Ministry of Public Health of Ukraine
Poltava State Medical University

Department of biological and bioorganic chemistry

Carbonyl compound aldehydes, ketones, carboxylic acids

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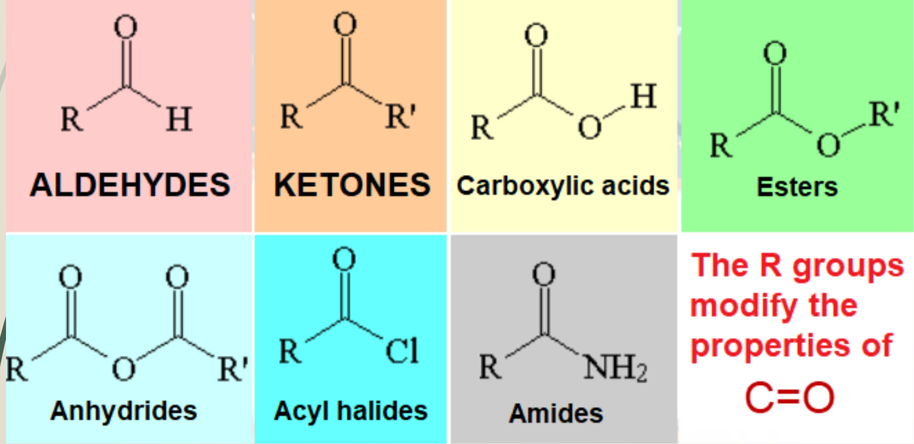
Lecture plan

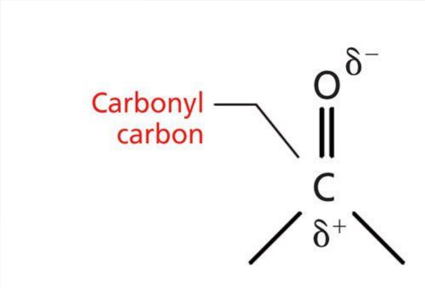
- The structure of the carbonyl group.
- Chemical properties of aldehydes.
- Chemical properties of ketones.
- Chemical properties of carboxylic acids.

The structure of the carbonyl group.

- The **carbonyl group** is a functional group composed of a carbon atom double-bonded to an oxygen atom: C=O.
- Carbonyl group **C=O** is present in **aldehydes, ketones, and carboxylic**



http://www.qorganica.es/QOT/T9/carbonilicos_e_exported/index.html



The oxygen has two lone pairs of electrons hanging around. These electrons make the oxygen more electronegative than carbon. The carbon is then partially postive (electrophillic) and the oxygen partially negative (nucleophillic).

Compounds containing a carbonyl group have higher melting and boiling points than hydrocarbons containing the same number of carbon atoms and are more soluble in polar solvents such as water. **The carbonyl group can enter into a variety of chemical reactions; nucleophilic reagents (electron-rich reagents) are attracted to the carbon atom, whereas electrophilic reagents (electron-seeking reagents) are attracted to the oxygen atom.**

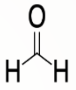
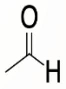
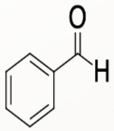
https://www.spectroscopyonline.com/view/carbonyl-group-part-i-introduction

Aldehydes.

- **The aldehyde** is a compound containing a functional group with the structure −CHO, consisting of a carbonyl center (a carbon double-bonded to oxygen) with the carbon atom also bonded to hydrogen and to any generic alkyl or side chain R group.

There are two general ways of naming aldehydes:

- The first method is based on the system used by the **IUPAC** and is often referred to as systematic nomenclature. This method assumes the **longest chain of carbon atoms** that contains the carbonyl group as the parent alkane. The aldehyde is shown by changing the suffix **-e** to **-al**. Because the carbonyl group of an aldehyde can only be on the end of the parent chain and, therefore, must be carbon 1, there is no need to use a number to locate it.
- The other method of nomenclature for aldehydes, referred to as **common nomenclature**, is to name them after the common name of the corresponding carboxylic acid; i.e., the carboxylic acid with the same structure as the aldehyde except that **—**COOH appears instead of **—**CHO. The acids are usually given a name ending in -ic acid. Aldehydes are given the same name but with the suffix -ic acid replaced by -aldehyde. Two examples are formaldehyde and benzaldehyde.

Structure	IUPAC (root names from alkanes)		Common (root names from common names of related carboxylic acids)	
	root	methane	root	formic acid
	aldehyde name	methanal	aldehyde name	formaldehyde
	root	ethane	root	acetic acid
	aldehyde name	ethanal	aldehyde name	acetaldehyde
	root	benzenecarboxylic acid	root	benzoic acid
	aldehyde name	benzenecarbaldehyde	aldehyde name	benzaldehyde

https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Supplemental_Modules_(Organic_Chemistry)/Aldehydes_and_Ketones/Nomenclature_of_Aldehydes_and_Ketones

Chemical properties of aldehydes.

