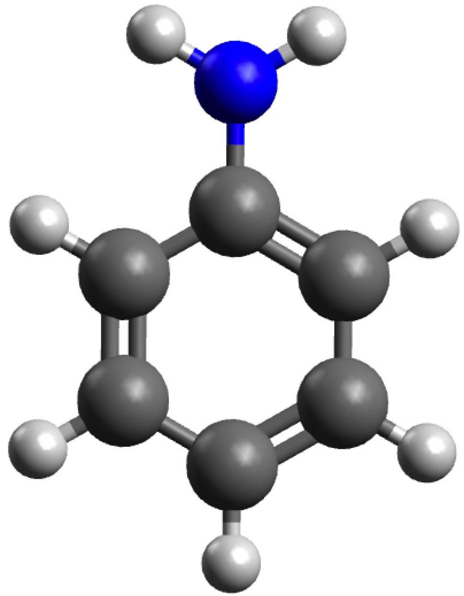


N-methyl-aminocyclohexane
methyl-cyclohexyl-amine

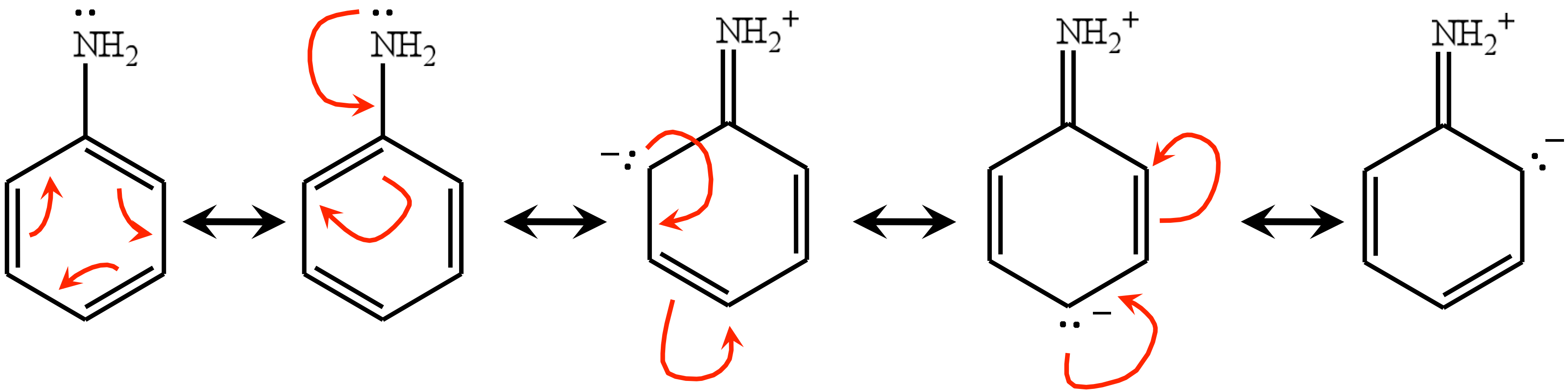
Aromatic amines



benzylamine
aminobenzene
phenylamine
aniline



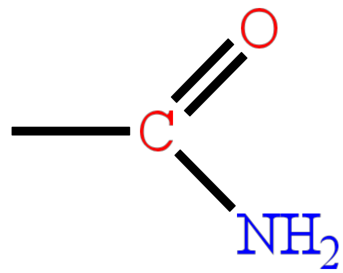
Aniline resonance
limit structures

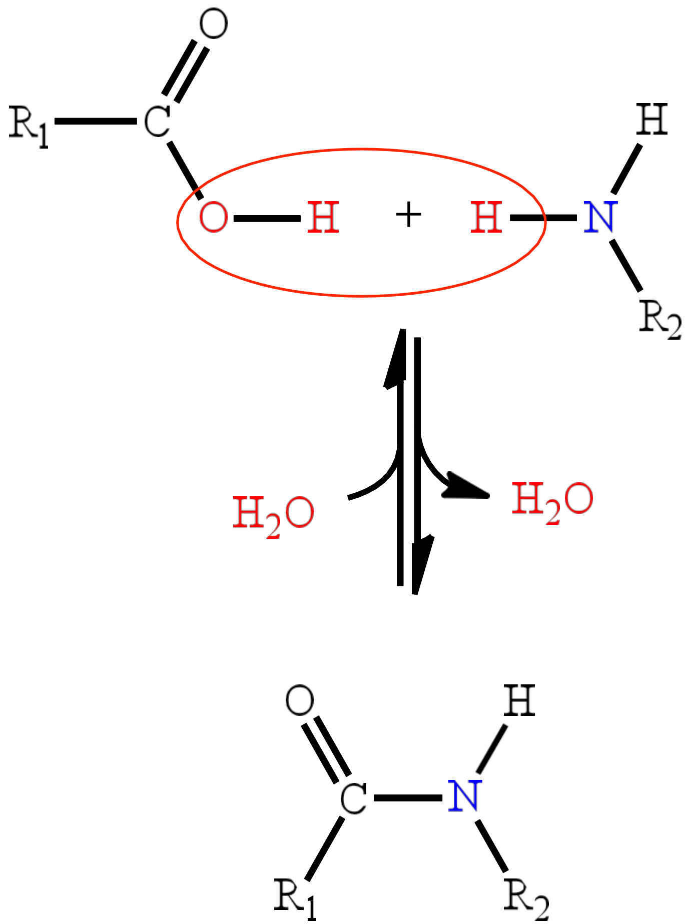


