ORGANIC CHEMISTRY

For General Medicine

Ďuračková Zdeňka

Institute of Medical Chemistry, Biochemistry and Clinical Biochemistry
Medical Faculty of Comenius University
Structure of organic compounds
(relation between structure and properties and functions of biologically important organic compounds)

Organic chemistry – chemistry of hydrocarbons and their derivatives

\[ \begin{array}{c}
\text{\element{6}{C}}
\end{array} \]

\[ 1s^2 \ 2s^2 \ 2p_x^1 \ 2p_y^1 \]

\[ \text{C} = \text{O} \]

Carbon in basic state
Structure of organic compounds
(relation between structure and properties and functions of biologically important organic compounds)

Organic chemistry – chemistry of hydrocarbons and their derivatives

\[ \text{C} = \text{O} \]

Carbon in basic state

\[ \text{O} = \text{C} = \text{O} \]

Carbon in excited state
Electron configuration of carbon

- basic state
- excited state
- 4 unpaired electrons – four covalent bonds
Basic principles of the structure of organic compounds

- carbon forms four covalent bonds
  \[ \text{\begin{array}{c}
  C
  \end{array}} \]

- all 4 bonds are equivalent (hybridization s-, and p-orbitals
  - equalization of all 4 bonds)

- between carbons can be simple, double, or triple bond
  (\(\sigma\) and \(\pi\) bond)
  \[ \text{\begin{array}{c}
  C - C - \\
  \text{C = C -} \\
  \text{C = C -}
  \end{array}} \]

- atoms of carbon form chains – simple straight, branched and cyclic forms

- between carbon atoms, atoms of oxygen, nitrogen or sulfur can be bound
Types of hydrocarbon structures

HYDROCARBONS

Acyclic (non-cyclic) → Non-saturated
Cyclic → Saturated
Alicyclic → Cycloalkanes
Aromatic → Cycloalkenes

Heterocyclic compounds (O, S, N, ...
Organic compounds – according to hydrocarbone chain arrangement

1. **Acyclic (non-cyclic)**
   - Unbranched (straight chain)
     - CH$_3$-CH$_2$-CH$_3$
   - Branched chain
     - CH$_3$-CH-CH$_3$

2. **Cyclic**
   - alicyclic (cyclic)
   - aromatic (arenes)
   - heterocyclic
Isomerism of organic compounds
(two or more compounds with identical molecular formula, but different structure)

Types of isomerism

• Constitutional \((n\text{-propanol, 2-propanol})\)
• Configuration (stereoisomerism)
  - geometrical (cis-, trans-) (fumaric, maleinic acids)
  - optical (chirality, D/L - isomers) (D-AA, L-AA)
• Conformation of molecules (chair, boat)
Relation between structure and biological properties

• **Isomerism**
  - identical sum (molecular) formula
  - different arrangement of atoms and atom groups (different structure)

1. **Constitutional isomerism**
  - different constitution placement of atoms or kind of bonds

- **carbon skeleton**
  n-butane: \( \text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \)
  isobutane: \( \text{CH}_3 - \text{CH} = \text{CH} - \text{CH}_3 \)

- **placement**
  1-propanol: \( \text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{OH} \)
  2-propanol: \( \text{CH}_3 - \text{CH} - \text{CH}_3 \)

- **placement of double bounds**
  1-butene: \( \text{CH}_2 = \text{CH} - \text{CH}_2 - \text{CH}_3 \)
  2-butene: \( \text{CH}_3 - \text{CH} = \text{CH} - \text{CH}_3 \)

- **Tautomerism** (oxo-enol, or lactam-lactim tautomerism)
  vinylalcohol: \( \text{CH}_2 = \text{CH} - \text{OH} \) → \( \text{CH}_3 - \text{C} = \text{O} \)
  acetaldehyde: \( \text{H} \)
Tautomerism - positional isomerism – reverse position of H and the double bond

\[ \text{CH}_2 = \text{CH} - \text{OH} \quad \rightarrow \quad \text{CH}_3 - \text{C} = \text{O} \]

Vinylalcohol

Ethanal
(acetaldehyde)

Guanine

Lactam – form

Lactim – form
Amino - / Imino-tautomerism

In DNA – They cause mutagenic mispairings during DNA replication
In RNA - Tautomeric nucleoside analogs have therapeutic applications as antiviral drugs because of their ability to induce lethal mutagenesis

(Klug & Cummings 1997)
Amino - / Imino-tautomerison

Change pairing from A-T to G-C

Use in antivirals
Configuration isomerism (stereoisomerism)

- different arrangement of atoms in space, the same connectivity (order of atoms and double bonds are identical)
- geometrical isomerism, cis – trans (maleic and fumaric acids) conditioned by the presence of double bond
  
  Maleic acid \((cis)\)  
  \[
  \begin{align*}
  \text{H} - \text{C} - \text{COOH} \\
  \text{H} - \text{C} - \text{COOH}
  \end{align*}
  \]

  Fumaric acid \((trans)\)  
  \[
  \begin{align*}
  \text{HOOC} - \text{C} - \text{H} \\
  \text{H} - \text{C} - \text{COOH}
  \end{align*}
  \]

- optical - conditioned by chiral carbon \(C^*\) (asymmetric carbon)
  - optical isomers - enantiomers
  - rotation of the plane of polarized light to the same degree but to opposite direction \(+ / -\)

  configuration D- a L-  
  \[
  \begin{align*}
  \text{H} - \text{C} = \text{O} \\
  \text{H} - \text{C}^* - \text{OH} \\
  \text{H} - \text{C} = \text{O} \\
  \text{HO} - \text{C}^* - \text{H}
  \end{align*}
  \]

  \[
  \begin{align*}
  \text{CH}_2\text{OH} \\
  \text{D}(+) - \text{glyceraldehyde} \\
  \text{CH}_2\text{OH} \\
  \text{L}(-) - \text{glyceraldehyde}
  \end{align*}
  \]
What does it mean + or - ????

An optically active substance (optically active carbon is present – C*) in solution is able to rotate the plane of polarised monochromatic light (light of only a single frequency) passing through a solution to the right or to the left.

