Organic chemistry

CARBOXYLIC ACIDS AND THEIR DERIVATIVES

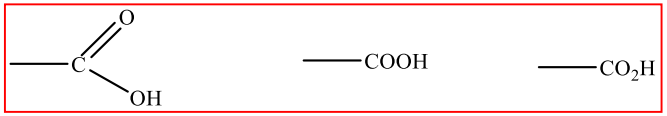
HETEROCYCLIC COMPOUNDS

Amino acids

ALKALOIDS

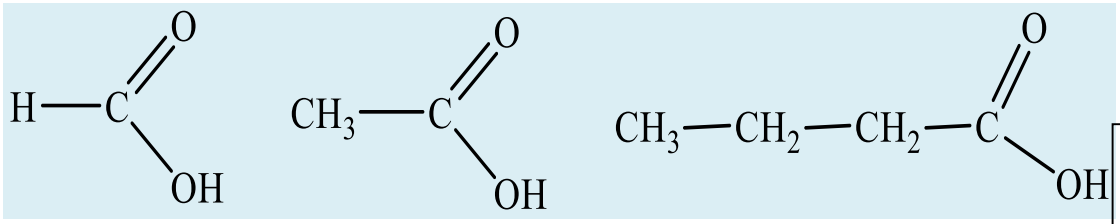
Prof. Dr. Nedeljko Manojlovic

CARBOXYLIC ACIDS



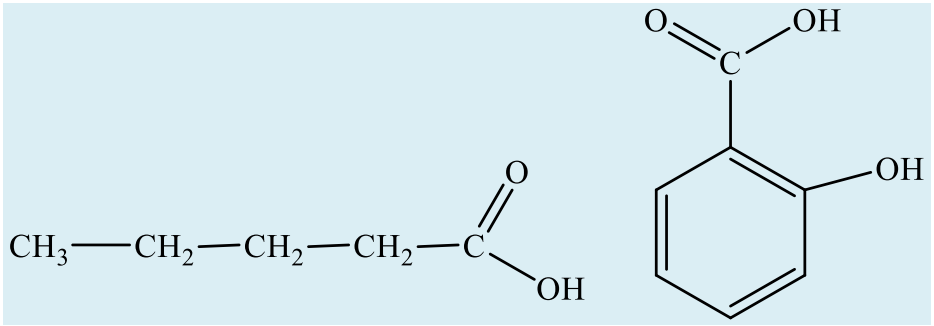
Carboxylic group

Aliphatic carboxylic acids have been known for a long time, so they have trivial names that indicate their sources.



formic acid acetic acid butyric acid

During the year, all the ants in the world produce more formic acid than all factories where it is

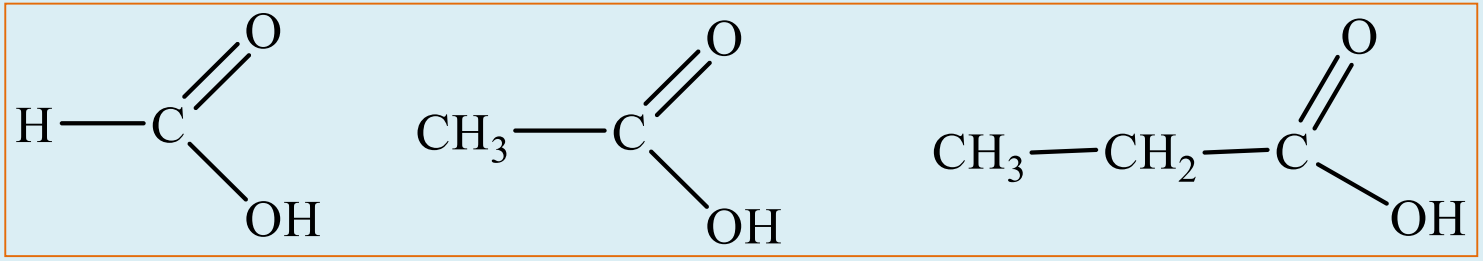


valeric acid salicylic acid

spinach contains oxalic acid

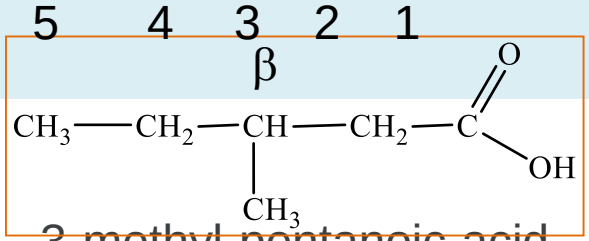
HOOC-COOH

According to the IUAC nomenclature, **the name of a carboxylic acid** is derived by determining the longest sequence in which the carboxyl group is located. The labeling of carbon atoms is done so that the first carbon atom is actually the carbon from the carboxyl group. The suffix **-ic acid** is added to the name of hydrocarbons with the same number of carbon atoms.



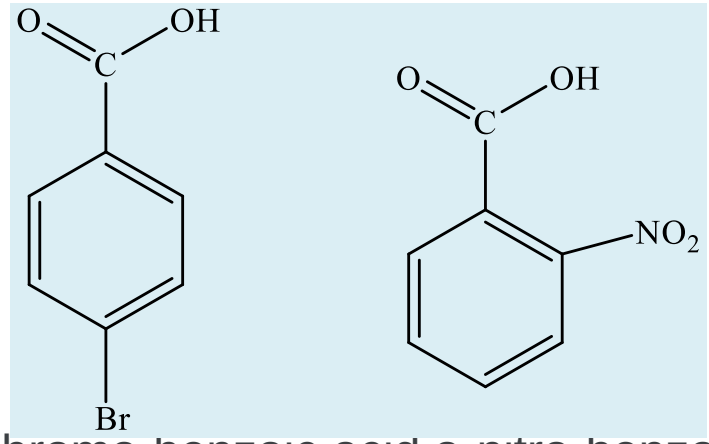
methane acid ethane acid propanoic acid

Marking of carbon atoms can also be done with letters, where the first adjacent carbon atom to the carboxyl group is α carbon, the next is β...

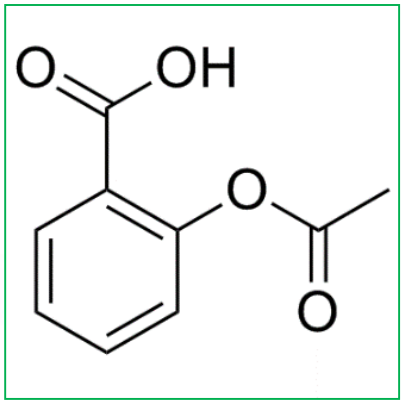


3-methyl-pentanoic acid
β-methyl-pentanoic acid

- Aromatic acids are considered derivatives of the parent acid, benzoic acid.

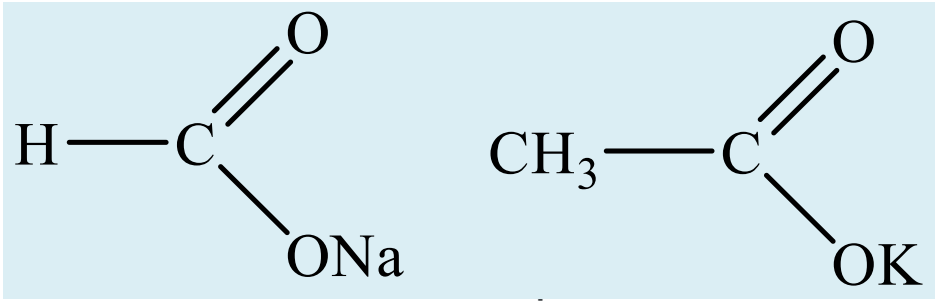


p-bromo-benzoic acid o-nitro-benzoic acid



Aspirin is acetylsalicylic acid

The names of salts are obtained by removing the suffix -ic from the name of the acid and adding the suffix -at.



sodium methanate potassium ethanoate

- **According to the character of the hydrocarbon residue R**

Acyclic (saturated and unsaturated)

Cyclic (cycloalkane, aromatic)

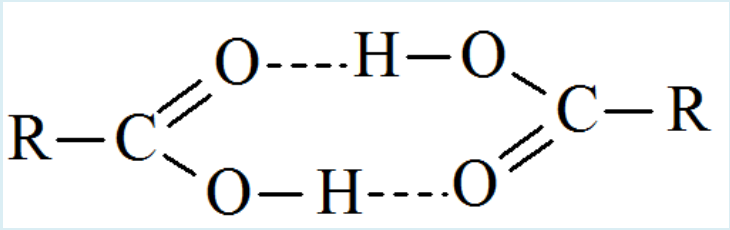
Heterocyclic

- **According to the number of carboxyl groups**

Monocarboxylic

Dicarboxylic

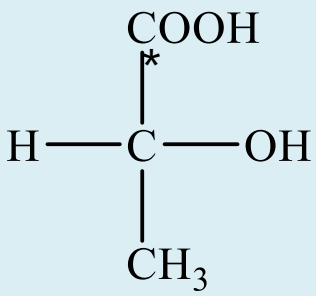
Tricarboxylic acids



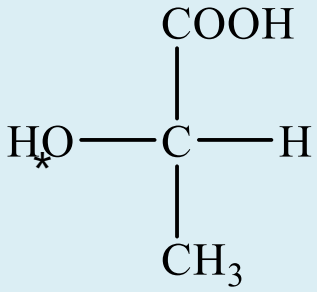
Dimeric form of carboxylic acids

Lactic (milk) acid

- Found in cheese, sour milk and sauerkraut (L or D)
- It accumulates in muscle.
- It has one chiral carbon atom and occurs in two enantiomeric forms, D- and L-lactic acid
- Salts of lactic acid are called lactates.



D-(-)- lactic acid



L-(-)- lactic acid

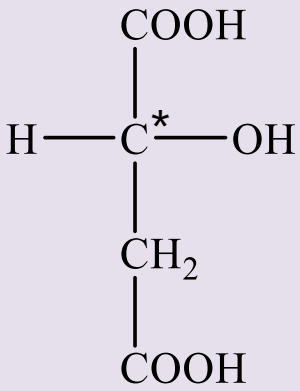
Malic acid

Monooxysuccinic or malic acid

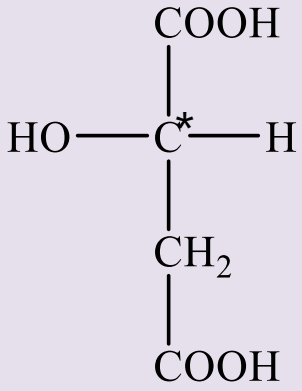
It is found in the unripe fruits of apples, gooseberries, grapes, etc.

It has one asymmetric carbon atom

Salts of malic acid are called malates



D-(-)-malic acid



L-(-)- malic acid

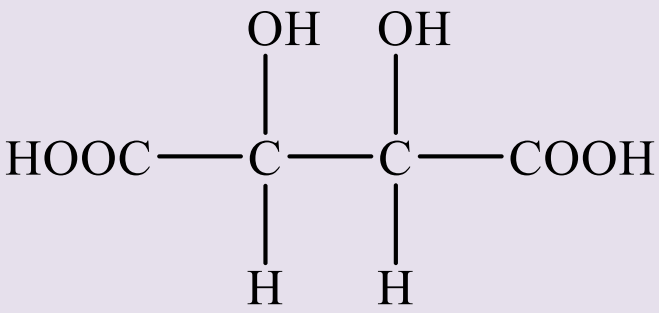
Tartaric acid

Tartaric acid is dioxysuccinic acid

It is found in fruits, mostly in grape juice (K-hydrotartrate).

Salts are called tartrates

It is an ingredient of "stone of wine"



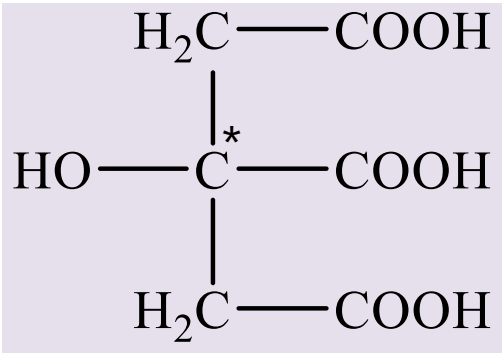
Tartaric acid

Citric acid

Citric acid, 2-oxypropane-1,2,3-tricarboxylic acid

It is found in the fruits of raspberries, gooseberries, grapes, while unripe lemons contain 6-7%.

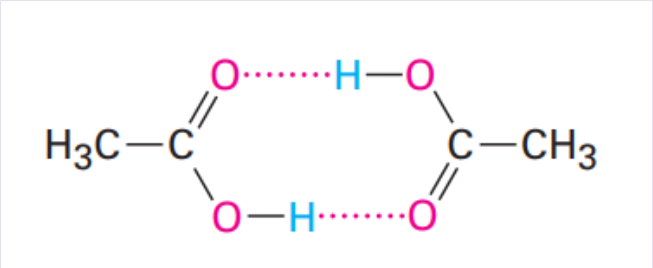
The salts are called citrates



Citric acid

Physical features

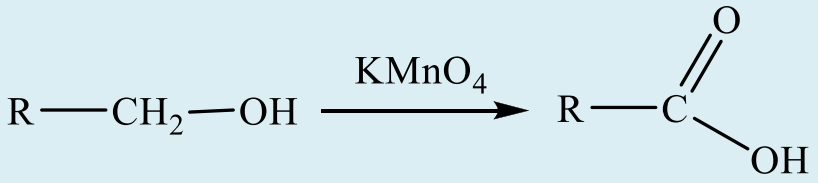
- The first four carboxylic acids are well soluble in water, the fifth only partially, while the others are almost insoluble.
- They are soluble in less polar solvents such as ether, alcohol, benzene, etc.
- They have a higher boiling point than alcohol, and this is due to the possibility of forming two hydrogen bonds



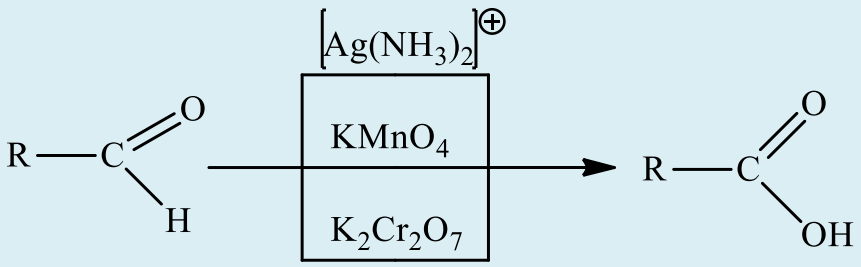
- The lower aliphatic acids, formic and acetic, have a sharp irritating smell. Butyric and valeric acid have an unpleasant smell.