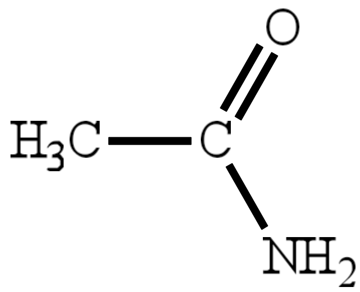
ortho *para* *ortho*

Amides

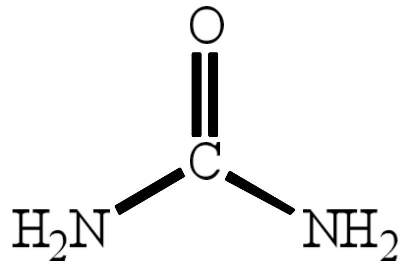
The amide functional group has formula –$CONH_2$ and is obtained by reaction of a carboxylic acid with an amine





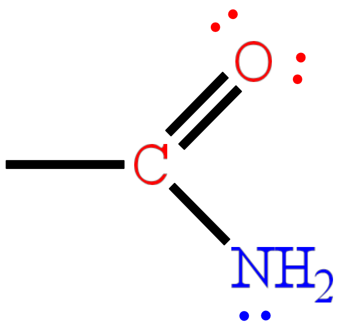


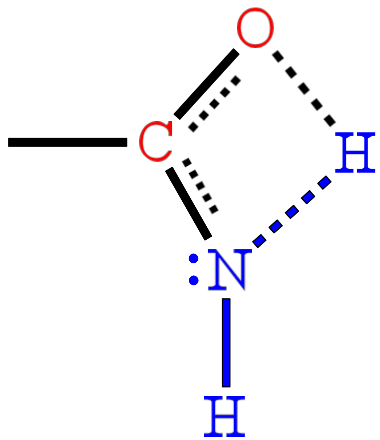
acetamide
(acetic amide)