Diagram: Not linear polarised light, Linear polarised light, plane of polarisation, clockwise rotation, anti-clockwise rotation.
Conformation of molecules

➢ Arrangement in space

➢ Rotation of atom groups around axis passing two carbon atoms linked by simple bond

Example: two conformations of cyclohexane:

Chair

Boat
low-molecular weight compounds (molecules, ions, radicals) react with substrate

**Nucleophilic** – donor of electrons to substrate for new bond formation is reagent: $\text{OH}^-$, $X^-$ (halogenid), $\text{H}_2\Theta$, $\text{NH}_3$

$$\text{Nu}^- + -\text{C}^+ \rightarrow \text{Cl}$$

**Electrophilic** – acceptor of electrons from substrate for new bond formation is reagent: $^+\text{SO}_3\text{H}$, $^+\text{NO}_2$, $\text{Cl}^+$, $\text{H}^+$

$$\text{E}^+ + \text{CH}_2=\text{CH}^- \ldots$$
INDUCTIVE EFFECT, I
( for σ- bond) – related to saturated hydrocarbons

- effect of polar bond on polarisation of neighbouring bonds
- direction of polarisation is identical with polarity of original bond
- effect is dependent on distance

**Negative inductive effect** – I
- atom, resp. group of atoms linked to carbon, which attracts electrons:
  - F, –Cl, –Br, –I, =O, –OR, –SR, –NH₂, –NO₂

**Positive inductive effect** + I
- atom, resp. group of atoms, which push electrons back:
  - CH₃ (alkyls)
MESOMERIC EFFECT, \( M \)  

Characteristic for \( \pi \) electrons

- transformation of polar group effects the conjugation system of double bonds

**Negative mesomeric effect \(-M\)**

- groups attracting electrons
- dilution of electron density on neighbouring double bonds
- groups: \(-\text{NO}_2\), \(-\text{COH}, =\text{C}=\text{O}, -\text{COOH}, -\text{C}=\text{N}^-\)

\[
\begin{align*}
+M & \quad -M \\
\begin{array}{c}
\text{6 } \pi \\
\text{electrons}
\end{array} & \quad \begin{array}{c}
\text{10 } \pi \\
\text{electrons}
\end{array}
\end{align*}
\]

\[
\begin{align*}
+M & \quad -M \\
R - \text{CH} = \text{CH} - \text{C} = \text{O} & \quad \text{H}
\end{align*}
\]
Possitive mesomeric effect, +M

➢ groups that repel (press out) electrons

➢ thickening of electrons on adjacent carbons with double bonds

➢ groups: -NH₂, -OH, -OR, -SH, -SR, -X (halogens)
Reactivity of hydrocarbons

- **Saturated hydrocarbons (alkanes)**
  - substitution (radical reaction, catalyst, UV)
  - elimination (dehydrogenation) (catalyst) (Pt, enzyme)

- **Non-saturated hydrocarbons (alkenes, alkynes)**
  - addition: hydrogenation (hydrogenation) → alkanes
  - halogeneration (halogenation) → dihalogenalkanes
  - halogeneration derivatives → monohalogenalkanes
  - water → hydroxy derivatives (alcohols)

- oxidation – cleavage of bond

- **Aromatic hydrocarbons**
  - substitution: halogenation
    - (electrophilic substitution)
    - sulphonation
    - nitration
    - acylation
    - alkylation
  - halogenation
  - Cl
  - SO₃H
  - NO₂
  - CO-R
  - CH₂-CH₃
REACTIONS of ORGANIC COMPOUNDS

1. Addition

\[
2H + CH_2 = CH_2 \rightarrow CH_3 - CH_3
\]

2. Substitution (displacement of atom/atom group)

\[
CH_3 - CH_2 - Cl + OH^- \rightarrow CH_3 - CH_2 - OH + Cl^- + H_2O
\]

3. Elimination

\[
CH_3 - CH - CH - CH_2 \rightarrow CH_3 - CH = CH - CH_3
\]

2 - butanol \[\rightarrow\] 2 - butene
Prefix de - ..... 
Elimination of something - double bond is formed

Dehydration

\[
\begin{align*}
\text{CH}_3 - \text{CH} - \text{CH} - \text{CH}_2 & \xrightarrow{- \text{H}_2\text{O}} \text{CH}_3 - \text{CH} = \text{CH} - \text{CH}_3 \\
\text{2 – butanol} & \rightarrow \text{2 – butene}
\end{align*}
\]

Dehydrogenation

\[
\begin{align*}
\text{CH}_3 - \text{CH} - \text{CH} - \text{CH}_2 & \xrightarrow{- 2\text{H}} \text{CH}_3 - \text{CH} = \text{CH} - \text{CH}_3 \\
\text{butan} & \rightarrow \text{2 – butene}
\end{align*}
\]

Deamination

\[
\begin{align*}
\text{CH}_3 - \text{CH} - \text{CH} - \text{CH}_2 & \xrightarrow{- \text{NH}_3} \text{CH}_3 - \text{CH} = \text{CH} - \text{CH}_3 \\
\text{2 – aminobutan} & \rightarrow \text{2 – butene}
\end{align*}
\]
HYDROCARBONS

Acyclic (aliphatic) hydrocarbons

Alkanes:

- Saturated hydrocarbons, simple (σ) bonds, binding angle 109°
- Homologic chain, -CH₂- homologic increase, molecular formula CₙH₂n+2
- Non-polar compounds, soluble in non-polar solvents, insoluble in H₂O
- Small reactivity, characteristic reaction - substitution (temperature, UV radiation)
  - Example: methane, ethane, propane, butane, pentane, hexane, isobutane
Alkenes

- non-saturated hydrocarbons, double bond ($\pi$), binding angle 120°
- homologous chain, sum formula $C_nH_{2n}$
- high reactivity, characteristic reaction – addition (Markovnik rule)

\[
CH_2 = CH_2 + HOH \rightarrow CH_2 - CH_2
\]

ethene (ethylene) \hspace{1cm} ethanol

\[
CH_2 = CH_2 + 2H \rightarrow CH_3 - CH_3
\]

ethene \hspace{1cm} ethane

catalyst
Dienes (2 double bonds)

- cumulated, conjugated or isolated double bonds
- high reactivity, important reaction – addition polymerisation

\[
n \quad \text{CH}_2 = \text{C} - \text{CH} = \text{CH}_2 \quad \text{-----} \quad -[\text{-CH}_2 - \text{C} = \text{CH} - \text{CH}_2^-]_n^- \]  

2-methyl-1,3-butadiene  

isoprene  

natural rubber polymer of isoprene

- Isoprenoids (for example: terpenes, steroids)
Alkynes

- non-saturated hydrocarbons, triple bond ($\pi$), binding angle 180°

- homologous chain, sum formula $\text{C}_n\text{H}_{2n-2}$

- high reactivity, characteristic reaction – addition

\[
\text{CH} \equiv \text{CH} + \text{HCl} \rightarrow \text{CH}_2 = \text{CH} - \text{Cl}
\]

Ethyne (acetylene)    chloroethene (vinylchloride)

\[
\text{CH} \equiv \text{CH} + \text{HOH} \rightarrow [\text{CH}_2 = \text{CH} - \text{OH}] \rightarrow \text{CH}_3 - \text{C} = \text{O}
\]

Ethyne (acetylene)    vinylalcohol    ethanal (acetaldehyde)