Obtaining carboxylic acids

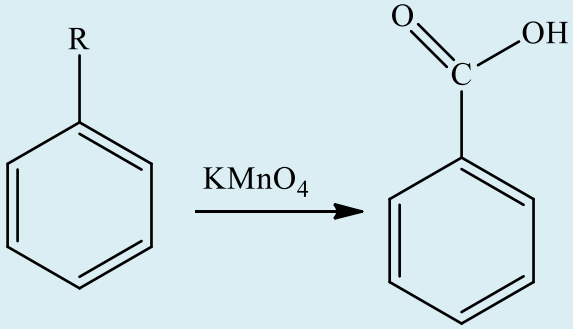
1. Oxidation of primary alcohols



2. Aldehyde oxidation

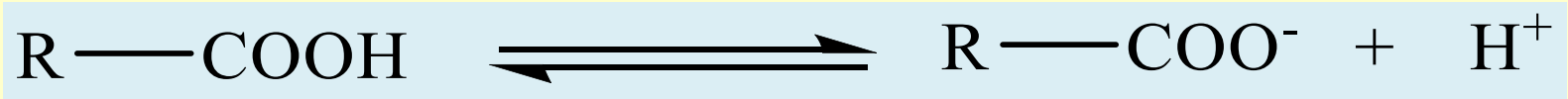


3. Oxidation of alkyl-benzene



Reactions of carboxylic acids

1. Acidity. Salt formation



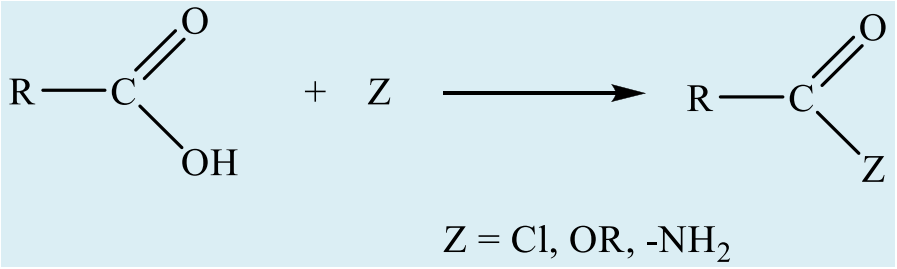
Electron-withdrawing groups and halogens enhance the acidity of carboxylic acids.

The closer such a substituent is to the carboxyl group, the stronger the acid.

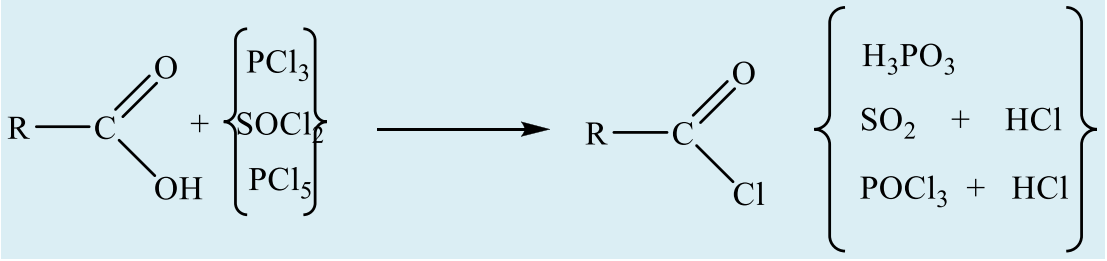
The greatest influence on the acid strength of halogens has the atom of fluorine, chlorine, bromine and the smallest atom of iodine.

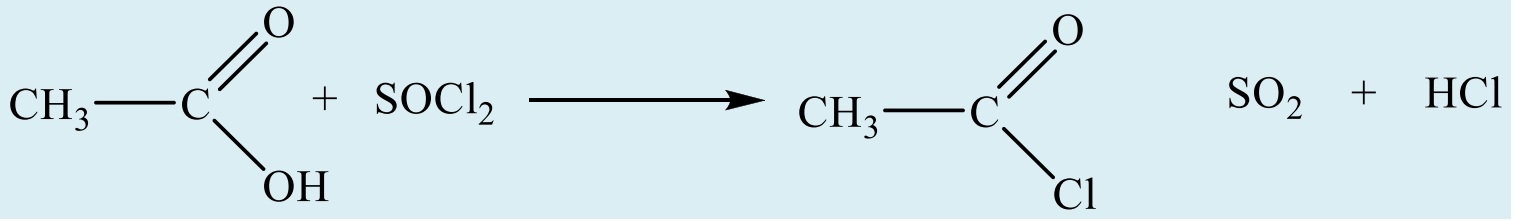
If there are more halogens in the acid molecule, the acid is stronger

2. Obtaining functional derivatives



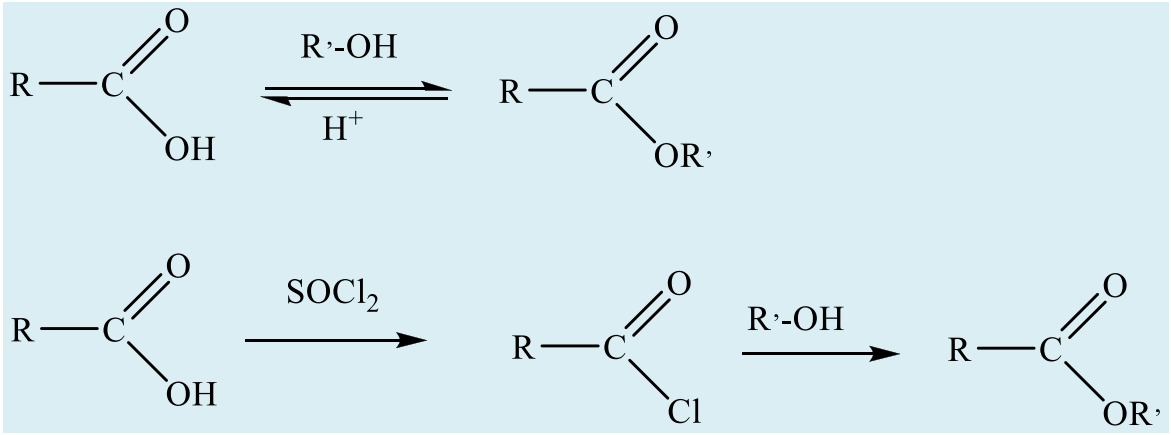
- 2a. Conversion to acid chlorides

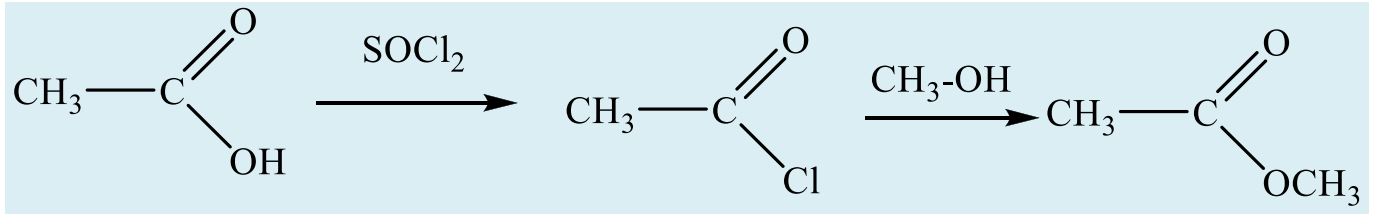




Ethanoyl chloride

2b. Obtaining esters (esterification)

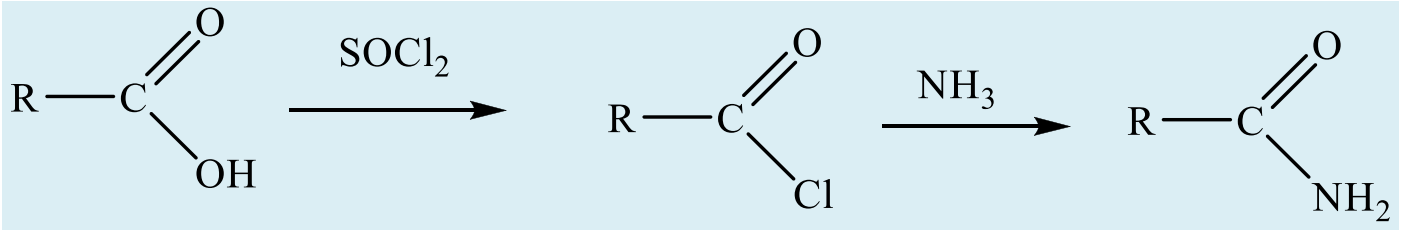




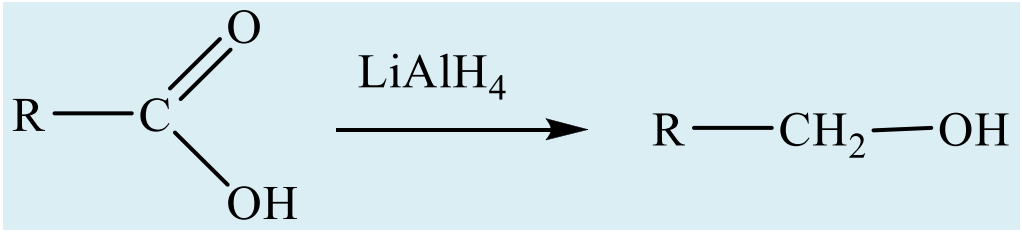
methyl ethanoate

methyl acetate

2c. Obtaining amides



3. Reduction



3. Ring substitution in aromatic acids.

The -COOH group is a deactivating group and directs further electrophilic aromatic substitution in the meta position.

Aromatic carboxylic acids undergo the following electrophilic aromatic substitution reactions:

Sulfonation

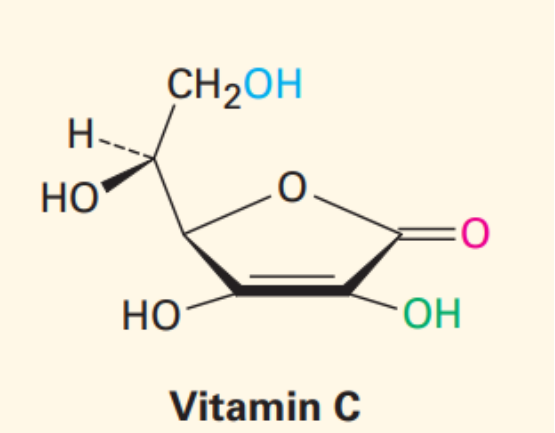
Nitrification

Halogenation

Alkylation

Acylation

Vitamin C



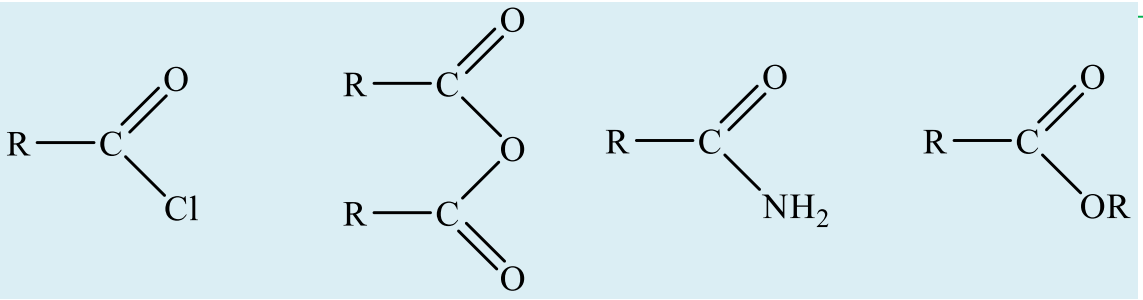
Vitamin C

discovered (1928)
structurally characterized (1933)
synthesized in the laboratory (1933)

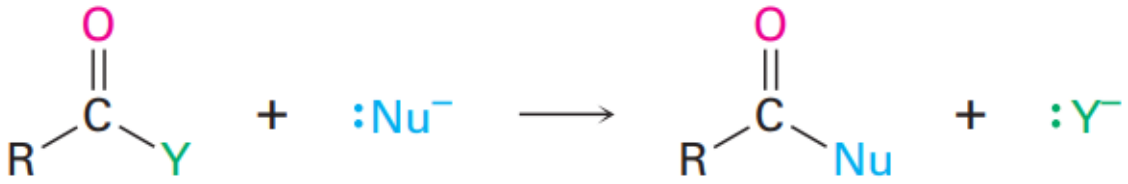
Vitamin C is used as a food preservative, a “flour improver” in bakeries, and an animal-food additive.

