SACCHARIDES

Saccharides

occur widely in the nature, present in all types of cells

- the major nutrient for heterotrophs
- energy stores (glycogen, starch)
- components of structural materials (glycosaminoglycans)
- parts of important molecules
  (nucleic acids, nucleotides, glycoproteins, glycolipids
- signalling function (recognition of molecules and cells,
  antigenic determinants)

Saccharides are polyhydroxyaldehydes and polyhydroxyketons

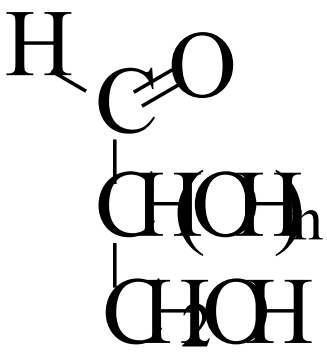
Classification according to the number of monosaccharide units n:

- monosaccharides
- oligosaccharides: n = 2-10
- polysaccharides: n > 10

(hundreds to thousands monosaccharide units)

Monosaccharides

Aldoses



Aldehyde group

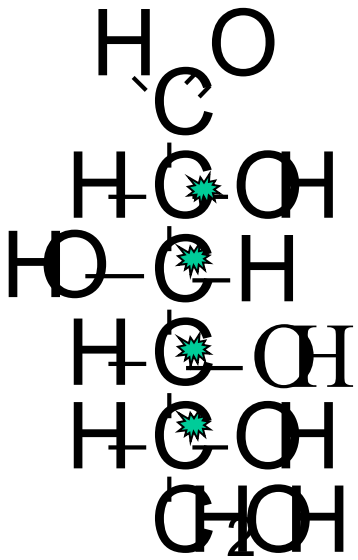
Ketoses

Keto group

Trioses	tetroses	pentoses	hexoses	heptoses

Stereoisomerism and optical activity of saccharides

Secondary alcoholic groups -CH-OH in monosaccharides are chiral centers



D-glucose

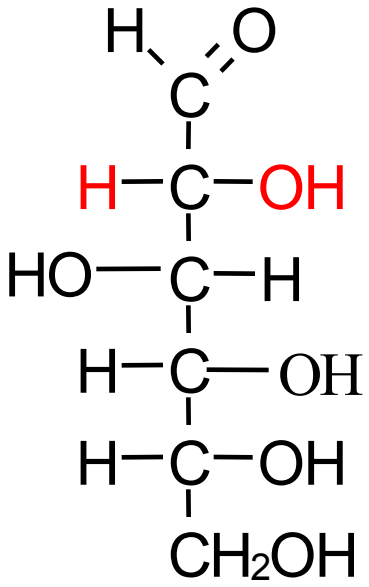
-**chiral centres** are mostly carbon atoms that bind four different groups
those atoms are often called "asymmetric" carbon atoms.

saccharides exists in form of **stereoisomers**

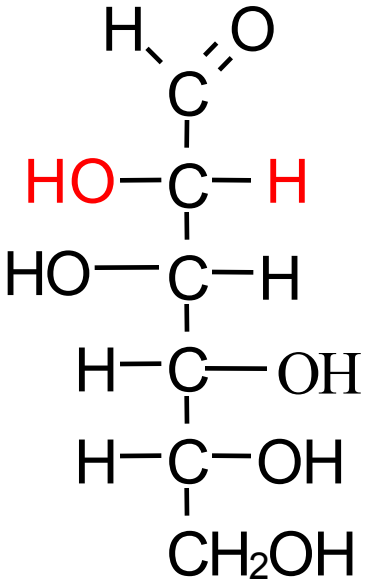
Stereoisomers

Compounds with the same structural formula but different space arrangement

They differ in configuration



D-glucose



stereoisomer of D-glucose

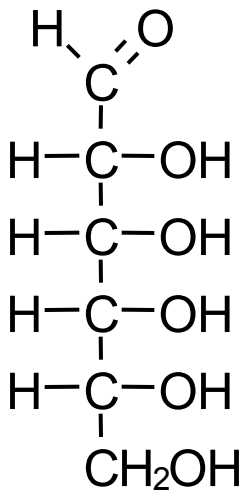
(one of many possible)

The number of streoisomers of given compound – equals 2^n

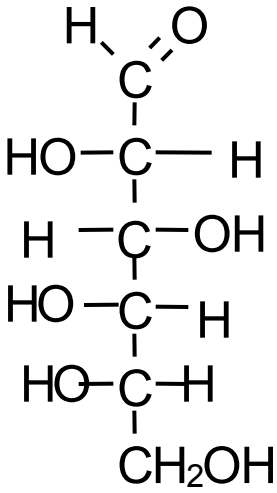
n-number of chiral centers

How many possible stereoisomers can be derived from glucose ?

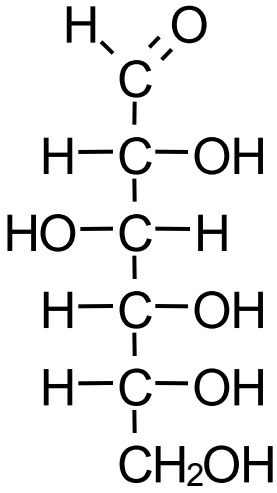
Structures of some isomeric aldohexoses (the total number of possible isomers is 16)



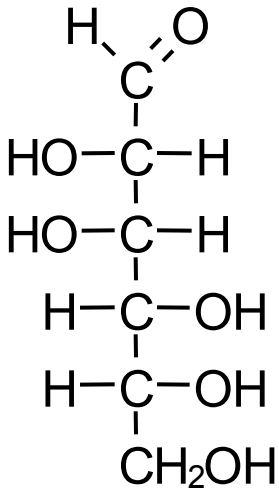
D-allose



L-glucose



D-glucose



D-mannose

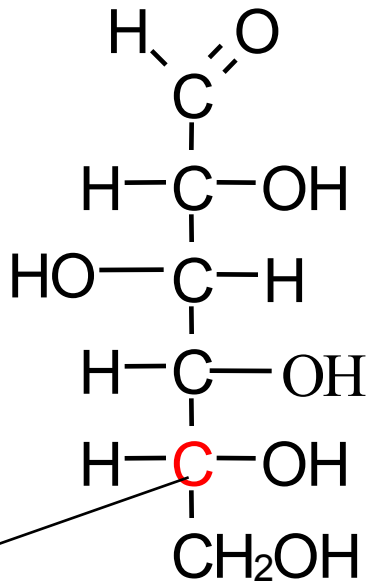
All of these monosaccharides have specific arrangement (configuration) on chiral centers

Assigning configurations D- and L-

(from Latin dexter and laevus)

Monosaccharides are classified as **D- or L-sugars** according to configuration at the **configurational carbon atom**

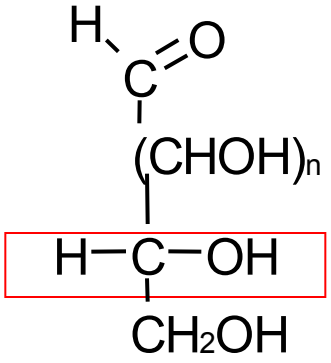
(the chiral carbon with the highest numerical locant)



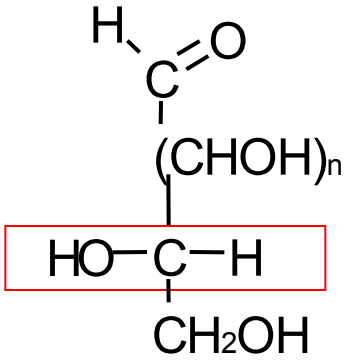
D - monosaccharide: OH- on configurational atom is to the right

L- monosaccharide: OH- on configurational atom is to the left

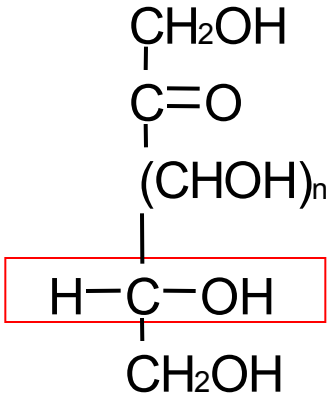
Common formulas of aldoses and ketoses



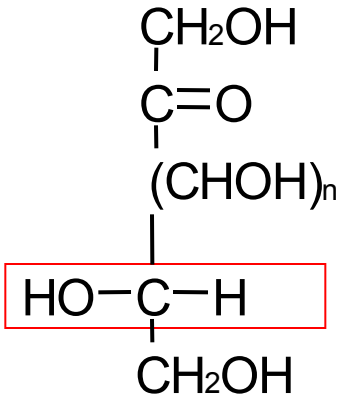
D-aldose



L-aldose



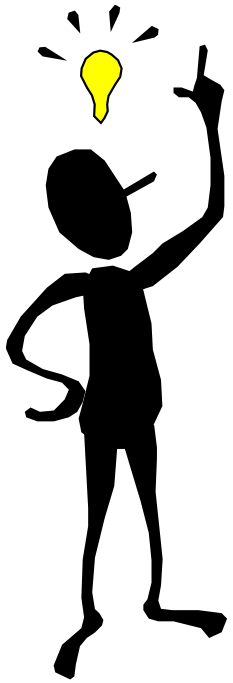
D-ketose



L-ketose

The configuration on the other chiral centers cannot be deduced from assignement D-, L-

(we must remember the configuration of the most common monosaccharides)



Optical activity of saccharides

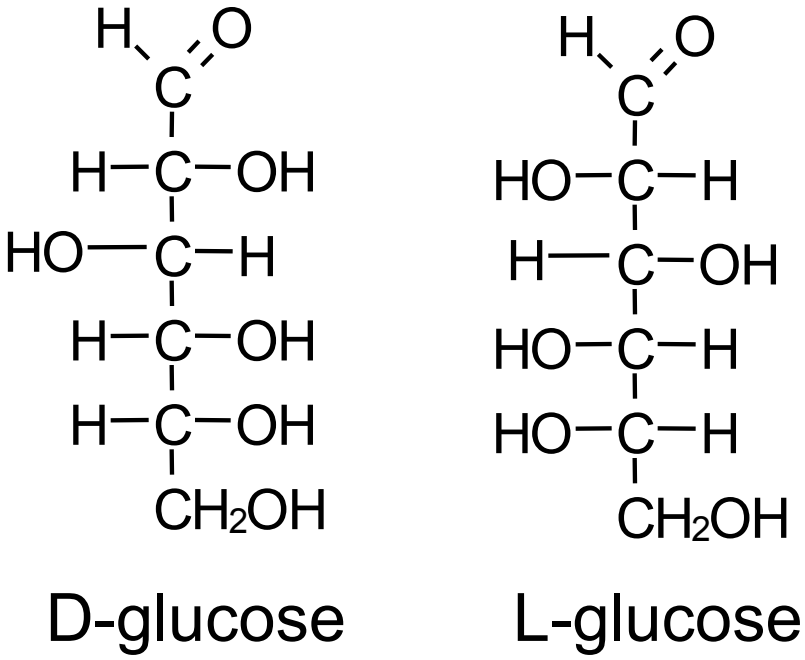
• Stereogenic centres in molecules of monosaccharides are the cause of their **optical activity**.

• Solutions of mono- and oligosaccharides turn the plane of polarized light.

• Optical activity is measured by using polarimeters and usually expressed as **specific optical rotation**.

• Dextrorotatory substances are marked (+), laevorotatory (–).

Each monosaccharide exists in form of two optical isomers (enantiomers)

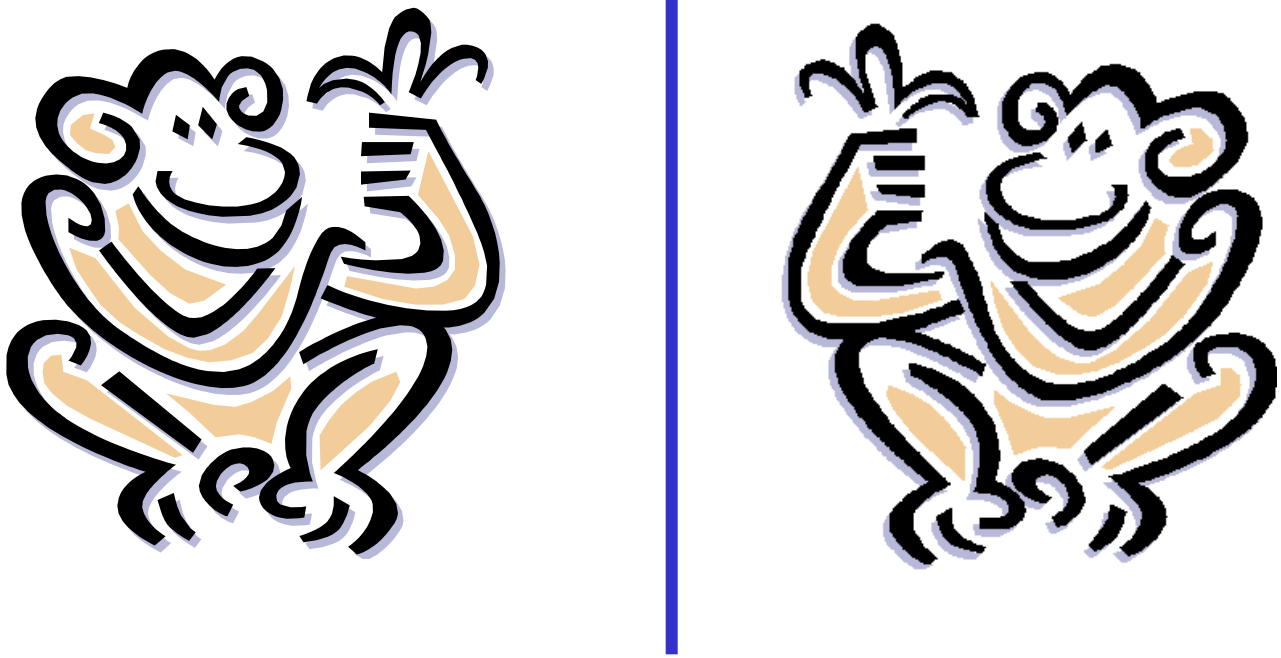


!!!!!! At all chiral carbons is opposite configuration

Optical isomers (enantiomers)

Specific pair of stereoisomers that differ in configuration at all chiral centers

(relation os a subject and its mirror image)



Enantiomers

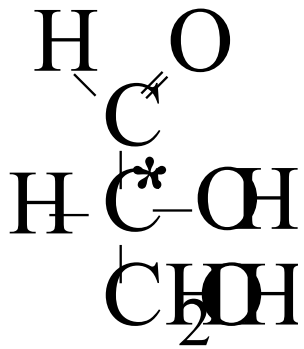
- have the same chemical properties
- they differ by the direction in which they rotate the plane of polarized light (the absolute value of specific optical rotation is the same)
- they differ in biological and pharmacological activity

Most monosacharides in mammals have configuration D.

Enzymes responsible for their metabolism are specific only for this configuration

The simplest monosaccharides (trioses)

glyceraldehyde



One chiral carbon

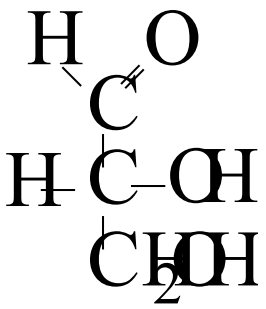
dihydroxyaceton

No chiral carbon

Glyceraldehyde

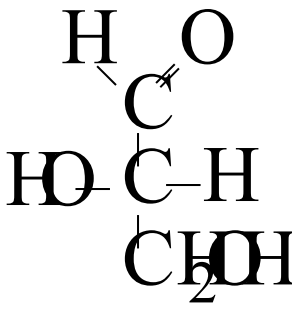
one chiral carbon ⇒ two enantiomers

D-glyceraldehyde



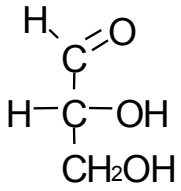
(-OH directs to the right)

L-glyceraldehyde

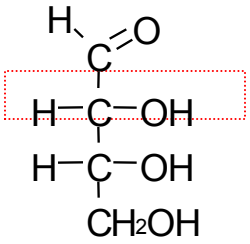


(-OH directs to the left)

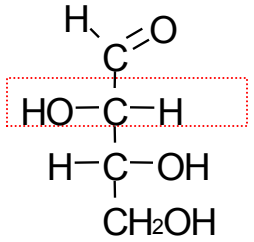
D-aldose tree – derived from D-glyeraldehyde