**Tautomerism** :

- enol-
Markovnik´s rule

Addition of

non-symetric hydrocarbon

non-symetric molecule

\[
CH_2 \neq CH - CH_3 + H - OH \rightarrow CH_2 - CH - CH_3
\]

1-propene \hspace{2cm} 2-propanol
Cyclic hydrocarbons

ALICYCLIC

For ex.: cyclopentane, cyclohexane, cyclohexene, cyclohexadiene, cyclopentanoperhydrophenantrene

Stereochemistry cyclohexane

➢ chair and boat form (bound angle 109°)
AROMATIC hydrocarbons (ARENS)

➢ basic hydrocarbon – **benzene** (benzol)

➢ aromatic character –
  - plane structure (120° bound angle)
  π – electrons are delocalized around whole circle
Polycyclic arens

- Toxicity of arens (benzene, benzpyrene)
- Stability towards oxidation
- Characteristic substitution reaction (nitration, halogenation, sulphonation)
- five- or six-membered rings with one or more heteroatoms
- condensed heterocyclic compounds with two or more heteroatoms

HETEROCYCLIC COMPOUNDS

- furane
- pyrrole
- thiophene
- imidazole
- thiazole
pyridine

pyrimidine

pyran (2H-pyran)

purine

pyrimidine + imidazole

indole

benzpyrole
Biologically important derivatives of heterocyclic compounds

Furan

Tiophene

Methyltiophene - in grill meat

Ribose

Deoxyribose
Biologically important derivatives of heterocyclic compounds

- Component of carboxylases – oxidative decarboxylation of alpha-oxoacids
- Metabolism of saccharides in brain

Thiamin – vitamin B1

Porphin – porphyrin - haeme
Biologically important derivatives of heterocyclic compounds - 3

imidazol

Biotin

Histidin

Purin
Biologically important derivatives of heterocyclic compounds

- Pyran
  - saturated

- Glucose

- Chroman ring

- Vitamin E

Chemical structures and their derivatives.
Biologically important derivatives of heterocyclic compounds

- Pyridin
- Amid of nicotinic acid
- Niacin
- Vitamin PP
- NAD^+
Biologically important derivatives of heterocyclic compounds - Pyrimidin nitrogen bases
Biologically important derivatives of heterocyclic compounds - 7

Uric acid

caffeine

theophilline
Biologically important derivatives of heterocyclic compounds

Indol benzene + pyrol → Tryptophan

→ Lysergic acid
### DERIVATIVES of HYDROCARBONS

- Replacing hydrogen atom/atoms in hydrocarbons with another atom or a group of atoms, so called **functional group**

### CHARACTERISTIC GROUPS and their marking

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<th>Characteristic group</th>
<th>Prefix</th>
<th>Affix</th>
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<td>— Cl</td>
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<td>— Br</td>
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<td>Iodo-</td>
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<td>Hydroxylimino-</td>
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<td>Nitrils</td>
<td>— C≡N</td>
<td>Cyano-</td>
<td>- nitril</td>
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</table>
HALOGEN DERIVATIVES

nucleophilic substitution

\[ \overset{\delta^+}{C} \overset{\delta^-}{X} + \overset{-}{OH^-} \leftrightarrow \overset{-}{H-C-OH} + \overset{-}{X^-} \]

High TOXICITY

Tyroxine – Tetraiodothyronine T4

– Triiodothyronine T3
HALOGENE DERIVATIVES of HYDROCARBONS

- insoluble in water, soluble in alcohols and ethers
- polar covalent bond between \(-\text{C} \rightarrow\) halogene

- **characteristic reaction**
- substitution (heterolytical cleavage of bonds), as alkylation reagents

- **practical use**
  - solvents for non-polar compounds (CCl\(_4\))
  - monomers for preparation of macromolecular compounds (PVC, artificial rubber, teflon),
  - in refrigerator industry (freons – dichloro-difluoromethane)
  - iodoform CHI\(_3\) – disinfection effects
  - insecticides
  - dioxins
  - narcotics (halotan, CF\(_3\)-CHBrCl)
Toxicity of halogen derivatives

- toxicity

- influence on central nervous system (CNS)
- tetrachlorodibenzo-dioxin – carcinogenic, teratogenic, mutagenic effects
  
  \[(c < 1\text{mg.l}^{-1})\text{ (dioxins)}\]

- cancerogens or suspected carcinogens (CHCl₃, CCl₄)

DDT – insecticide DichloroDiphenylTrichlorehthane

(1948 Paul Hermann Müller won Nobel Price for DDT discovery)
Key facts related to dioxins

- Dioxins are a group of chemically-related compounds that are persistent environmental pollutants.
- Dioxins are found throughout the world in the environment and **they accumulate in the food chain**, mainly in the fatty tissue of animals, mainly meat and dairy products, fish and shellfish.
- Dioxins are **highly toxic** and can cause **reproductive and developmental problems**, damage the **immune system**, interfere with hormones and also **cause cancer**.
- Due to the **omnipresence of dioxins**, all people have background exposure, which is not affecting human health. However, due to the highly toxic potential of this class of compounds, efforts need to be **undertaken to reduce current background exposure**.
- Prevention or reduction of human exposure is best done via **source-directed measures**, i.e. **strict control of industrial processes** to reduce formation of dioxins as much as possible.
Sources of dioxin contamination

➢ products of **industrial processes** or also result from **natural processes** (volcanic eruptions and forest fires)
➢ products of a wide range of **manufacturing processes** (smelting, chlorine bleaching of paper pulp, the manufacturing of some herbicides and pesticides)
➢ uncontrolled **waste incinerators** (solid waste and hospital waste) are often the worst culprits, due to incomplete burning
HYDROXYDERIVATIVES of HYDROCARBONS
(alcohols a phenols)

1. ALCOHOLS
Polarity of bond $R \rightarrow O \leftarrow H$ - reactivity of hydroxyderivatives

Dividing:
1. according to the place of -OH group bound in the chain

- primary (1-butanol) $\text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{OH}$
- secondary (2-butanol) $\text{CH}_3 - \text{CH}_2 - \text{CH} - \text{CH}_3$

- tertiary (tert. butanol) $\text{CH}_3 - \text{C} - \text{CH}_3$

50
2. According to a number of –OH groups

- monohydroxyderivatives (monohydric)

- dihydroxyderivatives (diols) (dihydric), ethanediol (ethyleneglycol)

- trihydroxyderivatives (triols) (trihydric), propanetriol (glycerol)

