Organic compounds containing oxygen, nitrogen and sulfur

Biologically important heterocycles

Bruno Sopko, Martina Srbová, Tereza Popelková
Organic compounds containing oxygen
Organic compounds containing oxygen

Hydroxyderivates
Ethers
Carbonylated compounds
Carboxylated compounds and derivatives
Electron configuration of oxygen atom:

\[ 1s^2 \quad 2s^2 \quad 2p^4 \]

In organic molecule oxygen is attached covalently

\[ -\overset{-}{O}\overset{-}{-} \]

\[ =\overset{-}{O} \]
- **Alcohols and phenols** (hydroxy derivates) – compounds with the hydroxyl (-OH)
  \[ \text{R} - \text{O} - \text{H} \]

- **Ethers** – compounds with alcoxy group (-OR)
  \[ \text{R} - \text{O} - \text{R} \]
- **Aldehydes and ketones** – carbonyl group
  \[
  \text{CH}_2\text{=O} \quad \text{R}\cd\text{C}=\ddot{\text{O}}
  \]

- **Carboxylic acids** – carboxyl group (COOH)
  \[
  \text{H}-\ddot{\text{O}}\cd\text{C}=\ddot{\text{O}} \quad \text{R}\cd\text{C}=\ddot{\text{O}}
  \]
Alcohols

Classification

- In 1° alcohol, only one carbon atom is attached to the carbon carrying the -OH group (primary carbon).
- In 2° alcohol two carbon atoms are attached to the carbon carrying the -OH group (secondary carbon).
- In 3° alcohol three other carbon atoms are attached to the carbon atom carrying the -OH group (tertiary carbon).
The number of hydroxyl groups, there are:

Monohydroxyderivatives (monohydroxy alcohols)

Polyhydroxy alcohols
- Diols (dihydroxyderivatives)
- Triols (trihydroxyderivatives)
- Tetrols (tetrahydroxyderivatives)

Phenols - OH attached primary to aromatic ring
H-bonds → solubility in water, higher boiling points than alkanes.
The –OH group generally makes the alcohol molecule polar.

The -OH group can form hydrogen bonds to one another and to other compounds.
Properties

Alcohols and phenols act as acids or bases

An alcohol + An alkoxide ion ⇌ An alcohol + An oxonium ion
ELIMINATION

dehydration

\[
\begin{array}{c}
\text{H} \\
\text{C} \quad \text{OH} \\
\text{C} \quad \text{C} \\
\end{array} \quad \rightarrow \quad \begin{array}{c}
\text{C} = \text{C} \\
\end{array} + \text{H}_2\text{O}
\]

element: glycolysis

\[
\begin{array}{c}
\text{C}_1\text{C}_2\text{OPO}_3^{2-} \\
\text{H} \quad \text{H} \quad \text{C} \quad \text{H} \\
\text{C} \quad \text{O} \quad \text{O} \quad \text{O} \\
\end{array} \quad \leftrightarrow \quad \begin{array}{c}
\text{C} \quad \text{C} \quad \text{O} \quad \text{O} \\
\text{H} \quad \text{H} \quad \text{C} \\
\end{array} + \text{H}_2\text{O}
\]

2-phosphoglycerate \quad \text{phosphoenolpyruvate}
Oxidation of alcohols
Methanol  $\text{CH}_3\text{-OH}$

Toxic substance, temporary blindness (15 ml), permanent blindness or death (30 ml)

Ethanol $\text{CH}_3\text{-CH}_2\text{-OH}$

Obtained by fermentation from sugar juices in the presence of yeast and temperature of less than 37° C
Oxidation of Ethanol in the Body

1 – Alcohol dehydrogenase
2 – Aldehyde dehydrogenase

Methanol $\rightarrow$ formaldehyde $\rightarrow$ formic acid

Ethanol – An Antidote in case of Methanol Poisoning
Ethylene glycol - ethane-1,2-diol
HO–CH₂–CH₂–OH

Used as a central heating and car antifreeze
toxic: 50 mL, lethal: 100 mL

Glycerol - propane-1,2,3-triol (glycerin)