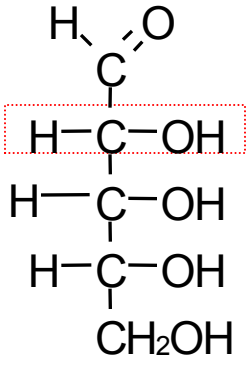
D-glyceraldehyde



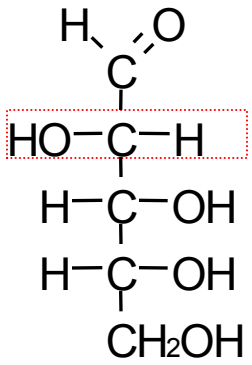
D-erythrose



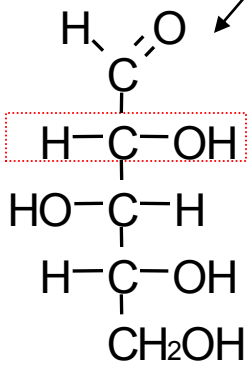
D-threose



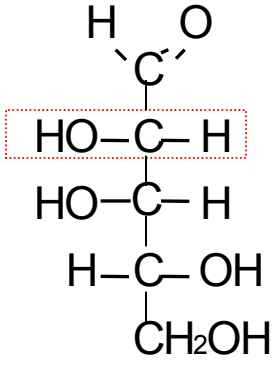
D-ribose



D-arabinose

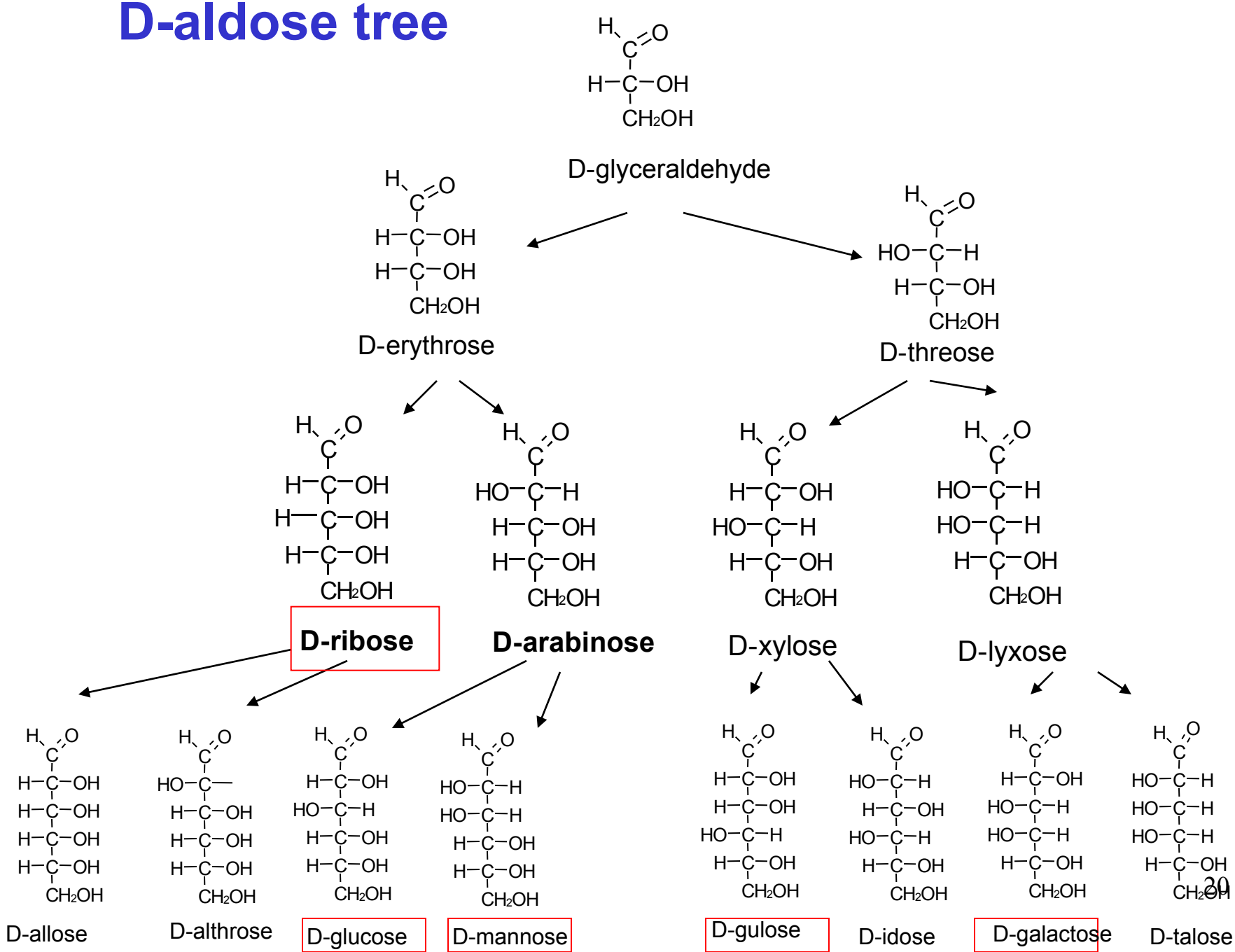


D-xylose



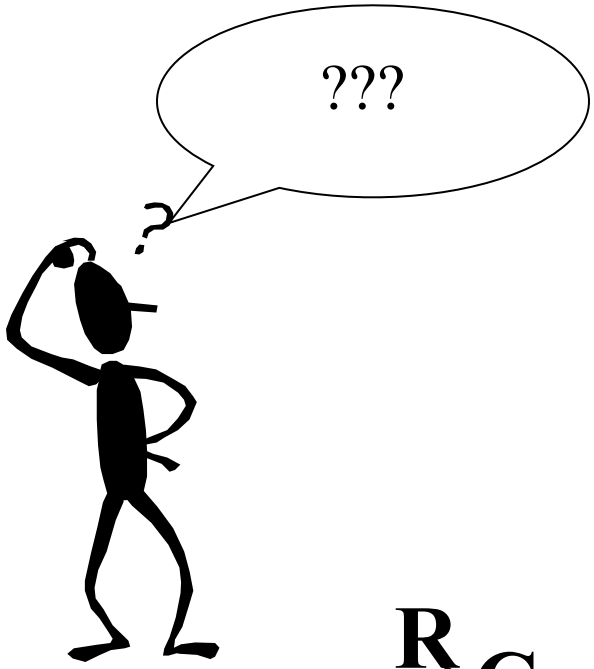
D-lyxose

D-aldose tree

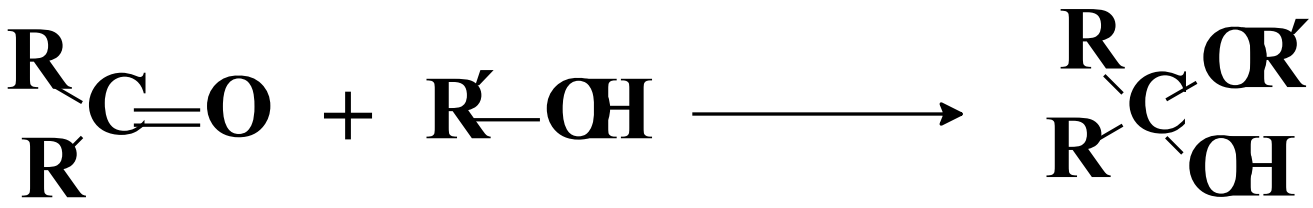


Cyclic forms of monosaccharides

Molecules of monosaccharides spontaneously form cyclic hemiacetal forms in solutions.

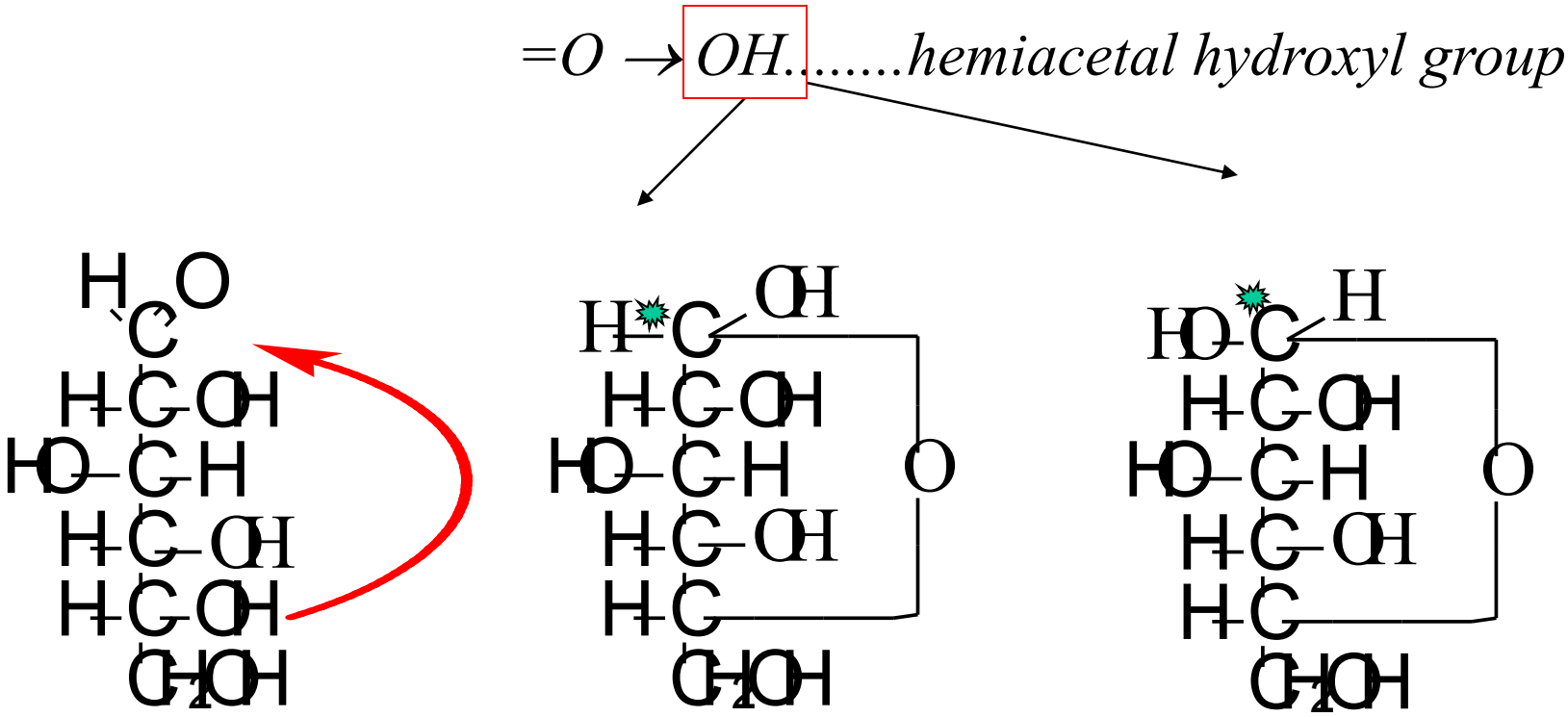


Hemiacetals are formed by reaction of carbonyl group with alcohol group



http://www.stolaf.edu/people/giannini/flashanimat/carbohydrates/glucose.swf

In cyclic forms of hemiacetals: -OH and -C=O originate from the same molecule



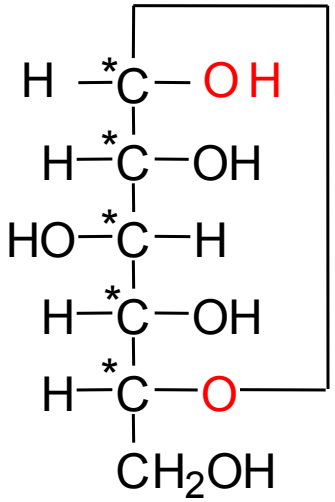
Cyklization:

C1 becomes chiral atom

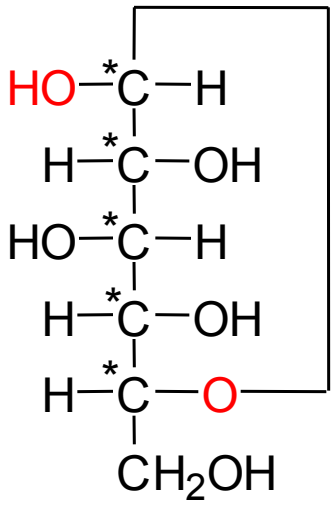
⇒ two new stereoisomers are formed – **anomers (α a β)**

α- anomer – the configuration on the anomeric carbon is the same as the configuration on the configurational carbon atom
(in D-forms is OH on the C1 on the right side)

β- anomer –the configuration on the anomeric carbon is opposite as the configuration on the configurational carbon atom
(in D-forms is OH on the C1 on the left side)



α

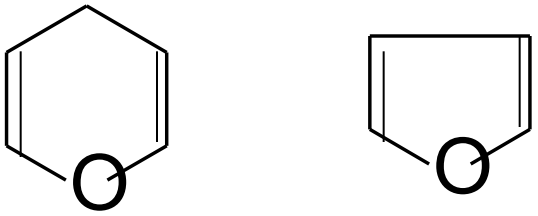


β

Names of the cyclic forms express the type of the cyclic form and the type of the anomer

Rings: six-membered **pyranoses**

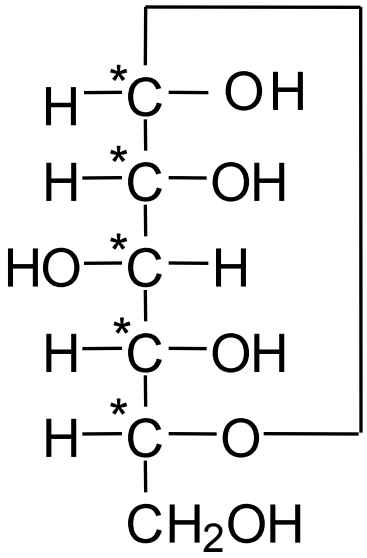
five-membered **furanoses**

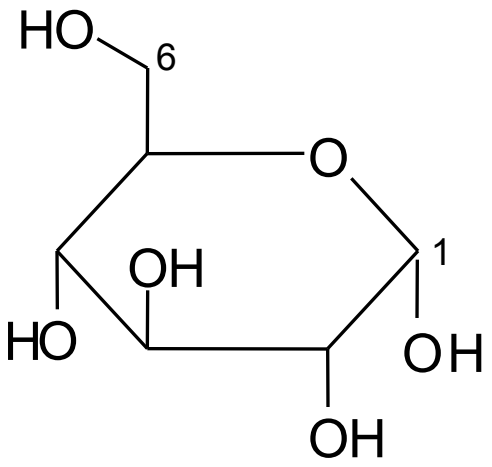


pyran

Projections of cyclic forms:

α-D-glucopyranose

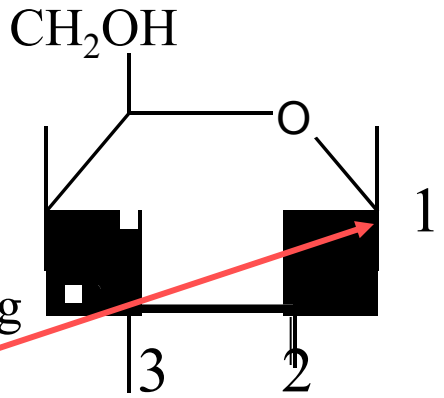




Fischer formula

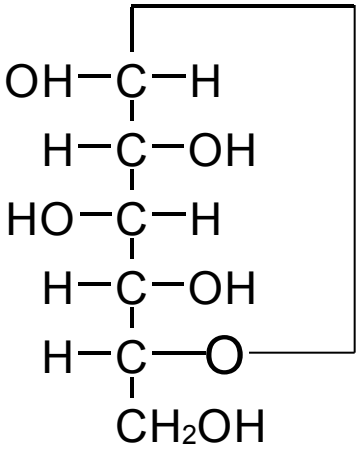
Haworth projection

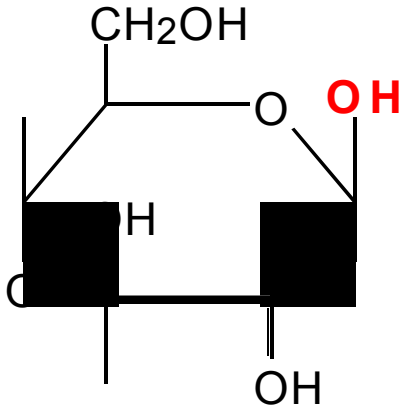
Rules for drawing Haworth projections (simplyfied)



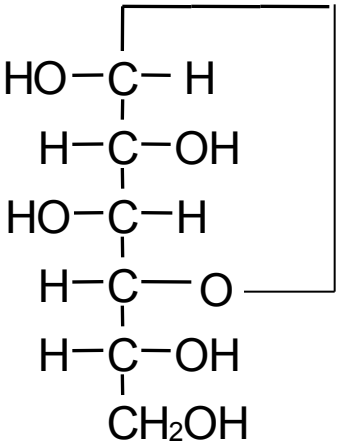
- Heterocycle is expressed by the pentagon or hexagon lying perpendicular to the plane of the paper
- Anomeric carbon is on the right-hand end
- Oxygen atom is behind
- The atoms are numbered clockwise around the ring
- Groups that appear to the right in the modified Fischer formula appear below the plane of the ring, those on the left appear above
- The CH_2OH group is directed abwards in D-sugars

Further possible cyclic forms of glucose

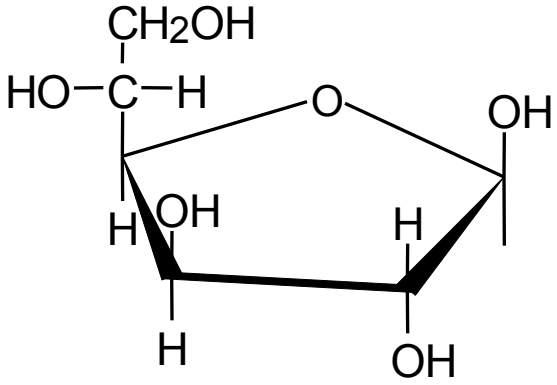




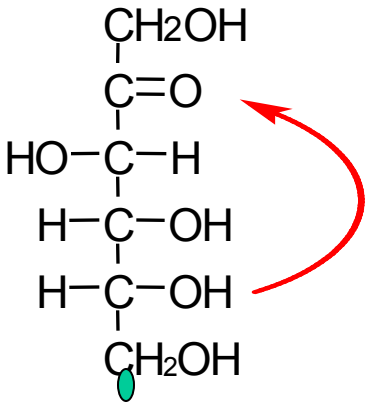
β - D-glucopyranose



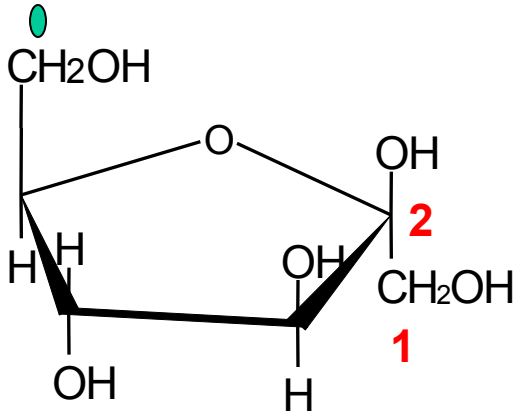
β-D-glucofuranose



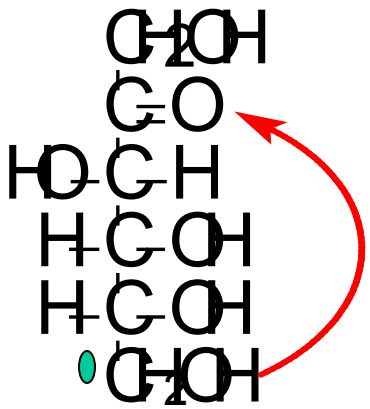
Cyclic forms of fructose

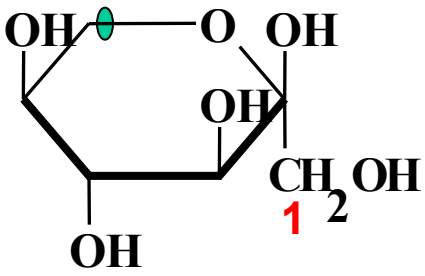


D-fructose



β-D-fructofuranose





β-D-fructopyranose

Don't confuse:

Enantiomers (optical antipodes): D- and L-form of the same monosaccharide, they differ in configuration at all chiral centres

Diastereomers – stereoisomers that differ in configuration at least at one chiral carbon and are equal in configuration at least at one chiral atom

Epimers – diastereomers differing in configuration at just one chiral carbon atom

Anomers - cyclic forms of the given monosaccharide that differ in configuration only on the anomeric carbon atom

Properties of monosaccharides

Soluble in water (polar)