- polyhydroxyderivatives (polyols) (saccharides)

\[
\begin{align*}
\text{ethyleneglycol} & : & \text{glycerol} & : & \text{glucose} \\
\CH_2 – \ OH & | & \CH_2 – \ OH & | & \CH_2\OH \\
\CH_2 – \ OH & | & \ CH – \ OH & | & \CH_2 – \ OH \\
\CH_2 – \ OH & | & \ CH – \ OH & | & \CH_2 – \ OH \\
\end{align*}
\]
Acidic character of alcohols

\[
\text{CH}_3\text{-CH}_2\text{-O-H} + \text{NaOH} \rightarrow \text{CH}_3\text{-CH}_2\text{-O}^- + \text{Na}^+ + \text{H}_2\text{O}
\]

Sodium alcoholate

Alkaline character of alcohols and ethers

\[
\text{CH}_3\text{-CH}_2\text{-O-H} + \text{H}^+\text{Cl}^- \rightarrow \text{CH}_3\text{-CH}_2\left[\text{H} - \text{O-H}\right]^+
\]

Alcoxonic salt

\[
\text{CH}_3 - \text{O} - \text{CH}_3 + \text{H}^+\text{Cl}^- \rightarrow \text{CH}_3\left[\text{H} - \text{O} - \text{CH}_3\right]^+
\]

Alcoxonic salt
HYDROXYDERIVATIVES

Oxidation of alcohols

R-CH₂-OH → ox -2H
R - alcohol

CH-OH → ox -2H

R-CH=O → ox H₂O
R – OH

R-C=O → ox
R – OH

bond cleavage between carbon atoms
3. Tertiary alcohols:

➢ stable against moderate oxidative reagents

➢ cleavage of - C – C - bond with strong oxidative reagent ($K_2Cr_2O_7$)
**Oxidation of diols**

- Ethylene glycol → glycolic acid
- Ethane diole → glyoxalic acid
- Dihydroxyacetone → glyceric acid

**Oxidation of triols**

- Glycerol → glyceraldehyde
- Glyceric acid
Hydrogen bond formation

$R - \overline{O} \leftrightarrow H$

$H \rightarrow \overline{O} - R$

Higher boiling point

cca 80°C

$H_3C - O - CH_3$

cca 40°C

$R - \overline{O} - R$

$R - \overline{O} - R$

$R - \overline{O} - R$
Esterification with organic acids

\[ R - OH + HOOC - R \rightarrow R - O - CO - R + H_2O \]

ester
Reaction with inorganic acids

Esterification of alcohols with sulphuric acid

\[ R\text{-}O\text{-}H + HO\text{-}SO_2\text{-}OH \rightarrow \text{H}_2\text{O} \]

Alcohol \quad H_2SO_4
Esterification of alcohols with sulphuric acid

\[ R - O - H + HO - SO_2 - OH \xrightarrow{- H_2O} R - O - SO_2 - OH \]

Alkylsulphate, ester of sulphuric acid

- heteropolysaccharides
  - chondroitinsulphate
  - dermatansulphate
- glycolipids
  - sulphatides
Esterification with nitric acid

HNO$_3$

\[
\begin{align*}
\text{CH}_2\text{-OH} & + \text{H-O-NO}_2 \quad \text{CH}_2\text{-O-NO}_2 \\
\text{CH-OH} & + \text{H-O-NO}_2 \quad \rightarrow \quad \text{CH-O-NO}_2 + 3 \text{H}_2\text{O} \\
\text{CH}_2\text{-OH} & + \text{H-O-NO}_2 \\
\end{align*}
\]

glyceroltrinitrate
(drug for heart diseases)

Alfred Nobel (1833-1896) → explosive compound
dynamit discovering (1867)
– Nobel foundation - 9 millions for Nobel prices
Reactions with inorganic phosphoric acid

$$R - \text{OH} + \text{HO} - \text{P} = \text{O} \quad \text{OH} \quad \overset{- \text{H}_2\text{O}}{\longrightarrow} \quad \text{R} - \text{O} - \text{P} = \text{O} \quad \text{OH}$$

monoester
Reaction with inorganic acids

\[ R - \text{OH} + \text{HO} - P = O \xrightarrow{- \text{H}_2\text{O}} R - O - P = O \]

\[ R - O - P = O + \text{HO} - R \xrightarrow{- \text{H}_2\text{O}} \text{monoester} \]
Reaction with inorganic acids

\[
\begin{align*}
R-\text{OH} + \text{HO}-\text{P} = \text{O} & \quad \rightarrow \quad \text{-H}_2\text{O} \\
\text{R}-\text{O}-\text{P} = \text{O} & \quad \rightarrow \quad \text{diester}
\end{align*}
\]

\[
\begin{align*}
\text{OH} + \text{HO}-\text{R} & \quad \rightarrow \quad \text{o}-\text{R} \\
\text{R}-\text{O}-\text{P} = \text{O} & \quad \rightarrow \quad \text{monoester}
\end{align*}
\]
Esterification of glycerol with phosphoric acid

\[ \text{H}_3\text{PO}_4 \]

\[
\begin{align*}
\text{CH}_2 \text{– OH} \\
\text{CH} \text{– OH} \\
\text{CH}_2 \text{– OH} \quad + \quad \text{H} \quad \text{– O} \quad \text{– P} \quad \text{= O} \\
\text{OH} \\
\text{OH} \\
\text{OH}
\end{align*}
\]

\[
\begin{align*}
\text{1CH}_2 \text{– OH} \\
\text{CH} \text{– OH} \\
\text{3CH}_2 \text{– O} \quad \text{– P} \quad \text{= O} \\
\text{OH} \\
\text{OH}
\end{align*}
\]

\[ \text{glycerol-3-phosphoric acid} \quad (\text{unit of complex lipids}) \]
- in the form of ions at different pH values of body fluids:
Esters of phosphoric acid, diphosphoric and triphosphoric acids in living systems

- Phosphoric acid
  \[ \text{O} \quad \text{HO–P–OH} \quad \text{OH} \]

- Diphosphoric acid
  \[ \text{O} \quad \text{HO–P–O–P–OH} \quad \text{OH} \quad \text{OH} \]

- Triphosphoric acid
  \[ \text{O} \quad \text{HO–P–O–P–O–P–OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \]

- Alkyl phosphate
  \[ \text{O} \quad \text{R-O–P–OH} \quad \text{OH} \]

- Alkyl diphosphate
  \[ \text{O} \quad \text{R-O–P–O–P–OH} \quad \text{OH} \quad \text{OH} \]

- Alkyl triphosphate
  \[ \text{O} \quad \text{R-O–P–O–P–O–P–OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \]
phosphoanhydric arrangement

\[
\begin{array}{c}
\text{O} \\
\uparrow \\
R - O - P - \overline{O} \sim P - OH \\
\downarrow \\
\text{OH} \\
\text{OH}
\end{array}
\]

protone-donor groups

phosphoester bond
ATP + H$_2$O $\rightleftharpoons$ ADP + Pi \hspace{1cm} \Delta G_0 \approx -32 \text{ kJ.mol}^{-1}$
PHENOLS