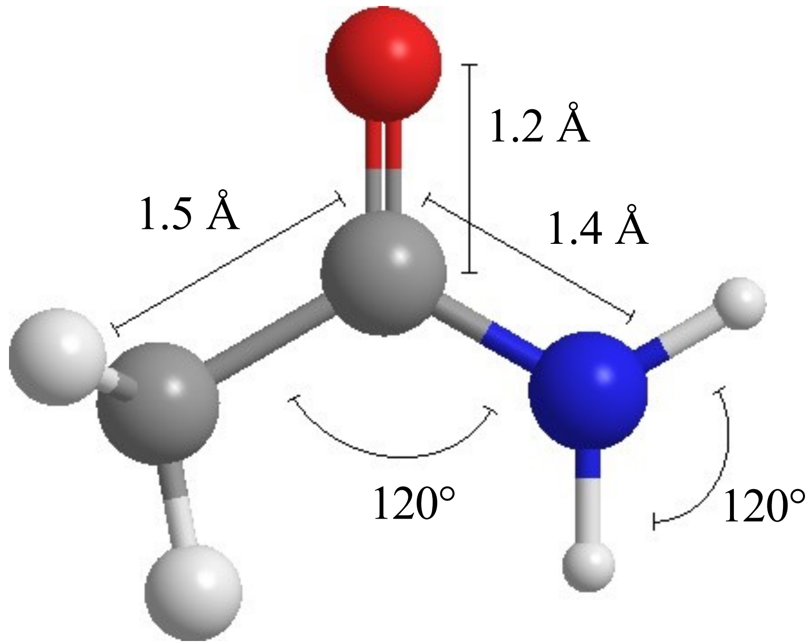
urea
(a diamide of carbonic acid)

The structure of the amide group allows the delocalization of the π binding orbital on three atoms C, O and N and this imposes the sp^2 geometry for the nitrogen in the delocalized O-C-N system: as a consequence amides have no basic character. To represent this structure, you can write the formula like this:





In this structure one of the nitrogen-linked hydrogen atoms is shared with the oxygen



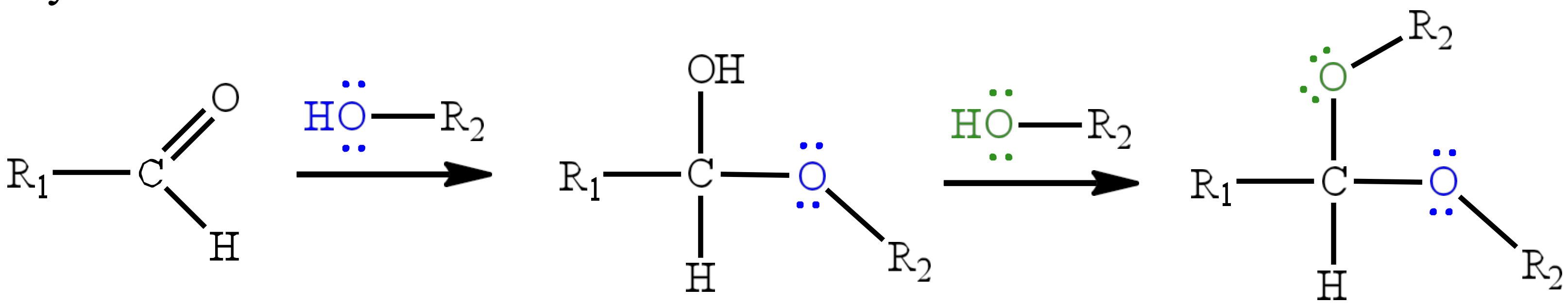
Functional groups deriving from the combination of other groups

The functional groups studied up to this point, account for more or less the most frequent compounds, but do not consider those compounds that derive from the reactions between groups.
The most reactive groups are those that contain oxygen

- anhydrides
- acetals and ketals
- esters

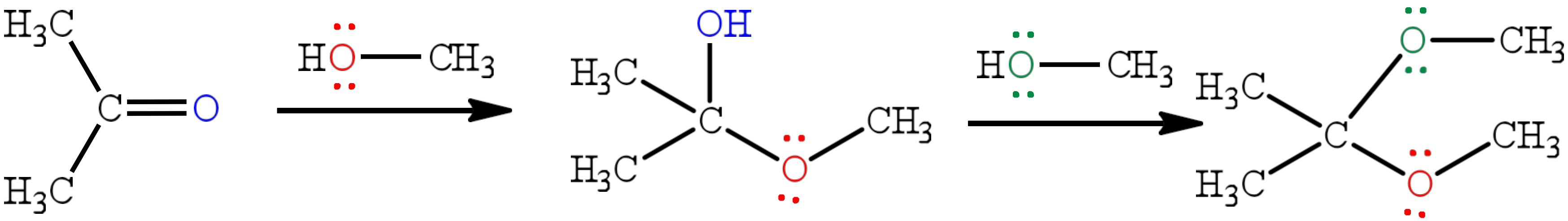
Acetals and ketals

The hemiacetals and acetals derive from the reaction of one or two alcohols with an aldehyde