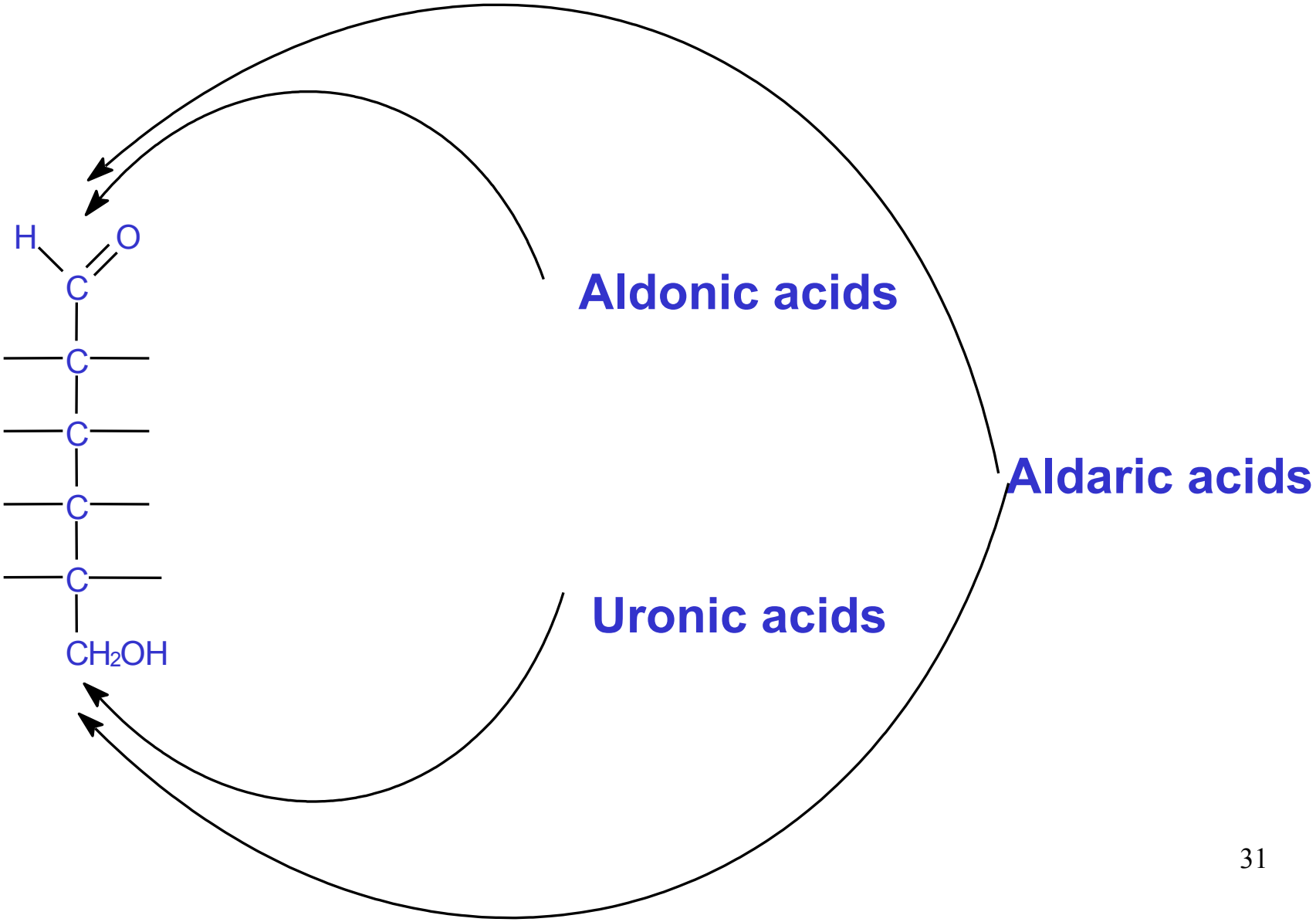
non soluble in organic solvents

Non-electrolytes

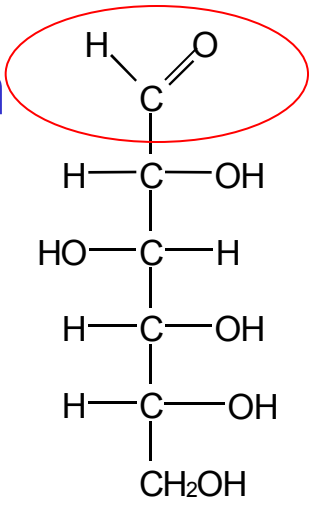
do not dissociate in aqueous solution

More or less sweet to the taste

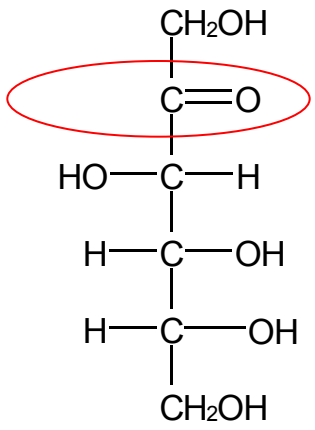
Oxidation of monosaccharides



Reduction of carbonyl group

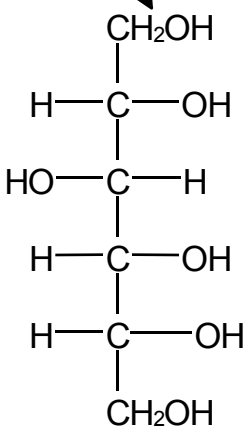


D-glucose

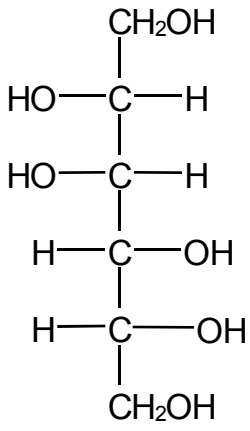


D-fructose

Reduction of fructose provides two alcohols



D-glucitol

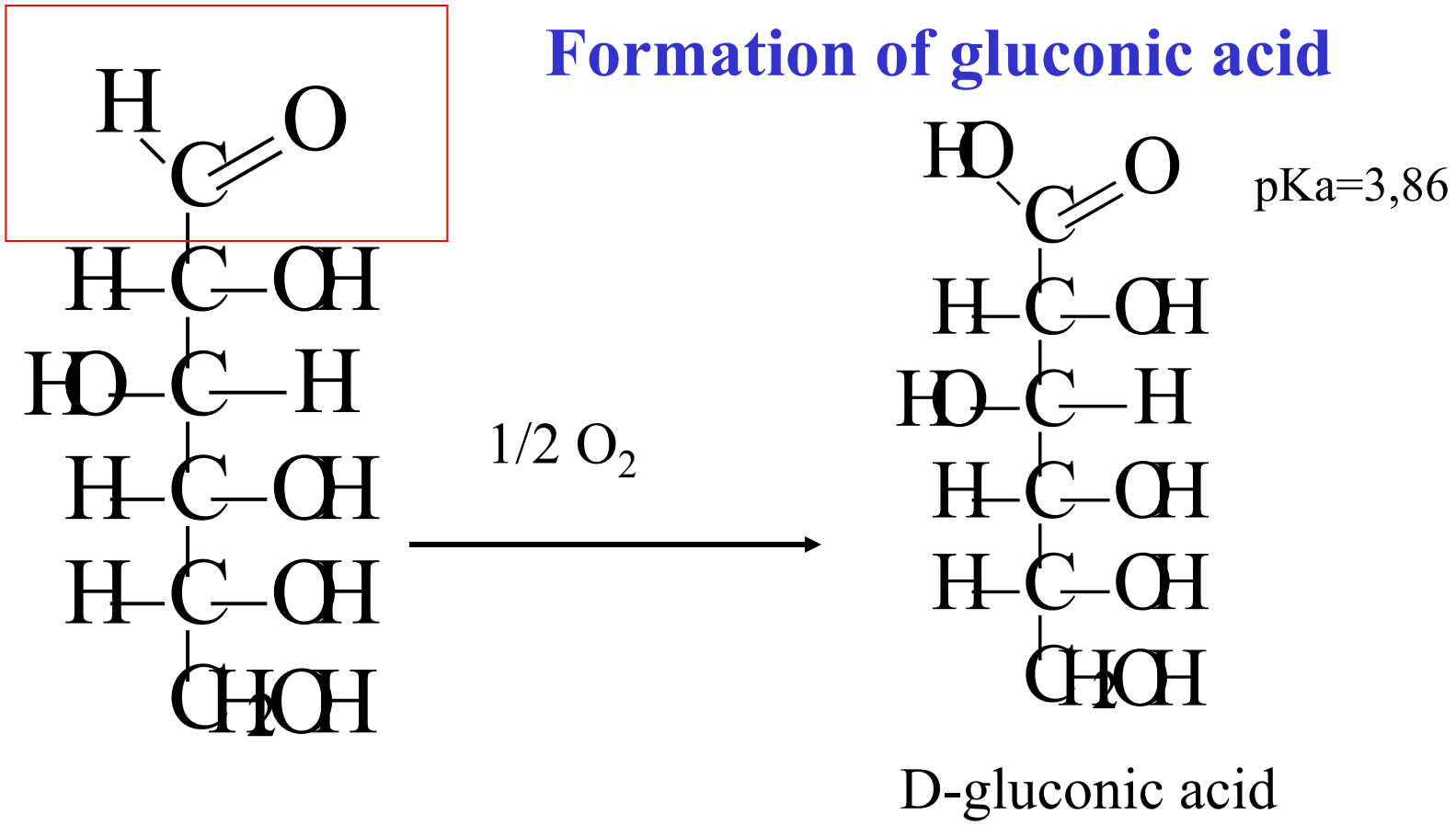


D-mannitol

Sugar alcohols

(alditols)

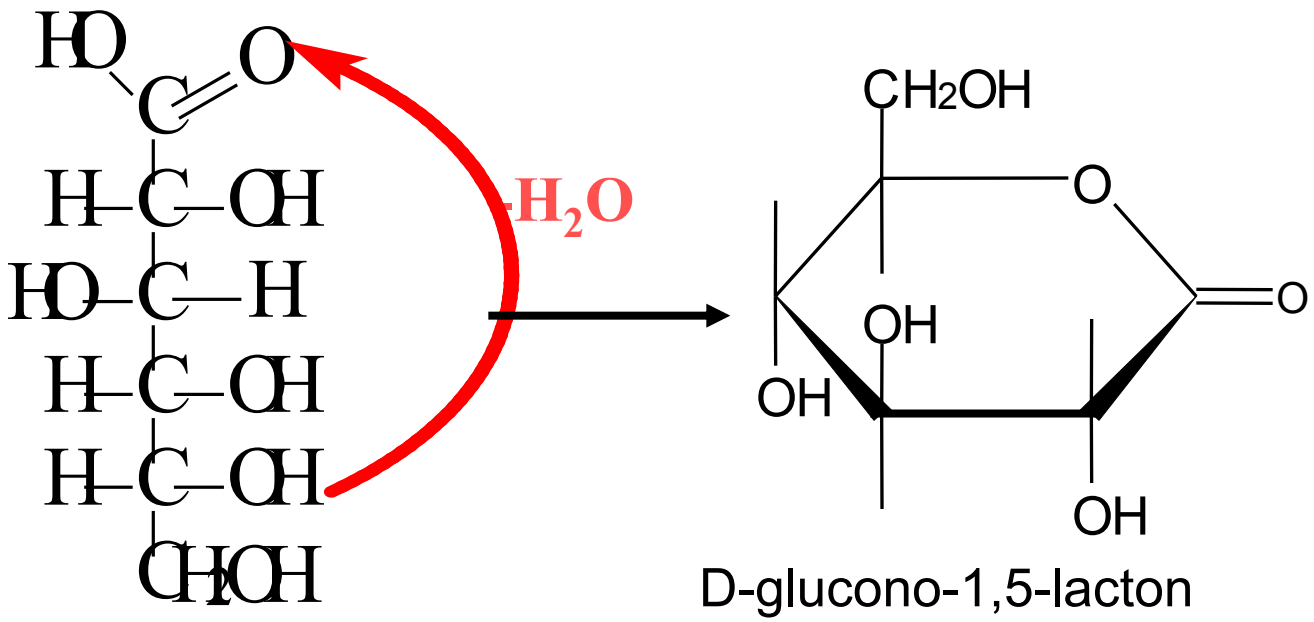
Formation of gluconic acid



D-gluconic acid

With acyclic form proceeds as oxygenation **(oxygen is bonded)**

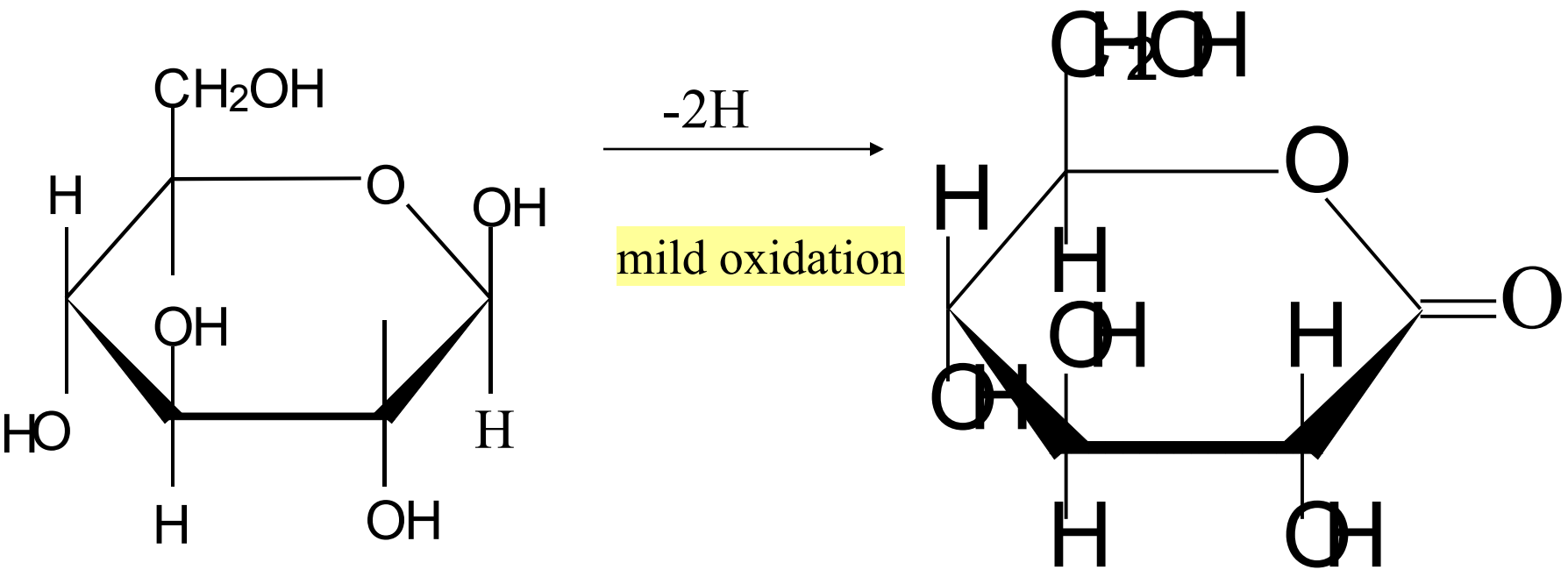
Formation of cyclic form of gluconic acid – lactone – it proceeds in aqueous solution



Lactones are „intramolecular (cyclic) esters“

They are formed in reaction between carboxylic and alkohol group in the same molecule, water is released

Gluconolactone is formed also by oxidation of cyclic form of glucose (proceeds as dehydrogenation) –

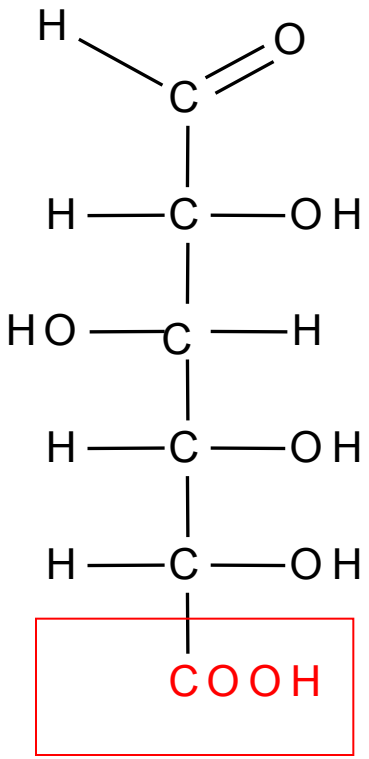


D-glucopyranose **D-glucono-1,5-lacton**

As in organism mainly cyclic form of glucose is present, this type of glucose oxidation is prevailing. Reaction is catalyzed by glucose-6P-dehydrogenase.

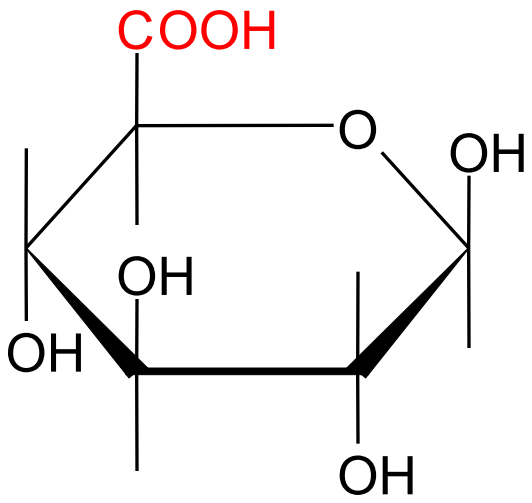
Uronic acids

Formed by double oxidation of the last carbon



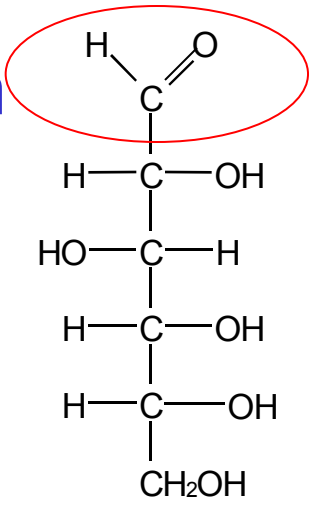
In organism it is formed by oxidation of cyclic form of glucose

(hemiacetal group is retained)

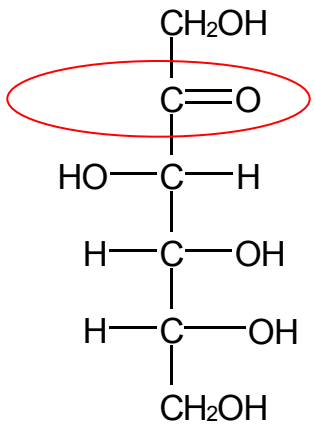


D-glucuronic acid

Reduction of carbonyl group

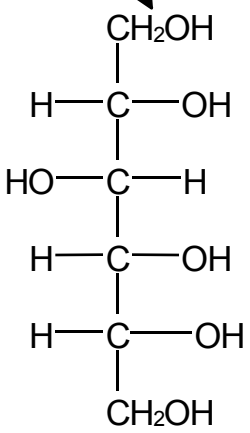


D-glucose

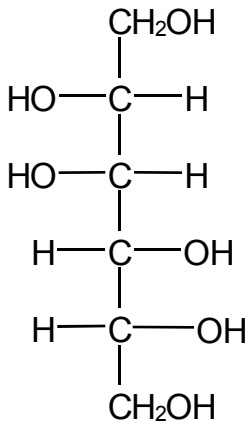


D-fructose

Reduction of fructose provides two alcohols



D-glucitol



D-mannitol

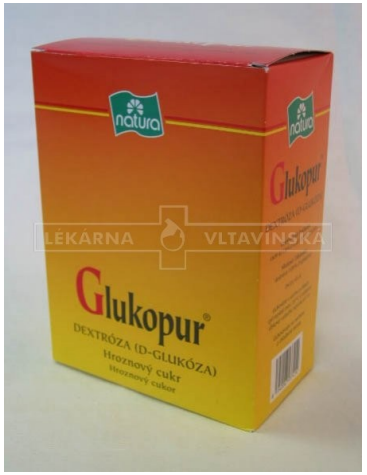
Sugar alcohols

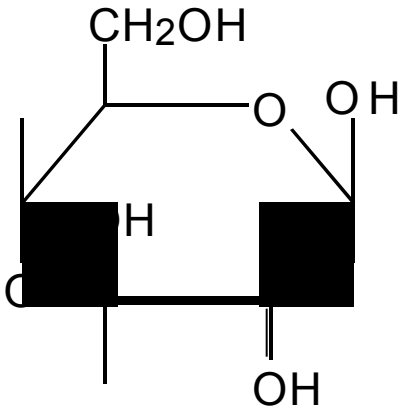
(alditols)

Important monosaccharides

D – Glucose

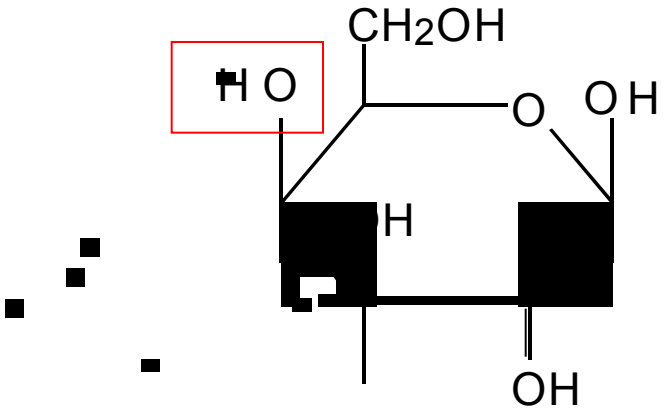
- most abundant sugar in the nature
  „grape sugar“
  contained in starch, glycogen and cellulose
- concentration in blood (3,3-5,5 mmol/l) is strictly regulated





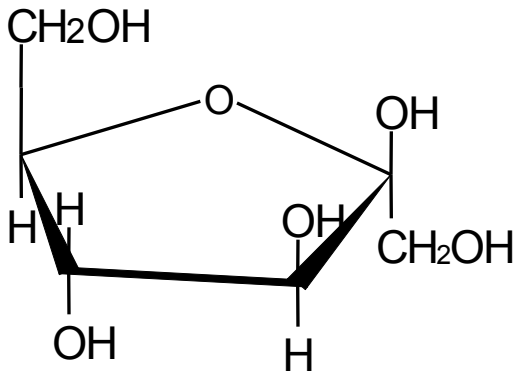
D - **Galactose**

- epimer of glucose – opposit configuration on C-4
- component of lactose (disaccharide), glycoproteins, glycolipids, proteoglycans