CH₂ - OH
\underline{CH} - OH
\underline{CH₂} - OH

-present as the backbone of several important biological compounds
• Reaction with acid yields esters - with nitric acid gives glyceroltrinitrate – nitroglycerin. Nitroglycerin is administered as a treatment for heart disease.
• The phosphoric acid esterifies primary –OH group to form 1-glycerophosphate acid.
• 1-glycerophosphate acid is an important metabolite and a structural component of complex lipids.
• **Inositol**: component of phospholipids
  (phosphatidylinositol)

• **Sphingosine** (2-amino-4-octadecene-1,3-diol)
  • component of brain phospholipids

• **Ethanolamine**: component of phospholipids

• **Choline**: component of phospholipids
  • Acetylcholine – acts as neurotransmitter
Phenols

- Dihydroxybenzenes

Catechol – part of catecholamines (epinephrine, norepinephrine)

Hydroquinone – oxidation → quinone, component of coenzyme Q (ubiquinone)
Aldehydes and Ketones

- Aldehydes and ketones have carbonyl group – polar, very reactive

- **Aldehydes** have the carbonyl carbon atom bonded to at least one hydrogen atom.

- **Ketones** have the carbonyl carbon atom bonded to two other carbons.

Nucleophilic addition

- ![Nucleophilic addition diagram](image)
Formaldehyde
Methanal

Acetaldehyde
Ethanal

Propionaldehyde
Propanal

Akrylaldehyde
Propenal

Acetone
propanone

Ethylmethyl ketone
Butanone

Cyclohexanone

Glyoxal
Ethandial

Benzaldehyde

Cinnamaldehyde
3-phenyl propenal

Acetophenone
Methylphenyl ketone

Benzophenone
Diphenyl ketone
Formation of Hemiacetals and Hemiketals

- An alcohol addition reversibly to an aldehyde or ketone produce hemiacetal or hemiketal and –OH group and OR$_1$ group are attached to the same carbon.

- Sugars contain both –OH and C=O groups that undergo these reactions.
Reactions of Aldehydes and Ketones with Amines

Aldehydes and ketones react with primary amines to form **imines - Schiff bases** (transamination, nonenzymatic glycation in diabetes).
Aldol condensation

\[ \text{glyceraldehyde-3-phosphate} + \text{dihydroxyacetonphosphate} \rightarrow \text{fructose-1,6-bisphosphate} \]
Carboxylic Acids

- Functional group is carboxyl group

- $R$ – can be aliphatic chain ($\text{CH}_3\text{CH}_2$-), cyclic molecule (including heterocycle) or aromatic molecule, exceptionally hydrogen ($\text{HCOOH}$).

- Involved in many vital function.

- Carboxyl group is polar and forms hydrogen bonds

Nucleophilic substitution (esterification)
Examples of monocarboxylic acids

- Formic acid
- Methanoic acid
- Acetic acid
- Ethanoic acid
- Propionic acid
- Propanoic acid
- Butyric acid
- Butanoic acid
- Isobutyric acid
- Isobutanoic acid
- Valeric acid
- Pentanoic acid
- Palmitic acid
- Hexadecanoic acid
- Stearic acid
- Octadecanoic acid
- Oleic acid
- Cis-9-octadecanoic acid
- Acrylic acid
- Propenoic acid
- Crotonic acid
- trans-2-butenoic acid
- Benzoic acid
- Benzenecarboxylic acid
- β-naphtoic acid
- 2-naphtalenecarboxylic acid
Examples of dicarboxylic acids

HOOC-COOH – oxalic acid
HOOC-CH$_2$-COOH – malonic acid
HOOC-CH$_2$-CH$_2$-COOH – succinic acid (citric cycle)
HCCO-CH$_2$-CH$_2$-CH$_2$-COOH – glutaric acid

Examples of unsaturated dicarboxylic acids

Maleic acid and fumaric acid are geometric isomers
Functional derivatives

Acyl group
ester
amide
acylhalogenide
anhydride
thioester
Substitutional derivatives
hydroxy -, keto-, amino-, halogen - acids

Hydroxy acids

- Lactic acid (lactate)
- Malic acid (malate)
- Citric acid (citrate)