Aldehydes are typically more reactive than ketones

due to the following factors:

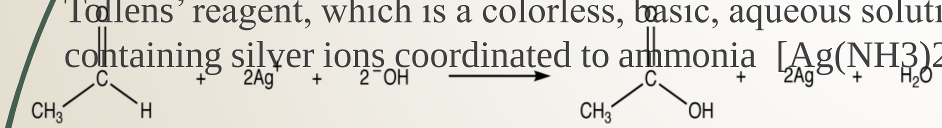
- Aldehydes are less hindered than ketones (a hydrogen atom is smaller than any other organic group).
- The carbonyl carbon in aldehydes generally has more partial positive charge than in ketones due to the electron-donating nature of alkyl groups.
- Aldehydes only have one e^- donor group while ketones have two.

Oxidation-reduction reactions of aldehydes

- The carbon atom of a carbonyl group has a relatively high oxidation state. The most common and characteristic oxidation reaction is the conversion of aldehydes to carboxylic acids: **RCHO → RCOOH**.
- Aldehydes can be reduced to primary alcohols:

$RCHO \rightarrow RCH_2OH$.

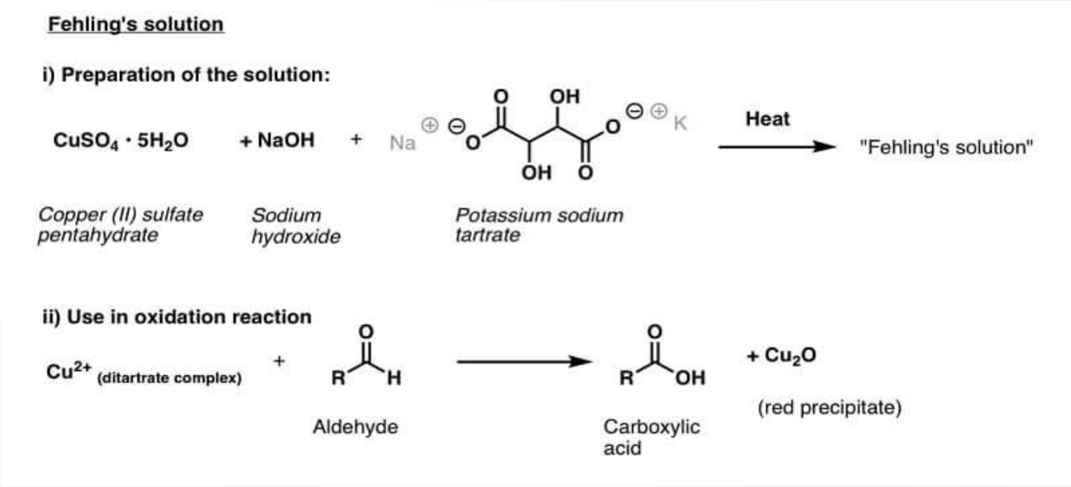
- Useful tests for aldehydes, Tollens' test, Trommers', Fehling's test, take advantage of this ease of oxidation by using Ag(+) and Cu(2+) as oxidizing agents (oxidants).
- **Tollens' test,** also known as silver-mirror test, is a qualitative laboratory test used to distinguish between an aldehyde and a ketone. It exploits the fact that aldehydes are readily oxidized, whereas ketones are not. Tollens' test uses a reagent known as Tollens' reagent, which is a colorless, basic, aqueous solution containing silver ions coordinated to ammonia [Ag(NH3)2+] .



$CH_3CHO + 2Ag^+ + 2\,^-OH \rightarrow CH_3COOH + 2Ag + H_2O$

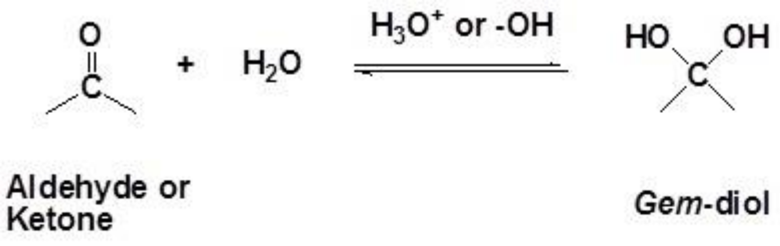
https://chem.libretexts.org/Courses/Brevard_College/CHE_202%3A_Organic_Chemistry_II/01%3A_Aldehydes_and_Ketones/1.05%3A_Oxidation_of_Aldehydes_and_Ketones

- **Fehling's test.**
- This test helps to do detect the presence of carbohydrates in a solution (**glucose in urine**), because the carbohydrates having free or potentially free carbonyl groups (aldehyde or ketone) can act as reducing sugars.
- Fehling's solution and Benedict's solution are variants of essentially the same thing. Both contain complexed copper(II) ions in an alkaline solution.
- Fehling's solution contains copper(II) ions complexed with tartrate ions in sodium hydroxide solution. Complexing the copper(II) ions with tartrate ions prevents precipitation of copper(II) hydroxide.
- Benedict's solution contains copper(II) ions complexed with citrate ions in sodium carbonate solution. Again, complexing the copper(II) ions prevents the formation of a precipitate - this time of copper(II) carbonate.