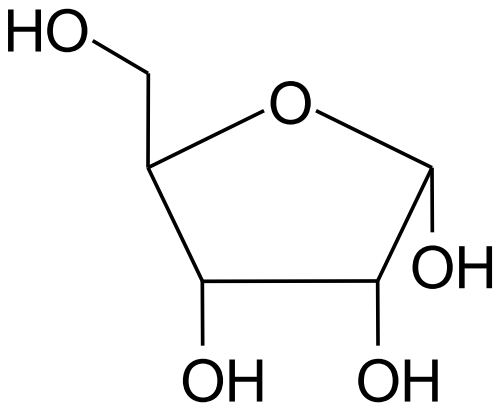
D – **fructose**

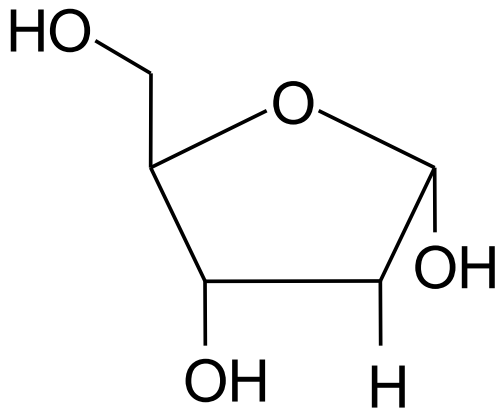
- „fruit sugar“
- most wideapread ketose
- free in honey, fruits
- component of sucrose



D-**ribose** a D-**2-deoxyribose**

- pentoses
- building unit of nucleic acids

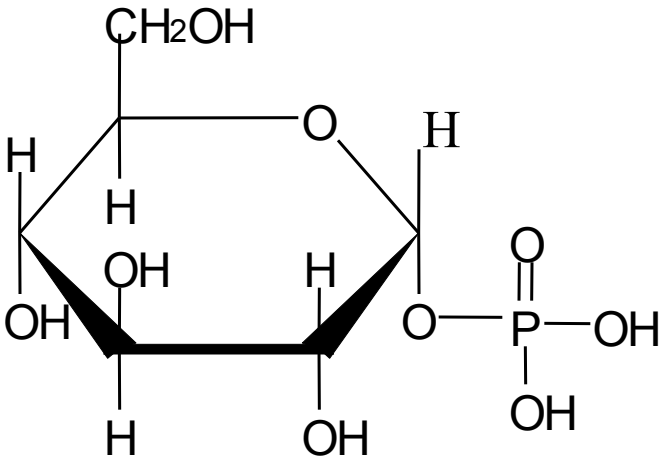




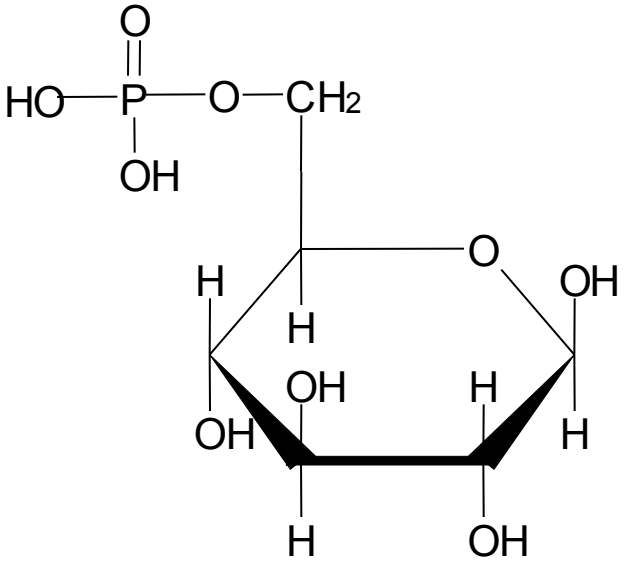
Derivatives of monosaccharides

Esters

- with phosphoric acid

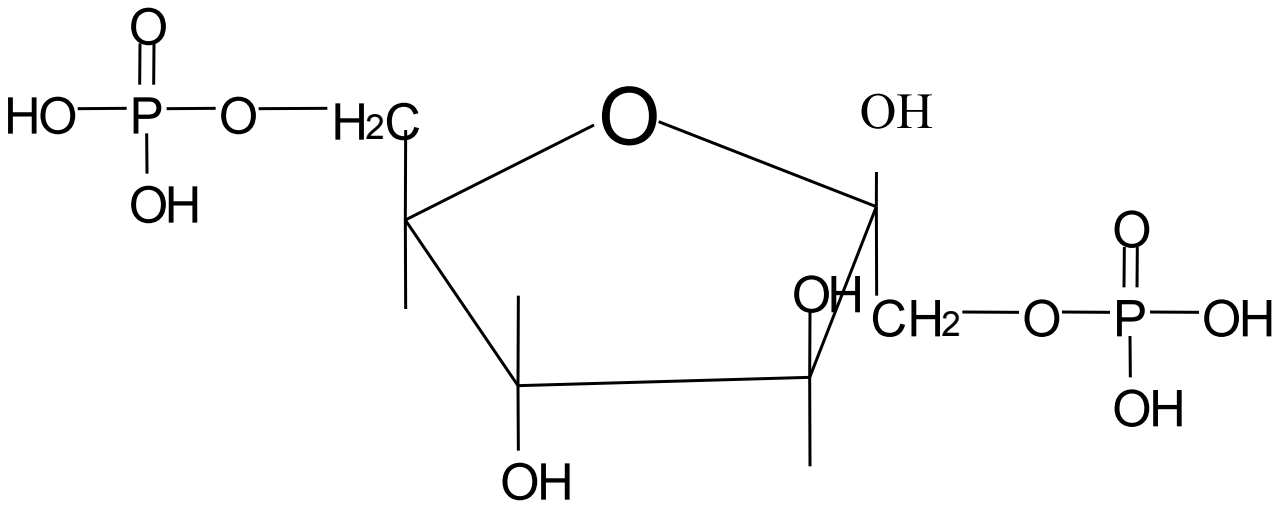


glucose-1-phosphate



glucose-6-phosphate

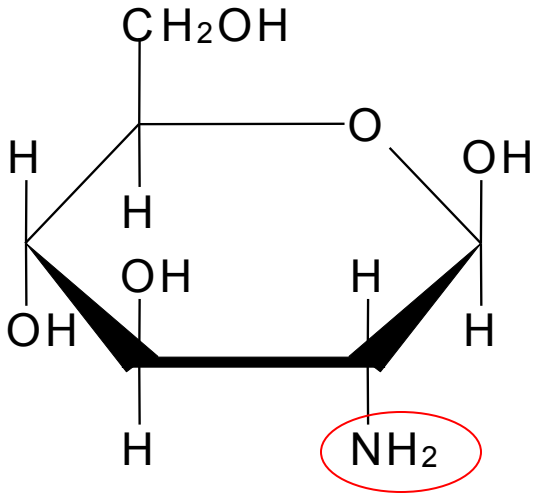
Intermediates in metabolism of glucose



fructose-1,6-bisphosphate

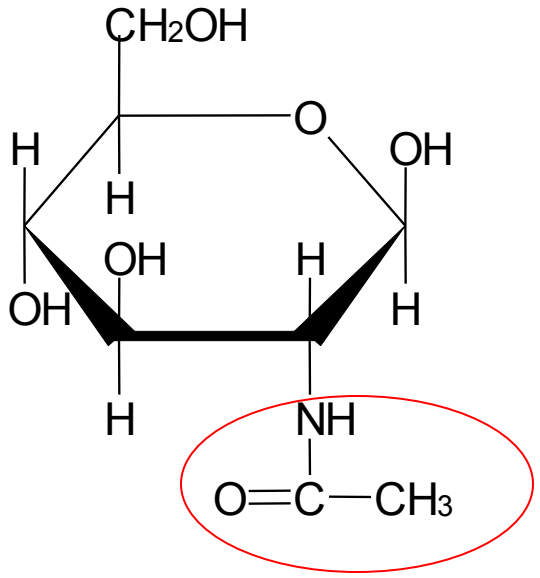
Intermediate in metabolism of glucose

Aminosugars



D-glucosamine

(2-amino-2-deoxy-D-glucose)

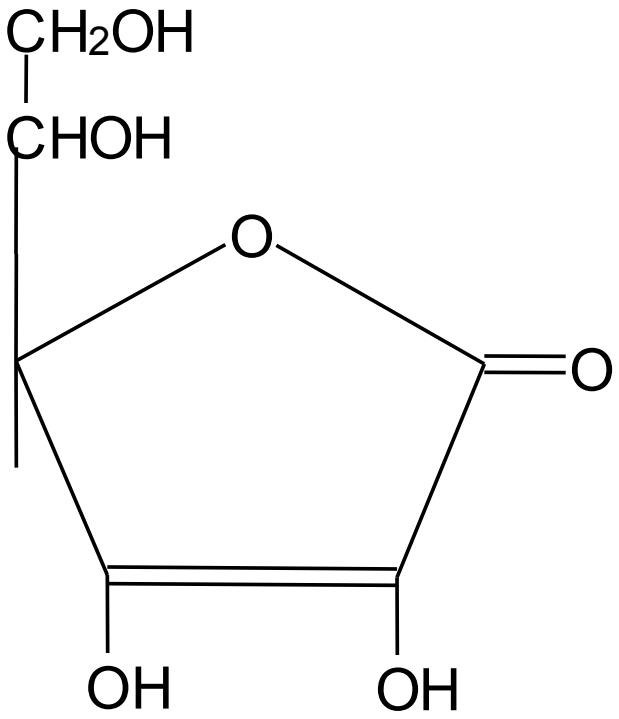


N-acetylglucosamine

Component of proteoglycans and glycoproteins

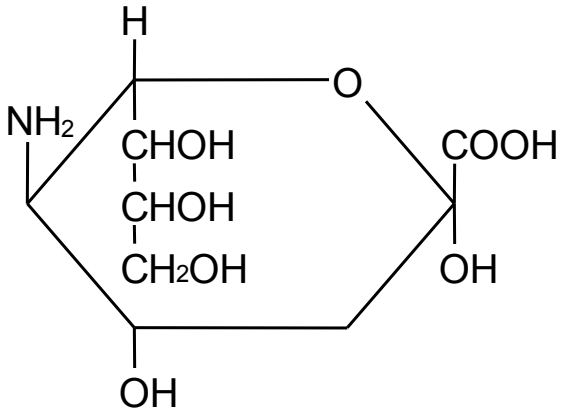
L-ascorbic acid

Derivative of L-gulonic acid

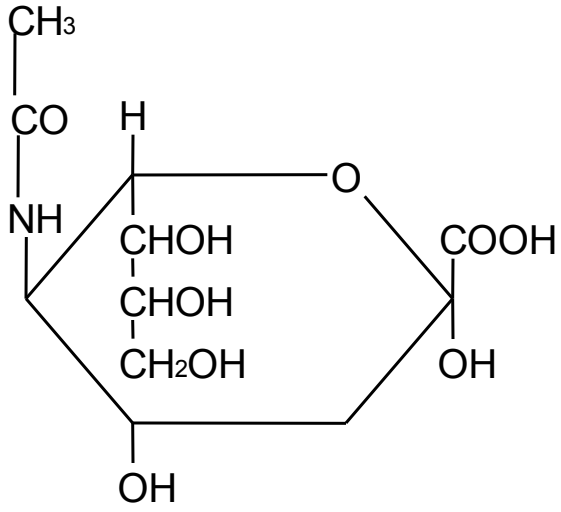


Weak diprotic acid

Sialic acids



Neuraminic acid

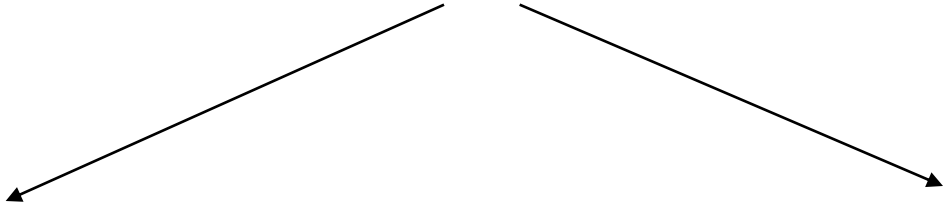


N-acetylneuraminic acid

Component of gangliosides, glycoproteins, proteoglycans

Glycosides

Derivatives of cyclic forms of monosaccharides arising by reaction on hemiacetal hydroxyl group of a saccharide :



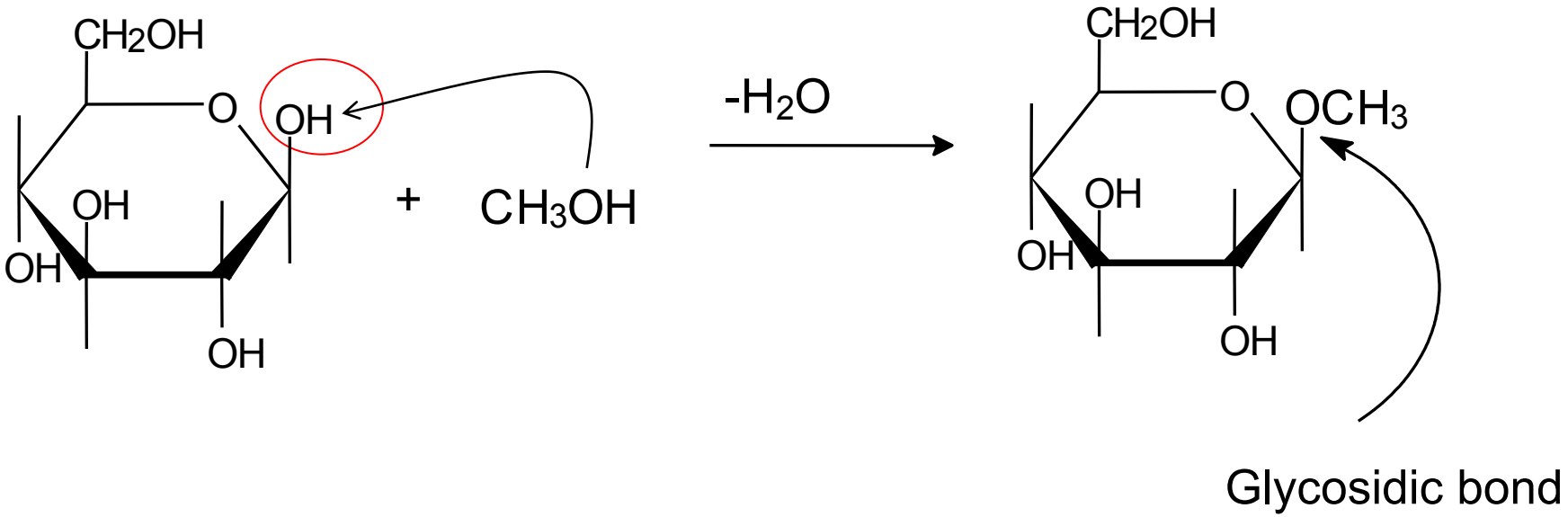
reaction with alcoholic or phenolic group of another compound

O-glycosides

with NH- group of another compound

N-glycosides

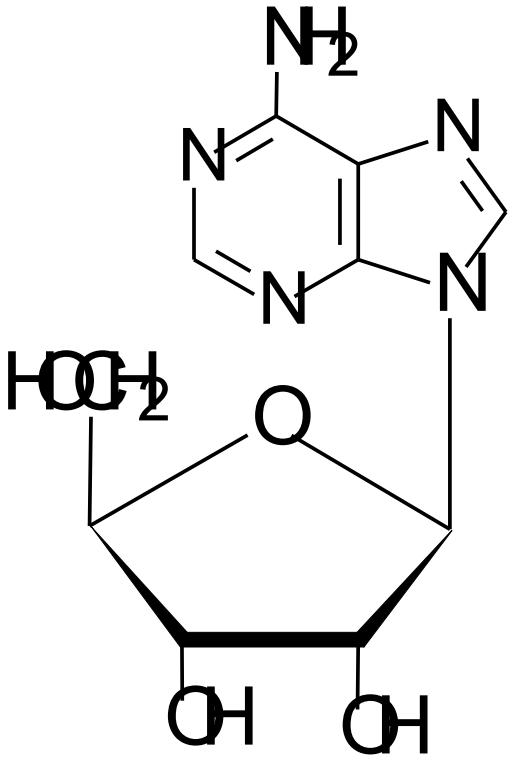
Formation of glycosidic bond



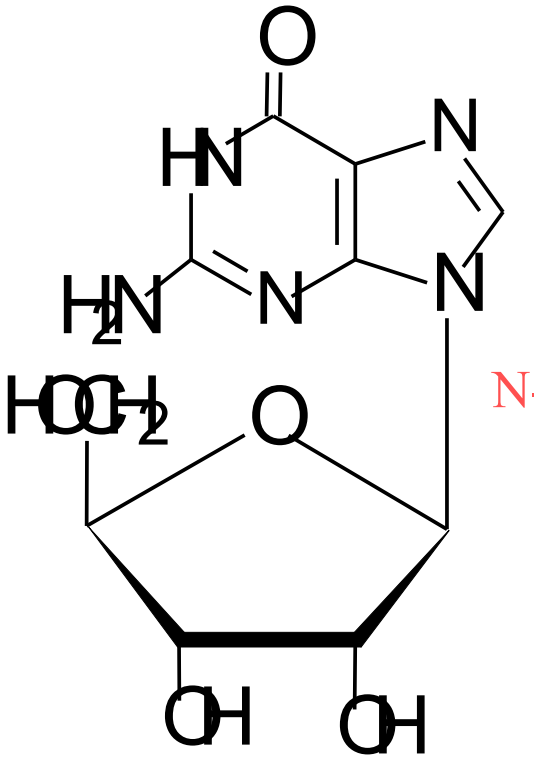
Methyl-β-D-glucopyranoside

N-glycosidic bond

nucleosides



adenosin



guanosin

N-glycosidid bond

Disaccharides

- The most important oligosaccharides
- Two monosaccharides joined by glycosidic bond

O-glycosides

two types of these sugars –
reducing and nonreducing disaccharides.