- one or more OH groups are linked directly to aromatic ring
- higher acidity of phenols in comparison to alcohols
- chemical reactions

Phenol

Hydroquinone

Salicylic acid
- **Acidic character of phenols** (higher than of alcohols)

\[
\text{OH} + \text{NaOH} \quad \rightarrow \quad \text{O}^- + \text{Na}^+ + \text{H}_2\text{O}
\]

**Sodium phenolate**

- **Toxicity of alcohols and phenols**
Oxidation of dihydroxyarenes – diphenols

- formation of quinones, cyclic conjugated diketones

\[
\text{OH} \quad \text{-2H} \quad \text{OH} \\
\text{OH} \quad \text{+2H} \\
\]

p-dihydroxybenzene (hydroquinone) \quad \text{p-benzoquinone (1,4-benzoquinone)}

- antioxidant function of phenols is related to reversible oxidation of diphenols to quinones (CoQ – ubiquinone in mitochondria)

- Desinfective properties of phenols (carbolic acid)
1,2-hydroquinone (pyrocatechol) → 1,2-benzoquinone

Resorcinol

Gallic acid

Pyrogalol
use in photograph, hair coloring

- CO₂

Tannins, antioxidant

bound to saccharide unit
Coenzyme Q

Involved in respiratory chain in mitochondria
Important for blood coagulation (prothrombin formation).

It is important for photosynthesis in plants.

Deficiency – malfunction of blood coagulation – risk of bleeding

Source – vegetable leaves
**OXO-compounds** (aldehydes and ketones)  
(polarisation of bond to oxygen)
Carbonyl group (oxo-group) - \( C = O \)
- all three atoms linked to carbonyl carbon form angle 120°
- they lie in one plane

Aldehydes
\[
\text{R} - \text{H} - \text{C} = \text{O}
\]

Ketones
\[
\text{R} - \text{C} = \text{O}
\]

- polarisation of group – reactivity of aldehydes and ketones
Chemical reactions of oxo-compounds

**Oxidation and reduction**

```
\[
\begin{align*}
\text{aldehyde} & \quad & \text{oxidation} & \quad & \text{carboxylic acid} \\
R - C - H & \quad \quad - 2H & \quad & R - \text{C} - \text{OH} \\
\text{reduction} & \quad & +2H \text{ (Ni)} & \quad & R - \text{CH}_2 - \text{OH} \\
& \quad & \text{or donor H atom} & \quad & \text{primary alcohol}
\end{align*}
\]
```
Oxidation - 2H

Reduction

relatively stable against oxidation

Ketone

O
R – C – R

Oxidation

OH
R – CH – R
secondary alcohol

catalyst Ni
or donor of H atoms
oxidation and reduction in living systems

(coenzymes of dehydrogenases as acceptors and donors of \( H \) atoms)

- NAD\(^+\) - acceptor of \( H^- \) (hydride ion) during the oxidation of alcohol

- NADH – reduced form of coenzyme – donor of \( H^- \) (hydride ions)

\[
\text{CH}_3\text{CH} = \text{OH} + \text{NAD}^+ \rightleftharpoons \text{CH}_3\text{C} = \text{O} + \text{NADH} + H^+ \\
\text{ethylalcohol} \quad \text{acetaldehyde}
\]
Redox properties

\[ R - \text{CH}_2 - \text{OH} \quad \text{H}_2\text{O} \quad R - \text{C} = \text{O} \]

Aldehyde

Reducing properties

\[ R - \text{C} = \text{O} \quad \text{Ox} \quad R - \text{CH}_2 - \text{OH} \]

Ketone
Addition and condensation reactions
- formation of hemiacetals and acetals

- hemiacetals are unstable
- hemiacetal *in cyclic form* (cyclic monosaccharides - relatively stable intermediates at the formation of acetals - glycosides)
Addition and condensation reactions
- formation of hemiacetals and acetals

- hemiacetals are unstable
- hemiacetal \textit{in cyclic form} (cyclic monosaccharides - relatively stable intermediates at the formation of acetals - glycosides)
Aldol condensation (aldehydes with $\alpha$-hydrogene)

$$\text{CH}_3-C-H + \text{CH}_3-\text{CH}_2-C-H \xrightarrow{\text{OH}^-} \text{CH}_3-\text{CH}-(\text{CH}_2-C-H)$$

3-hydroxyaldehyde = aldol

$$\text{CH}_3-C-H + \text{CH}_3-C-\text{CH}_3 \xrightarrow{\text{OH}^-} \text{CH}_3-\text{CH}-(\text{CH}_2-C-\text{CH}_3)$$

4-hydroxy-2-pentanone
Aldol condensation  (aldehydes with $\alpha$-hydrogene)

\[
\text{CH}_3 - \text{C} - \text{H} + \text{CH}_3 - \text{CH}_2 - \text{C} - \text{H} \xrightarrow{\text{OH}^-} \text{CH}_3 - \text{CH} - \text{CH} - \text{C} - \text{H}
\]

3-hydroxyaldehyde = aldol

\[
\text{CH}_3 - \text{C} - \text{H} + \text{CH}_3 - \text{C} - \text{CH}_3 \xrightarrow{\text{OH}^-} \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{C} - \text{CH}_3
\]

4-hydroxy-2-pentanone
Aldol condensation in metabolism

\[ \text{dihydroxyaceton-phosphate} \rightarrow \text{glyceraldehyde-phosphate} \]

\[ \text{aldolase} \]

\[ \begin{align*}
&\text{H}_2\text{C} \quad \text{O} \quad \text{P} \\
&\text{C} \quad \text{O} \\
&\text{HO} \quad \text{CH}_2
\end{align*} \]

\[ \text{fructose -1,6-bifosfate} \]
Condensation with primary amines - Formation of imines (Schiff bases)

\[ R - \text{CH} = O + H_2\text{N} - \text{CH}_3 \xrightarrow{-H_2\text{O}} R - \text{CH} = \text{N} - \text{CH}_3 \]  
- aldimine

\[ R - \text{C} = O + H_2\text{N} - \text{CH}_3 \xrightarrow{} R - \text{C} = \text{N} - \text{CH}_3 \]  
- ketimine

**Schiff bases**
- important intermediates of biochemical reactions
- binding of carbonyl compounds to free amino groups of proteins
Biological importance of Schiff bases formation

retinal (vitamin A) + H₂N—opsin → rhodopsin

- H₂O

Rhodopsin – red color pigment in the retina of the eye sensitive to light
Nonezymatic glycation of proteins

D-glucose + protein → aldimeine (Schiff base) → Ketoamine (fructosamine)
CARBOXYLIC ACIDS

