CARBOHYDRATES.

AMINO ACIDS.

POLYPEPTIDES AND PROTEINS.

NUCLEIC ACIDS.

Self-directed learning

1. Amino sugars (D-glucosamine, D-mannosamine, D-galactosamine), their properties

2. The concept of the mixed biopolymers: proteoglycans, glycoproteins, glycolipids

3. Reductive amination reactions. Pyridoxal catalysis

4. The qualitative tests for of α-amino acids.

5. The concept of the secondary structure of DNA. The role of hydrogen bonds in the formation of the DNA secondary structure. Complementarity of heterocyclic bases

CARBOHYDRATES. MONOSACCHARIDES. CLASSIFICATION.

Carbohydrates are classified on the basis of their acid-catalyzed hydrolysis products.
1) *monosaccharides* are the simplest carbohydrates, those that cannot be hydrolyzed into smaller simpler carbohydrates;
2) *oligosaccharides* are carbohydrates that hydrolyze to yield 2 — 10 molecules of a monosaccharide;
3) *polysaccharides* are carbohydrates that yield a large number of molecules of monosaccharide (> 10).

Monosaccharides are classified according to

(1) the number of carbon atoms (n) present in the molecule:

n=3 - triose n=5 - pentose

n=4 – tetrose n =6 - hexose

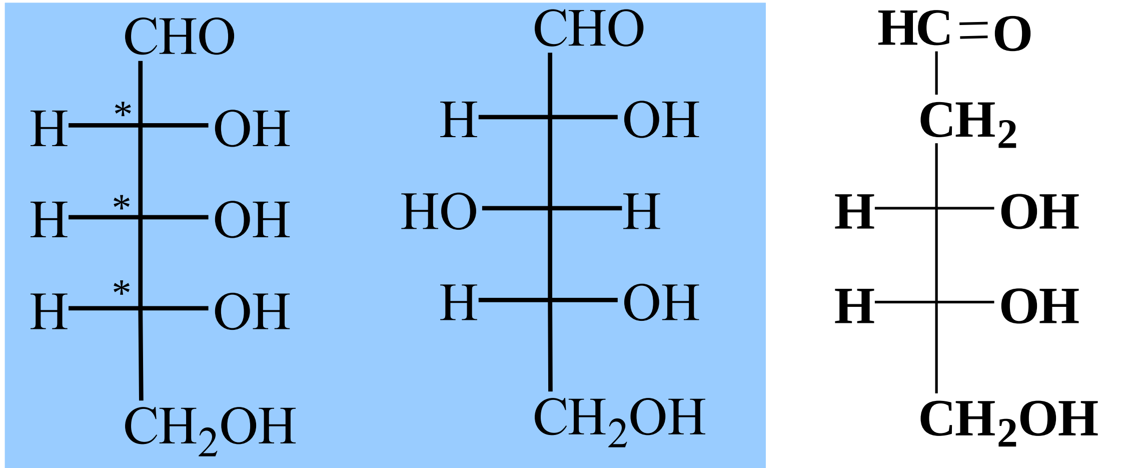
(2) whether they contain an aldehyde or keto group. A monosaccharide containing an aldehyde group is called an aldose; one containing a keto group is called a ketose.

STRUCTURAL FORMULAS FOR MONOSACCHARIDES.

Aldopentoses

$N = 2^n$

$N = 2^3 = 8$

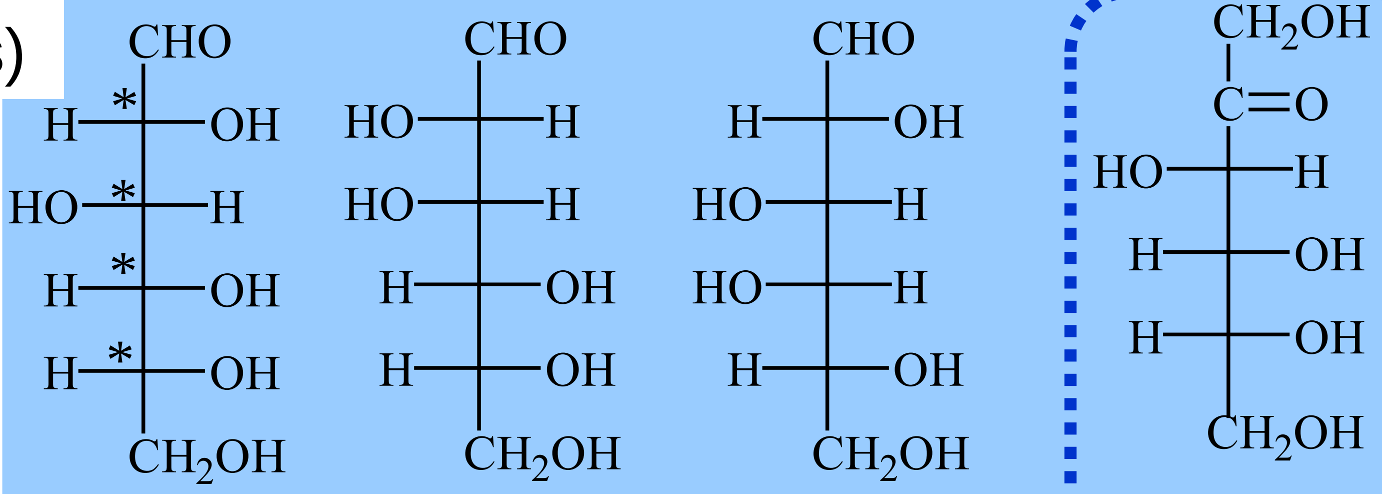


D-(-)-Ribose D-(+)-Xylose **2-deoxy-D-ribose**

D-mannose and
D-glucose are C2 **epimers.**
D-galactose and
D-glucose are C4 **epimers.**