Reducing disaccharides

- formed by a reaction between the anomeric hydroxyl of one monosaccharide and a **alcoholic hydroxyl group of another**

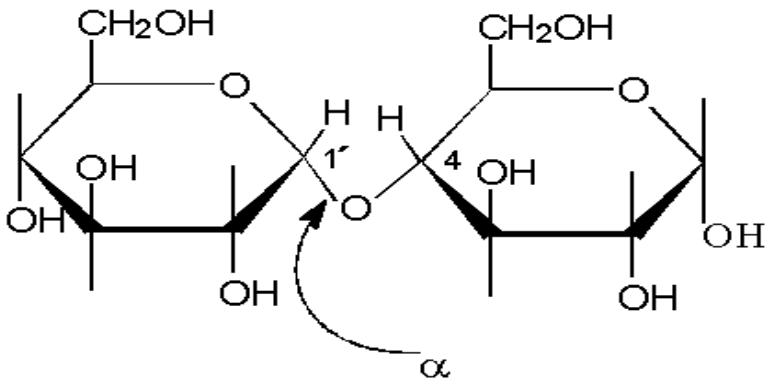
Nonreducing disaccharides

- both anomeric hydroxyl groups are linked in the glycosidic bond

a) Reducing disaccharides

Maltose

- „malt sugar“
- contained in malt, formed by enzymic hydrolysis of starch in the intestine
- 2 molecules of glucose, α - 1,4 glycosidic bond



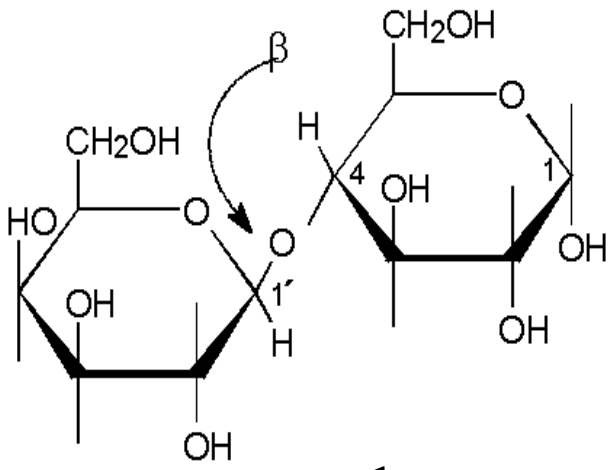
α - maltose

4-O-α-D-glucopyranosyl- α-D-glucopyranose

Lactose

- „milk sugar“
- galactose and glucose, β-1,4 glycosidic bond
- milk : cow 4-6%

  human 6%



α - lactose

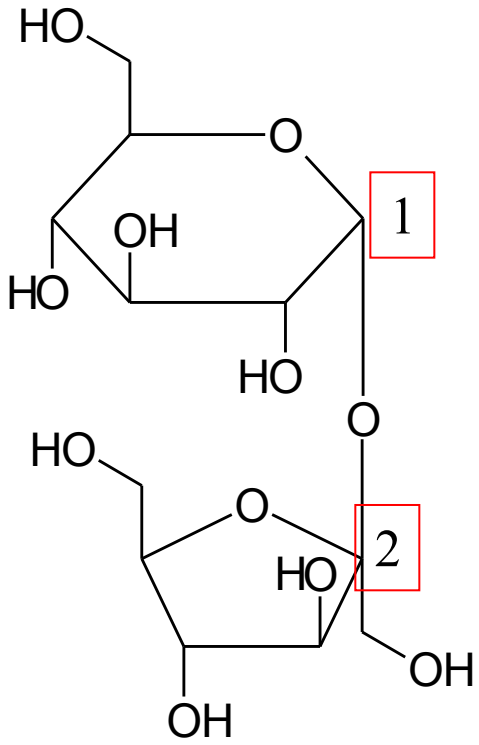
4-O-β-D-galactopyranosyl-α-D-glucopyranose

b) Nonreducing disaccharides

Sucrose

Beet/cane sugar

glucose a fructose
β-2,1 glycosidic bond



name: "glycosyl-glyco**side**"

β-D-fruktofuranosyl-α-D-glucopyranoside

Polysaccharides

- several hunreds to thousands monosaccharide units
- glycosidic bond : α - glycosidic bond vazba

  β - glycosidic bond

  mostly $1 \rightarrow 4$ a $1 \rightarrow 6$
- chains are linear or branched
- non soluble in water, some form colloidal solutions
- not sweet

Clasification of polysaccharides

Homopolysaccharides

Contain one type of monosaccharide

(starch, glycogen, cellulose, inulin)

Heteropolysaccharides

Contain two or more monosaccharides or their derivatives

(glycosaminoglycans, hyaluronic acid, glucofructans)

Biochemical significance of polysaccharides

- Store of energy

  starch (plants), glycogen (animals)

- Structural function

  cellulose (plants), proteoglycans of connective tissue (animals)

- Component of glycoproteins (affects biological function of proteins)

Starch

- lat. amylum,
- Storage polysaccharide of plants
- Main source of energy for human
- In hot water forms colloidal solution
- Monosaccharide subunit is D-glucose,
- two types of chains

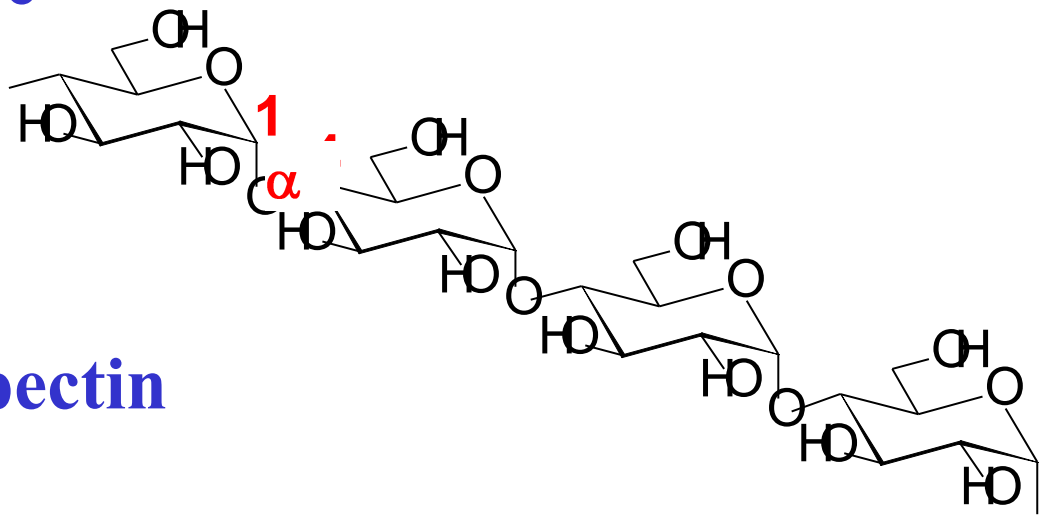
Amylose

- 20-30 %
- α-1,4 bonds
- linear (helix)
- soluble in water

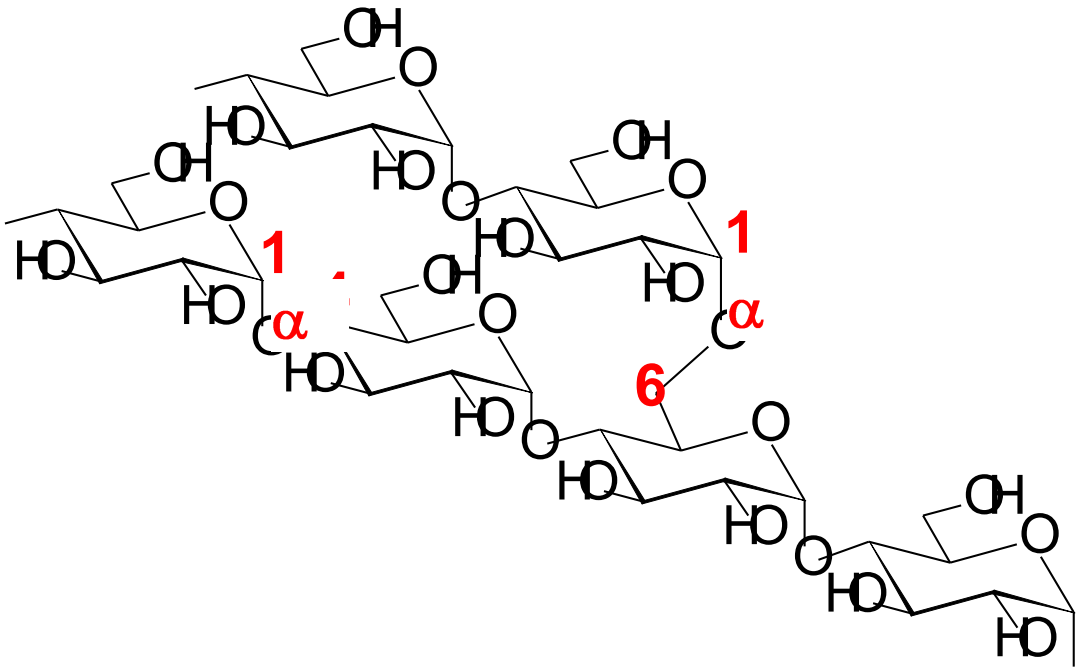
Amylopectin

- 70-80 %
- α-1,4 + α-1,6 bonds
- branched
- non soluble in water

Structure of amylose



Structure of amylopectin



Starch is the main source of saccharides in food

- it is digested by α-amylase in mouth and intestine
- α-amylase hydrolyses α-(1→4) glycosidic bonds
- the product of digestion is maltose, isomaltose, they are further digested by specific enzymes
- the final product of cleavage is glucose

Distinguish: : amylase x amylose !!!!

Glycogen

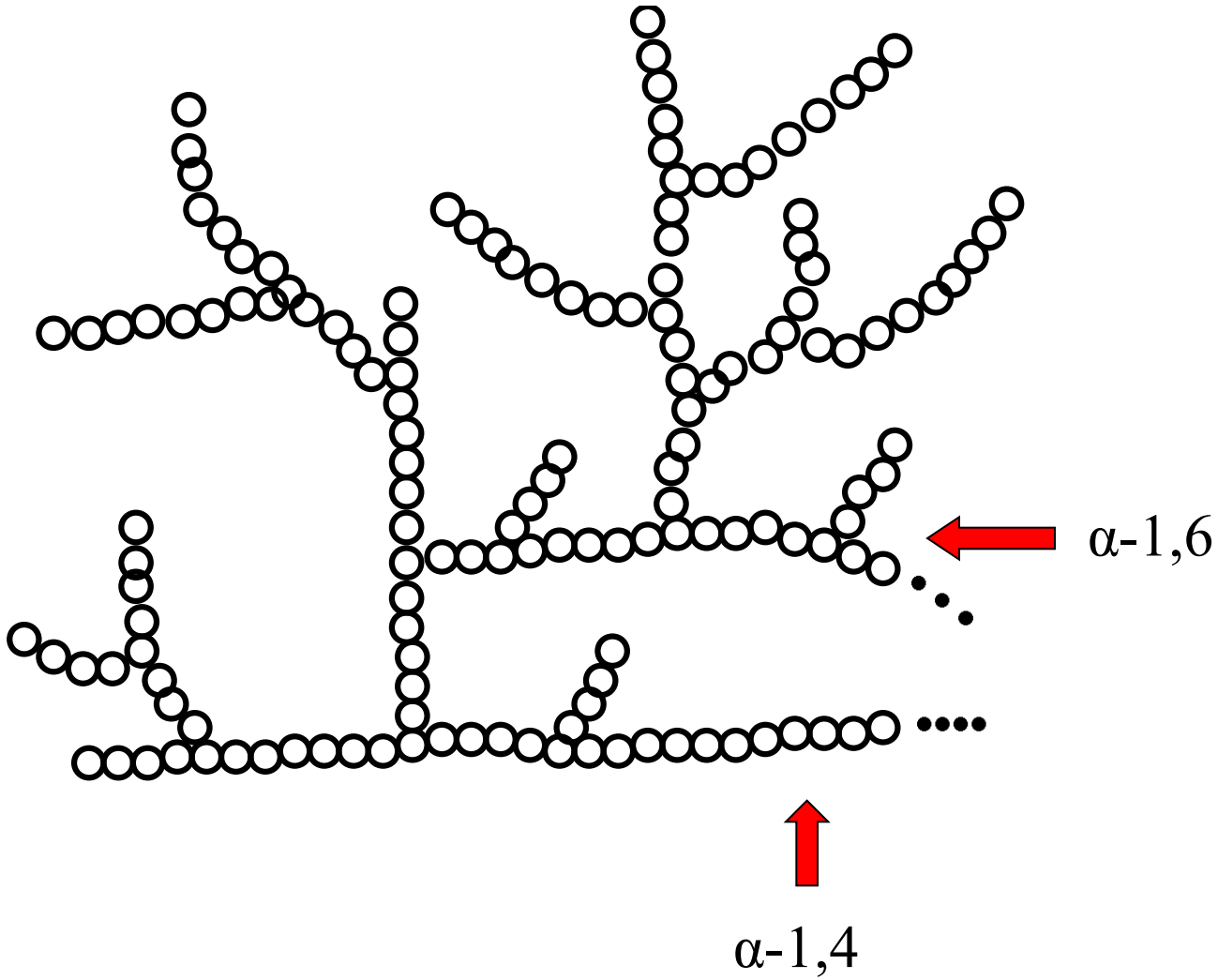
- storage substance in animals (liver, muscle)
- „animal starch“
- formed from sugars taken in food
- composed of glucose units
- structurally similar to amylopectin

  branched chain: bonds α-1,4 and α-1,6 → branching

Glycogen stores in man

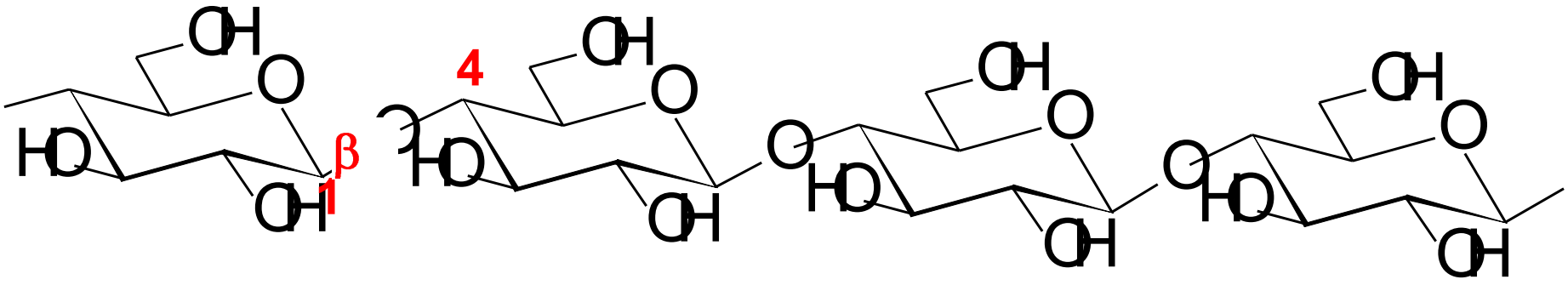
Liver	Muscle
4-6 % of liver mass	1-2 % of muscle mass

Glycogen branching

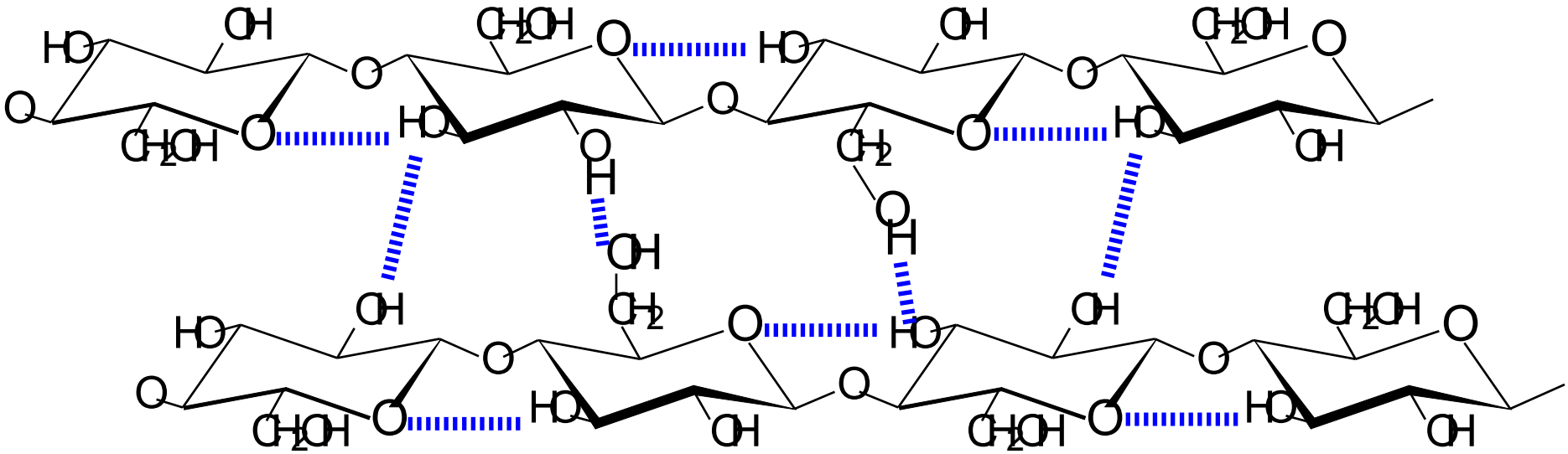


Cellulose

- Most abundant organic compound in plants
- Composed of D-glucose, bonds β-1,4
- Fibrous macromolecules joined by hydrogen bonds
- Not soluble in water
- Not digestible for humans and most animals, is the main component of dietary fibre



Intra- and inter- molecular hydrogen bonds in cellulose



Formation of fibers and bundles.

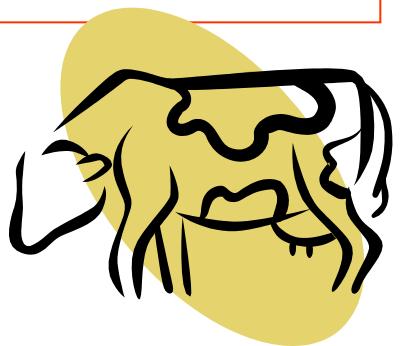
Cotton, wood, hemp, linen, straw, and corncobs are mainly cellulose

Cellulose cleavage

- bonds β-(1→4) can not be cleaved by α-amylase

Cellulose is not digestible by human

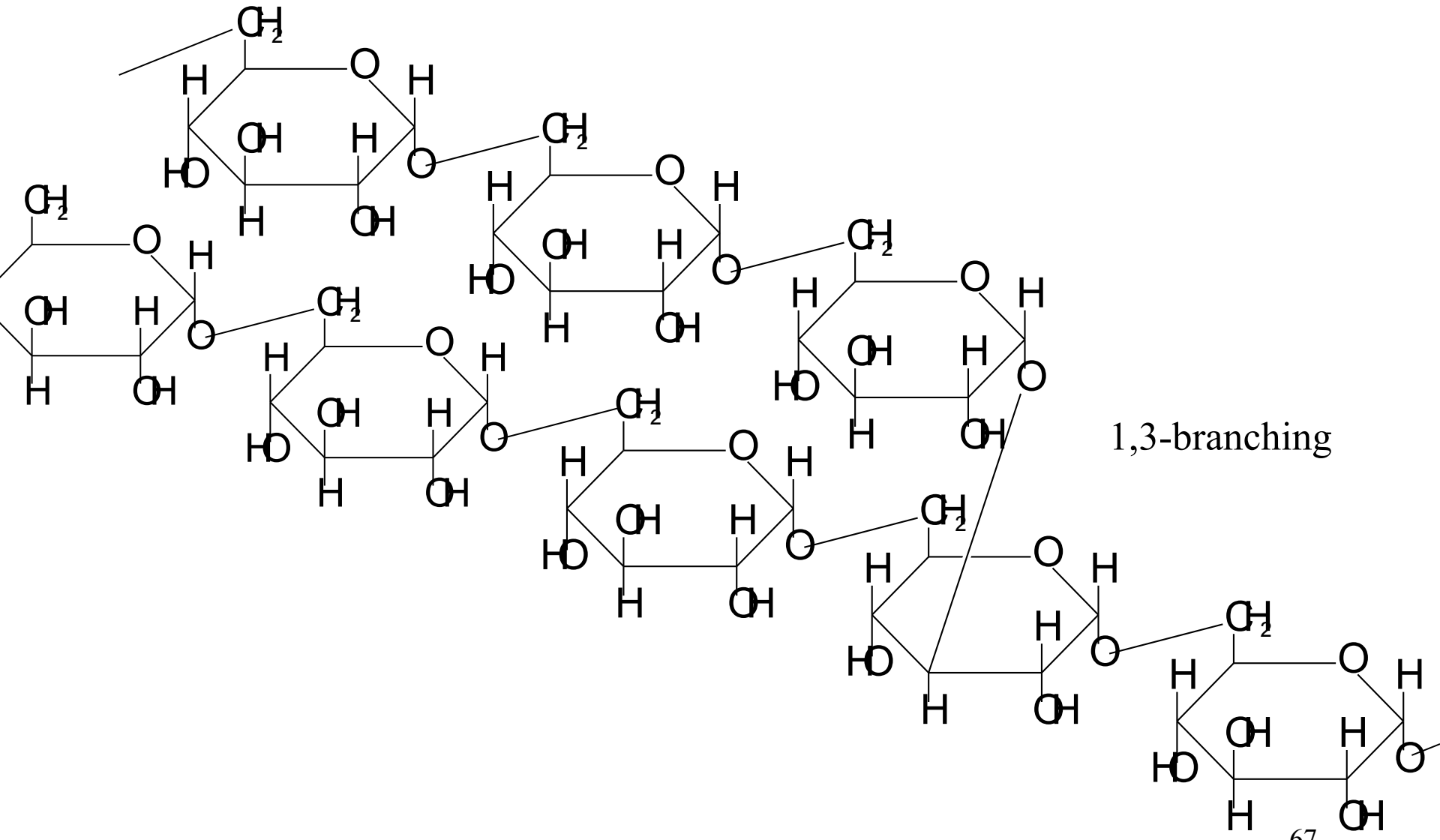
Ruminants have microorganisms in their digestion tract that are producing β-glucosidases – they can utilize cellulose as a source of glucose