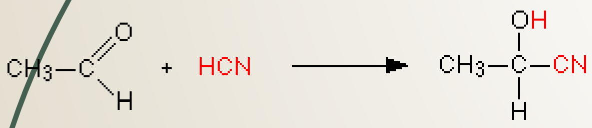
Reactions of nuclephilic addition (A_N)

Nucleophilic addition of H2O



Nucleophilic addition of HCN

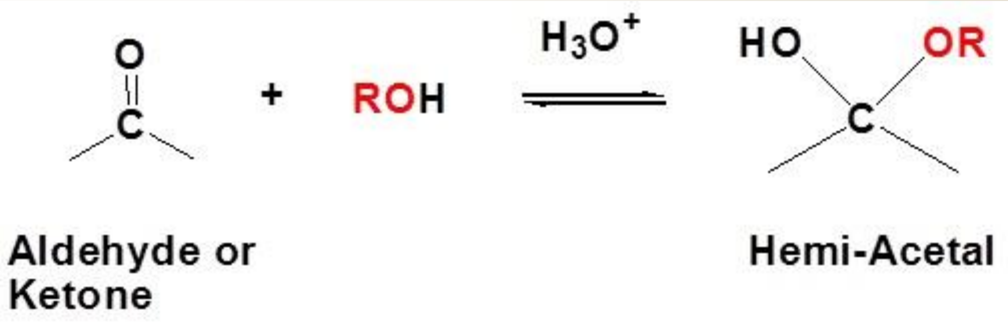
(formation of hydroxyalkanenitrile (cyanohydrins))

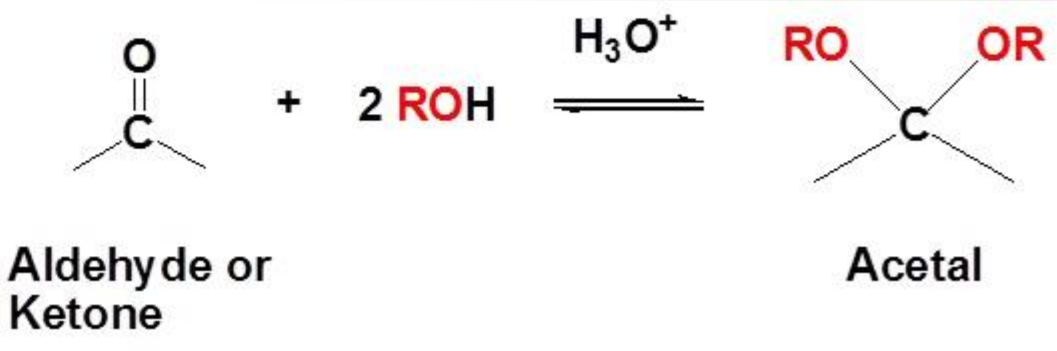


ethanale **2-hydroxy-2-methylpropanenitrile**

Nucleophilic addition of alkohols

(formation of hemiacetal and acetal)



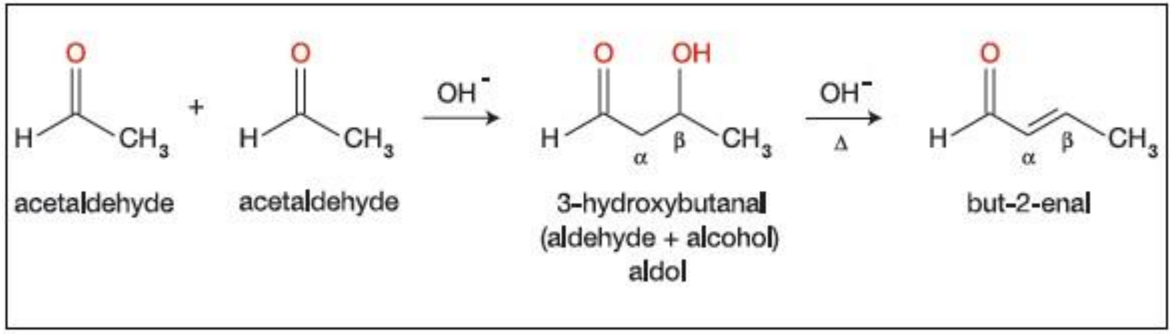


https://chem.libretexts.org/Courses/Athabasca_University/Chemistry_360%3A_Organic_Chemistry_II/Chapter_19%3A_Aldehydes_and_Ketones%3A_Nucleophilic_Addition_Reactions

The reaction of aldol condensation

- Aldol condensation reactions signify an essential class of reactions for the formation of carbon-carbon bonds. An aldol reaction involves the condensation of two carbonyl compounds to form a ß-hydroxyaldehyde or ß-hydroxyketone, the aldol product.

- The typical aldol reaction involves self condensation of the reactant ketone or aldehyde wherein one molecule adds to the other of the same type. An example of a self-condensation with acetaldehyde as the sole reactant.