aldehyde hemiacetal acetal

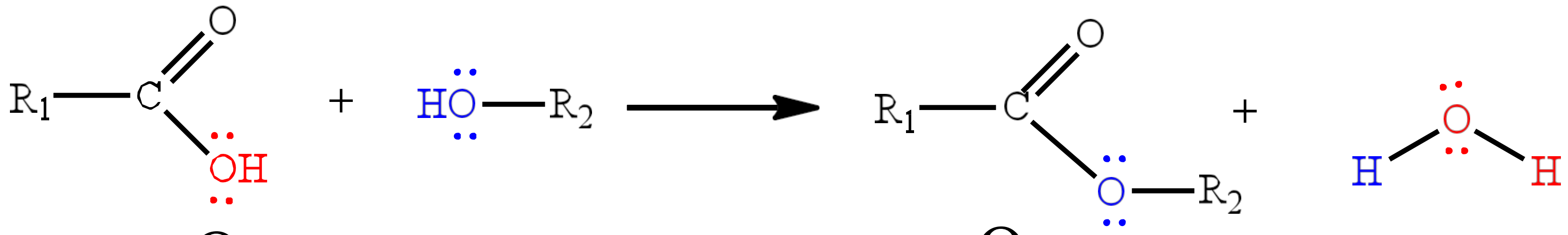
The hemiketals and ketals derive from the reaction of one or two alcohols with a ketone



ketone hemiketal ketal

Esters

The **ester** is the reaction product of an alcohol with an acid, with removal of a molecule of water



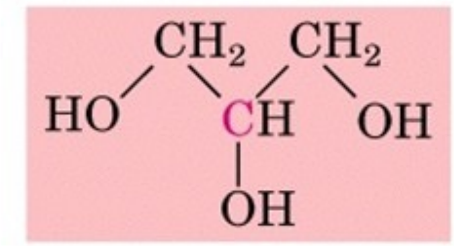
$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}OH + CH_3OH \rightleftharpoons CH_3\overset{\overset{\displaystyle O}{\|}}{C}{-}O{-}CH_3 + H_2O$$

acetic acid   methanol   methyl acetate

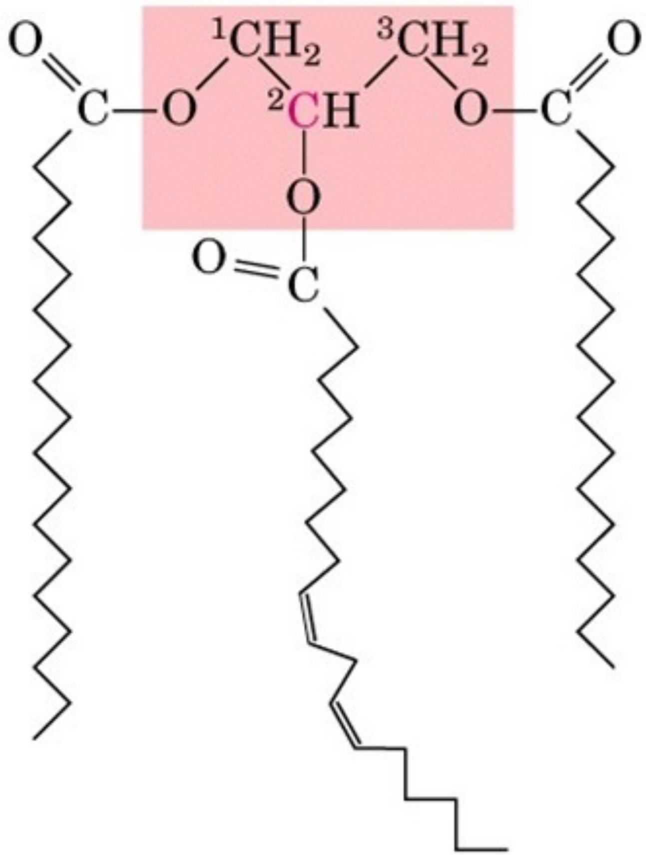
$$CH_3OH + H_3PO_4 \rightleftharpoons CH_3{-}O{-}PO_3H_2 + H_2O$$