Dextrans

- Polysaccharides containing D-glucose, bonds α-1,6
- Special type of branching (positions 3 and 4)
- Formed from saccharose by the action of bacteria
- Molecular mass 10 000 – 1 000 000
- Used as artificial substitute of blood plasma (at bleeding or therapy of burns)
- Highly branched dextrans prepared artificially are used as molecular sieves for gel chromatography

Structure of dextran



Dextran and caries

- bacterias of oral cavity (e.g.. *Streptococcus mutans*) cleave sucrose to glucose a fructose
- bacterial enzyme dextran transglucosylase catalyzes synthesis of dextran from glucose
- dextran is not soluble in water and resistant against salivary amylase, it builds up coatings on unclean teeth– it is a mixture of dextrans and bacterias
- bacterias metabolize fructose to lactic acid (pK_A = 3,86), that has corrosive effect on enamel

Heteropolysacharides

Glycosaminoglycans (mucopolysacharides)

- non-branched heteropolysacharides
- Components of proteoglycans and peptidoglycans
- formed by repeating disaccharide units:

$$-[\text{ glycosamin} - \text{uronic acid}]_n-$$

Glukosamin, galaktosamin

(often acetylated)

Glucuronic, galacturonic, iduronic

Specific –OH groups may be sulfated

Major types of glycosaminoglycans (GAG)

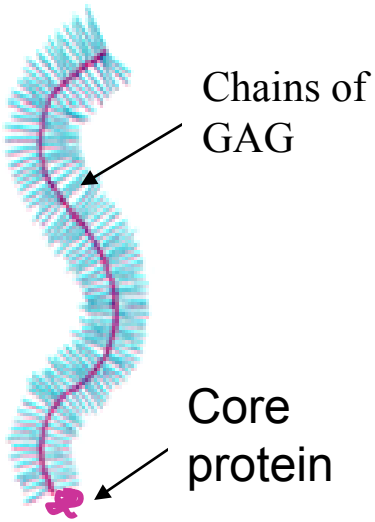
Heteroglycan	Compositon
• hyaluronic acid	• Glc-NAc, Glc-UA
• chondroitin-4-sulfate	• Gal-NAc-4-sulfate, Glc-UA
• chondroitin-6-sulfate	• Gal-NAc-6-sulfate, Glc-UA,
• keratansulfate	• Gal-NAc, sulfate
• heparin	• Glc-NAc, Glc/Ido-UA, sulfate
• dermatansulfate	• Gal-NAc, Glc/Ido-UA, sulfate

Heparin

- Prevents blood clotting in vivo + in vitro
- Forms the complex with antitrombin
- It is released from basophillic granules of mast cells
- Therapeutically used to prevent and treat tromboses, after IM, surgical operations etc.
- Preparation of uncoaguable blood

Glycosaminoglycans are often components proteoglycans

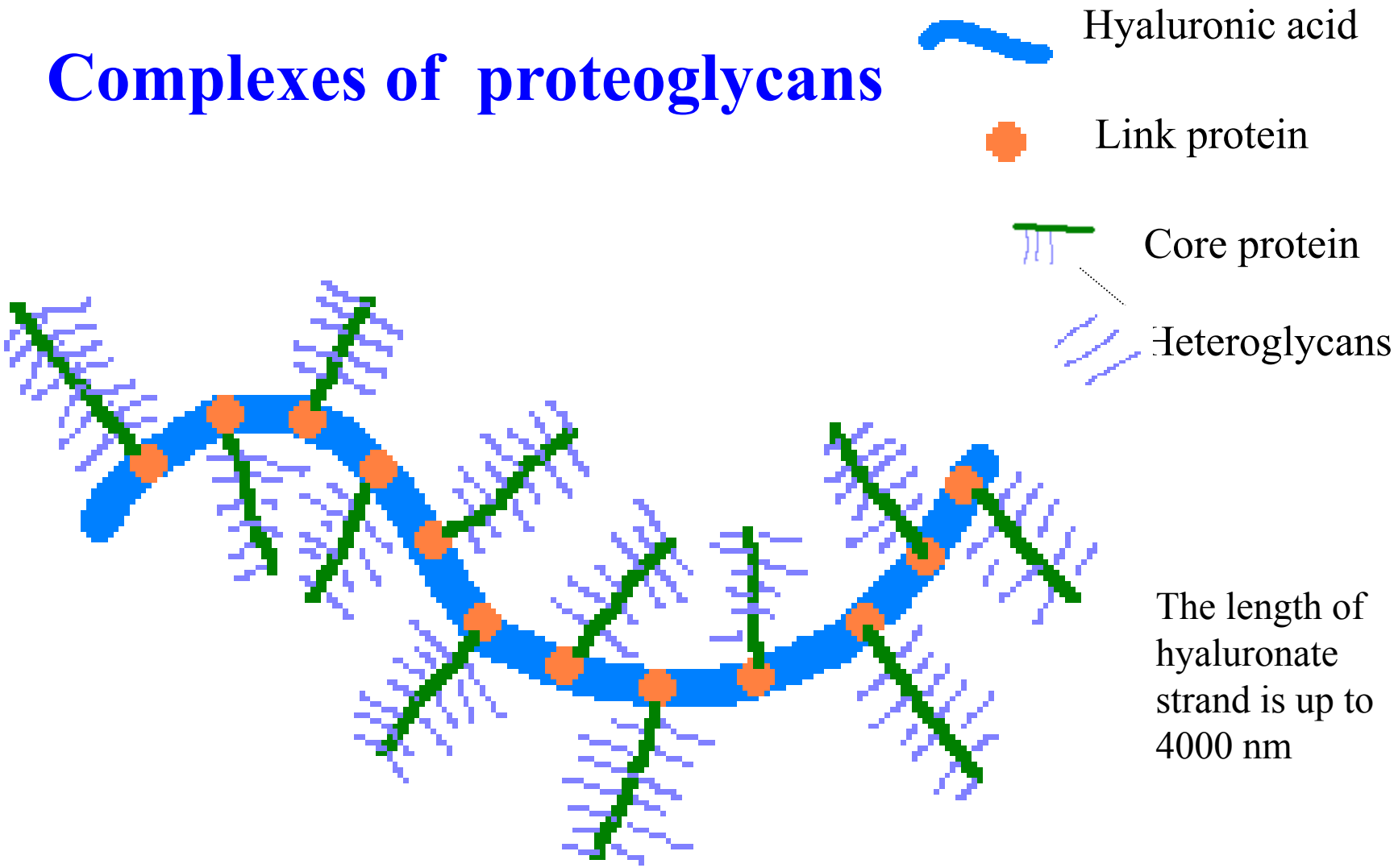
It resembles a bottle-brush



Proteoglycans

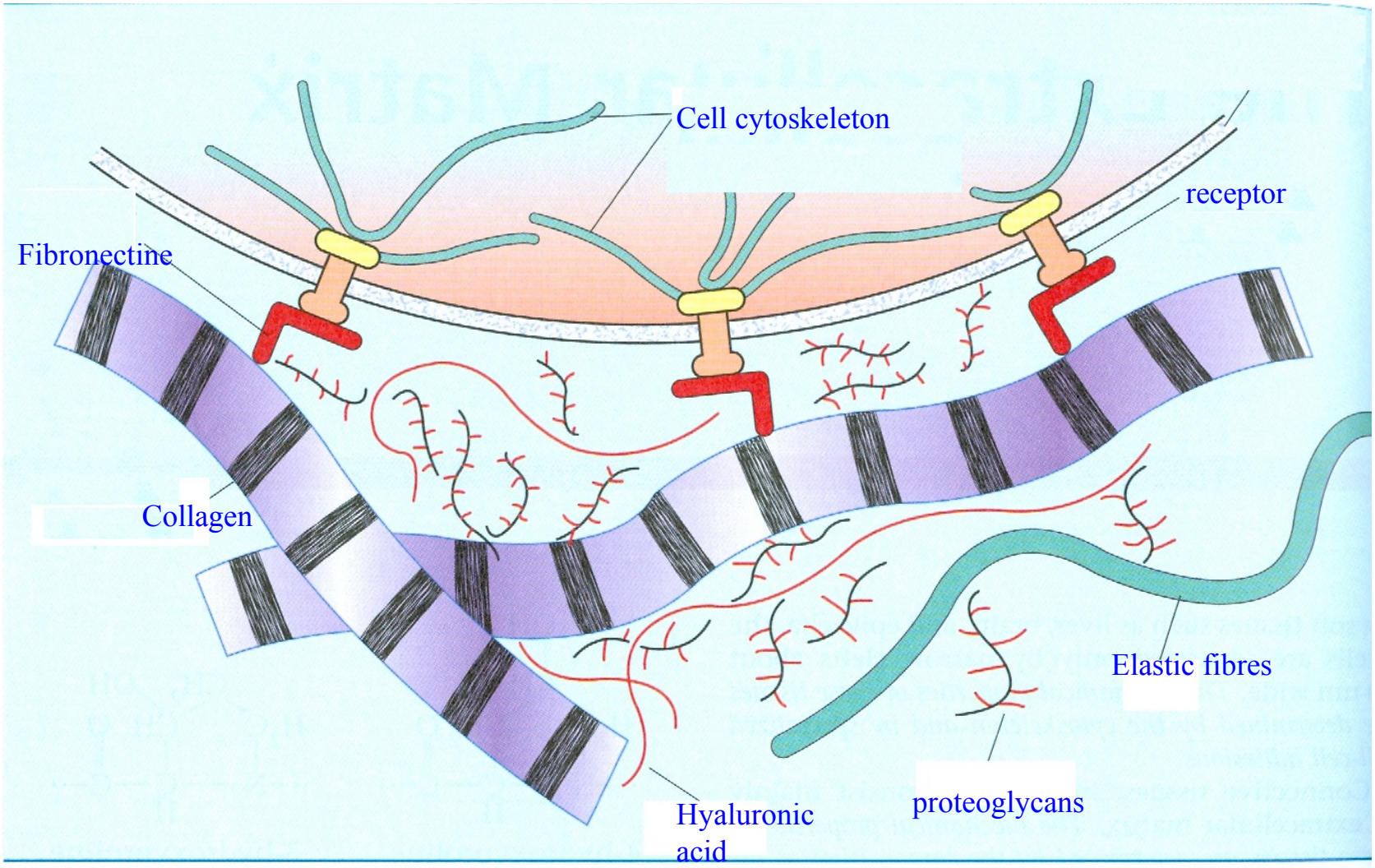
- complexes of glycosaminoglycans and specific proteins
- content of heteroglycans up to 95 %, chains of 10-100 saccharide units
- most often O-glykosidic bond between a protein and glycan, end-sequence Gal-Gal-Xyl
- present mainly in extracellular matrix of animals

Complexes of proteoglycans



Core proteins are associated with hyaluronate by link proteins

Main components of extracellular matrix

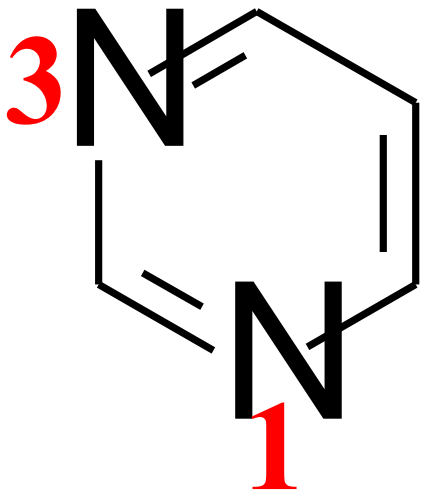


Meisenberg, Simmons:Principles of Medical Biochemistry

Nucleosides a nucleotides

Pyrimidine a derivatives

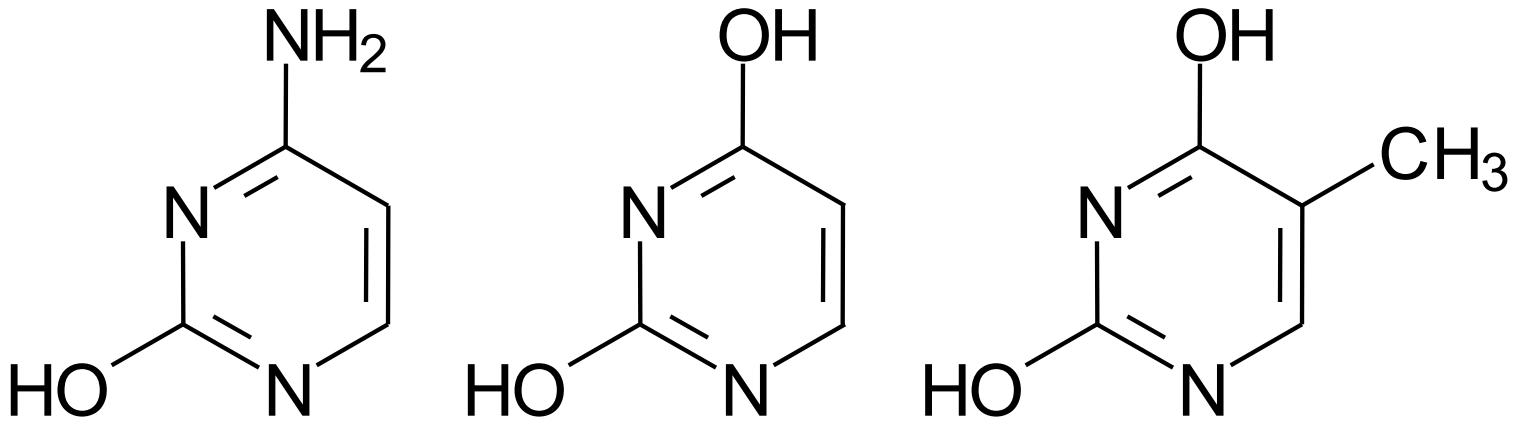
Numbering



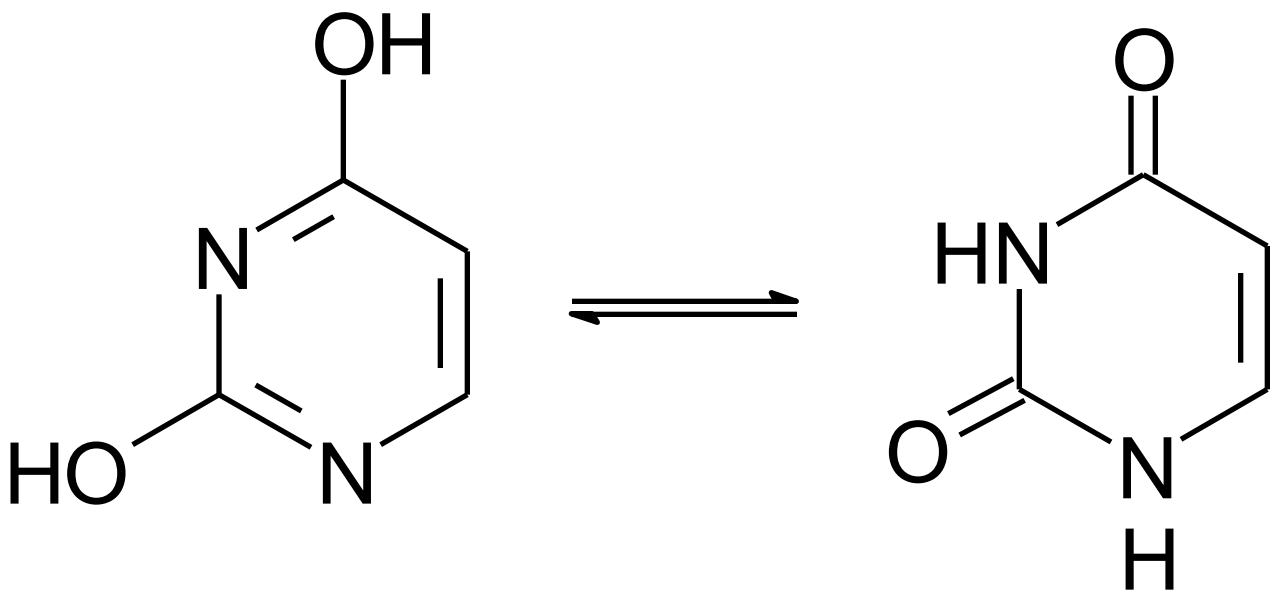
1,3-diazine

Pyrimidine bases

cytosine	uracil	thymine
2-hydroxy-4-aminopyrimidine	2,4-dihydroxypyrimidine	2,4-dihydroxy-5-methylpyrimidine



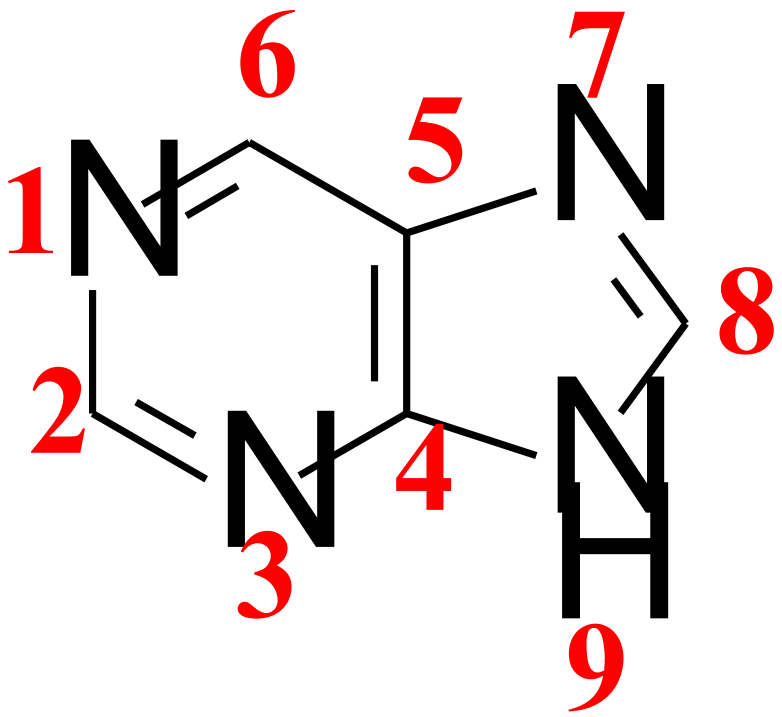
Tautomerism of pyrimidine bases



lactime form (weakly acidic)

lactam form (more stabile)