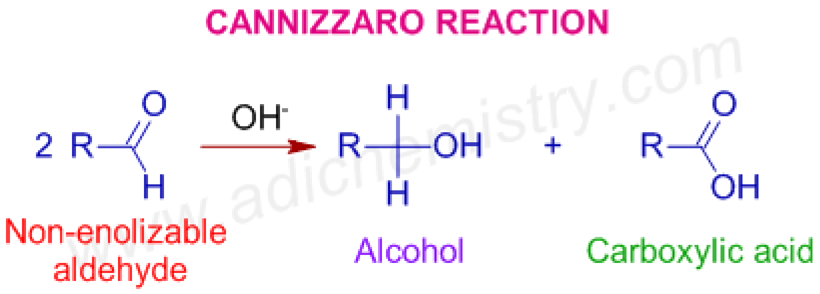


Aldolases there are enzymes that catalyses an aldol reaction (creating an aldol) or its reverse (cleaving an aldol), such as fructose-bisphosphate aldolase of glycolysis and gluconeogenesis.

https://www.azom.com/article.aspx?ArticleID=8887

The reaction of disproportionation (dismutation, Cannizzaro’s).

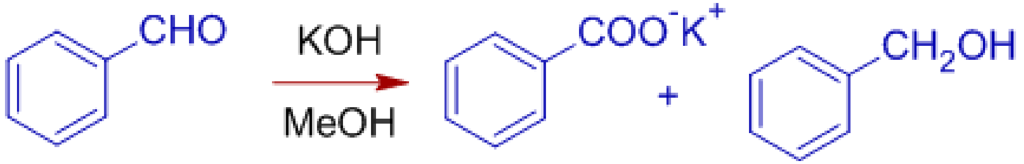
The **Cannizzaro reaction**, named after its discoverer Stanislao Cannizzaro, is a chemical reaction that involves the base-induced disproportionation of two molecules of a non-enolizable aldehyde (formaldehyde and benzaldehyde): one molecule of aldehyde is **reduced** to the corresponding **alcohol**, while a second one is **oxidized** to the **carboxylic acid**.



Formaldehyde is disproportionated to formic acid and methyl alcohol.

$$2\,HCHO \xrightarrow{NaOH} HCOO^{-}Na^{+} + CH_3OH$$

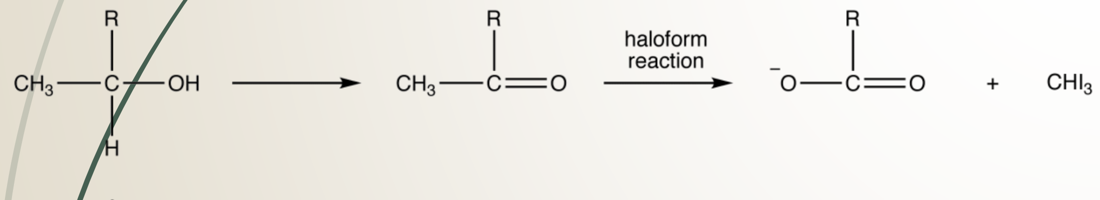
Benzaldehyde can be converted to benzoic acid and benzyl alcohol.



https://www.adichemistry.com/organic/namedreactions/cannizzaro/cannizzaro-1.html

Haloform reactions of aldehydes and ketones

The haloform reaction is the reaction of a methyl ketone with chlorine, bromine, or iodine in the presence of hydroxide ions to give a carboxylate ion and a haloform. There is one aldehyde that undergoes the haloform reaction, which is acetaldehyde.



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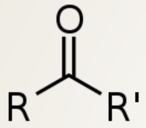
When the halogen used is iodine, the haloform reaction can be used to identify methyl ketones because iodoform is a yellow solid with a characteristic odor. The test is known as the iodoform test. Alcohols also give a positive iodoform test because, under the reaction conditions, they are oxidized to the corresponding methyl ketone, or, in the case of ethanol to acetaldehyde, which is the only aldehyde that undergoes haloform reaction.

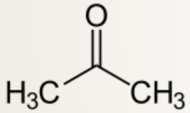
https://chem.libretexts.org/Bookshelves/Ancillary_Materials/Reference/Organic_Chemistry_Glossary/Haloform_Reaction#:~:text=The%20haloform%20reaction%20is%20the,haloform%20reaction%2C%20which%20is%20acetaldehyde.

Ketones.

Ketones contain a carbonyl group linked to two carbon-containing radicals:



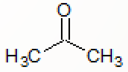
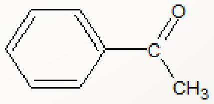
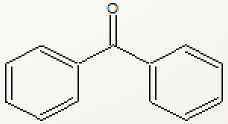
The simplest ketone is propanone or acetone with the formula:



Acetone - one of the types of ketone bodies (they also include acetoacetic and beta-hydroxybutyric acids), is synthesized in the liver and serves as a source of energy for the brain and muscles (especially the myocardium). An increase in blood concentration - ketonemia, is characteristic of fasting, an insulin-dependent type of diabetes mellitus.

Ketone derivatives are: - ketoses – monosaccharides such as fructosab ribulose;
- steroid hormones (testosteron);
-purine, pyrimidine nitogenouse bases;
-Ketoacids (acetoacetic, oxalic, keto-glutaric) ets.