Acetylsalicylic acid (Aspirin)

p-Aminosalicylic acid
Keto acids

enolform  
\[
\text{COOH} \\
\text{C-OH} \\
\text{CH}_2
\]

\[\overset{\text{Spontaneously}}{\rightarrow}\]

ketoform  
\[
\text{COOH} \\
\text{C}=\text{O} \\
\text{CH}_3
\]

Pyruvic acid  
\textit{pyruvate}

Oxaloacetic acid  
\textit{oxalacetate}

\[\text{CO}_2\text{H} \\
\text{C}=\text{O} \\
\text{CH}_2 \\
\text{CO}_2\text{H}\]

\[\text{CO}_2\text{H} \\
\text{C}=\text{O} \\
\text{CH}_2 \\
\text{CO}_2\text{H}\]

\[\alpha\text{-ketoglutaric acid} \]
\[\alpha\text{-ketoglutarate}\]
glycolysis

Pyruvate $\rightarrow$ Lactate

Lactate dehydrogenase

NADH + H$^+$ $\rightarrow$ NAD$^+$
Organic compounds containing nitrogen
Nitrogen compounds

Types of bonds in nitrogen compounds:
Nitro compounds: R-NO₂

- Hydrogen substituted for NO₂
- Originate from nitration of hydrocarbons (HNO₃)

Examples:
- chloramphenicol (antibiotic)
- trinitrotoluene
Amines: R-NH₂

- organic derivates of ammonia

Properties of amines:
- basicity of amines (the unshared pair of electrons on the nitrogen atom)
- form hydrogen bonds (the polarity of the carbon-nitrogen bond)
- form nitrosoamines (nitrites in food may cause cancer)

\[
\text{R–N–H} + \text{HNO}_2 \rightarrow \text{R–N–N=O} + \text{H}_2\text{O}
\]
Importance of amines:

The most important organic bases

In biochemistry:

- Quaternary ammonium salts
- Biogenic amines
- Amino acids
- Proteins
- Alkaloids
Quaternary ammonium salts:

\[
\begin{array}{c}
R \\
\text{N} \\
R' \\
\text{R''} \\
\text{R'''} \\
+ \\
\end{array}
\]

Choline:
- the constituent of phospholipids (lecithin)

\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \text{NH} \text{CH}_2 \text{CH}_2 \text{OH} \\
\text{choline} \\
\end{array}
\]

Acetylcholine:
- neurotransmitter (parasympathetic nervous system)

\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \text{NH} \text{CH}_2 \text{CH}_2 \text{O} \text{CCH}_3 \\
\text{acetylcholine} \\
\end{array}
\]
**Biogenic amines:**

- from amino acids by decarboxylation
- constituents of biomolecules, neurotransmitters

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>Amine</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serine</td>
<td>Ethanolamine</td>
<td>Phospholipids</td>
</tr>
<tr>
<td>Cysteine</td>
<td>Thioethanolamine</td>
<td>Component of coenzyme A</td>
</tr>
<tr>
<td>Threonine</td>
<td>Aminopropanol</td>
<td>Component of vitamin $B_{12}$</td>
</tr>
<tr>
<td>Aspartate</td>
<td>$\beta$-Alanine</td>
<td>Component of coenzyme A</td>
</tr>
<tr>
<td>Glutamate</td>
<td>$\gamma$-Aminobutyrate</td>
<td>Neurotransmitter (GABA)</td>
</tr>
<tr>
<td>Histidine</td>
<td>Histamine</td>
<td>Mediator, neurotransmitter</td>
</tr>
<tr>
<td>Dopa</td>
<td>Dopamine</td>
<td>Neurotransmitter</td>
</tr>
<tr>
<td>5-hydroxytryptophan</td>
<td>Serotonin</td>
<td>Mediator, neurotransmitter</td>
</tr>
</tbody>
</table>
Biogenic amines – examples:

- GABA
- Serotonin
- Histamine

Diagram:

- Pantoic acid
- β-Alanine
- Thioethanolamine

- Diphosphate
- Adenine
- Coenzyme A
- Ribose-3-phosphate
Adrenaline and amphetamines:

**Catecholamines (adrenaline and noradrenaline)**
- biogenic amines with catechol group derived from tyrosine
- hormones (the adrenal medulla), neurotransmitters (sympathetic nervous system)