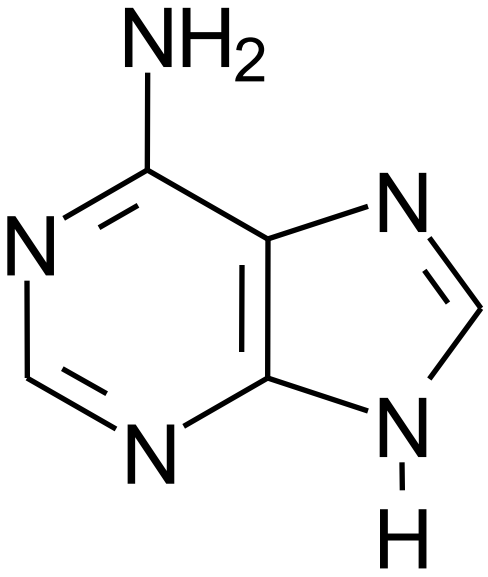
Purine and derivatives



Purine has special numbering

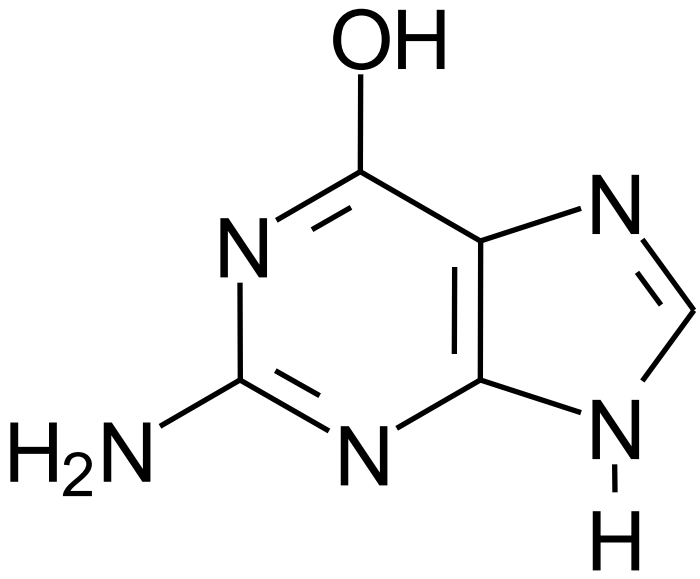
Purine bases

adenine



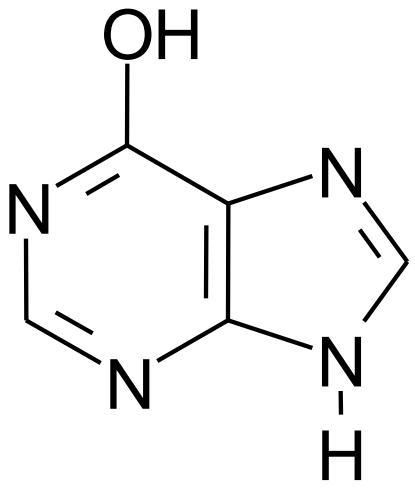
6-aminopurine

guanine



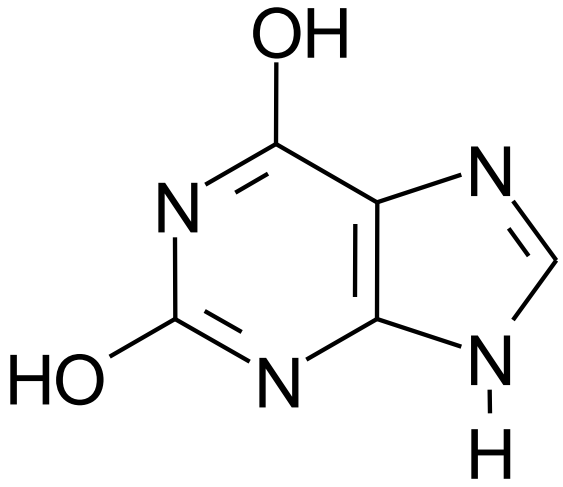
2-amino-6-hydroxypurine

hypoxantine



6-hydroxypurine

xantine

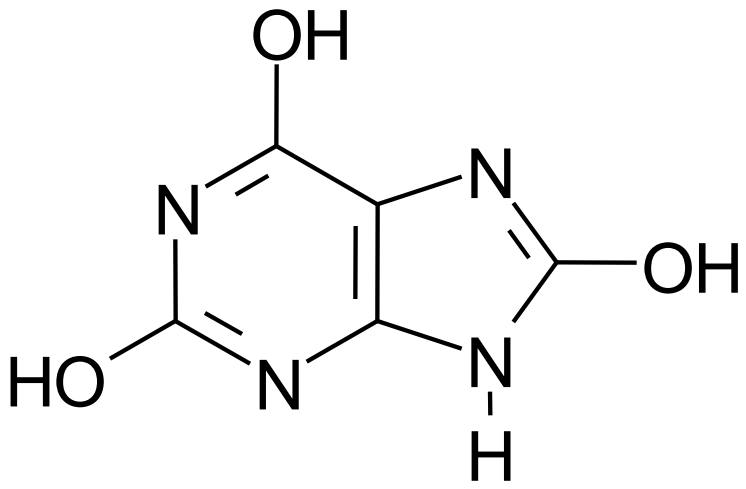


2,6-dihydroxypurine

They are formed by metabolism of purine bases

Uric acid

(acidum uricum)

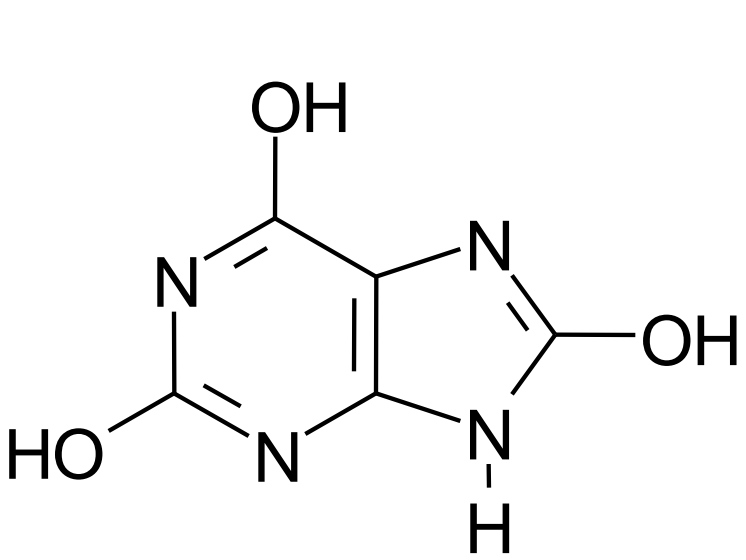


2,6,8-trihydroxypurine

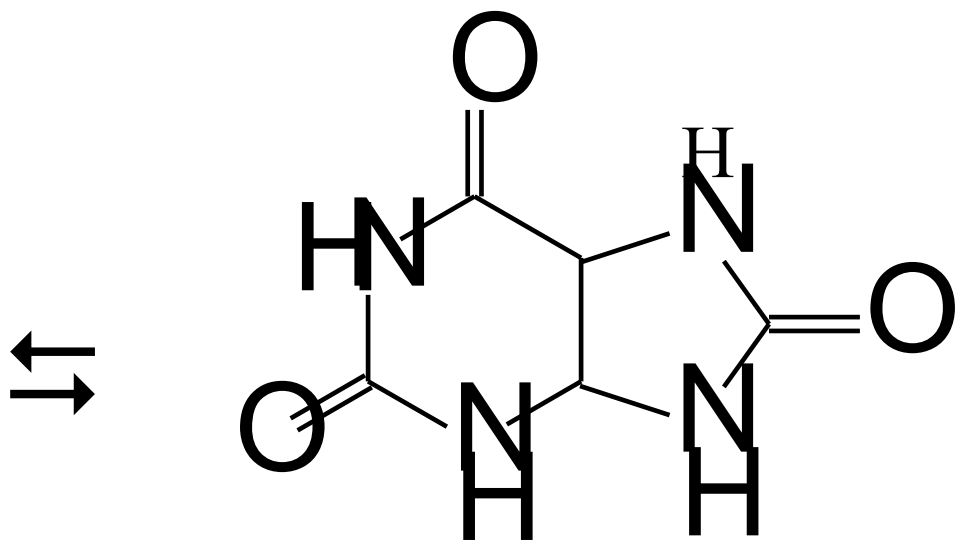
At mammals: final product of purine bases metabolism

Uricotel organisms (most of reptiles and birds): it is formed from amino acids.

Tautomeris forms of uric acid



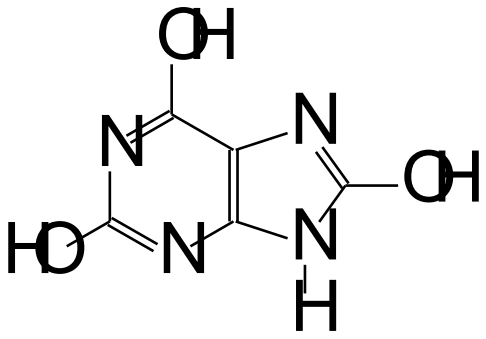
lactime



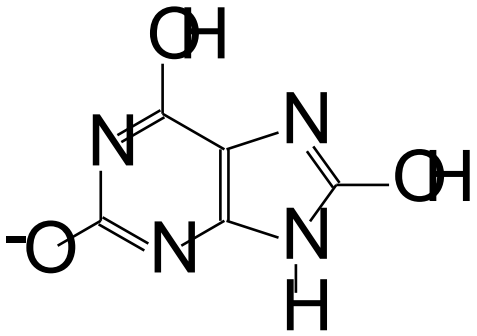
lactame

Lactime form is diprotic acid

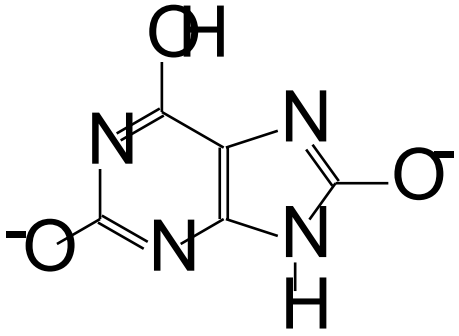
$pK_{A1} = 5,4$ $pK_{A2} = 10,3$



uric acid



hydrogenurate

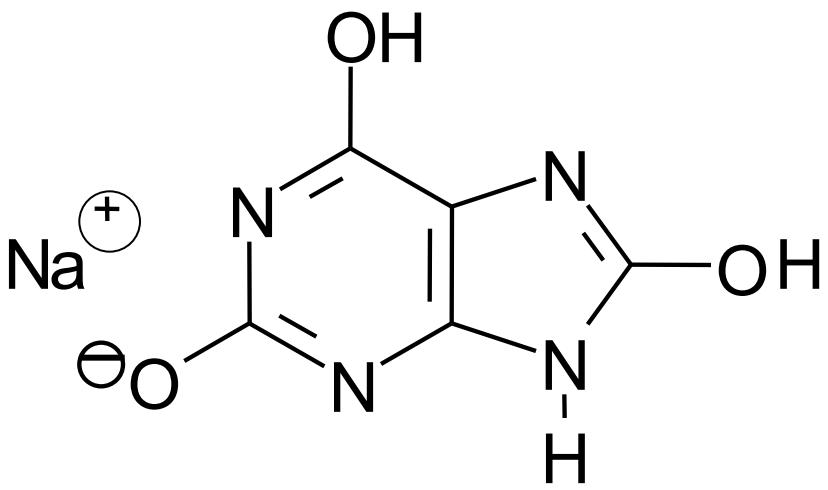


urate

2,6,8-trihydroxypurine

Uric acid is very bad soluble in water or in acidic medium

It dissolves in alkaline medium and forms salts (urates and hydrogenurates)



Sodium hydrogenurate

Consequences of bad solubility in human body

Under patological conditions

- Formation of renal stones
- deposition in joints and tissues (gout)

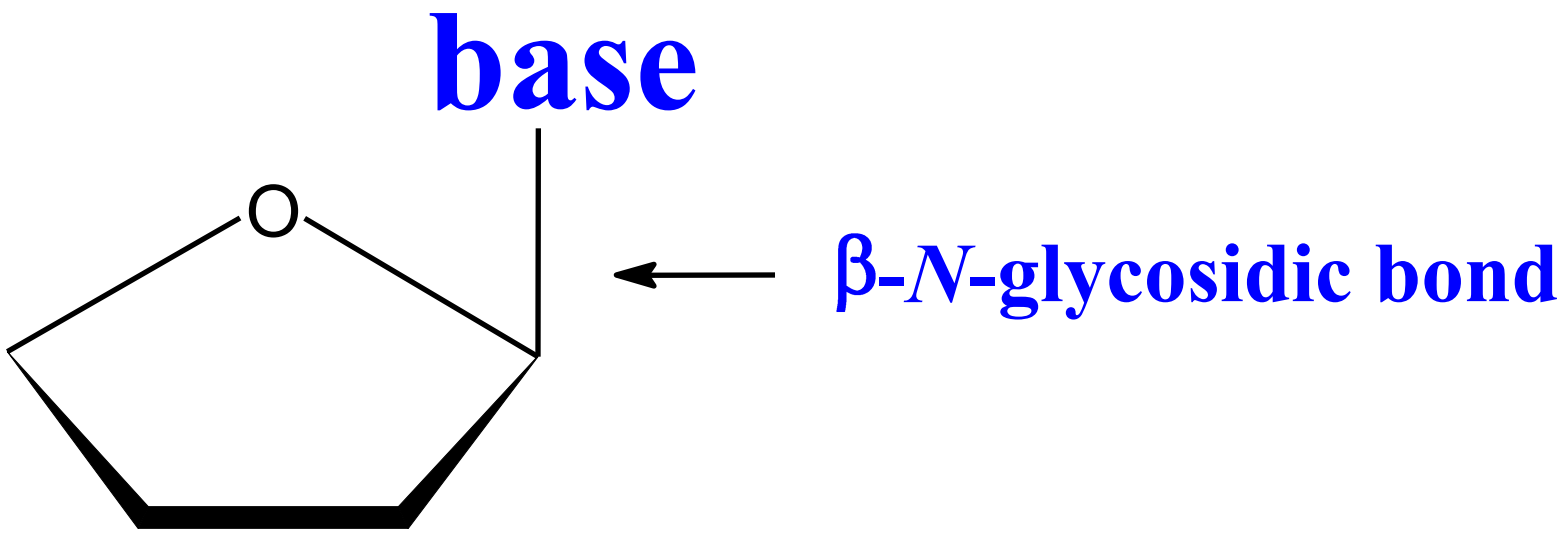
Nucleosides

base + ribose

base + 2-deoxyribose

β-N-glycosidic bond

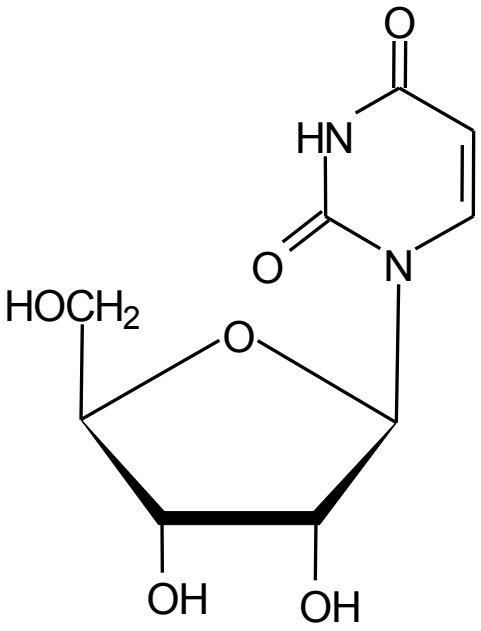
General structure of nucleoside



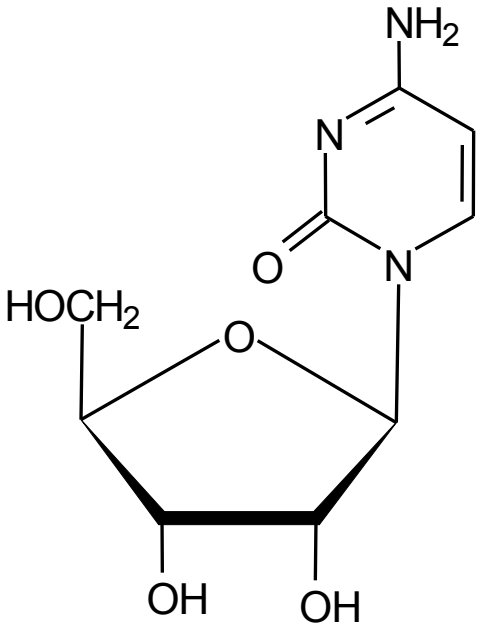
Names of nucleosides

- Trivial names
- Derived from names of bases
- ending -idine (pyrimidine nucleosides)
- přípona -osine (purine nucleosides)