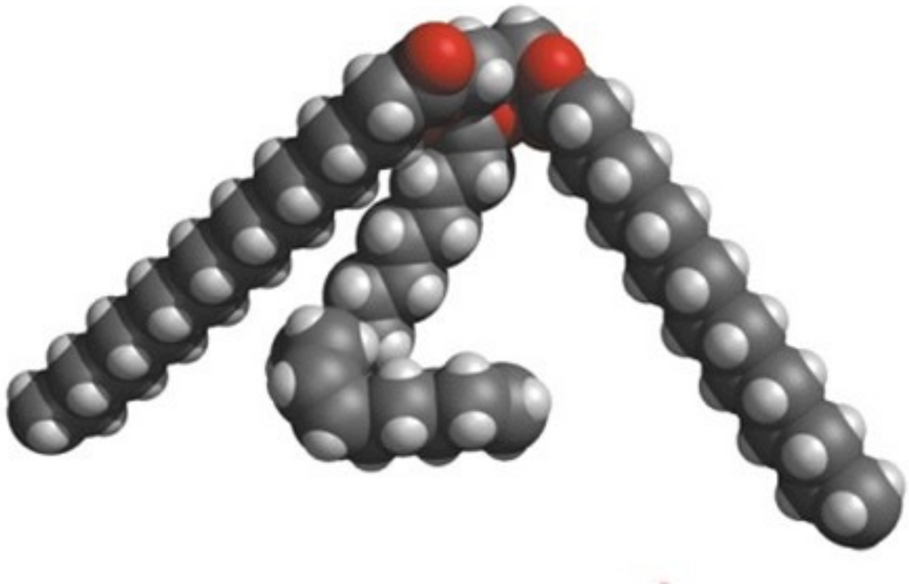
methanol   phosphoric acid   methyl phosphate

Triglycerides: glycerol esters with three fatty acids (lipid).



glycerol





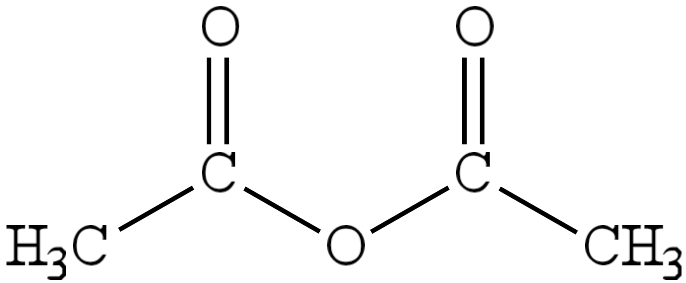
1-stearoyl-2-lineoyl-3-palmitoyl-glycerol

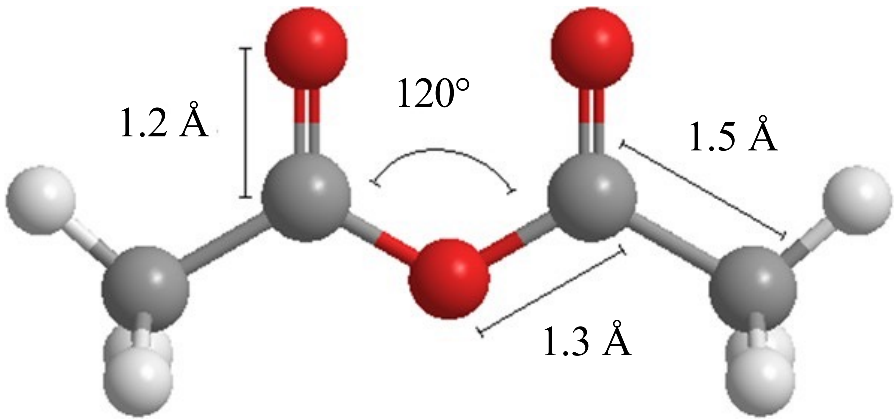
Anhydrides

an anhydride is the reaction product between two acids, with the elimination of a water molecule