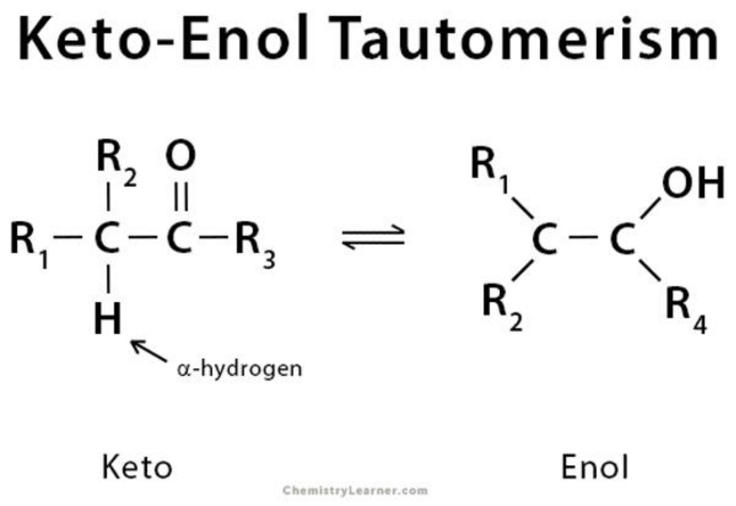
- The IUPAC system of nomenclature assigns a characteristic suffix of **-one** to ketones.

Compound	Systematic	Common
	propane ↓ propanone	acetone or dimethyl ketone
	1-phenylethane ↓ 1-phenylethanone	acetophenone or methyl phenyl ketone
	benzophenone	diphenyl ketone

https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Supplemental_Modules_(Organic_Chemistry)/Aldehydes_and_Ketones/Nomenclature_of_Aldehydes_and_Ketones

Chemical properties of ketones.

- Keto-enol tautomerization
- Ketones that have at least one alpha-hydrogen, undergo keto-enol tautomerization; the tautomer is an enol. Tautomerization is catalyzed by both acids and bases. Usually, the keto form is more stable than the enol.



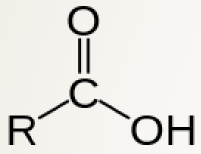
https://www.chemistrylearner.com/keto-enol-tautomerism.html

- C-H bonds adjacent to the carbonyl in ketones are more acidic than the C-H bonds in alkane. The relative acidity of the α-hydrogen is important in the enolization reactions of ketones and other carbonyl compounds. The acidity of the α-hydrogen also allows ketones and other carbonyl compounds to react as nucleophiles at that position, with either stoichiometric and catalytic base.

- Ketones are also weak bases, undergoing protonation on the carbonyl oxygen in the presence of Brønsted acids.
- An aldehyde differs from a ketone in that it has a hydrogen atom attached to its carbonyl group, making aldehydes easier to oxidize. Ketones do not have a hydrogen atom bonded to the carbonyl group, and are therefore more resistant to oxidation. They are oxidized only by powerful oxidizing agents which have the ability to cleave carbon–carbon bonds.

Carboxylic acids.

- A **carboxylic acid** is an organic acid that contains a **carboxyl group** (COOH) attached to an R-group. The general formula of a carboxylic acid is:



- Carboxylic acids are commonly identified by their trivial names. They often have the suffix -ic acid. IUPAC-recommended names also exist; in this system, carboxylic acids have an -oic acid suffix. For example, butyric acid (C3H7CO2H) is butanoic acid by IUPAC guidelines.

- Carboxylic acids occur widely. Important examples include the amino acids and fatty acids.

Formula	Common Name	IUPAC Name
$HCOOH$	formic acid	methanoic acid
CH_3COOH	acetic acid	ethanoic acid
CH_3CH_2COOH	propionic acid	propanoic acid
$CH_3(CH_2)_2COOH$	butyric acid	butanoic acid
$CH_3(CH_2)_3COOH$	valeric acid	pentanoic acid

Classification of carboxylic acids.

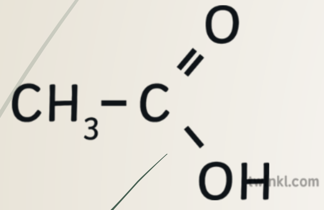
- **According to the number of carboxyl groups**, carboxylic acids are divided into:
monocarboxylic (one -COOH group), **dicarboxylic** (two -COOH groups), etc.

- **Depending on the structure of the hydrocarbon radical to which the carboxyl group is linked**, carboxylic acids are:
aliphatic (for example, acetic or acrylic), **alicyclic** (for example, cyclohexanecarboxylic), or **aromatic** (benzoic, phthalic).

Examples of carboxylic acids

Acetic acid

Acetic acid (ethanoic acid)

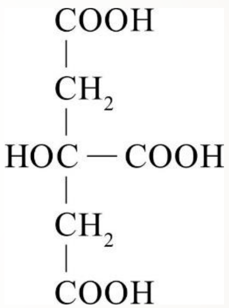


At physiological pH, acetic acid is usually fully ionised to acetate.