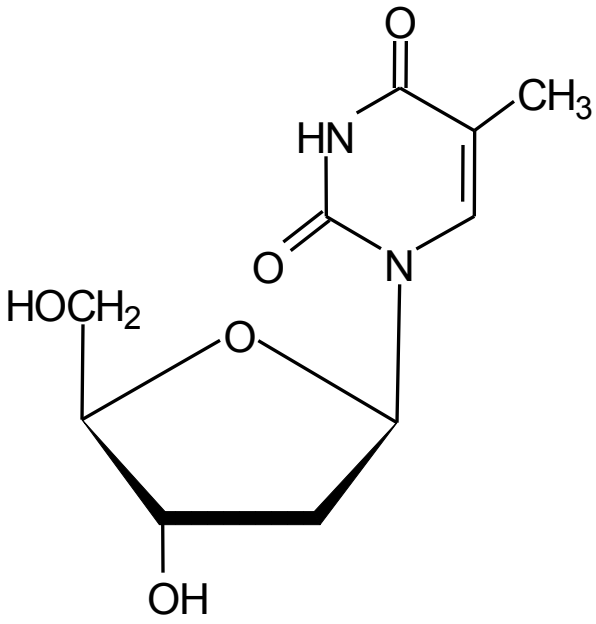
Pyrimidine nucleosides



uridine

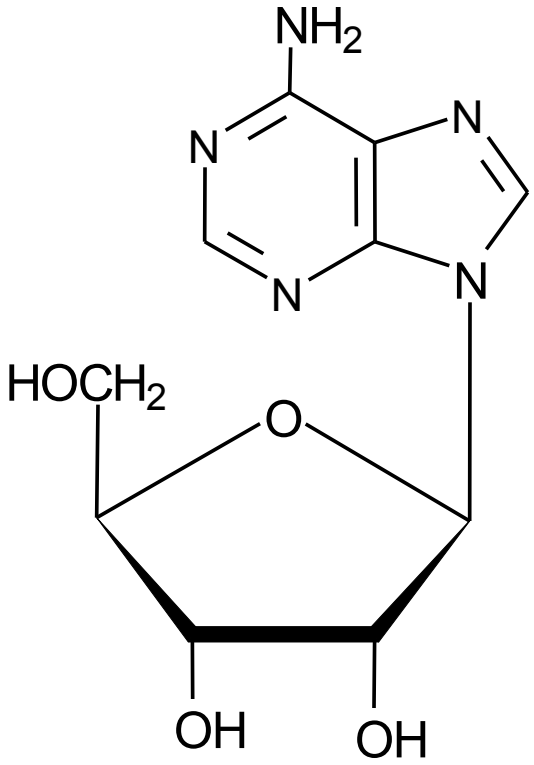


cytidine

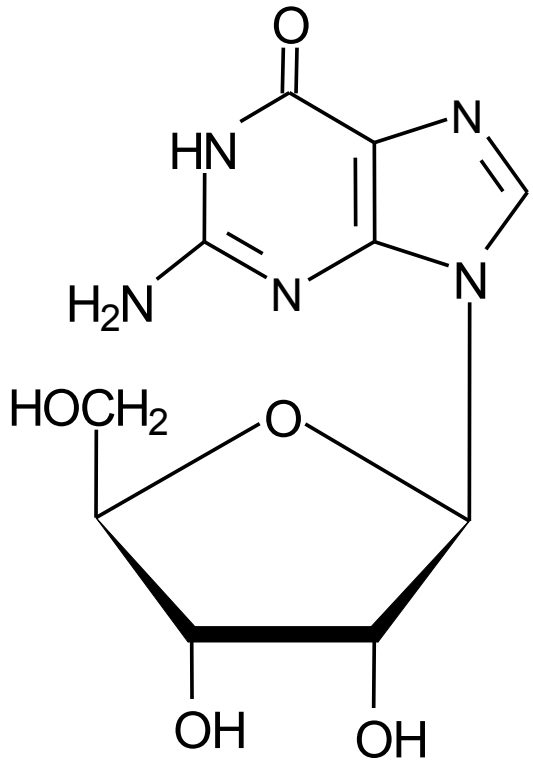


thymidine

Purine nucleosides

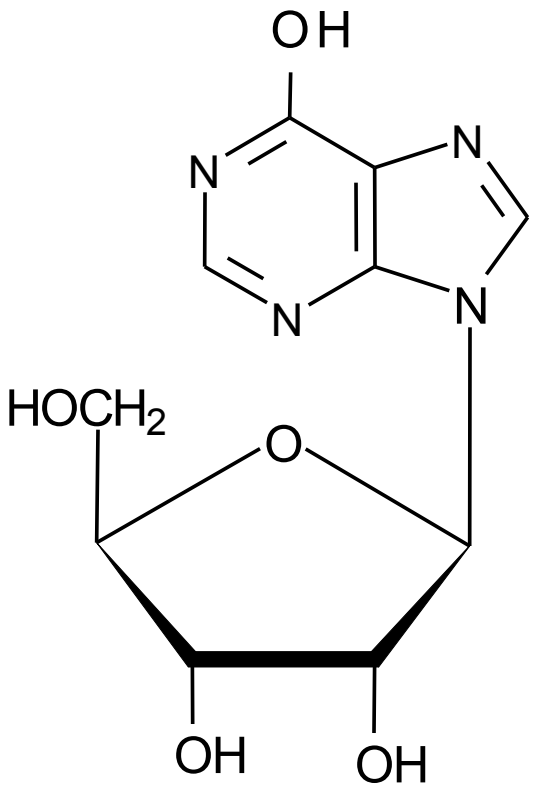


adenosine

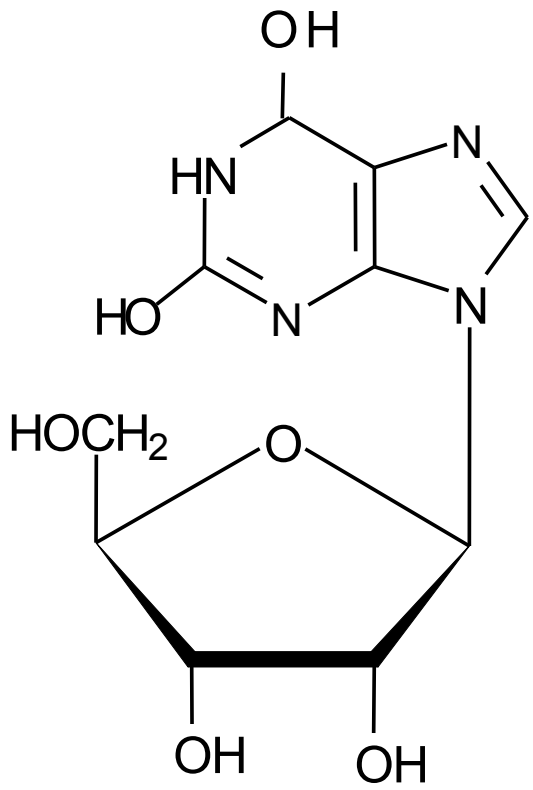


guanosine

Purine nucleosides



inosine



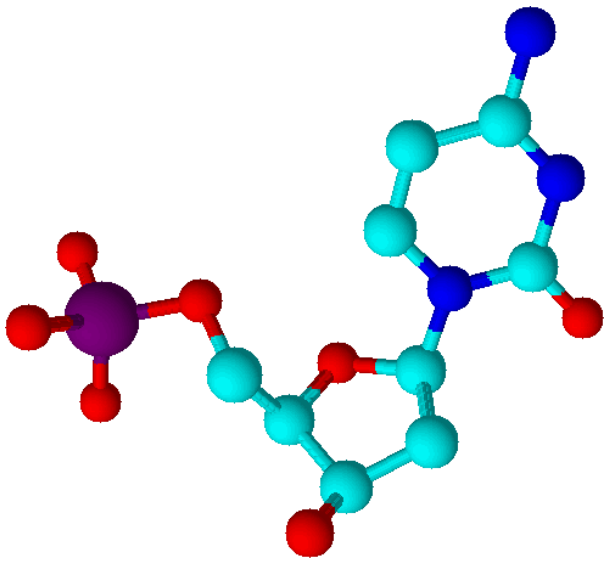
xanthosine

Nucleotides

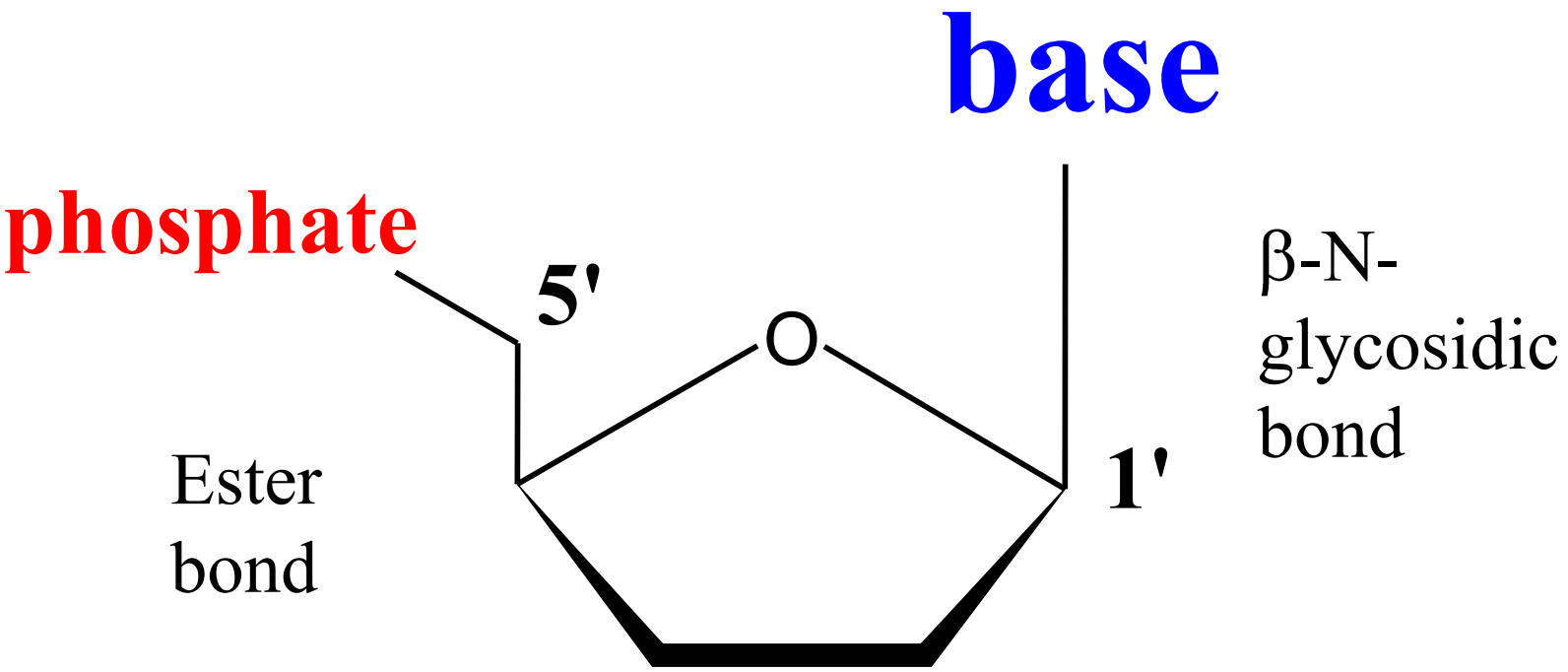
Nucleoside + phosphoric acid

bound by ester bond to: ribose ($C_{2'}$,$C_{3'}$, $C_{5'}$)

deoxyribose ($C_{3'}$,$C_{5'}$)



General structure of nucleotide



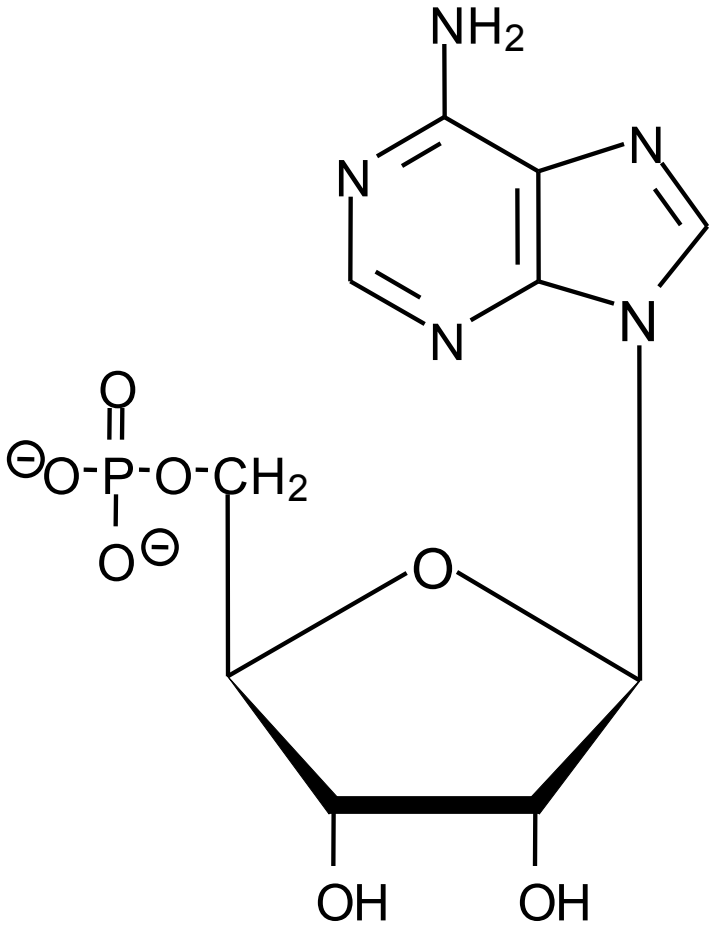
Names of nucleotides

- nucleoside + 5‘-mono(di, tri) + phosphate
- abbreviations AMP, ADP, ATP …….....

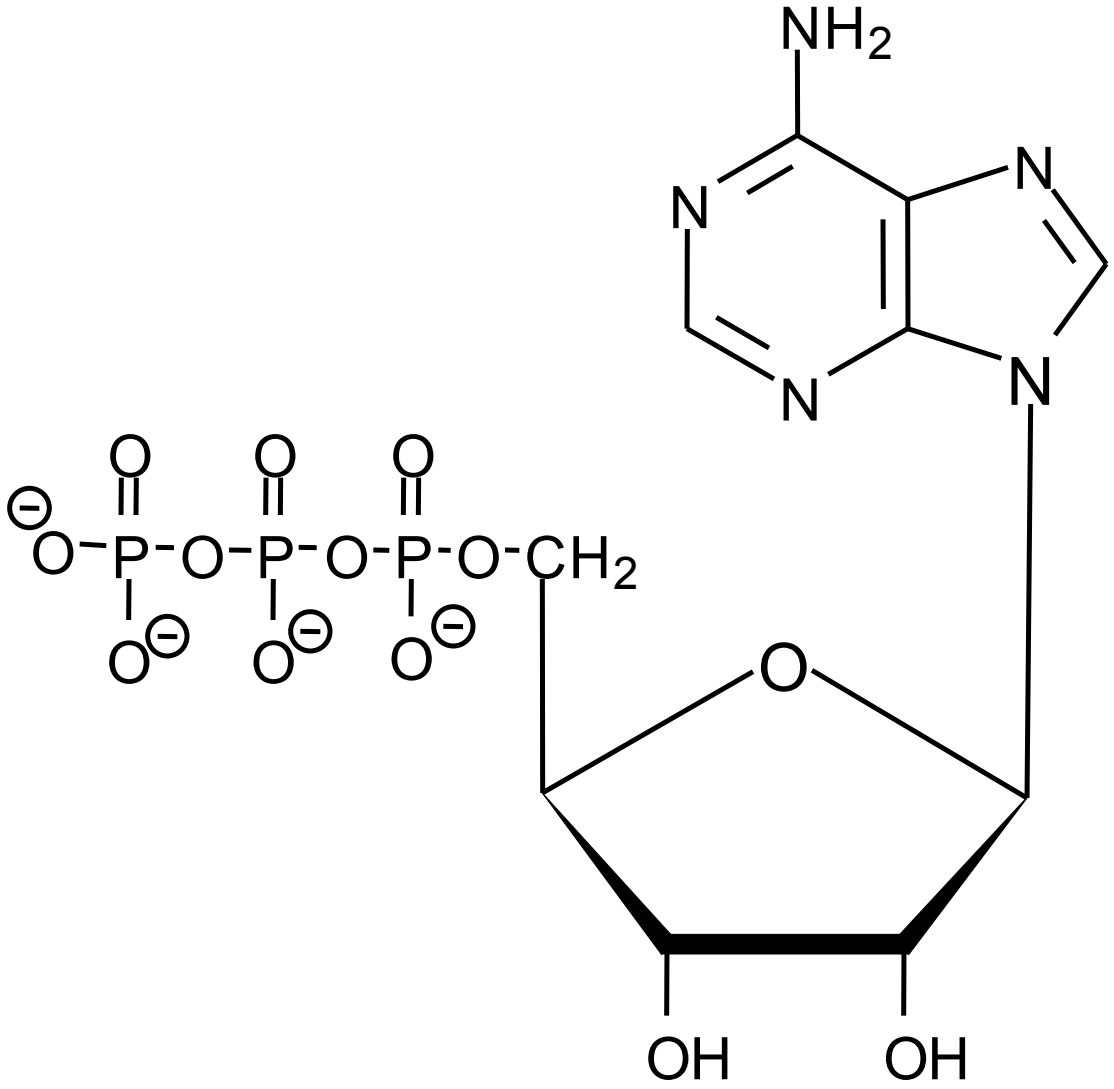
Significance of nucleotides

- Building blocks of nucleic acids
- Macroergic compounds (ATP, CTP, UTP)
- Second messengers (cAMP, cGMP)
- Cofactors of enzymes
- syntetic analogs - therapeutics

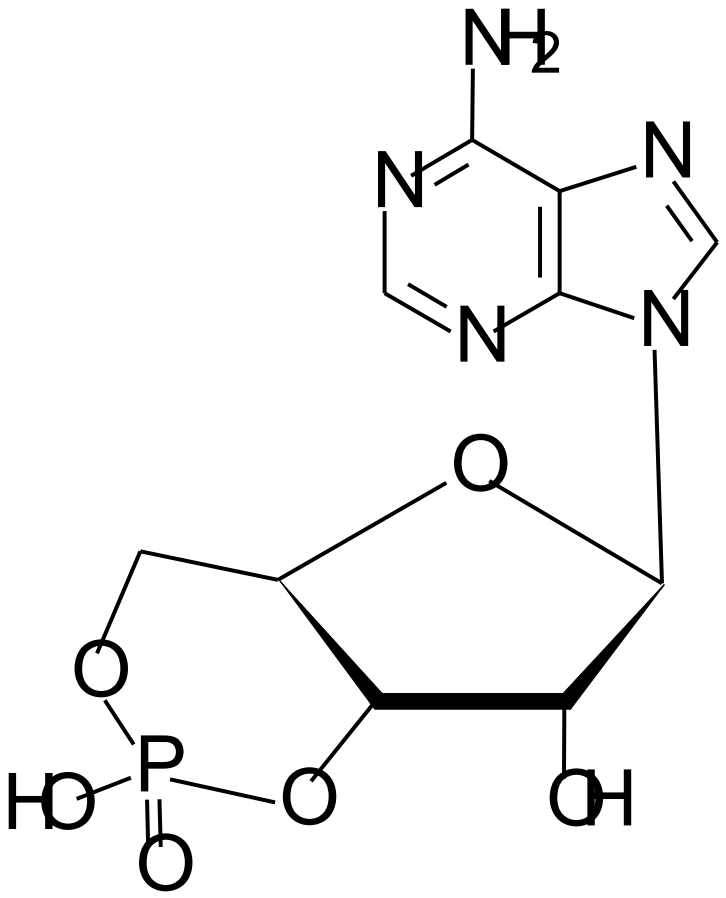
Adenosin-5´- monophosphate (AMP)



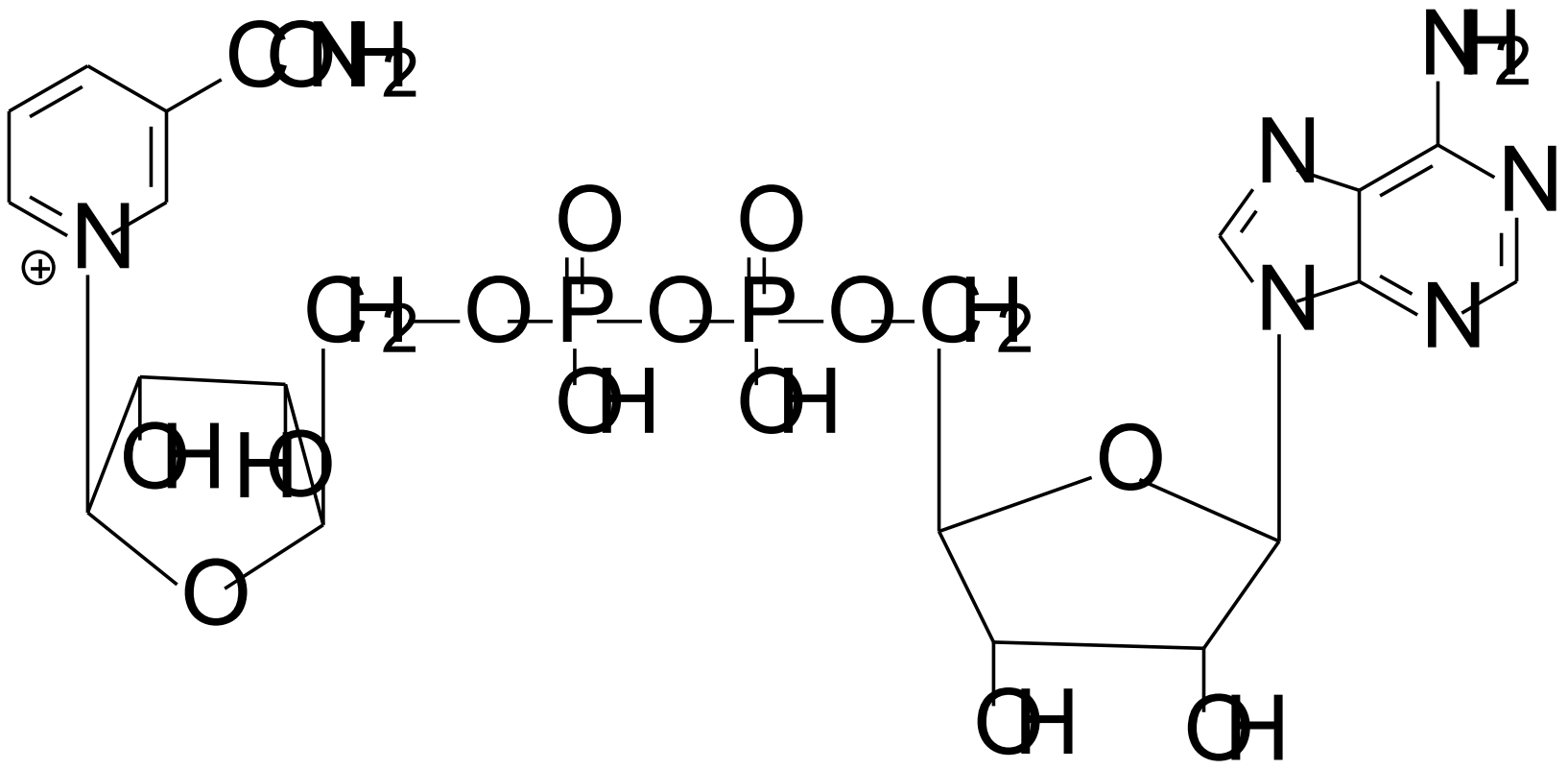
Adenosine-5´- triphopshate (ATP)



cAMP – secondary messenger



NAD^+ is dinucleotide



Flavine adenine dinucleotide (FAD)