$$2\ CH_3COOH \rightleftharpoons CH_3CO{-}O{-}CO{-}CH_3 + H_2O$$

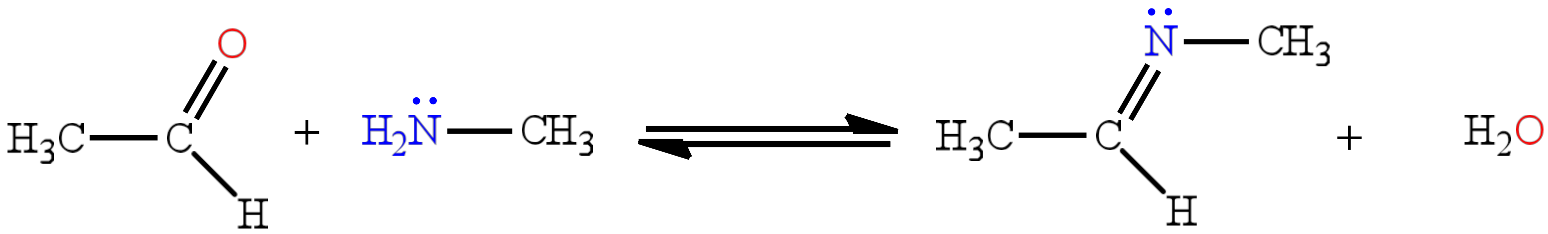
acetic acid — acetic anhydride



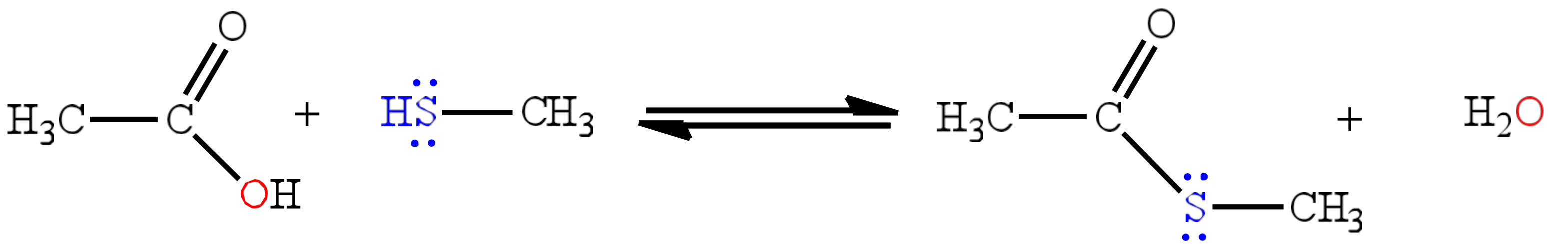


Other important reactions and compounds

Among the characteristic reactions of functional groups, the reactions between aldehydes and amines and those between carboxylic acids and thioalcohols are quite important

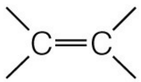
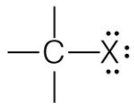
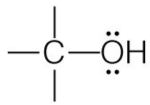
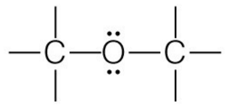
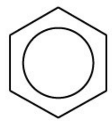


ethanal methyl amine Schiff base (an aldimine)



