

The most important chemical reactions in metabolism

The metabolic pathways of the human organism form an *extensive network* of interconnected reactions that often share *common intermediates*. Chemical transformations of individual substances are usually classified according to a general mechanism common to all substances undergoing a given reaction. For example, *decarboxylation is the splitting of CO₂ from the carboxyl group, where the substrate may be different carboxylic acids*.

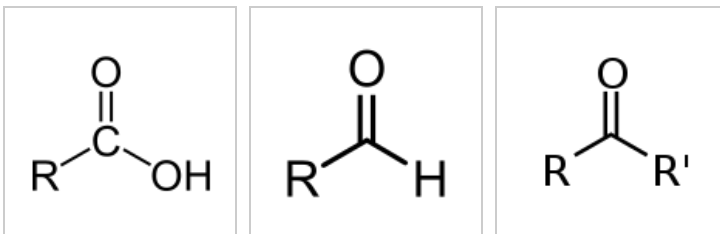
Alcohols, carbonyl compounds and carboxylic acids

Alcohols, carbonyl compounds and carboxylic acids are important substrates for many reactions of metabolic pathways of organisms.

Alcohols contain the functional group **–OH**. Depending on the number of OH groups in the molecule, alcohols can be *one-, two- or polybasic*. Furthermore, depending on which carbon atom the OH group binds to, we distinguish between *primary, secondary and tertiary* alcohols.

Primárni	$\text{R}-\text{CH}-\text{OH}$
Sekundární	$\begin{array}{c} \text{R}_1 \\ \text{R}_2 \end{array} \text{CH}-\text{OH}$
Terciárni	$\begin{array}{c} \text{R}_1 \\ \text{R}_2 \\ \text{R}_3 \end{array} \text{C}-\text{OH}$

Aldehydes with ketones form a group of carbonyl compounds. The functional group of aldehydes is the group **–CHO**, in ketones **–C=O**. Of this group of substances, the most important substrates are probably the reactions of **carboxylic acids**, characterized by the presence of the functional group **–COOH, and their derivatives**.



carboxyl group

Aldehyde group

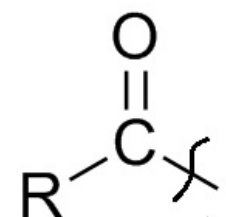
ketone group

Significant reactions of alcohols, aldehydes and carboxylic acids

1. Formation of anions and acyls derived from carboxylic acids
2. Dehydrogenation and hydrogenation (oxidation and reduction)
3. Esterification

Formation of anions and acyls derived from carboxylic acids

The carboxyl group is capable of *dissociation, with the degree of dissociation for individual acids given by dissociation constant. Carboxylic acids are weak, which means that their dissociation is only partial. The acid thus gives rise to the anion (group –COO[–])*. After splitting off the whole –OH group from the carboxyl group, its **acyl** is formed.



Acile

Dehydrogenation and hydrogenation (oxidation and reduction)

During the chemical reaction, **dehydrogenation, the H** is removed from the molecule.

The obtained hydrogen can then be used for the formation of a proton gradient in mitochondria and for energy gain (ATP). The introduction of hydrogen **into a molecule is called** hydrogenation. In the body, dehydrogenation and hydrogenation occur, for example, in the following processes:

Oxidation of single bonds to double bonds



These reactions occur, for example, in **Krebs cycle**, at **β -oxidation of fatty acids** or **desaturation reactions**, which aim at the synthesis of unsaturated fatty acids.

Mutual conversion of alcohols, aldehydes / ketones and carboxylic acids

Alcohols, carbonyl compounds and carboxylic acids *form a series* differing from each other in the degree of oxidation / reduction.

The general scheme of their mutual transformation is as follows (oxidation takes place towards the carbonyl compound and carboxylic acid, reduction in the opposite direction):

- **Primary alcohol \rightleftharpoons aldehyde \rightleftharpoons carboxylic acid**



- **Secondary alcohol \rightleftharpoons ketone**



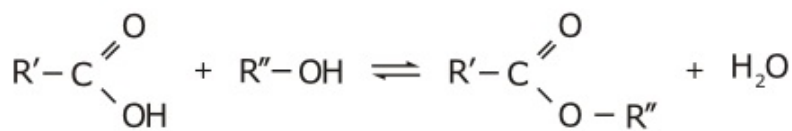
- **Tertiary alcohol**

"Slight" oxidation does not take place (it can be oxidized only with simultaneous splitting of the carbon chain).

An example of oxidation is the formation of *dihydroxyacetone phosphate* (DHA-P) from **glycerol-3-phosphate** (cofactor is **FAD**), through which glycerol enters glycolysis or gluconeogenesis according to the current needs of the organism.

Esterification

Esterification is the reaction of a carboxylic acid with an alcohol, producing an **ester** *and water*:



The most important carboxylic acids, their anions and acyls

Saturated monocarboxylic acids

C	Systematic name	Trivial name	Latin name	Acyl	Anion
1	methane	ant	<i>ac. formicum</i>	formyl	formate
2	Ethan	Vinegar	<i>ac. aceticum</i>	acetyl	acetate
3	Propane	propionic	<i>ac. propionicum</i>	propionyl	propionate
4	Butane	butter	<i>ac. Butyricum</i>	Butyryl	butyrate
5	pentane	Valérová	<i>ac. Valericum</i>	Valeryl	valerate
12	Dodecanese	Laurova	<i>ac. Lauricum</i>	Lauryl	laurate
16	hexadecane	Palmito	<i>ac. palmiticum</i>	Palmitoyl	palmitate
18	Octadecane	Stearova	<i>ac. stearicum</i>	stearoyl	Stearate