- Shift of $\pi$- electrons in group $\overset{\text{\textrightharpoonup}}{\text{C} = \text{O}}$

- Polarisation of $- \text{O} \leftrightarrow \text{H}$ bond

- Mostly weak acids, $K(\text{ionis. const.}) = \text{near to } 10^{-5}$

- According to the number of $- \text{COOH}$ groups: mono-, di- and tricarboxylic acids

- Saturated and unsaturated
Examples of saturated mono- and dicarboxylic acids

<table>
<thead>
<tr>
<th>Monocarboxylic acids</th>
<th>Dicarboxylic acids</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>formula</strong></td>
<td><strong>Name</strong></td>
</tr>
<tr>
<td></td>
<td>substituional</td>
</tr>
<tr>
<td>HCOOH</td>
<td>Metanoic</td>
</tr>
<tr>
<td>CH₃ COOH</td>
<td>Ethanoic</td>
</tr>
<tr>
<td>CH₃ CH₂ COOH</td>
<td>Propanoic</td>
</tr>
<tr>
<td>CH₃(CH₂)₂ COOH</td>
<td>Butanoic</td>
</tr>
<tr>
<td>CH₃(CH₂)₃ COOH</td>
<td>Pentanoic</td>
</tr>
<tr>
<td>CH₃(CH₂)₄ COOH</td>
<td>Hexanoic</td>
</tr>
</tbody>
</table>
### Important dicarboxylic and hydroxy-acids

<table>
<thead>
<tr>
<th>Acid name</th>
<th>formula R-COOH</th>
<th>salt name</th>
<th>R-COO⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxalic</td>
<td>HOOC–COOH</td>
<td>Oxalate</td>
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</tr>
<tr>
<td>Malonic</td>
<td>HOOC–CH₂–COOH</td>
<td>Malonate</td>
<td></td>
</tr>
<tr>
<td>Succinic</td>
<td>HOOC–(CH₂)₂–COOH</td>
<td>Succinate</td>
<td></td>
</tr>
<tr>
<td>Glutaric</td>
<td>HOOC–(CH₂)₃–COOH</td>
<td>Glutarate</td>
<td></td>
</tr>
<tr>
<td>Fumaric (trans-form)</td>
<td>HOOC–CH=CH-COOH</td>
<td>Fumarate</td>
<td>Maleic (cis-form)</td>
</tr>
<tr>
<td>Maleate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactic</td>
<td>CH₃–CH–COOH</td>
<td>Lactate</td>
<td></td>
</tr>
</tbody>
</table>
### Important dicarboxylic, hydroxy- and oxo- acids II

<table>
<thead>
<tr>
<th>Acid name</th>
<th>formula</th>
<th>R-COOH</th>
<th>salt name</th>
<th>R-COO⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-Hydroxybutyric</td>
<td>CH₃–CH–CH₂–COOH</td>
<td>3-Hydroxybutyrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malic</td>
<td>HOOC–CH–CH₂–COOH</td>
<td>Malate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tartaric</td>
<td>HOOC–CH–CH–COOH</td>
<td>Tartarate</td>
<td></td>
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</tr>
<tr>
<td>Citric</td>
<td>CH₂–COOH</td>
<td>Citrate</td>
<td></td>
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<tr>
<td>Pyruvic</td>
<td>CH₃–CO–COOH</td>
<td>Pyruvate</td>
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</tr>
<tr>
<td>Acetoacetate</td>
<td>CH₃–CO-CH₂-COOH</td>
<td>Acetoacetate</td>
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</tr>
<tr>
<td>Oxalacetic</td>
<td>HOOC-CO–CH₂-COOH</td>
<td>Oxalacetate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-Oxoglutaric (α-ketoglutaric)</td>
<td>HOOC–(CH₂)₂–CO–COOH</td>
<td>2-Oxoglutarate (α-ketoglutarate)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxalosuccinic</td>
<td>HOOC–CO–CH(COOH)CH₂(COOH)</td>
<td>Oxalosuccinate</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Chemical reactions

1. **Neutralisation - salt formation**

\[
\text{Acetic acid} + \text{NaOH} \rightarrow \text{Ch}_3\text{–COO}^- \text{Na}^+ + \text{H}_2\text{O}
\]

Acetic acid \quad \text{sodium acetate}

Sodium and potassium salts – well soluble in water

\[
\text{(COOH)}_2 + \text{Ca(OH)}_2 \rightarrow \text{(COO)}_2 \text{Ca} + \text{H}_2\text{O}
\]

Oxalic acid \quad \text{calcium oxalate - insoluble (urine stones)}

- organic acids at pH near to 7.4 form in cells salts
- dissociated in the form of anions \quad \text{R – COO}^-
- soaps – sodium and potassium salts of fatty acids
  - palmitic acid \quad \text{CH}_3\text{–(CH}_2\text{)}_{14}\text{ - COO}^+\text{Na}^-
  - stearic acid \quad \text{CH}_3\text{–(CH}_2\text{)}_{16}\text{ - COO}^+\text{K}^+
2. Decarboxylation

\[ \text{propanoic acid} \quad \overset{\text{- CO}_2}{\longrightarrow} \quad \text{ethane} \]

\[ \text{Oxalosuccinic acid} \quad \overset{\text{- CO}_2}{\longrightarrow} \quad \text{Fumaric acid} \quad \overset{\text{dehydrogenation}}{\longrightarrow} \quad \text{Succinic acid} \]
1. Functional derivatives
- substitution of – H or - OH group of carboxyl with another atom or atom group
- esters, thioesters, halogenides, amides, anhydrides

2. Substitution derivatives
- substitution of hydrogen atom/s in side chain of carboxylic acids with another atom or atom group
- hydroxyacids, oxoacids, amino acids, halogene acids
DERIVATIVES of CARBOXYLIC ACIDS

Acyl- + O

- M (salt)
  - X (halogenides)
  - NH$_2$ (amides)
  - O – R (esters)
  - O – CO – R (anhydrides)
  ≡ N (nitriles)

Functional derivatives
3. **Nucleophilic substitution reactions**

- formation of functional derivatives (esters, amides, anhydrides, halogenides)
- substitution of –OH group in carboxyl by nucleophile (esterification)

\[
\begin{align*}
\text{Formic acid} & \quad \text{Methyl formiate} \\
H^- \overset{\text{H}^+}{\rightleftharpoons} H^+ O\overset{\text{H}_2\text{O}}{\rightarrow} \text{CH}_3 \quad \text{Methylester of formic acid}
\end{align*}
\]
Synthesis of aspirin

Charles Frederic Gerhardt (1853)

2-Hydroxybenzoic acid (salicylic acid) + Acetic acid

esterification

- H₂O

Acetylsalicylic acid (aspirin)