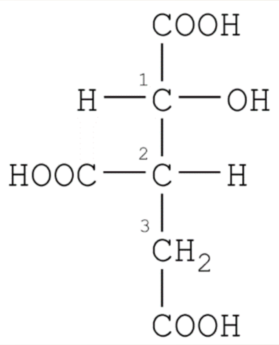
The acetyl group, formally derived from acetic acid, is fundamental to all forms of life. Derivate of acetic acid - acetyl coenzyme A, (acetyl-CoA). It is acetic acid, binded with coenzyme A. Acetyl-CoA is central metabolit of many biochemical processes (Krebs cycle, synthesise of fatty acids, cholesterol, metabolism of some amino acids, ets.).

Citric, isocitric acids

Citric acid or 2-Hydroxypropane-1,2,3-tricarboxylic acid:



Isocitric acid or1-Hydroxypropane-1,2,3-tricarboxylic acid:



Citric and isocitric acids are examples of tricarboxylic acids.

Citratic and isocitric asids are intermediates in the Tricarboxylic Acid cycle cycle (TCA, or Krebs cycle), - central metabolic pathway.

Examples of carboxylic acids

Succinic acid

Succinic acid (1,4-Butanedioic acid):

$HOOC-CH_2-CH_2-COOH$

It is a dicarboxylic saturated acid.

The name comes from the Latin succinum, which means amber. In living organisms, succinic acid takes the form of an anion. Succinate is produced in mitochondria in the tricarboxylic acid cycle. And then, in the same cycle, it is converted into fumarate by the enzyme succinate dehydrogenase. This enzyme is part of complex 2 of the electron transport chain, which is involved in the production of ATP.

Malonic acid

Malonic acid (propanedioic acid):

$HOOC-CH_2-COOH$

It is a dicarboxylic saturated acid.

Malonic acid is the classic example of a competitive inhibitor of enzyme succinate dehydrogenase. Inhibition of this enzyme decreases cellular respiration and ATP synthesis.

Fumaric acid

Fumaric acid **(***trans*-1,2-Ethylenedicarboxylic acid,2-Butenedioic acid)**:**
$HOOC-CH=CH-COOH$
It is dicarboxylic unsaturated acid.
Fumaric aci is metabolit of Citric Acid cycle and Urea cycle.

Examples of carboxylic acids

Oxalic acid

Oxalic acid (ethanedioic acid):

HOOC-COOH

It is a dicarboxylic acid .
Oxalic acid is a competitive inhibitor of the enzyme lactate dehydrogenase (LDH). LDH catalyzes the reversible conversion of pyruvate to lactic acid (the end product of anaerobic glycolysis).
Oxalic acid salts - oxalates can cause kidney stones.
In addition, they enhance the crystallization of uric acid in the kidneys. Enters the body with food (tomatoes, grapes, citrus fruits)

Glutaric acid

Glutaric acid (Propane-1,3-dicarboxylic acid 1,3-Propanedicarboxylic acid, Pentanedioic acid, n-Pyrotartaric acid):

HOOC-CH2- CH2-CH2-COOH

Glutaric acid is naturally produced in the body during the metabolism of some amino acids, including lysine and tryptophan. Defects in this metabolic pathway can lead to a disorder called glutaric aciduria, where toxic byproducts build up and can cause severe encephalopathy.

Chemical properties of carboxyl group.

The carboxyl **(COOH)** group is so-named because of the *carb*onyl group (C=O) and hydr*oxyl* group.

In the carboxyl group, everyone is polar. The carbon atom is in a state of sp2 hybridization. It forms three σ-bonds: two with oxygen atoms and one with a hydrogen atom in formic acid or carbon in molecules of other carboxylic acids. σ-bonds are located in one plane, the angle between them is close to 120◦.

The carbon atom forms another bond with the oxygen atom of the carbonyl group. The unhybridized p-orbitals of the carbon atom and the carbonyl oxygen atom overlap to form a π-bond.

In the carbonyl group, the electron density is shifted towards the oxygen atom due to its high electronegativity. As a result, a partial positive charge arises on the carbonyl carbon atom. The carbon atom seeks to compensate for the positive charge and attracts the lone pair of electrons of the oxygen atom of the hydroxyl group.