- has antiscorbutic properties

Carboxylic Acid Derivatives



acid chloride anhydrides amide ester

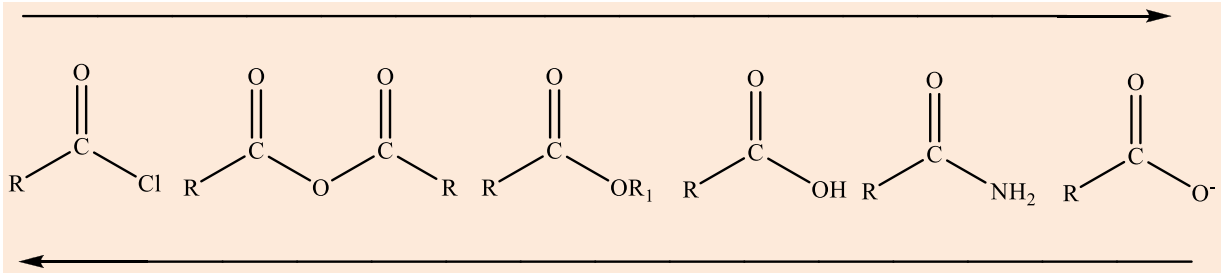


nucleophilic acyl substitution reaction

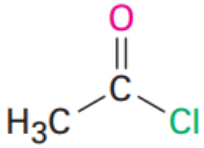
- polar compounds
- Amides have unusually high boiling points because they can form strong intermolecular hydrogen bonds.

Reactivity of Carboxylic Acid Derivatives

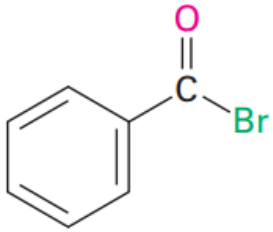
increased stability due to resonantion



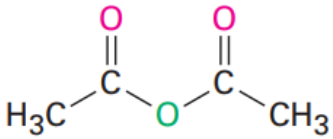
Increased reactivity



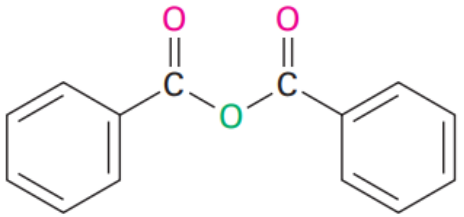
Acetyl chloride



Benzoyl bromide

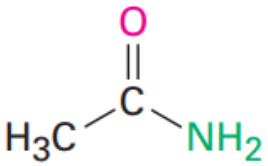


Acetic anhydride

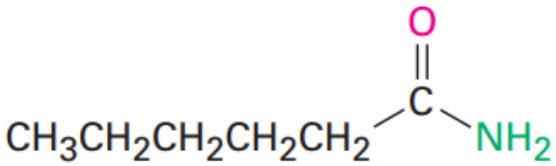


Benzoic anhydride

Amides



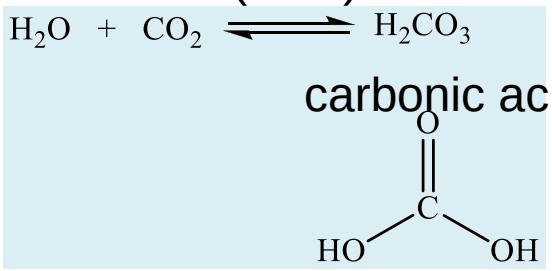
Acetamide

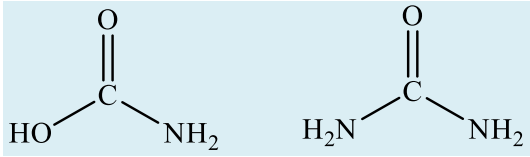


Hexanamide

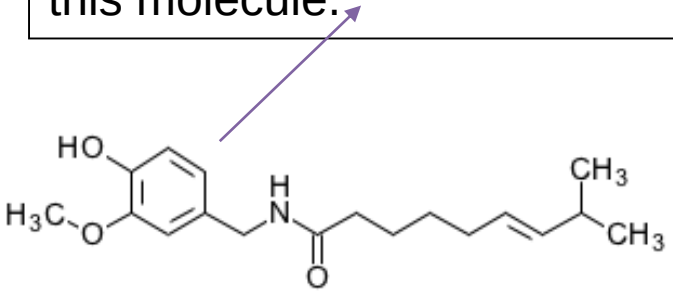
Diamide of carbonic acid

Urea (urea)



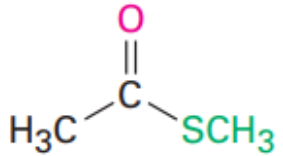


Chili peppers contain the molecule capsaicin. It irritates mammals, but not birds, because they do not have a receptor for this molecule.



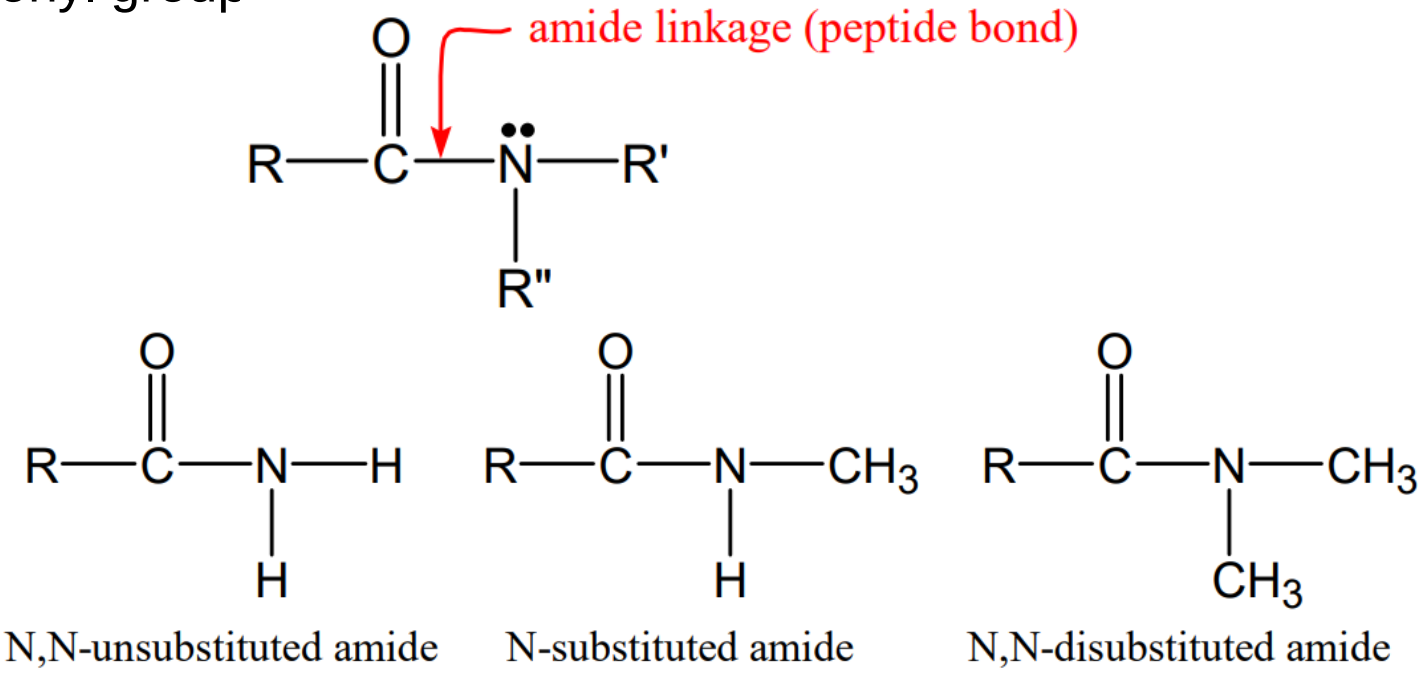
Capsaicin has the amide group.

Thioesters, RCOSR

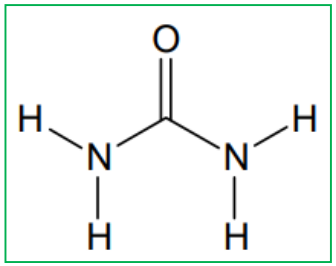


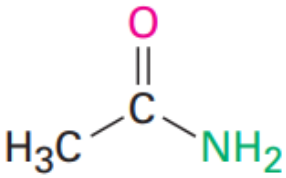
Methyl thioacetate

Amides contain a nitrogen which is directly attached to a carbon in a carbonyl group

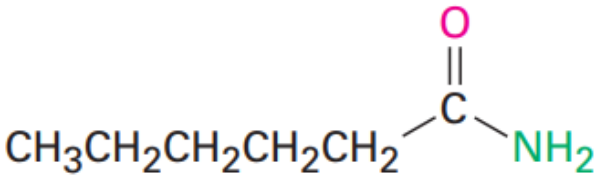


Urea is the major organic component of urine; about 25 g are excreted every day by humans.





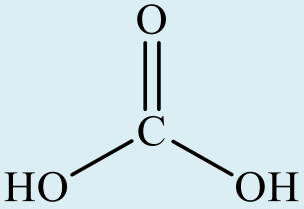
Acetamide



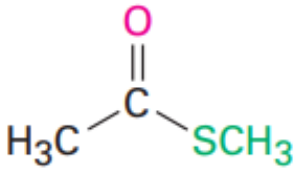
Hexanamide

Diamide of carbonic acid
Urea (urea)

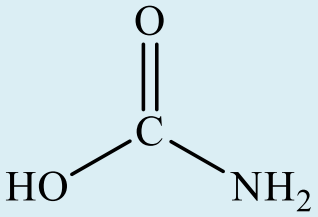
carbonic acid



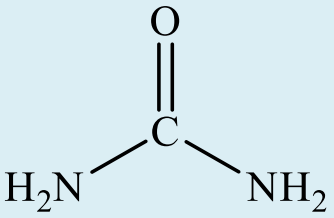
Thioesters,
RCOSR



Methyl thioacetate

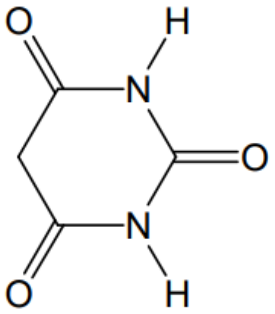


monoamide

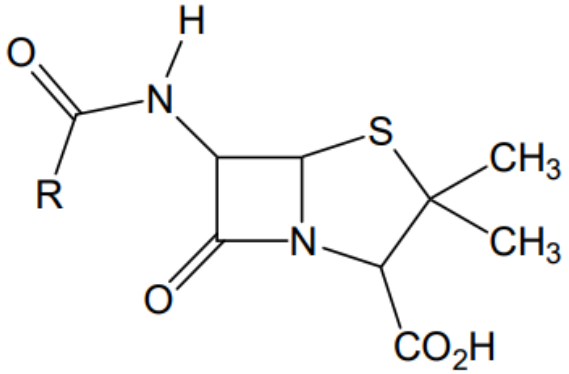


diamide
(urea)

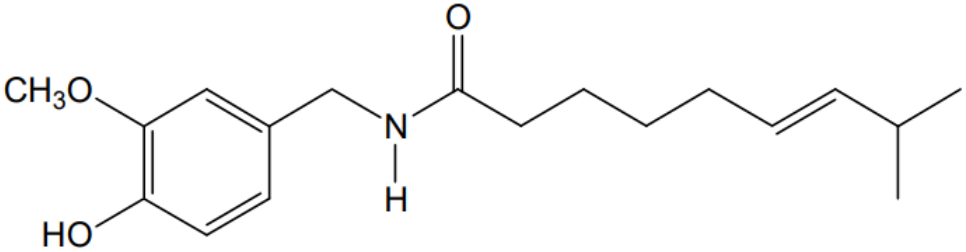
Some important amides



Barbituric acid



Penicillin

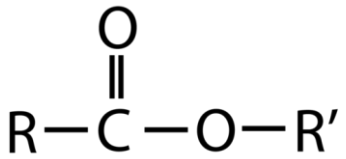


Chili peppers contain the molecule capsaicin. It irritates mammals, but not birds, because they do not have a receptor for this molecule.

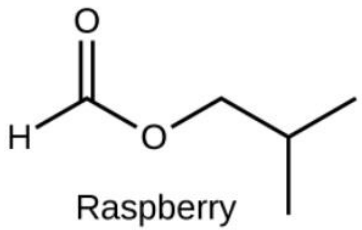
Penicillin is an antibiotic compound produced by the molds Penicillium notatum and Penicillium chrysogenum; it was discovered by Alexander Fleming in 1928

Esters

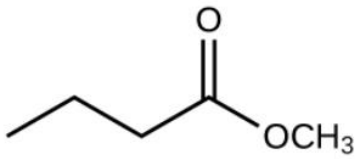
Ester is an organic compound that is a derivative of a carboxylic acid in which the hydrogen atom of the hydroxyl group has been replaced with an alkyl group.