1899 The First Bottle of Aspirin
Transport of *acyl* in biochemical reactions

- coenzyme A, (CoA ~ SH) - activation of carboxylic acids

```
R – COOH + HS – CoA → Acyl-
```

- thioesters – active form of carboxylic acids (acyls)

```
CH₃ – CO ~ S-CoA   acetyl – CoA
```

```
CH₃ – CO ~ CoA  the key intermediate of metabolism of lipids, saccharides and proteins
```

- substrate for Krebs cycle (citric acid cycle)
2. Hydrolysis of esters

\[ \text{R} - \text{CO} - \text{O} - \text{R}_1 + \text{HOH} \rightarrow \text{R} - \text{COOH} + \text{R}_1 - \text{OH} \]

Ester \hspace{2cm} Acid \hspace{2cm} Alcohol

**Alkaline hydrolysis of esters, so called saponification:**

\[ \text{R} - \text{CO} - \text{OR}_1 + \text{NaOH} \rightarrow \text{R} - \text{COO}^- \text{Na}^+ + \text{R}_1 - \text{OH} \]

R – rest of fatty acid \hspace{2cm} Salt of fatty acid

**Soap** – sodium or potassium salt of fatty acids
Amides of carboxylic acid

\[ R-C-OH + NH_3 \rightarrow R-C-NH_2 + H_2O \]

Amide of carboxylic acid

Amide of nicotinic acid
Niacin
Vitamin PP

NAD^+
- Substitution derivatives

\[ \gamma(4) \quad \beta(3) \quad \alpha(2) \quad 1 \]

\[ R - \text{CH}_2 - \text{CH}_2 - \text{CH} - \text{C} \]

\[ \text{H} \]

\[ \text{O} \]

\[ \text{OH} \]

- \( \text{X} \) (halogene of carboxylic acid)
- \( \text{OH} \) (hydroxy acids)
- \( \text{NH}_2 \) (amino acids)
- \( = \text{O} \) (aldehyde- and oxo-acids)
α- Hydroxy acids

α-hydroxy acids eliminate water to lactides at higher temperature

\[
\begin{align*}
\text{CH}_3 - \text{CH} - \text{COOH} + \text{HO} \quad \rightarrow \quad \text{CH}_3 - \text{CH} - \text{CO} - \text{O} - \text{CH} - \text{CH}_3 \\
\text{OH} \quad \text{HOOC} \quad \text{CH} - \text{CH}_3 \\
\end{align*}
\]

- 2 H₂O

lactide

Cyclic diester
β- a γ- Hydroxy acids

β–hydroxy acids eliminate water (dehydrated) to unsaturated acids at higher temperature:

\[ \beta \text{-CH}_3 - ^3\text{CH} - \text{CH}_2 - ^1\text{COOH} \xrightarrow{-\text{H}_2\text{O}} \text{CH}_3 - \text{CH} = \text{CH} - \text{COOH} \]

3–Hydroxybutanoic acid → 2- Butenoic acid

γ–hydroxy acids dehydrated to lactons at higher temperature:

\[ \gamma \text{-R} - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{C}=\text{O} \xrightarrow{-\text{H}_2\text{O}} \text{R-CH-CH}_2-\text{CH}_2-\text{C}=\text{O} \]

γ–hydroxy acid → γ–lactone
Oxidation of hydroxy acids

Lactic acid

CH₃ – CH – COOH

OH

+2H

CH₃ – C – COOH

-2H

Pyruvic acid

β – hydroxybutyric acid

CH₃ – CH – CH₂ – COOH

OH

+2H

CH₃ – CO – CH₂ – COOH

-2H

Acetoacetic acid
Reaction of β-oxoacids important in the metabolism of fat

\[ \text{Acetoacetic acid} \xrightarrow{\text{NADH + H}^+ \text{ hydrogenation}} \text{CH}_3\text{C}-\text{CH}2\text{COOH} \]

\[ \text{CH}_3\text{C}-\text{CH}2\text{COOH} \xrightarrow{\text{ketone forming cleavage}} \text{CH}_3\text{CH}-\text{CH}2\text{COOH} \]

\[ \text{CH}_3\text{C}-\text{CH}2\text{COOH} \xrightarrow{(OH^-) \text{ acid forming cleavage}} 2 \text{CH}_3\text{COOH} \]

\[ \text{CH}_3\text{C}-\text{CH}2\text{COOH} \xrightarrow{\text{hydrogenation}} \text{OH} \]

\[ \beta\text{-Hydroxybutyric acid} \]

\[ \text{CH}_3\text{CO}-\text{CH}_3 \]

\[ \text{Acetone} \]

\[ 2 \text{CH}_3\text{COOH} \]

\[ \text{Acetic acid} \]
Ketone bodies in the organism

In trace amount in blood, urine
At higher concentration in urine – ketonuria (ketoacidosis) (starvation, diabetes)

\[
\text{CH}_3 - \text{CO} - \text{CH}_2 - \text{COOH} \quad \text{acetoacetic acid}
\]

\[
\text{CH}_3 - \text{CH} - \text{CH}_2 \text{COOH} \quad \beta - \text{hydroxybutyric acid}
\]

\[
\text{CH}_3 - \text{CO} - \text{CH}_3 \quad \text{acetone}
\]
Transamination

Glutamic acid + Phenylpyruvic acid ⇌ 2-oxo-glutaric acid + Phenylalanine
Citrate cycle
Krebs Hans Adolf (1900 - 1981)

Nobel price for physiology and medicine, 1953

Discovery of citric acid cycle

He was born in Hildesheim (Germany) in the family of Judaic physician. After studying medicine he studied also chemistry in Berlin for one year.

His most important discovery was Citric cycle (Krebs cycle).
Citrate formation from Oxaloacetate and Acetyl-CoA
Citrate/Isocitrate isomerisation

Citrate

Iso-citrate

Cis-aconitate

aconitase

H₂O

H₂O
Oxalosuccinate and α-oxoglutarate formation

\[
\begin{align*}
\text{Isocitrate} & \quad \text{Isocitrate dehydrogenase} \\
\text{NAD}^+ & \quad \text{NADH} + H^+ \\
\text{CH}_2\text{-COO}^- & \quad \text{CO}_2 \\
\text{H-C} & \quad \text{H-C} \\
\text{HO-C} & \quad \text{O=C-COO}^- \\
\text{Isocitrate} & \quad \text{Alpha-ketoglutarate} \\
\text{NAD}^+ & \quad \text{NADH} + H^+ \\
\text{CH}_2\text{-COO}^- & \quad \text{CO}_2 \\
\text{CH}-\text{COO}^- & \quad \text{O=C-COO}^- \\
\text{Oxalosuccinate} &
\end{align*}
\]
Succinyl-CoA formation
Succinate formation

\[ \text{CoA-S} \xrightarrow{\text{HOH}} \text{CH}_2 \text{CH}_2 \text{COO}^- \rightarrow \text{CH}_2 \text{COO}^- + \text{GTP} + \text{CoA-SH} \]