![Chemical structures of adrenaline and noradrenaline](image1)

**Amphetamines**
- mimic the action of catecholamines
- abuse drugs

![Chemical structures of amphetamine and methamphetamine](image2)
Alkaloids:

- naturally occurring chemical compounds containing basic nitrogen atoms
- important biological properties

Examples:

Atropine – blocks acetylcholine receptors

Cocaine – stimulative effect

Reserpine – sedative

Ephedrine – bronchodilator
Opium and opiates:

= morphine alkaloids

➤ important in medicine, abuse

➤ bind to the opioid receptors

Examples:

Opium, morphine – analgetic, the immature seed pods of opium poppies

Codeine – analgetic, antitussive

Heroin – synthesizes from morphine

Methadone -therapy of heroin addiction
Amides: R-CO-NH$_2$

- an amino group or substituted amino group bonded to a carbonyl carbon

Properties:
- not basic (the carbonyl group draws electrons away from the nitrogen)
- formation of the peptide bond –NH$_2$ + HOOC- (enzyme-catalyzed)
- The great stability toward hydrolysis (the peptide bond is stable, enzymatic hydrolysis)
Asparagine, glutamine:

The peptide bond:
Carbamate and urea

= carbonic acid amides (H$_2$CO$_3$)

Carbamate

Urea

Carbamoyl phosphate

- intermediate in: urea cycle

the formation of pyrimidines

Carbamoyl phosphate
Urea

- the end-product of protein metabolism in mammals
- produced only in the liver (urea cycle)
- soluble in water (excreted in the urine)

- biuret test (detection of peptide bonds and urea) - heating - biuret in alkaline environment with $\text{Cu}^{2+}$ - purple
Creatine

In muscle metabolism, energy for contraction

Creatinine

In a nonenzymatic reaction from creatine
Excreted in the urine
Barbiturates

- Barbituric acid derivates:

- sedatives, hypnotics, narcotiks

Pentobarbital

Phenobarbital
Imines: R-C=N-R

Schiff bases

- functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group

Mechanism of transamamination:

\[
\text{Pyridoxal phosphate} + \text{AA} \rightarrow \text{Pyridoxal phosphate+AA}
\]
Organic compounds containing sulfur
# Sulfur compounds

Structurally similar to oxygen compound

<table>
<thead>
<tr>
<th>R-O-H</th>
<th>R-S-H</th>
<th>R-O-R</th>
<th>R-S-R</th>
<th>R-O-O-R</th>
<th>R'-S-S-R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Thioalcohol = Mercaptans</td>
<td>Ether</td>
<td>Thioether = Sulfide</td>
<td>Peroxide</td>
<td>Disulfide</td>
</tr>
</tbody>
</table>
Thiols: R-SH (sulfhydryl group)

Properties:
- Not form hydrogen bonds
- Stronger acids than alcohols
- Easily oxidized → disulfide

Examples:
- Cysteine
- Glutathione
Disulfides: R-S-S-R

Disulfide-bonded cystein residues

- The disulfide bond forms when the two thiol groups are oxidized (reverse reaction)
- Protein conformation!
Glutathione

- An antioxidant (elimination of $H_2O_2$ and organic hydroperoxides)

Reduced form of glutathione (monomer)  
Oxidized form of glutathione (dimer, disulphide)
Sulfides: R-S-R

Examples:

**Methionine**

**S-Adenosylmethionine (SAM)**

= sulphonium ion

- Highly reactive methyl group (an important methylation agent)!
Sulfonic acids: $R\text{-SO}_3\text{H}$

Examples:

**Taurin**

= derivate from cysteine

**Sulfonamides**

- important chemoterapeutics
Biologically important heterocycles
<table>
<thead>
<tr>
<th>Name</th>
<th>Formula</th>
<th>Biologically important derivates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furan</td>
<td><img src="image" alt="Furan" /></td>
<td>Furanoses (sugars)</td>
</tr>
</tbody>
</table>
| Pyrrole| ![Pyrrole](image) | Porphin (heme, vit. B<sub>12</sub> - cobalamin)  
Bilirubin  
Proline, Hydroxyproline |
| Indole | ![Indole](image) | Tryptophan, Serotonin, Melatonin  
LSD, Psilocybin |
| Imidazole | ![Imidazole](image) | Histidine, Histamine  
Biotin (vit. H) |
<table>
<thead>
<tr>
<th>Name</th>
<th>Formula</th>
<th>Biologically important derivates</th>
</tr>
</thead>
</table>
| Thiazole     | ![Thiazole formula](image) | Thiamine (vit. B₁)  
Penicillin       |
| Pyran        | ![Pyran formula](image)   | Pyranoses (sugars) |
| Benzopyran (chroman) | ![Benzopyran formula](image) | Tocopherol (vit. E) |
| Pyridine     | ![Pyridine formula](image) | Nicotinamide (vit. B₃)  
Pyridoxal (vit. B₆) |
<table>
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<th>Name</th>
<th>Formula</th>
<th>Biologically important derivates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrimidine</td>
<td><img src="image" alt="Pyrimidine" /></td>
<td>Nucleotide bases (U,T,C)\nPhenobarbital\nVit. $B_1$</td>
</tr>
<tr>
<td>Purine</td>
<td><img src="image" alt="Purine" /></td>
<td>Nucleotide bases (A,G)\nHypoxanthine\nCaffeine\nUric acid</td>
</tr>
<tr>
<td>Pteridine</td>
<td><img src="image" alt="Pteridine" /></td>
<td>Folic acid (vit. $B_9$)</td>
</tr>
<tr>
<td>Isoalloxazine</td>
<td><img src="image" alt="Isoalloxazine" /></td>
<td>Riboflavin (vit. $B_2$)</td>
</tr>
</tbody>
</table>
**Heme**
- complexed with protein in hemoglobin, myoglobin, cytochroms
- 4 pyrrole rings coordinated with Fe$^{2+}$
- side chains: methyl, propionyl, vinyl

**Bilirubin**
- degradation product of heme (cleavage and reduction)
- excreted in the bile
Tryptophan
- an amino acid (serotonin and melatonin precursor)

Serotonin
- a neurotransmitter (mood control)
- many antidepressant drugs increase the level of serotonin in the brain

Melatonin
- a hormone (produced in response to the light-dark cycle → regulates circadian rhythms)
- an antioxidant → protective effects
Histidine

- an amino acid (histamine precursor)

Histamine

- a neurotransmitter (the major mediator of the allergic response → vasodilation, bronchoconstriction)
- antihistamines (block histamine from binding to its receptor)

Biotin (vit. H)

- in liver, egg yolk, yeast products, legumes, nuts
- function: carboxylation (the coenzyme of the carboxylases)
Thiamine (vit. B₁)
- contains two heterocyclic rings
- in grain, yeast products, pork
- its deficiency (beriberi → neurological disturbances, cardiac insufficiency, and muscular atrophy)
- function: oxidative decarboxylation

Tocopherol (vit. E)
- in cereals, liver, eggs, seed oil
- function: antioxidant in membranes
**Nicotinamide (niacin)**
- in meat, yeast products, fruit, vegetables
- its deficiency (pellagra → skin damage, digestive disturbances, depression)
- function: in the coenzymes NADH and NADPH (dehydrogenases)

![Nicotinamide structure]

**Pyridoxal (vit. B₆)**
- in meat, vegetables, grain products
- function: the coenzyme in the amino acid metabolism

![Pyridoxal structure]
Nucleotide bases derived from pyrimidine

- in nucleic acids

- a nucleic acid base is N-glycosidically linked to ribose or 2-deoxyribose
- the sugar is esterified with phosphoric acid
Nucleotide bases derived from purine

- in nucleic acids, ATP, NADP, FAD, CoA
- degradation of purine nucleotides → uric acid (excreted)

Adenine
(in both RNA and DNA)

Guanine
(in both RNA and DNA)

Uric acid

Anhydride bonds
An ester bond

ATP

- the most important form of chemical energy in cells
Folic acid
- in fresh green vegetables, liver
- its deficiency (megaloblastic anemia)
- function: coenzyme in C<sub>1</sub> metabolism (nucleotide biosynthesis)

Riboflavin
- in milk, eggs
- function: in the coenzymes FMN and FAD (oxidation and reduction)
Thank you for your attention