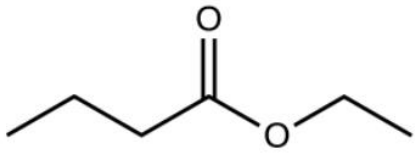
General formula for esters



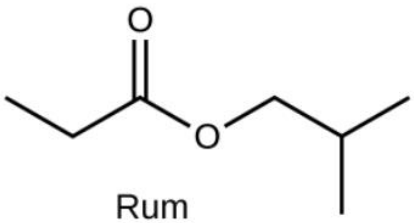
Raspberry
iso-butyl formate



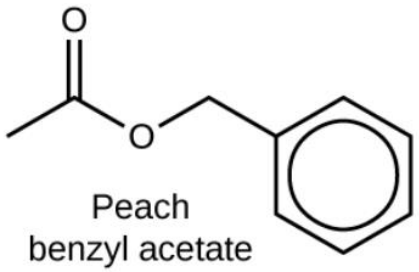
Apple
butyl acetate



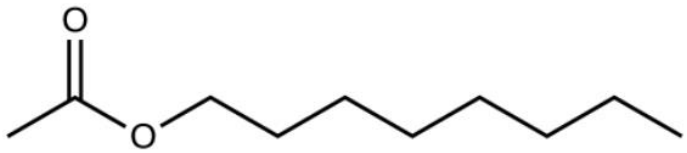
Pineapple
ethyl butyrate



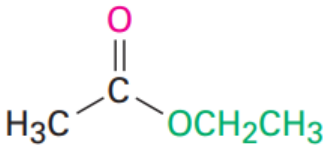
Rum
propyl isobutyrate



Peach
benzyl acetate

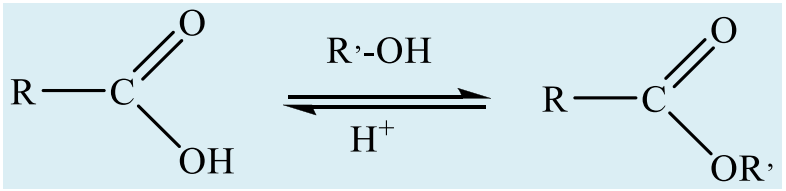


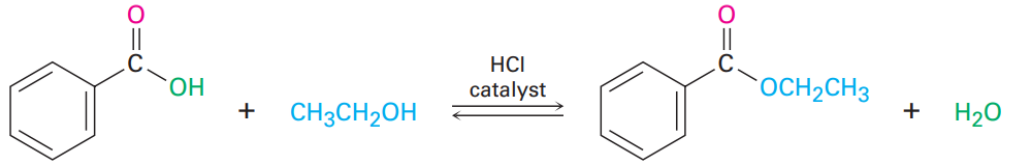
Orange
octyl acetate



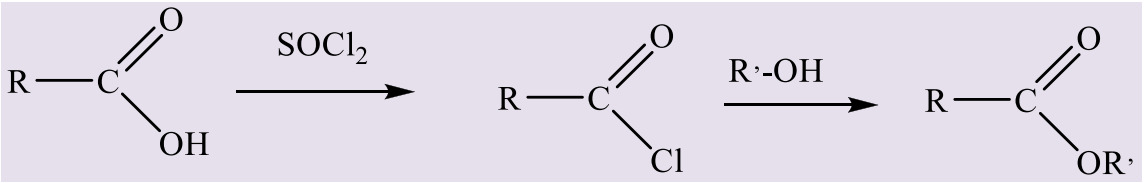
Ethyl acetate

1. Esters are obtained from acids and alcohols (esterification).

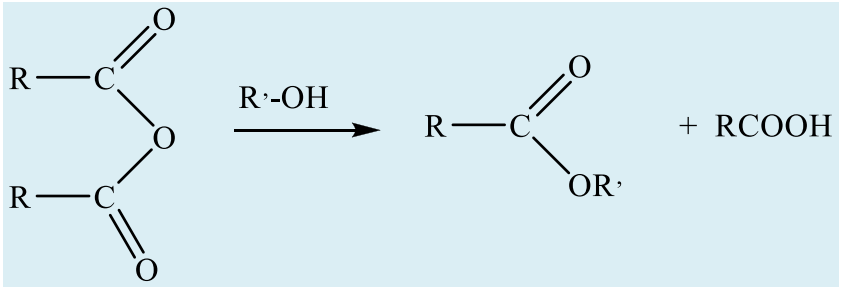




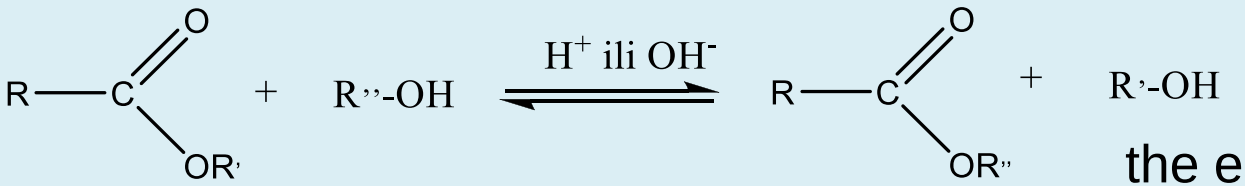
Benzoic acid **Ethyl benzoate (91%)**



2. Esters are obtained from acid chlorides or acid anhydrides



3. Esters are obtained from other esters. Transesterification



Ester 1 Ester 2

the ester reacts with alcohol

- esters are found in all cells: they are the basic ingredients of fats, oils and waxes, phosphate esters of sugar and those found in nucleic acids and phospholipids are known

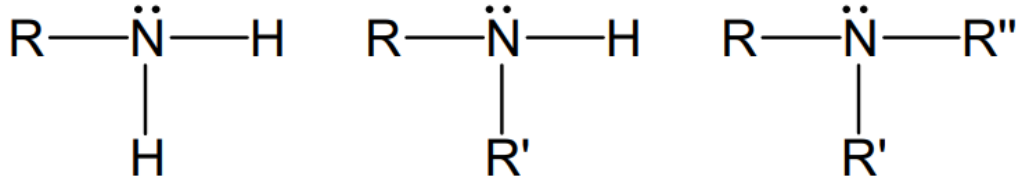
- Application: solvents and aromas

Esters ketones aldehides terpenes

Esters have characteristic smells (flowers)

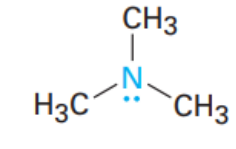
Amines

- General formula of amines is R-NH_2.
- Amines are divided into

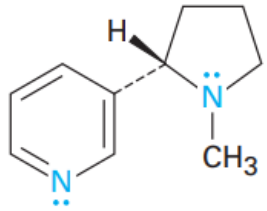


1° Amine **2° Amine** **3° Amine**

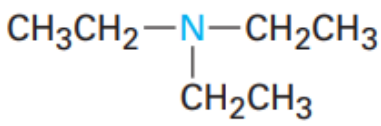
Alkaloids contain an amino group
Morphine is used in medicine



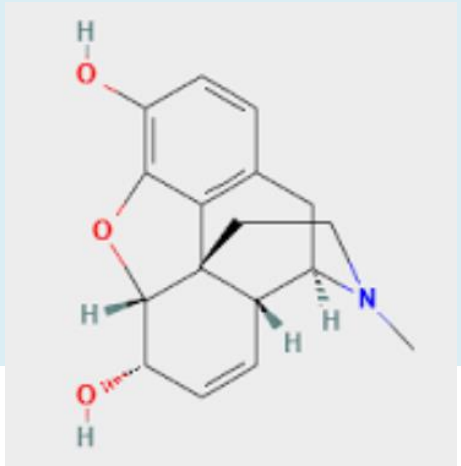
Trimethylamine

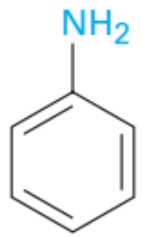


Nicotine



Triethylamine



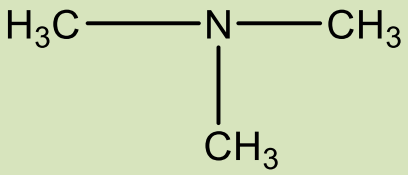


Aniline

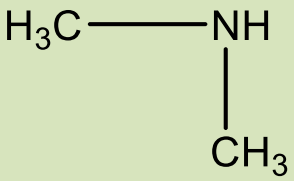
Physical properties

- Amines are polar compounds
- Except for tertiary amines, all of them can form hydrogen bonds
- They have a higher boiling point than non-polar compounds of similar molecular weight
- Amines containing up to six carbon atoms are soluble in water
- Aromatic amines are generally poisonous

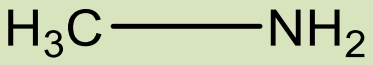
- The names of aliphatic amines are obtained by adding the suffix -amine to the name of the alkyl radical.



trimethylamine

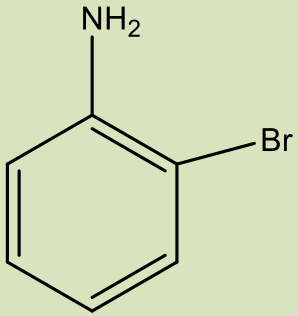


dimethylamine



methylamine

- The names of aromatic amines are derived from the simplest aromatic amine aniline



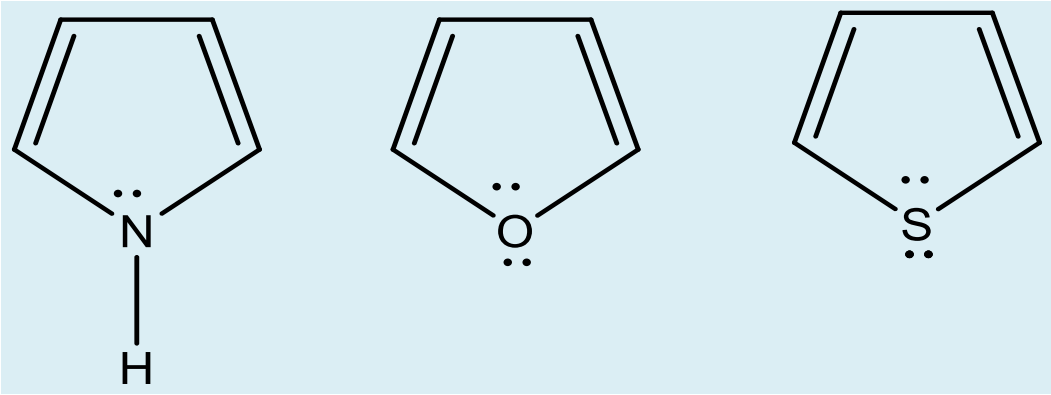
o-bromo-aniline

Heterocyclic compounds

- Cyclic compounds in which, apart from carbon, one or more other elements-heteroatoms (N, S, O, P...) are part of the ring.
- The size of the ring in the heteroatom molecule varies greatly - from three-membered to multi-membered.
- The most widespread are five-membered and six-membered heteroatoms.

Heterocyclic compounds in DNA molecule

Five-membered heterocyclic compounds with one heteroatom



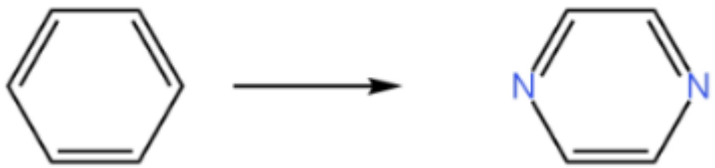
Pyrrole Furan Thiophene

Electrophilic Aromatic Substitution (EAS)

- Pyrrole, furan and thiophene undergo electrophilic substitution (halogenation, nitration, sulfonation, acylation) and are more reactive than benzene in these reactions.

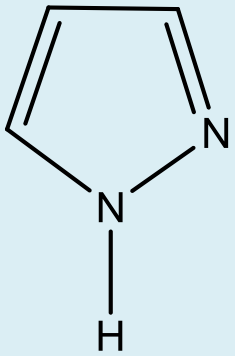
- Electrophilic attack takes place in position 2.

Hetero atom	Valency	Prefix
O	2	Oxa
N	3	Aza
S	2	Thia
P	3	Phospha
As	3	Arsa
Si	4	Sila

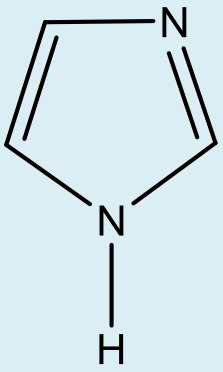


benzene 1,4-diazabenzene

Five-membered heterocyclic systems with two nitrogens (diazoles)

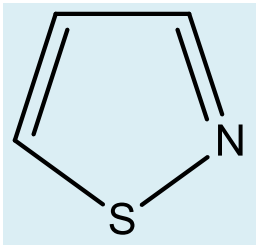


1,2-diazole (pyrazole)

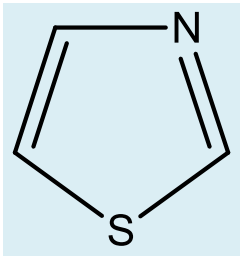


1,3-diazole (imidazole)

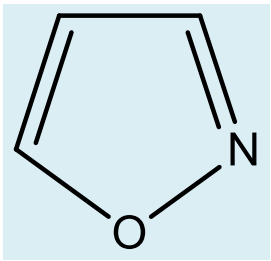
Five-membered heterocyclic systems with sulfur and nitrogen



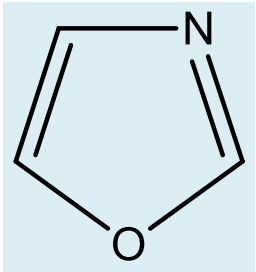
1,2-thiazole (isothiazole)



1,3-thiazole (thiazole)



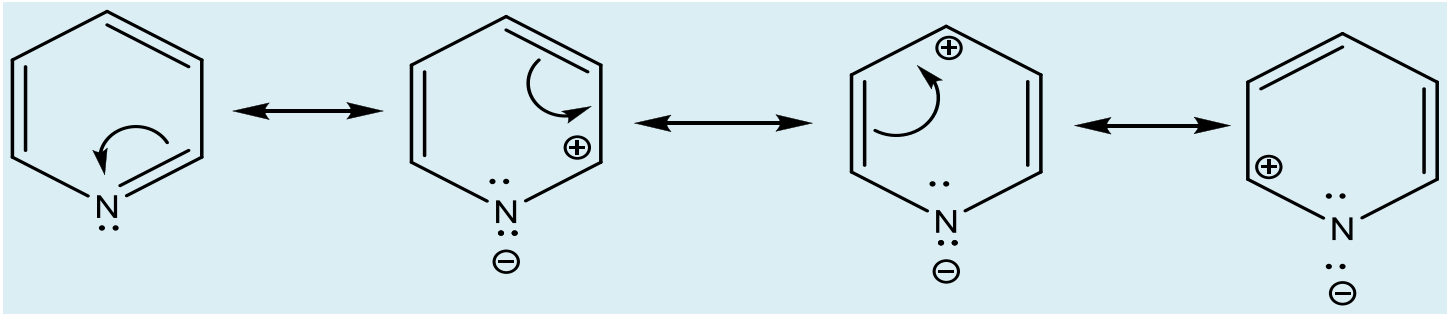
1,2-oxazole (isoxazole)



1,3-oxazole (oxazole)

Six-membered heterocyclic compounds with one heteroatom

- The most important compound is pyridine.
- Pyridine is a stronger base than pyrrole, but much weaker than aliphatic amines



pyridine

Chemical reactions of pyridine

1. Nucleophilic substitution

It behaves similarly to benzene which is substituted with an electron-withdrawing group

It takes place very easily, especially in the 2nd and 4th positions.