Saturated dicarboxylic acids

C	Systematic name	Trivial name	Latin name	Acyl	Anion
2	Etandi	Štavelová	<i>ac. oxalicum</i>	oxalyl	oxalate
3	Propandiová	Malonova	<i>ac. malonicum</i>	Malonyl	malonate
4	Butandi	amber	<i>ac. succinicum</i>	succinyl	succinate
5	Pentondia	glutaric	<i>ac. glutaricum</i>	Glutaryl	glutarate
6	hexandium	adip	<i>ac. adipicum</i>	Adipoyl	adipate

Unsaturated monocarboxylic acids

C	Systematic name	Trivial name	Latin name	Acyl	Anion
18:1	<i>cis</i> -octadec-9-eno	oil	<i>ac. oleicum</i>	oleoyl	oleate
18:2 (ω-6)	<i>cis,cis</i> -octadeca-9,12-dienova	linoleic	<i>ac. linoleicum</i>	Linoloyl	linolate
18:3 (ω-3)	<i>cis,cis,cis</i> -octadeca-9,12,15-trienová	Linolenic	<i>ac. linolenicum</i>	Linolenoyl	Linolenate
20:4 (ω-6)	<i>cis,cis,cis,cis</i> -eikosa-5,8,11,14-tetraenová	arachidonová	<i>ac. arachidonicum</i>	arachidonyl	arachidonát

Unsaturated dicarboxylic acids

C	Systematic name	Trivial name	Latin name	Acyl	Anion
4	<i>cis</i> -butendi	Malein	<i>ac. maleicum</i>	Maleinyl	maleate
4	<i>trans</i> -butendi	Fumarova	<i>ac. fumaricum</i>	Fumaroyl	fumarate

Carboxylic acid derivatives

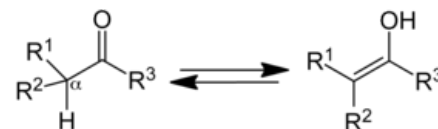
C	Systematic name	Trivial name	Latin name	Acyl	Anion
3	2-oxopropane	pyrogrape	<i>ac. pyruvicum</i>	Pyruvyl	pyruvate
3	2-hydroxypropane	milk	<i>ac. lacticum</i>	lactoyl	lactate
4	3-oxobutaneous	acetoacetic		acetoacetyl	acetoacetate
4	3-hydroxybutane	β-hydroxybutyric			β-hydroxybutyrate
4	2-hydroxybutanedia	apple	<i>ac. malicum</i>	Maloyl	Malate
4	2-oxobutanidium	oxaloacetic			oxaloacetate
5	2-oxopentandia	α-ketoglutar		α-ketoglutaryl	α-ketoglutarate
6	2-hydroxypropane-1,2,3-tricarboxylic	lemon	<i>ac. citricum</i>		citrate

Hydroxy acids and keto acids

Hydroxy acids in addition to the –COOH group also contain the –OH group replacing one –H. **Keto acids** or **oxo acids** contain in the molecule in addition to the group –COOH also the group =O replacing one –H. Their mutual conversion is relatively common in metabolic pathways.

An example is the relatively common *keto-enol tautomerism* in metabolism. It converts two forms of organic compounds:

- *ketoform* (or *oxoform*) contains double-bonded oxygen as a group =O,
- *enolform*, which contains a double bond between carbons and one of them binds –OH group (i.e. contains the structure $R^1-CH=C(OH)-R^2$).



The mutual transformation of the two forms represents the **migration of the hydrogen atom** or the proton, accompanied by the **swapping of the single bond** and the adjacent **double bond**.

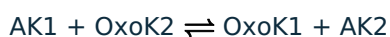
Amino acids and oxo acids

Amino acids and oxo acids are substitution derivatives of carboxylic acids. Amino acids contain in the molecule in addition to the –COOH group also the group –NH₂, oxo acids group =O. Their mutual transformations are frequent in the organism, for example, there is a **NH₂ group for group =O** and vice versa.

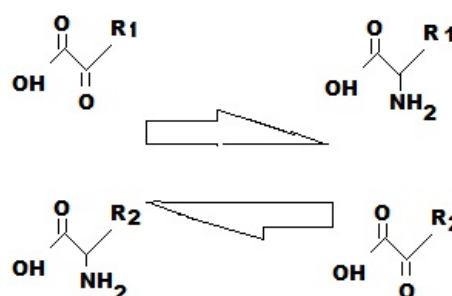
These transformations occur mainly in two processes:

Transamination

In this reaction, the amino acid is a donor –NH₂ of the oxo acid group. From the corresponding oxo acid, an amino acid is formed, and the original amino acid becomes an oxo acid:



TRANSAMINASE



Oxidative deamination

It is the formation of oxo acid from the amino acid **by removing –NH₂ group, which is released as ammonia (NH₃)**. **Oxidative deamination is one of the important reactions through which amino acids initiate the process of their degradation**. In the human body, they

take place mainly in the liver, and the released ammonia is broken down in **urea synthesis**. This reaction is mainly catalyzed by glutamate dehydrogenase.

Decarboxylation and carboxylation

Decarboxylation removes the carboxyl group, which is released as a **CO₂** molecule and replaced by a proton. They are significant, for example, for

- conversion of amino acids to *biogenic amines* (e.g. in the synthesis of many neurotransmitters),
- dehydrogenation of 2-keto acids – pyruvate dehydrogenase reaction and two reactions of the Krebs cycle.

Carboxylation is the opposite reaction, involving the introduction of a COOH group into the molecule. It occurs, for example, in

- fatty acid synthesis,
- gluconeogenesis.