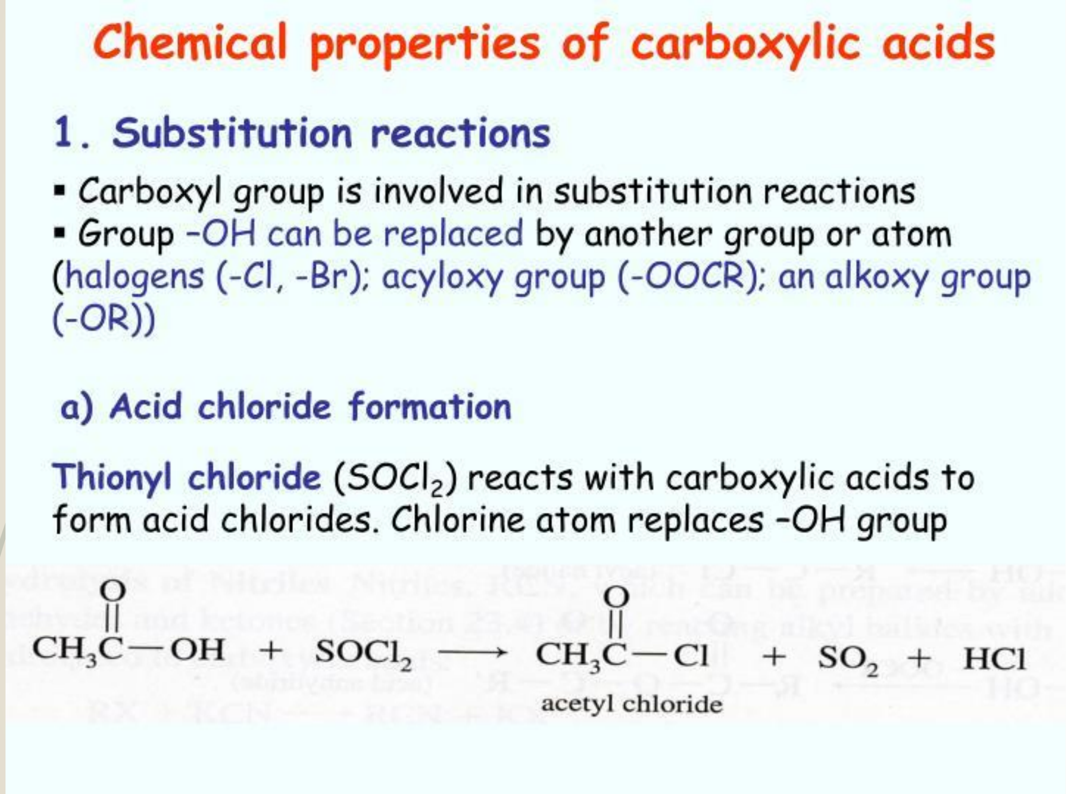
In turn, the oxygen atom pulls off the electron density along the O-H bond from the hydrogen atom of the hydroxyl group.

As a result, the bond between oxygen and hydrogen atoms in the hydroxyl group becomes more polar and the hydrogen atom acquires increased mobility, which greatly simplifies its separation in the form of a proton (H +). As a result of the mutual influence of atoms in the carboxyl group, the C = O bond is stronger than in the carbonyl group of aldehydes, and the O-H bond is less strong than in alcohols.

The acidic properties of carboxylic acids are due to the shift of the electron density to the carbonyl oxygen atom and the resulting strong polarization of the O - H bond (in comparison with alcohols and phenols), as a result of which the separation of the hydrogen atom in the form of a proton is facilitated. Carboxylic acids, unlike alcohols, dissociate to form hydrogen ions H.

For carboxylic acids, in contrast to aldehydes, addition reactions at the double bond> C = O are not characteristic, due to a decrease in the positive charge on the carbonyl carbon atom by the oxygen atom of the hydroxo group.

Chemical properties of carboxylic acids.



Chemical properties of carboxylic acids

1. Substitution reactions

- Carboxyl group is involved in substitution reactions
- Group –OH can be replaced by another group or atom (halogens (-Cl, -Br); acyloxy group (-OOCR); an alkoxy group (-OR))

a) Acid chloride formation

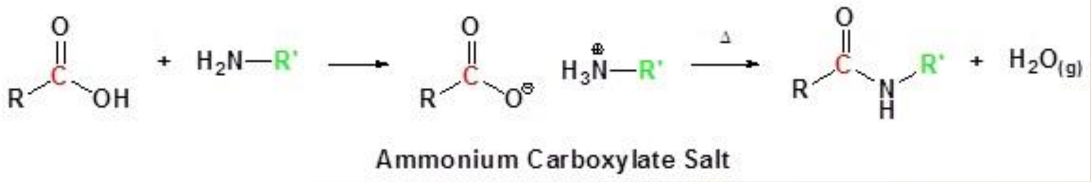
Thionyl chloride ($SOCl_2$) reacts with carboxylic acids to form acid chlorides. Chlorine atom replaces –OH group

$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}-OH + SOCl_2 \longrightarrow CH_3\overset{\overset{\displaystyle O}{\|}}{C}-Cl + SO_2 + HCl$$

acetyl chloride

https://www.slideserve.com/taite/carboxylic-acids

Conversion of a Carboxylic Acid to an Amide

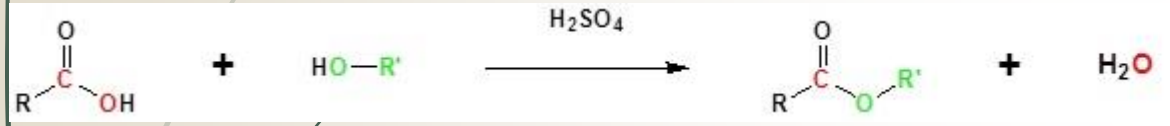


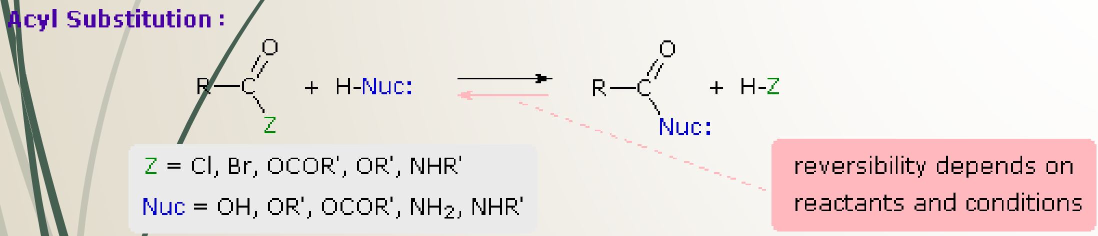
https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Supplemental_Modules_(Organic_Chemistry)/Carboxylic_Acids/Reactivity_of_Carboxylic_Acids/Fischer_Esterification