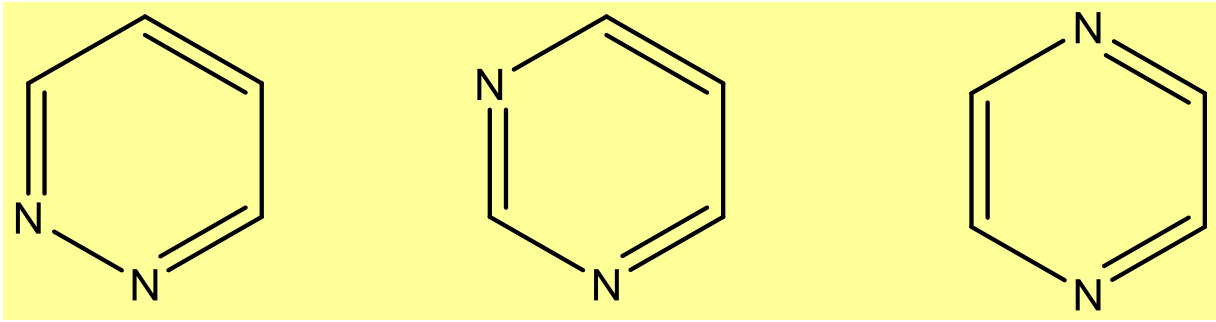
2. Electrophilic substitution

It behaves like a highly deactivated benzene derivative

Nitration, sulfonation and halogenation can only be carried out under drastic conditions, and acylation is not carried out even then

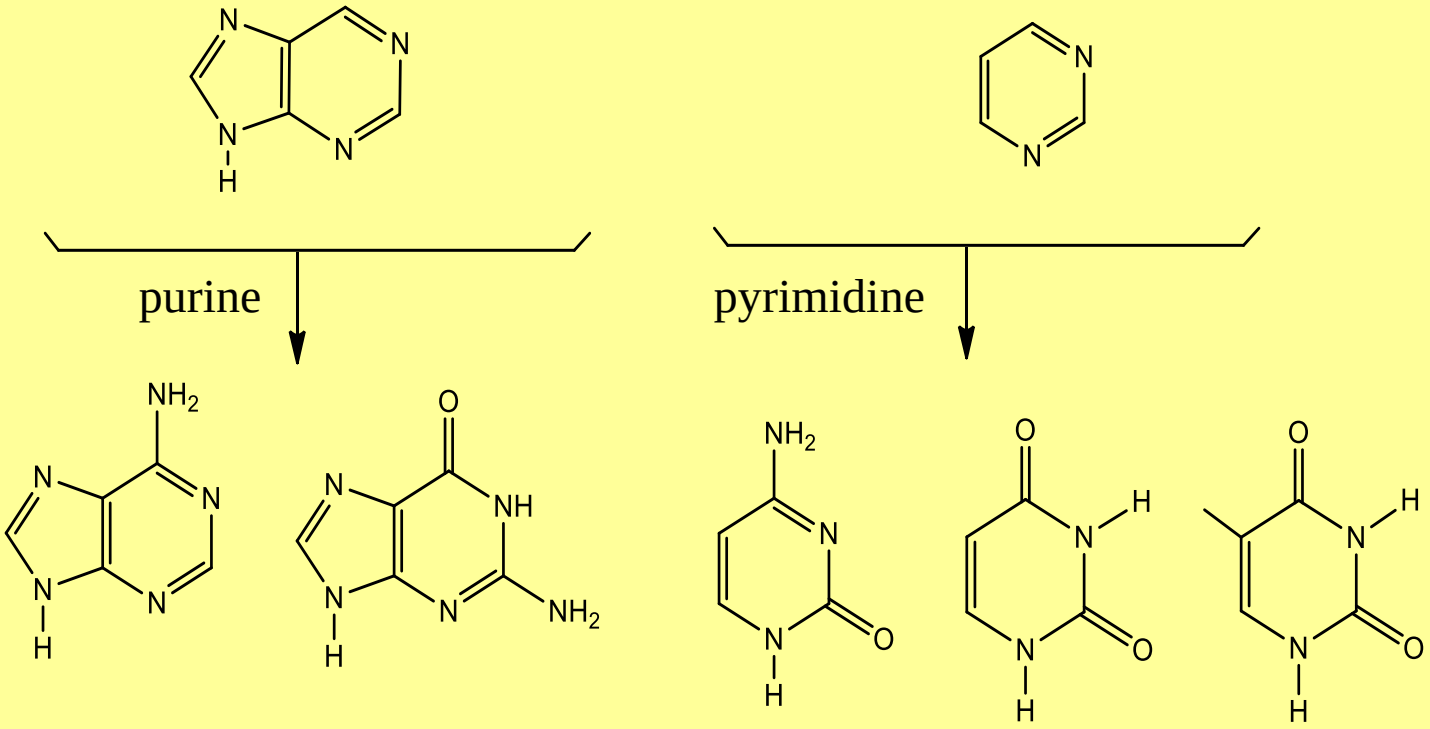
Substitution occurs in position 3.

Six-membered heterocyclic compounds with two heteroatoms



1,2-diazine (pyridazine) 1,3-diazine (pyrimidine) 1,4-diazine (pyrazine)

Purine and pyrimidine bases

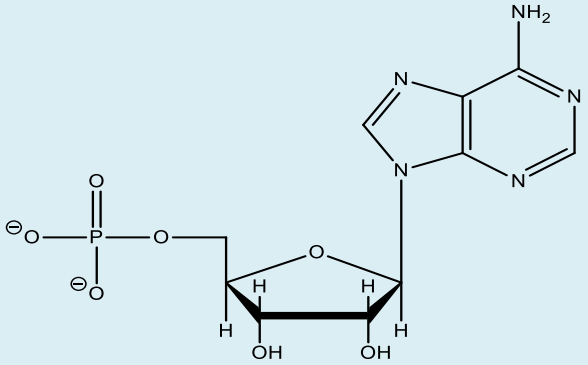


adenine (A) guanine (G) cytosine (C) uracil (U-only in RNA) timine (T-only in DNA)

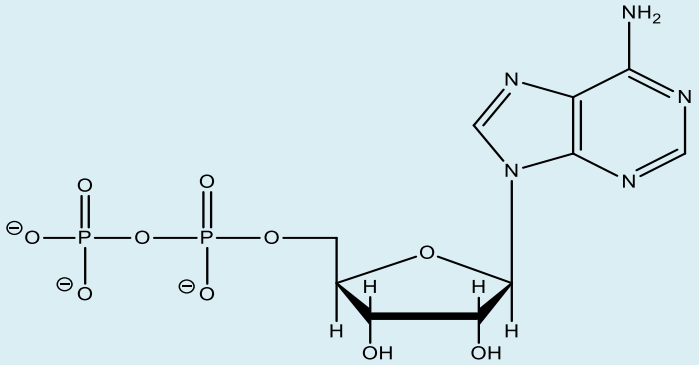
МЕДИЦИНСКИ ФАКУЛТЕТ
УНИВЕРЗИТЕТ У КРАГУЈЕВЦУ

THE MEDICAL FACULTY
UNIVERSITY OF KRAGUJEVAC

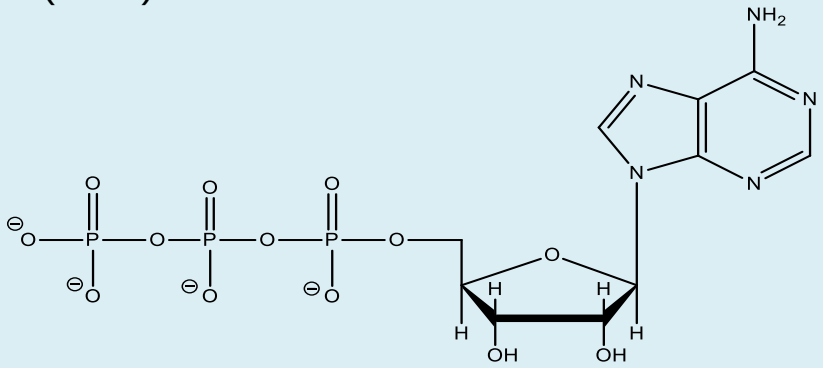
Important mononucleotides



adenosine monophosphate
(AMP)



adenosine diphosphate
(ADP)



adenosine triphosphate
(ATP)

Toxicological chemistry

A poison, or toxicant, is a substance that is harmful to living organisms because of its detrimental effects on tissues, organs, or biological processes.

Toxicology is the science of poisons.

Classification of Toxic Agents

A. Heavy Metals

- by increasing the presence of heavy metals in air, water, soil, and food, and
- by changing the structure of the chemical.

B. Solvents and Vapors

C. Radiation and Radioactive Materials

D. Dioxin/Furans

E. Pesticides

F. Plant Toxins

G. Animal Toxins

Substance	LD_{50} (g/kg)	Substance	LD_{50} (g/kg)
Strychnine	0.005	Chloroform	1.2
Arsenic trioxide	0.015	Iron(II) sulfate	1.5
DDT	0.115	Ethyl alcohol	10.6
Aspirin	1.1	Sodium cyclamate	17

Air pollution

Ozone, Nitrogen dioxide, sulphur dioxide, Carbon monoxide,

Acid rain

Sulphuric, nitric acids, sulphur dioxide, nitric acid and nitrogen oxides.

Lead pollution

Water pollution

Arsenic

Mercury and methylmercury

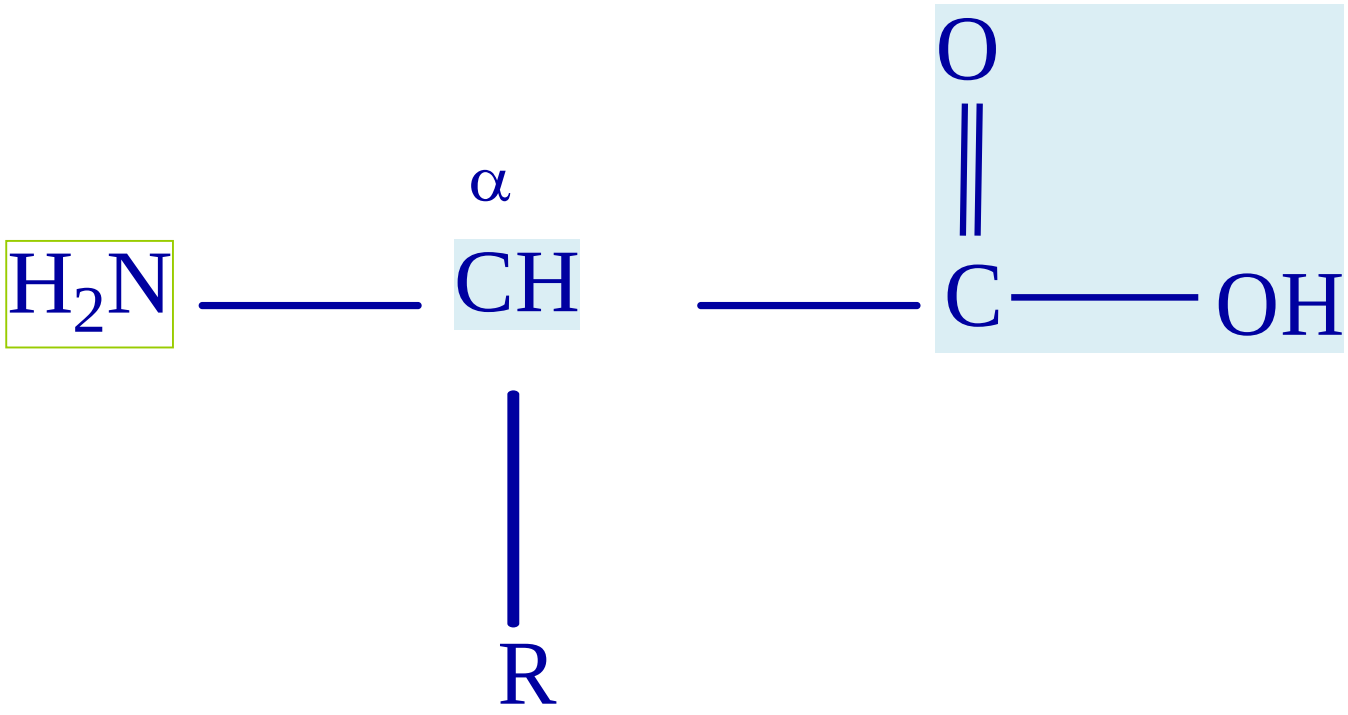
Plant toxins

Primary biomolecules

- carbohydrates
- amino acids
- proteins
- lipids

Primary biomolecules

Proteins, fats, and carbohydrates are main nutrients found in foods and drinks.