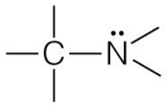
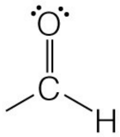
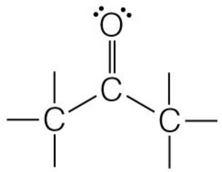
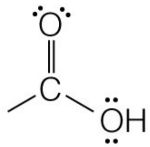
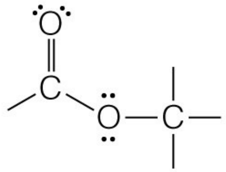
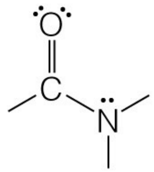
acetic acid methane thiol methyl thioacetate (a thioester)

Summary of Important Families of Organic Compounds

	Family						
	Alkane	**Alkene**	**Alkyne**	**Aromatic**	**Haloalkane**	**Alcohol**	**Ether**
Functional group	C—H and C—C bonds		—C≡C—	Aromatic ring			
General formula	RH	$RCH{=}CH_2$ $RCH{=}CHR$ $R_2C{=}CHR$ $R_2C{=}CR_2$	$RC{\equiv}CH$ $RC{\equiv}CR$	ArH	RX	ROH	ROR
Specific example	CH_3CH_3	$CH_2{=}CH_2$	$HC{\equiv}CH$		CH_3CH_2Cl	CH_3CH_2OH	CH_3OCH_3
IUPAC name	Ethane	Ethene	Ethyne	Benzene	Chloroethane	Ethanol	Methoxymethane
Common name[a]	Ethane	Ethylene	Acetylene	Benzene	Ethyl chloride	Ethyl alcohol	Dimethyl ether

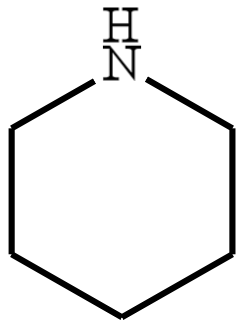
[a]These names are also accepted by the IUPAC.

Summary (cont.)

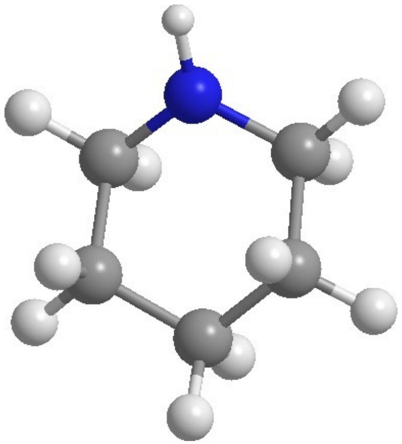
Family						
Amine	**Aldehyde**	**Ketone**	**Carboxylic Acid**	**Ester**	**Amide**	**Nitrile**
						$-C\equiv N$
RNH_2 R_2NH R_3N	$R\overset{\overset{O}{\|}}{C}H$	$R\overset{\overset{O}{\|}}{C}R'$	$R\overset{\overset{O}{\|}}{C}OH$	$R\overset{\overset{O}{\|}}{C}OR'$	$R\overset{\overset{O}{\|}}{C}NH_2$ $R\overset{\overset{O}{\|}}{C}NHR'$ $R\overset{\overset{O}{\|}}{C}NR'R''$	RCN
CH_3NH_2	$CH_3\overset{\overset{O}{\|}}{C}H$	$CH_3\overset{\overset{O}{\|}}{C}CH_3$	$CH_3\overset{\overset{O}{\|}}{C}OH$	$CH_3\overset{\overset{O}{\|}}{C}OCH_3$	$CH_3\overset{\overset{O}{\|}}{C}NH_2$	$CH_3C\equiv N$
Methanamine	Ethanal	Propanone	Ethanoic acid	Methyl ethanoate	Ethanamide	Ethanenitrile
Methylamine	Acetaldehyde	Acetone	Acetic acid	Methyl acetate	Acetamide	Acetonitrile

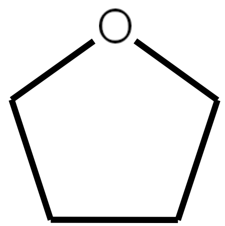
Heterocyclic compounds

Heterocycles are cyclic, aromatic or aliphatic compounds, containing atoms other than carbon. Among the important aliphatic heterocyclics:

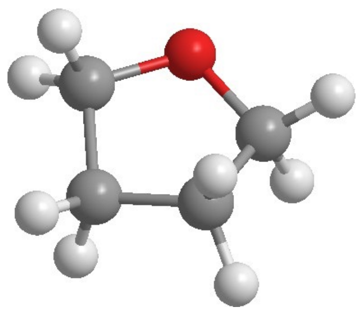


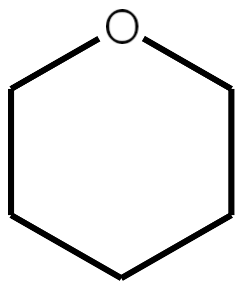
piperidine



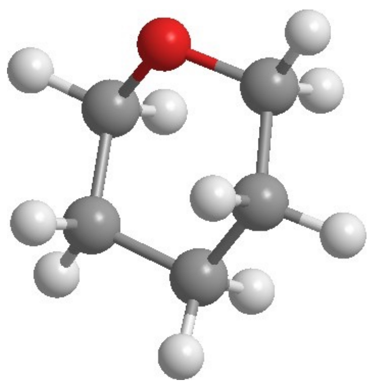


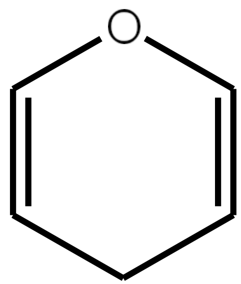
tetrahydrofuran



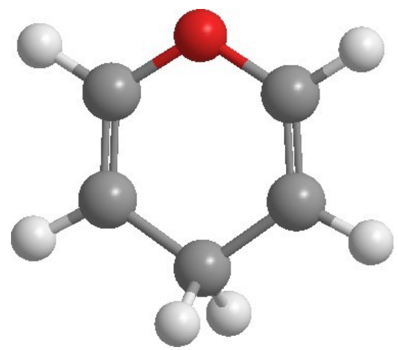


tetrahydropyran

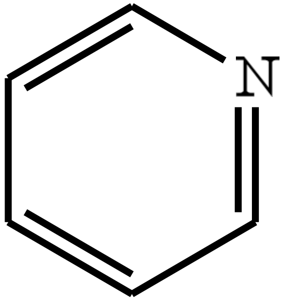




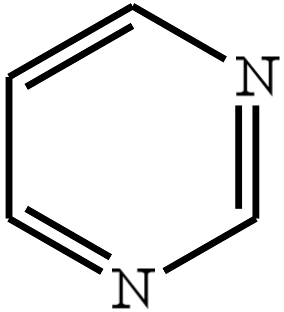
pyran



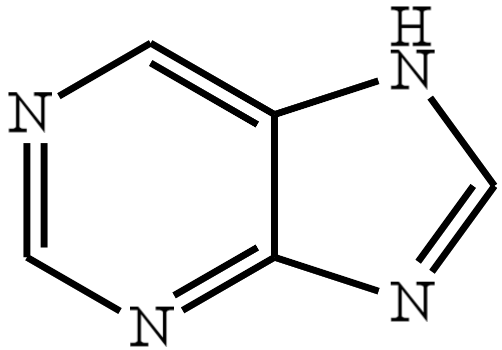
Important aromatic heterocycles :



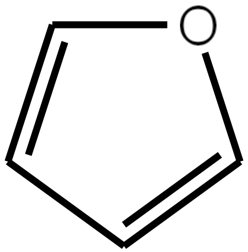
pyridine



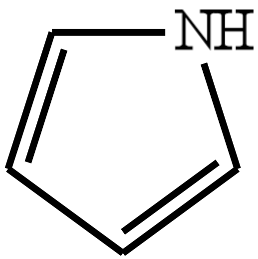
pyrimidine



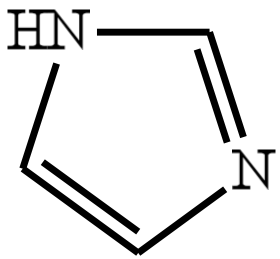
purine



furan



pyrrole



imidazole