Chemical properties of carboxylic acids.

Esterification

Esterification is the esterification of a carboxylic acid by heating it with an alcohol in the presence of a strong acid as the catalyst.



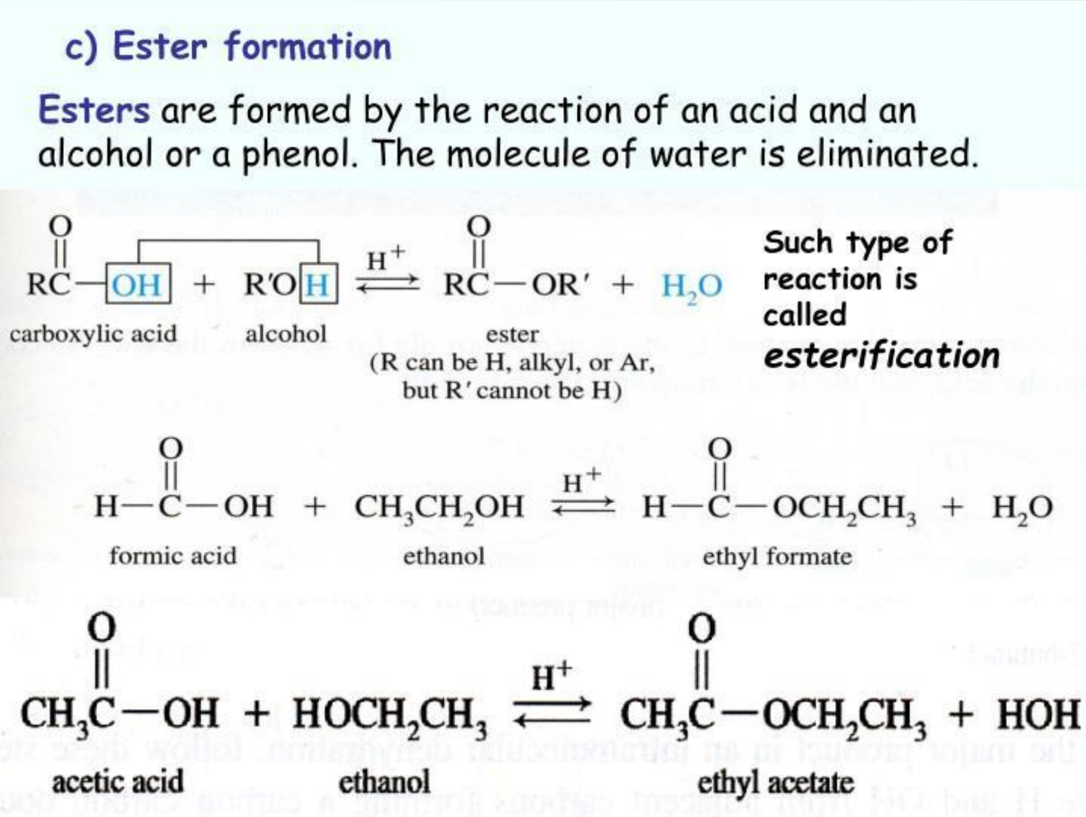


Z = Cl, Br, OCOR', OR', NHR'

Nuc = OH, OR', OCOR', NH_2, NHR'

reversibility depends on reactants and conditions

https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Supplemental_Modules_(Organic_Chemistry)/Carboxylic_Acids/Reactivity_of_Carboxylic_Acids/Fischer_Esterification



c) Ester formation

Esters are formed by the reaction of an acid and an alcohol or a phenol. The molecule of water is eliminated.

$$RCOOH + R'OH \overset{H^+}{\rightleftharpoons} RCOOR' + H_2O$$

(R can be H, alkyl, or Ar, but R′ cannot be H)

Such type of reaction is called ***esterification***

$$H{-}\overset{O}{\overset{\|}{C}}{-}OH + CH_3CH_2OH \overset{H^+}{\rightleftharpoons} H{-}\overset{O}{\overset{\|}{C}}{-}OCH_2CH_3 + H_2O$$

$$CH_3\overset{O}{\overset{\|}{C}}{-}OH + HOCH_2CH_3 \overset{H^+}{\rightleftharpoons} CH_3\overset{O}{\overset{\|}{C}}{-}OCH_2CH_3 + HOH$$

https://www.slideserve.com/taite/carboxylic-acids

Sources of information

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