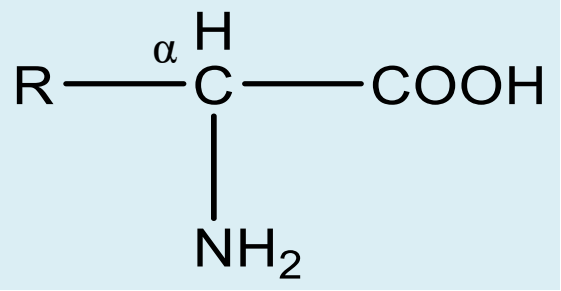
amino acid structure

Amino acids and proteins

Amino acids

- Amino acids are compounds that contain an amino (-NH_2-) and a carboxyl group (-COOH)

- There are a large number of amino acids in nature, but about 20 are used for protein synthesis.
- Essential amino acids - the human body cannot synthesize them, but they must come from food.
- The essential amino acids are: Arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.
- α- Amino acids



Non essential amino acids can be made by humans

Physical Properties:

- Colourless
- Crystalline in nature
- Tasteless (tyrosine), sweet (glycine, alanine)
- Melting point above 200•C
- Soluble in polar solvent and

Insoluble in non polar solvent

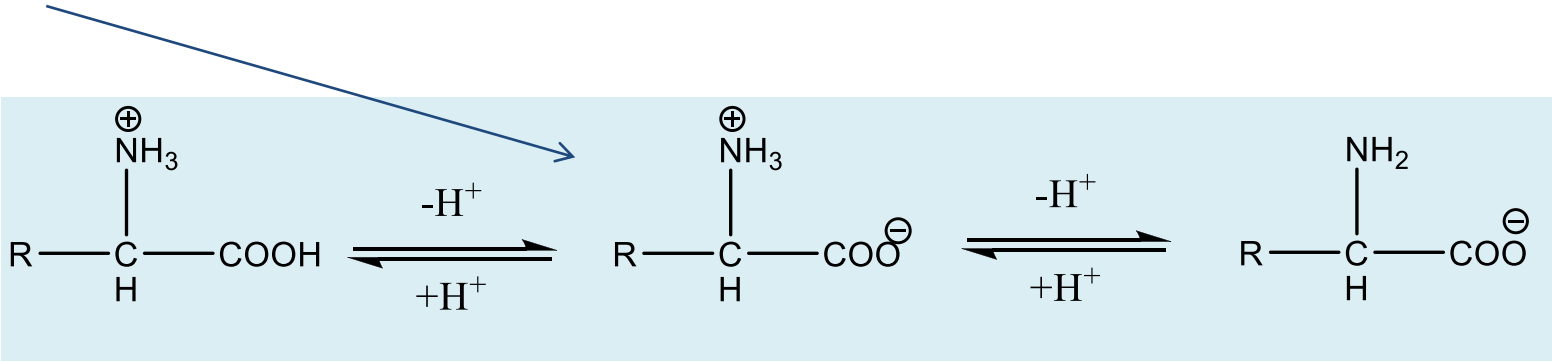
- Have absorbance at 280nm

All amino acids possess optical isomers due to the presence of asymmetric α-carbon atoms.

- Amino acids are amphoteric compounds, because due to their functional groups they can react both as acids (-COOH) and as bases ($-NH_2$)

- Due to the negative inductive (-I) effect of the $-NH_2$ group, amino acids are stronger acids than carboxylic acids, and weaker bases than primary amines - a consequence of the -I effect of the –COOH group

- In aqueous solution, they are found in the form of dipole ions (zwitter ions) or salts

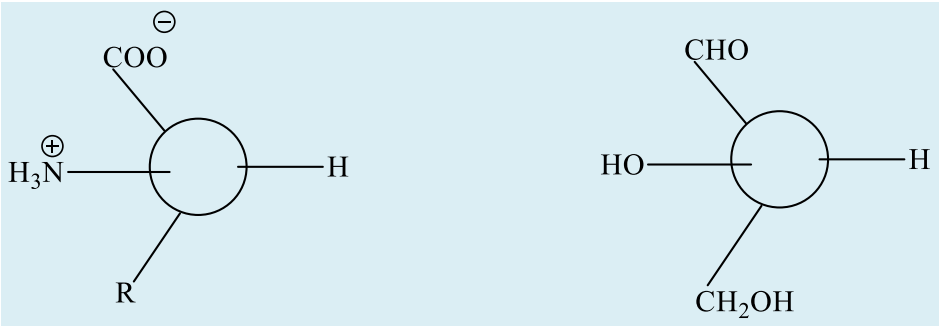


- In which form the amino acid will be found in aqueous solution depends on:

- of amino acid nature
- pH values - in highly acidic solutions, amino acids are found in cationic form, and in strongly basic solutions in anionic form

- **Isoelectric point** - pH value at which the concentration of the dipole ion is maximum, while the concentrations of cationic and anionic forms are very low and equal

Configuration of natural amino-acids

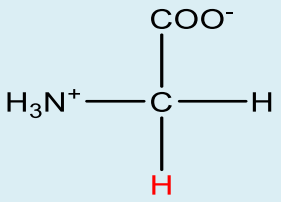


L-amino acid L-glyceraldehyde

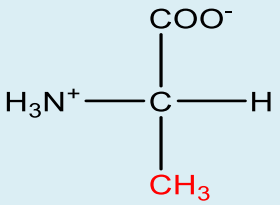
Classification of amino acid

Amino acids can be classified according to polarity of R-group

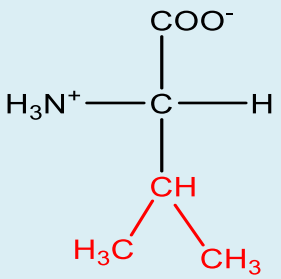
- Non-polar amino acids - aliphatic - R group