+ GDP + Pi
Fumarate formation
Malate formation through water addition

Fumarate $\xrightarrow{\text{fumarase}}$ Malate

$\text{H}_2\text{O}$
Malate dehydrogenation

Malate dehydrogenase

\[ \text{NAD}^+ \rightarrow \text{NADH} + H^+ \]

Malate

\[ \text{HCO}_2^- \text{C} \text{OH} \text{CH}_2 \text{CO}_2^- \]

Oxaloacetate

\[ \text{C} \equiv \text{O} \text{CH}_2 \text{CO}_2^- \]
Derivatives of $\text{H}_2\text{CO}_3$ $\rightarrow$ NaHCO$_3$  Na$_2$CO$_3$  inorganic salts

- **Formic acid**
- **Carbonic acid**
- **Phosgene**
- **Urea**
- **Iminourea - guanidine**
- **Thiourea**

 oxidation

$\text{HOOC} - \text{OH} = \text{HO} - \text{C} - \text{OH}$

$\text{H}_2\text{N} - \text{C} - \text{NH}_2$

$\text{H}_2\text{N} - \text{C} - \text{NH}_2$

$\text{H}_2\text{N} - \text{C} - \text{NH}_2$
Macroergic compounds

Carbamoyl phosphate

phosphoenolpyruvate

1,3–bisphosphoglycerate
Free energy releases through hydrolyses of phosphates of some macroergic compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\Delta G^0$ (kJ.mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphoenolpyruvate</td>
<td>-61.86</td>
</tr>
<tr>
<td>Carbamoyl phosphate</td>
<td>-51.41</td>
</tr>
<tr>
<td>Acetyl phosphate</td>
<td>-43.05</td>
</tr>
<tr>
<td>Creatine phosphate</td>
<td>-43.05</td>
</tr>
<tr>
<td>ATP (na ADP)</td>
<td>-30.51</td>
</tr>
<tr>
<td>Glucose-1-phosphate</td>
<td>-30.51</td>
</tr>
<tr>
<td>Glucose-6-phosphate</td>
<td>-13.79</td>
</tr>
<tr>
<td>Glucose-3-phosphate</td>
<td>-9.19</td>
</tr>
</tbody>
</table>
Organic compounds of nitrogen

Amines
- primary \( R-\text{NH}_2 \)
- secondary \( R-\text{NH}-R \)
- tertiary \( R-N-R \)

Basic properties
Formation of ammonium salts

\[ R-\text{NH}_2 + H^+ \rightarrow R-\text{NH}_3^+ \]
AMINODERIVATIVES OF HYDROCARBONS

AMINOFENOS - Catecholamines

BIOGENIC AMINES
- decarboxylation of aminoacids

\[
\begin{align*}
\text{serine} & \quad \xrightarrow{\text{CO}_2} \quad \text{ethanolamine} \\
\text{noradrenaline} & \quad \text{adrenaline}
\end{align*}
\]
Biological important amines formation

histidine $\xrightarrow{\text{CO}_2}$ histamine
Lysine

\[ \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH} - \text{COOH} \]

\[ \text{NH}_2 \]

\[ \text{CO}_2 \]

Cadaverine

\[ \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 \]

\[ \text{NH}_2 \]

\[ \text{NH}_3 \]

Pyrrolidine

Putrid process
In dunghill
Reaction of amines with nitric acid/nitrates

Primary amine

$$R - CH_2 - NH_2 + HNO_2 \rightarrow R - CH_2 - OH + N_2 + H_2O$$

Secondary amine

$$\begin{array}{c}
R \\
\text{NH} + HO-N=O \\
R
\end{array} \rightarrow \begin{array}{c}
R \\
\text{N-N=O} + H_2C \\
R
\end{array}$$

nitrosoamine

Carcinogen  !!
ALCALOIDS

🌟 natural compounds with nitrogen – basic properties
🌟 occurrence: products of aminoacid metabolism in plants
🌟 nitrogen - as heterocycle
🌟 in water insoluble
🌟 bitter taste

💀 strong effect on organisms, high doses are toxic
➢ **Alcaloids derived from pyridine**

- **nicotine** – isolated from tabacco leaf
  - lethal dose for man - 50 mg

➢ **Alcaloids derived from thropane**

- **atropine** - has very specific effect on the body – is used in treating colitis, renal and biliary colic, peptic ulcer and irritable bowel syndrome

- **cocaine** - local analgetic

➢ **Alcaloids derived from chinoline and isochinoline**

- **morphine** - a potent opiate analgesic medication
- **codeine** – make softer caugh
- **heroin** (diacetylmorphine) - a semi-[synthetic opioid drug](#) synthesized from morphine, a derivative of the [opium poppy](#) - is used as an analgesic.

  Frequent and regular administration is associated with tolerance and physical dependence, which may develop into [addiction](#).

➢ **Alcaloids derived from indole** (produced by the ergot fungus and some plants)

- **lysergid** (LSD) – hallucinogens

➢ **Alcaloids derived from purine**

- **copheine**
- **theobromine**
- **theophyline**

Analeptics stimulate CNS, but did not influence significantly psychic functions.
ORGANIC COMPOUNDS OF SUPHUR

- Thiols \( R{-}SH \) (disulphides, thioesters)
- Sulphides \( R{-}S{-}R \) (sulphoxides, sulphons)
- Sulphonic acids, sulphonamides \( R – SO_3H \)
- Heterocyclic compounds with sulphur (thiophene, thiazol)

\[ \begin{align*}
\text{S} & \quad \text{N} \\
\text{thiophene} & \quad \text{thiazol}
\end{align*} \]
Tiols and sulfides

Amino Acid Cysteine

Aminoacid methionine
Redox reaction of thiols

\[ \text{oxid} \quad \text{R} - \text{SH} + \text{HS} - \text{R} \quad \text{red} \quad \text{R} - \text{S} - \text{S} - \text{R} + \text{2H} \]
Disulfides formation

\[ \text{Cysteine} + 2H \xrightarrow{\text{[reduction]}} \text{Cystine} - 2H \xleftarrow{\text{[oxidation]}} \text{Cysteine} \]
Redox reactions of thiols – structure of proteins is changed

\[
\text{Oxidation} - 2\text{H} \quad \leftrightarrow \quad \text{Reduction} + 2\text{H}
\]
Oxidation of glutathione

\[ \text{OOC-CH-CH}_2\text{-CH}_2\text{-CO-NH-CH-CO-NH-CH}_2\text{-COO}^- + 2\text{H} \rightarrow \text{GSSG} + 2\text{H} \]
Thank you for your attention........