Glycine

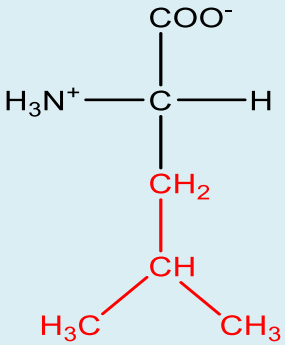


Alanine

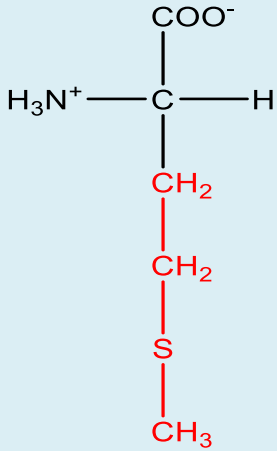


Valine *

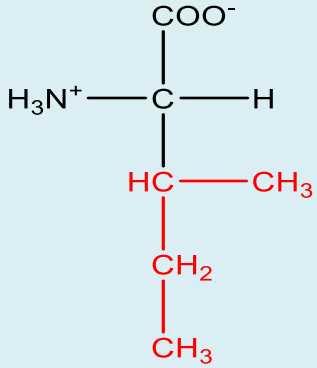
*-essential amino acid



Leucine *

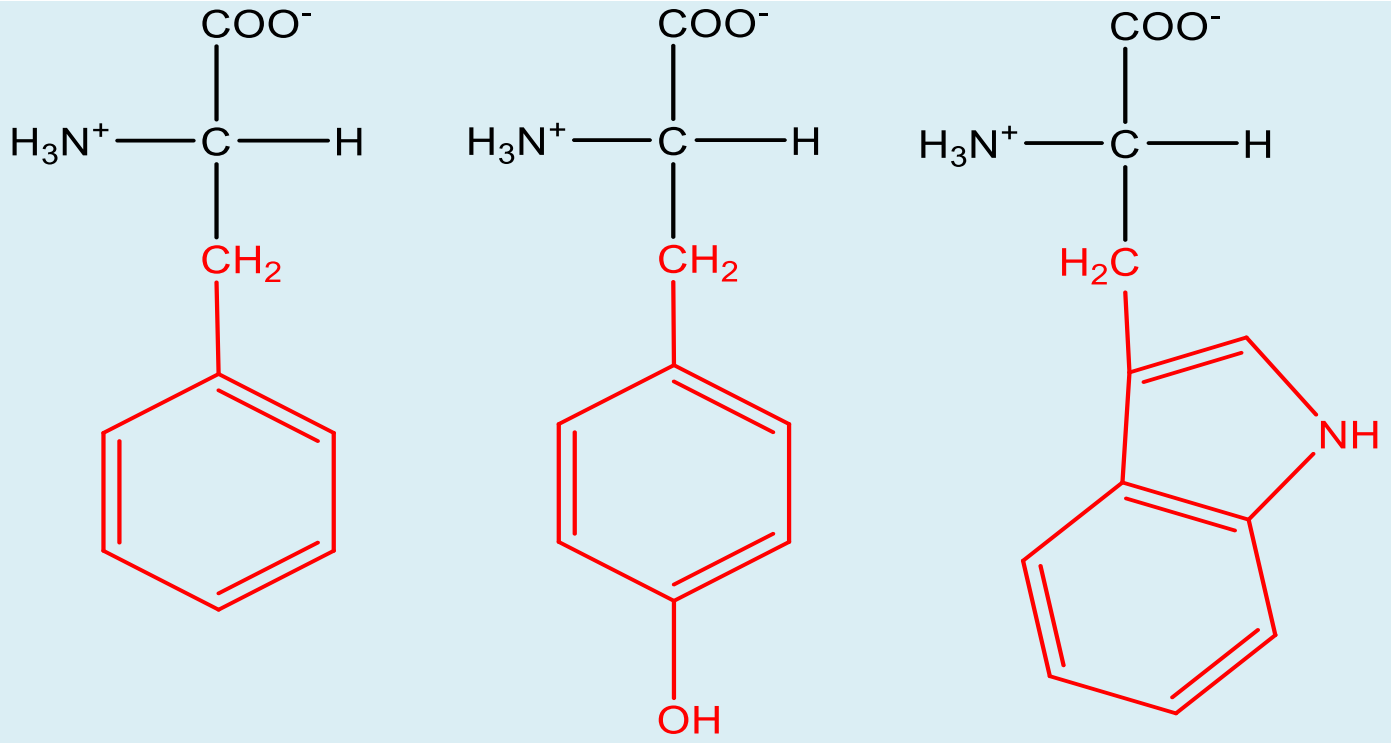


Methionine *



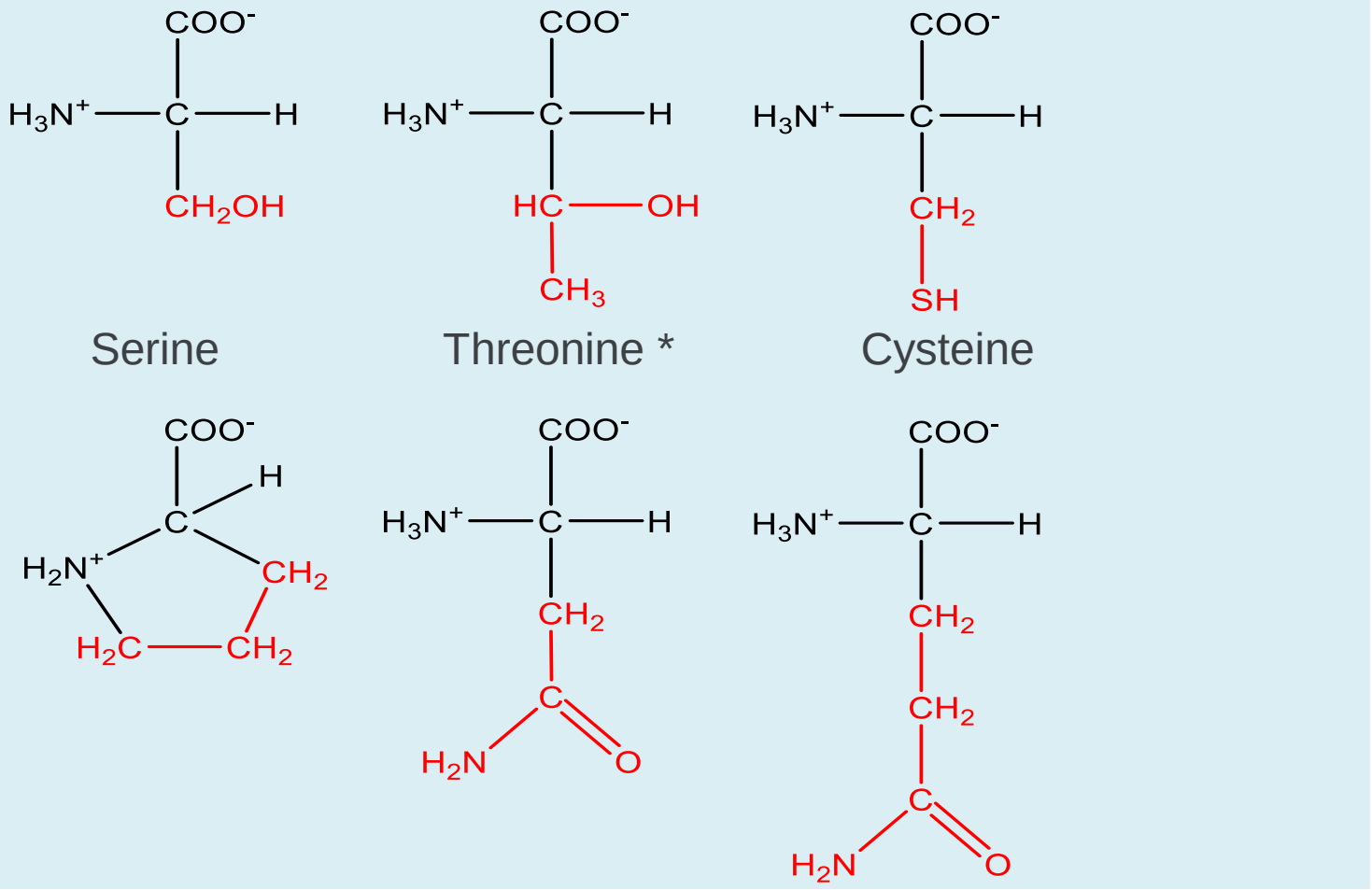
Isoleucine *

- Non-polar amino acids - aromatic - R group



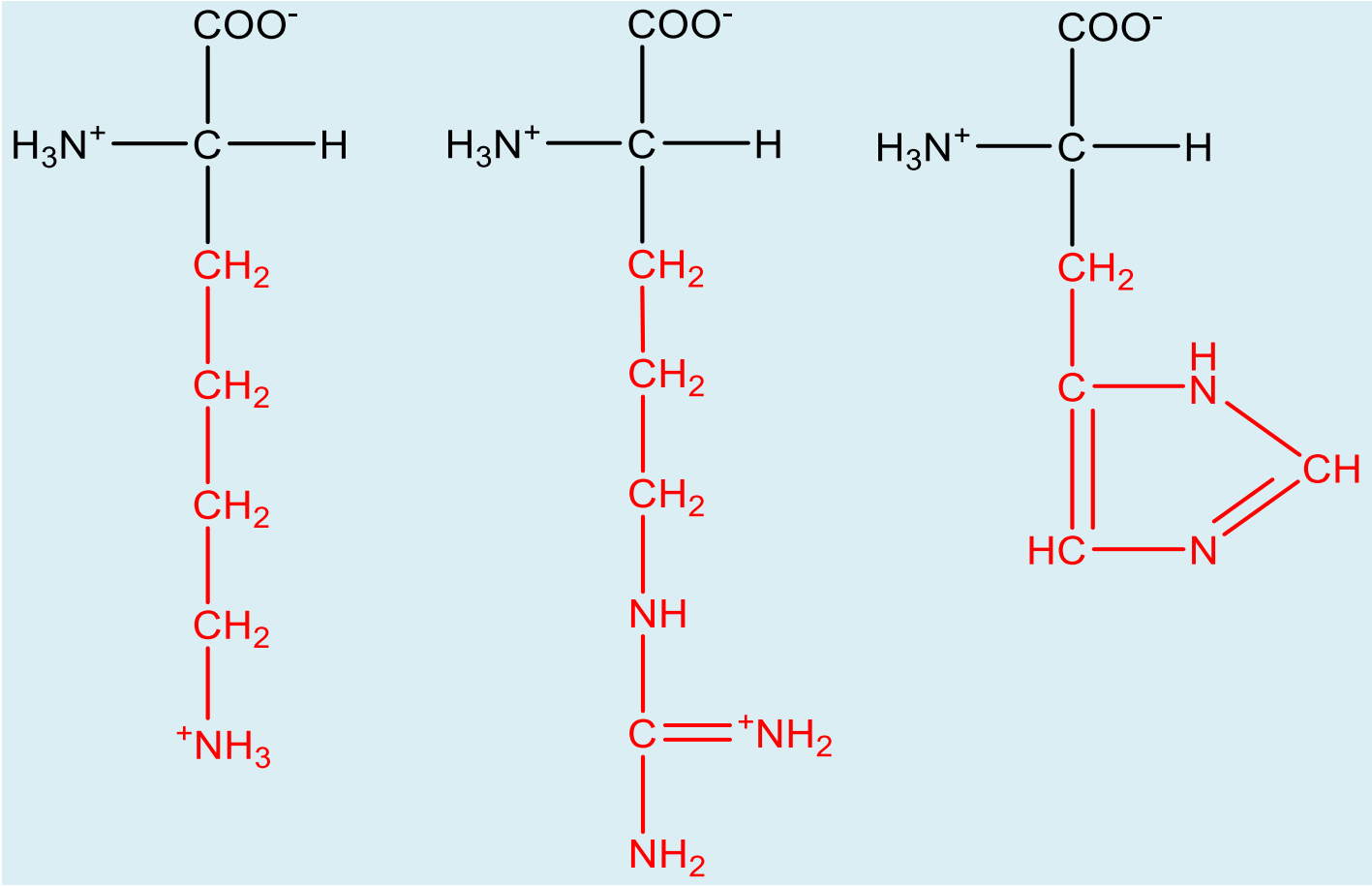
Phenylalanine * Tyrosine Tryptophan *

- Polar amino acids - charged -R group



- Polar amino acids - positively charged -R group

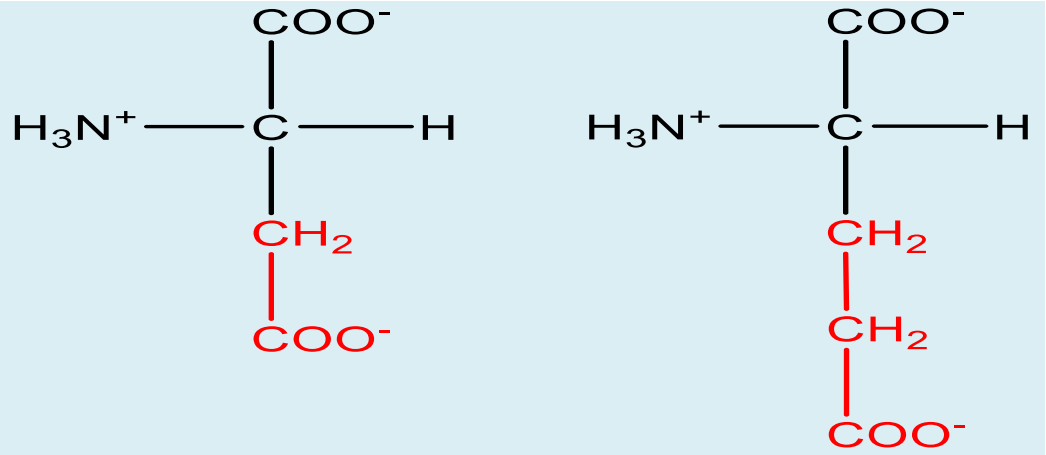
(Basic amino acids)



Lysine * Arginine * Histidine *

- Polar amino acids - negatively charged -R group

(Acidic amino acids)



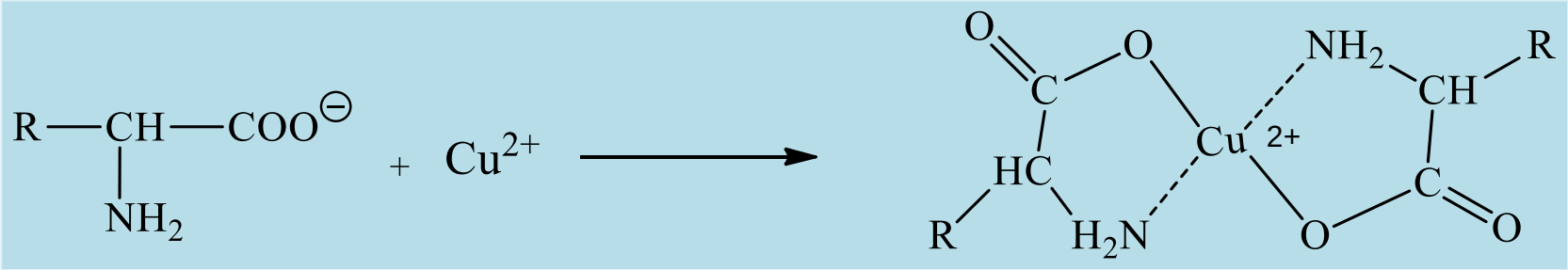
Aspartic acid

Glutamic acid

Amino acid reactions

Reactions of the carboxyl group

chelate formation

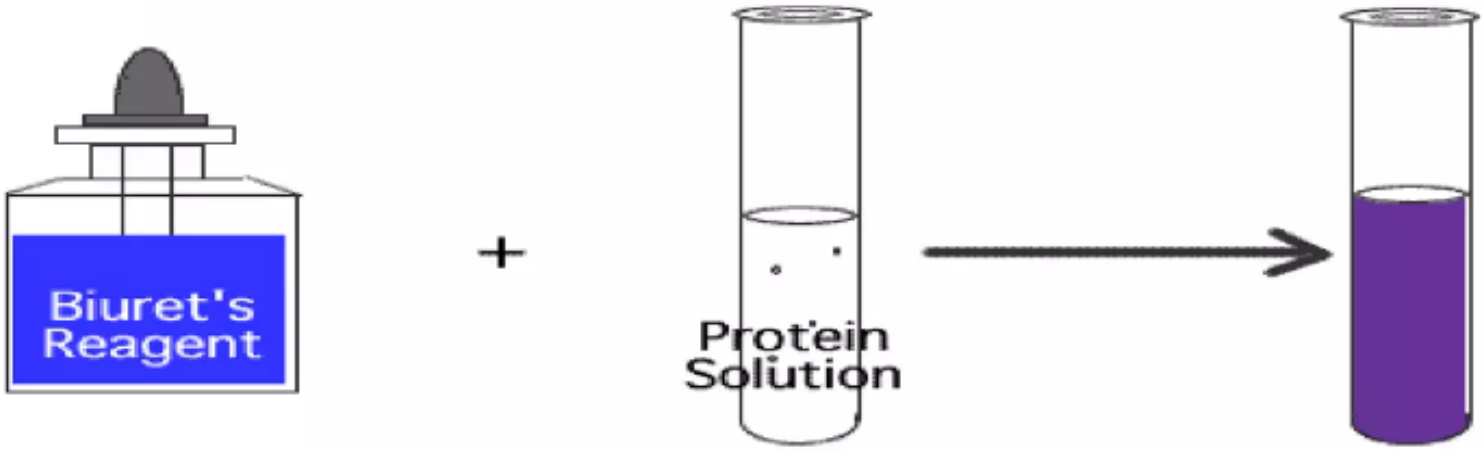


Procedure :

Add 30 drops oof albumin into test tube .

Then add 5 drops of CusO4

And then 10 drops of NaOH .



Amino acids in pharmaceuticals, food and cosmetics industry

5-HTP (5-hydroxytryptophan) used for experimental treatment of depression

L-DOPA (L-dihydroxyphenylalanine) is used for Parkinson's treatment in the treatment of sleeping sickness.

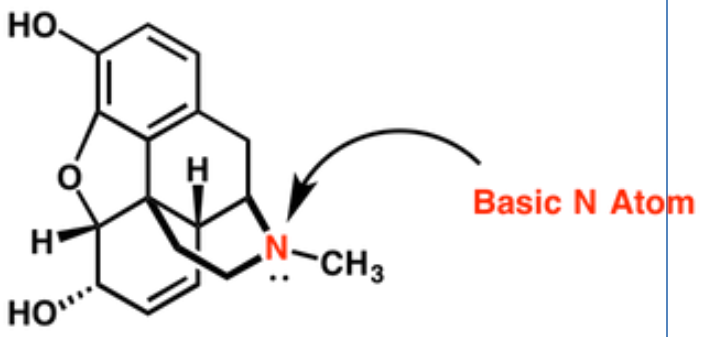
Amino acids are used in the synthesis of some cosmetics.

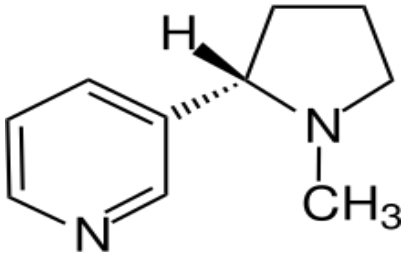
Glutamic acid is used in the food industry as a flavor enhancer

Aspartame (aspartylphenylalanine 1-methyl ester) is used as an artificial sweetener.

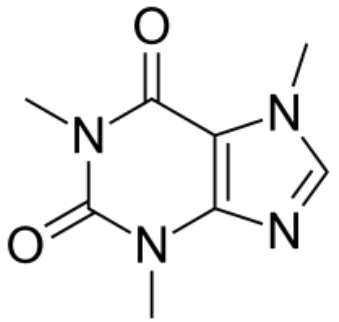
Alkaloides

- basic nitrogenous secondary metabolites, mainly of plant origin and with a pronounced physiological effect.
- not all alkaloids are basic,
- not all alkaloids are of plant origin.
- mostly colorless, crystalline substances,





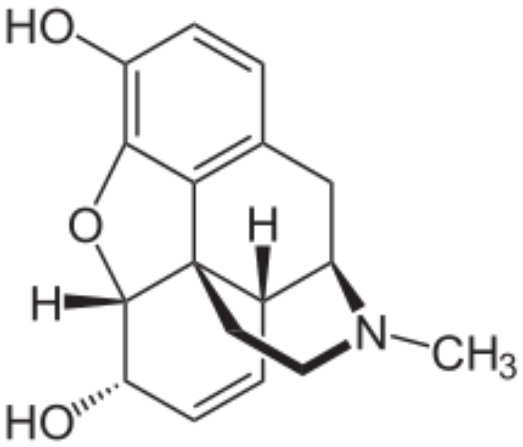
nicotine



caffeine from tea and coffee

- nicotine are liquids with a characteristic smell.
- serotonin and tangerine are of animal origin.

Morphine is the most abundant alkaloid obtained from poppy strow (3-25%).
Opium contains 0.2-3% codeine, which is the methyl ether of morphine.



morphine

Poppy straw

It is mainly used as a pain medication.

Opium is a CNS depressant and very effective painkiller.

HPLC analysis of alkaloids

HPLC = high performans liquid chromatography

Identification of component in extracts.

Quantification of component in the mixures.

HPLC chromatogram of standard alkaloides

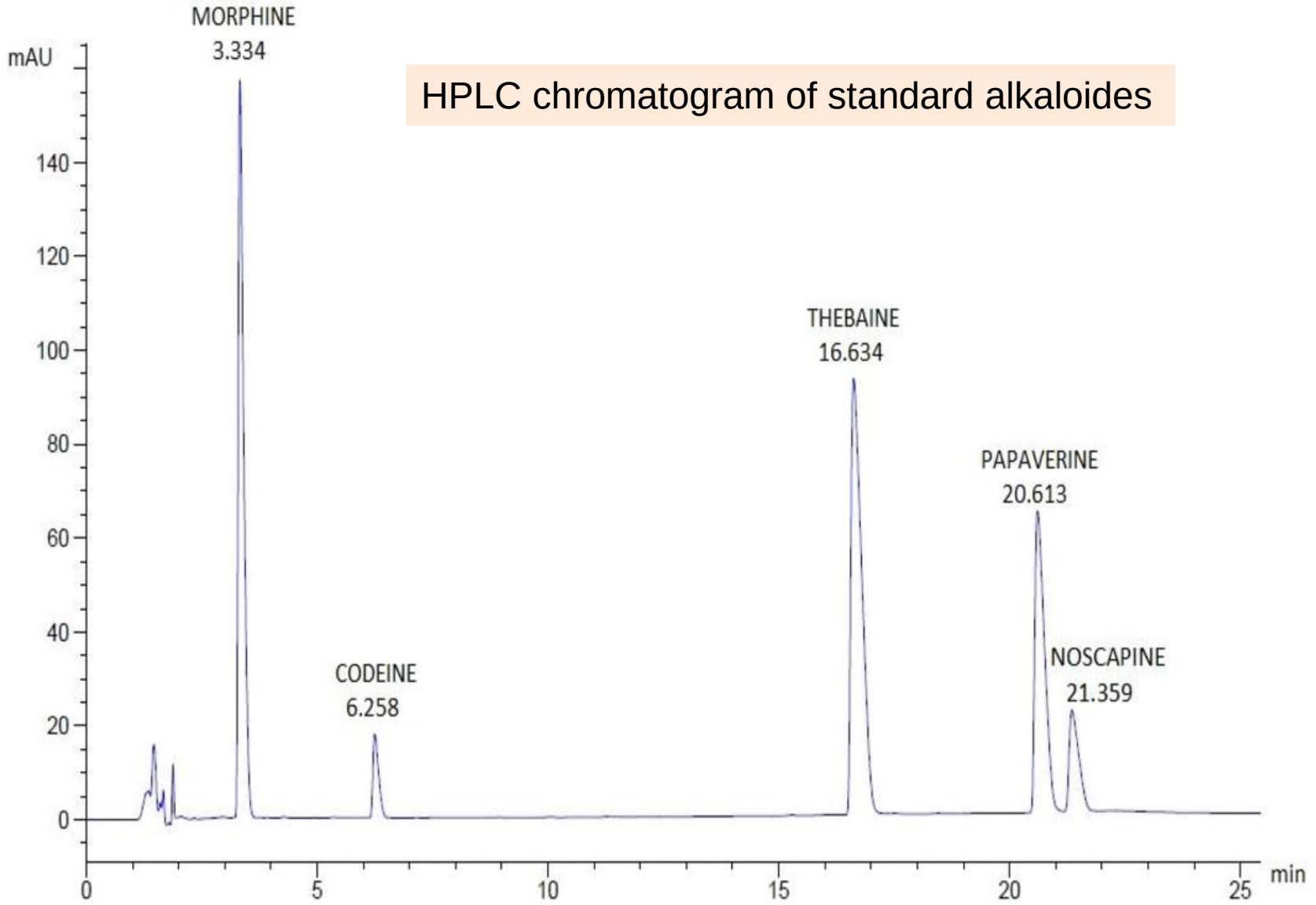


Figure 1 Alkaloid standard chromatogram. Morphine, codeine, thebaine, papaverine and noscapine standards. Ascentis Express F5 column, MF A: 5% acetonitrile, MF B: acetonitrile : glacial acetic acid:

HPLC chromatogram of Poppy strow

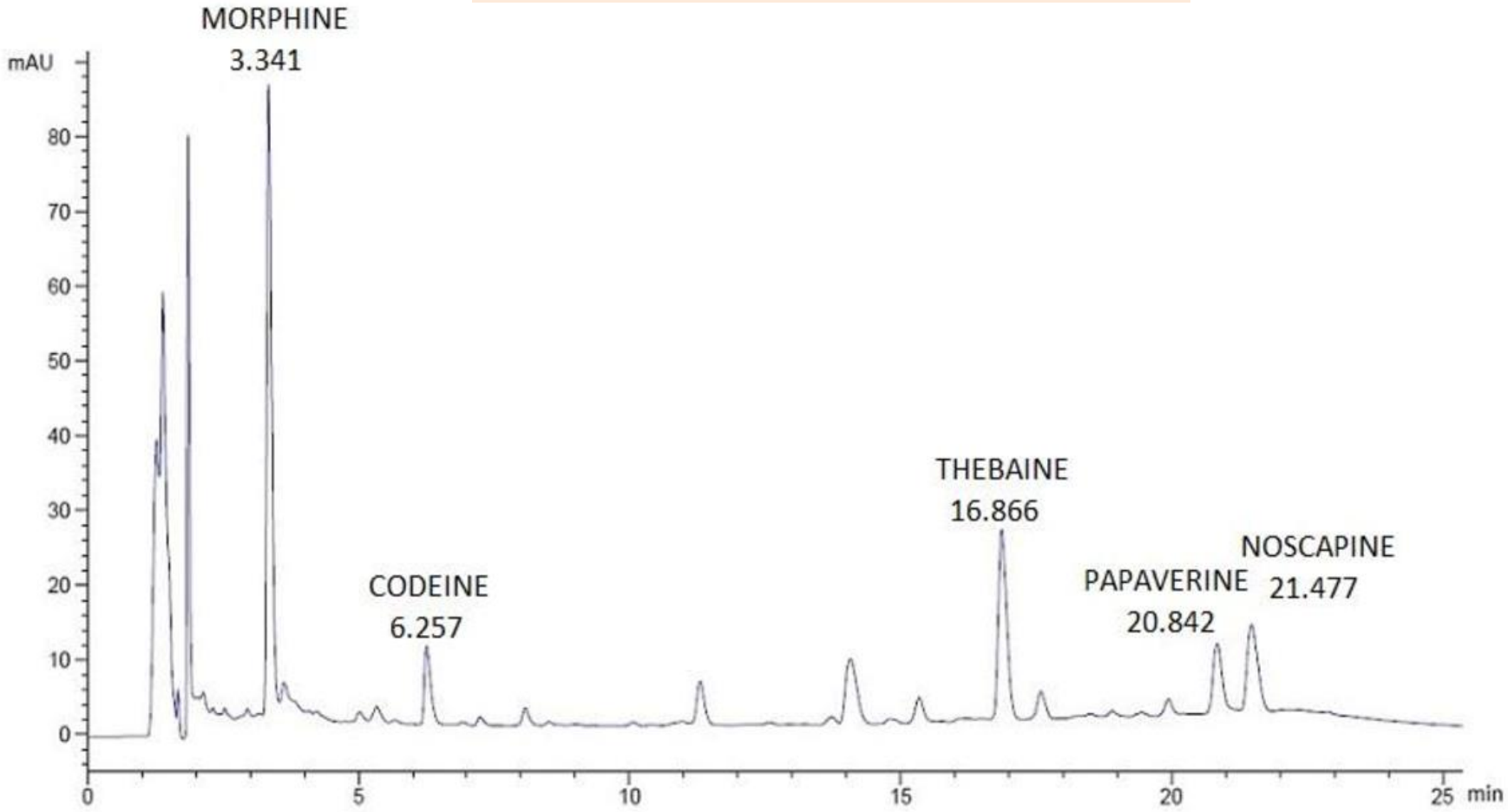


Figure 2 Poppy straw sample chromatogram. Ascentis Express F5 column, MF A: 5% acetonitrile, MF B: acetonitrile : glacial acetic acid: triethylamine = 97.9 : 2 : 0.1, 1 ml . min^{-1}, UV/VIS detection, 284 nm.

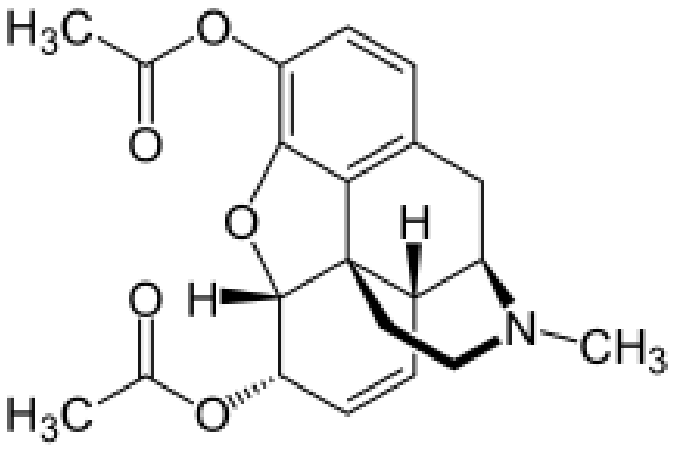
Table 3 Opium alkaloid contents determined in poppy straw samples

Laboratory sample number	Opium alkaloid content (wt. %)				
	Morphine	Codeine	Thebaine	Papaverine	Noscapine
559	0.04	0.01	below LOQ	below LOQ	below LOQ
3977	0.16	0.03	below LOQ	below LOQ	below LOQ
654	0.28	0.10	0.01	0.02	0.03
591	0.39	0.06	below LOQ	0.01	0.04
641	0.44	0.08	below LOQ	0.10	0.03
6087	0.55	0.17	0.01	below LOQ	0.03
6084	0.66	0.19	0.01	below LOQ	0.02
628	0.83	0.17	below LOQ	below LOQ	0.01
6089	0.95	0.14	0.06	0.01	0.02
551	1.47	0.35	0.05	below LOQ	0.02

Heroin (diacetylmorphine) is recreational drug for its euphoric effects.

It is typically injected, usually into a vein, but it can also be snorted, smoked, or inhaled.

Heroin is the most addictive narcotic.



Heroin

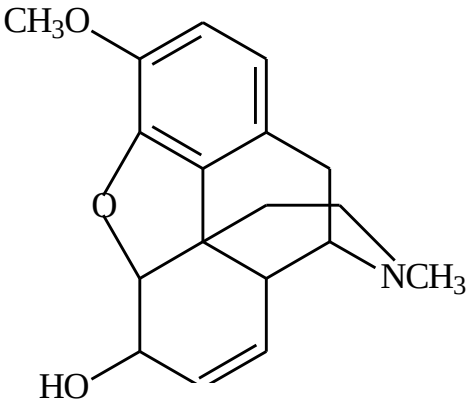
white crystalline powder

Codeine

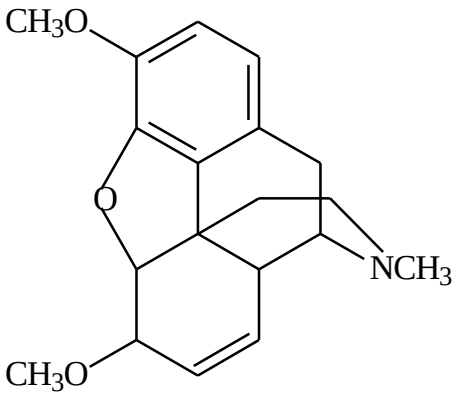
Opium contains 0.2-3% codeine.

It is mainly used as a pain medication mild to moderate pain.

Codeine is an opiate.

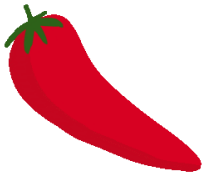


Codeine



Tebaine

Codein is used as an antitussic (means to prevent cough)

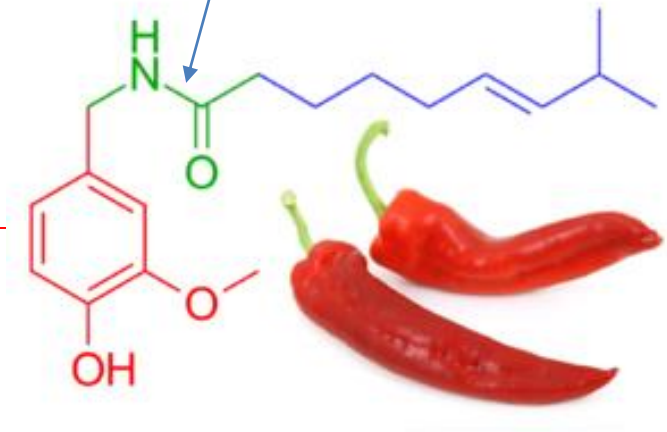


Capsaicin

is alkaloid and an active component of chili peppers.

Capsaicin is used as an analgesic.

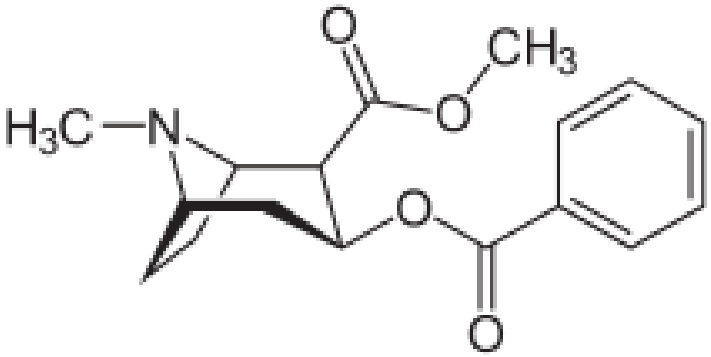
Capsaicin has the amide group.



Carolina is the hottest pepper in the world.

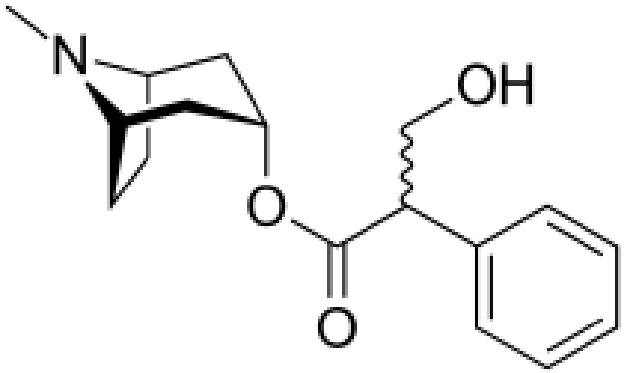
Cocaine is a tropane alkaloid that acts as a central nervous system (CNS) stimulant.

It is obtained by extracting the plant Erythroxylum coca.



Cocaine is a dangerous and addictive drug.

Crack (rock)
For smoking



Atropine

Atropine is used to dilate pupils for eye examinations

Cleopatra used atropine to dilate the pupils.

Mescaline is a hallucinogenic liquid alkaloid isolated from some species of cactus (peyote).

Mescaline has been used by the Indians to improve fitness and in religious rituals.