Aldohexoses
(diastereomers)

$N = 2^4 = 16$

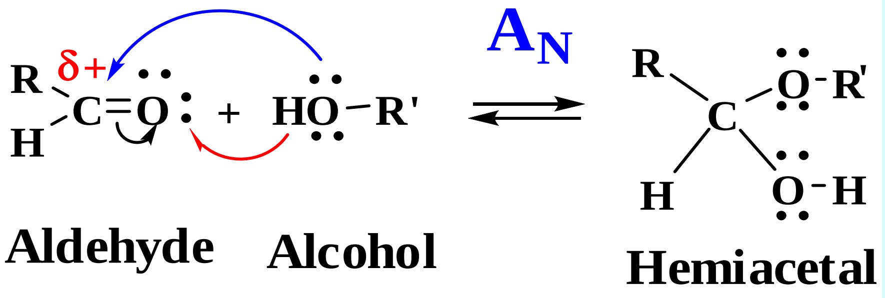


D-Glukose D-Mannose D-Galactose D-Fructose

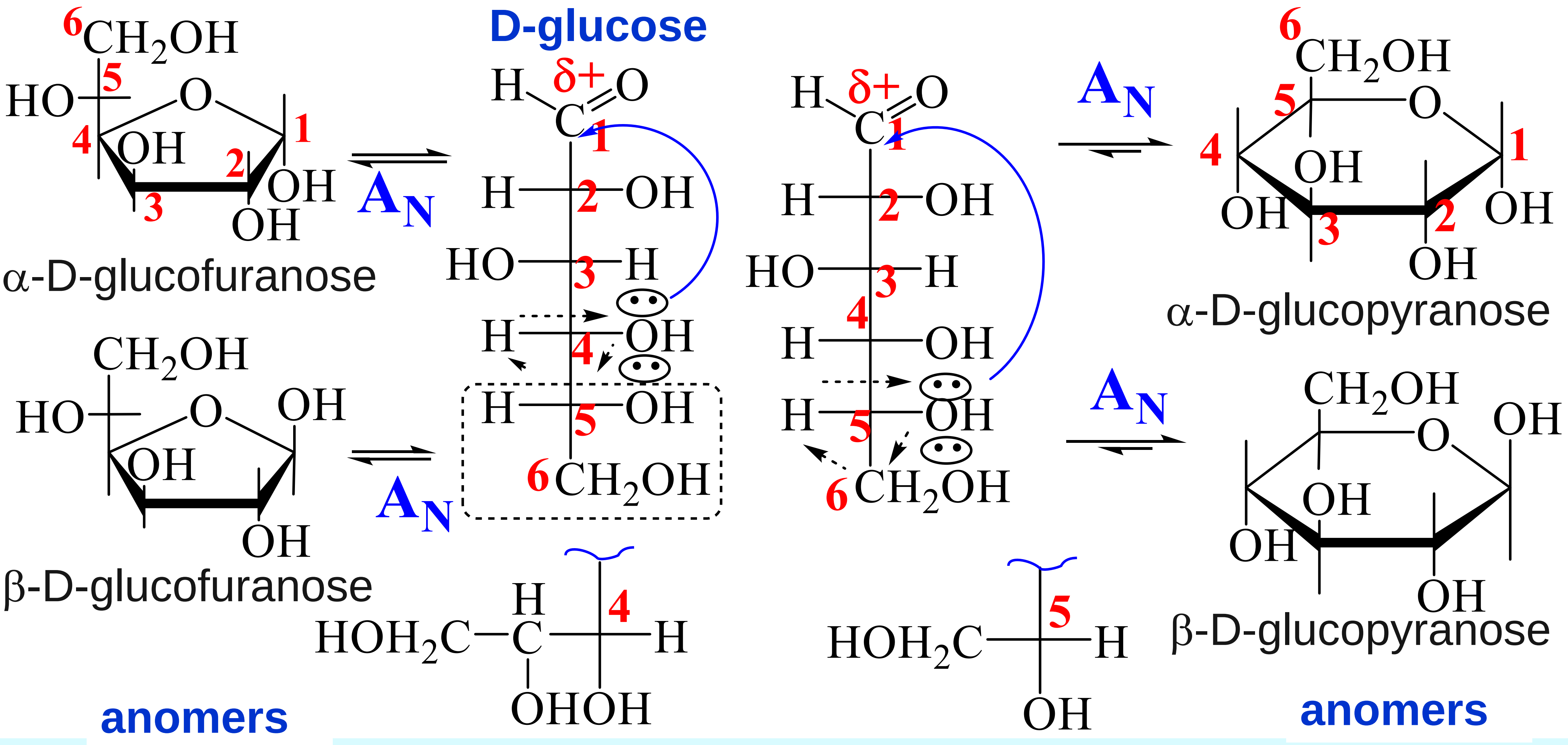
The D-,L-families of monosaccharides designates in a basis of configuration of highest numbered stereocenter

Ketohexose

CYCLO-OXO TAUTOMERIZATION OF MONOSACCHARIDES

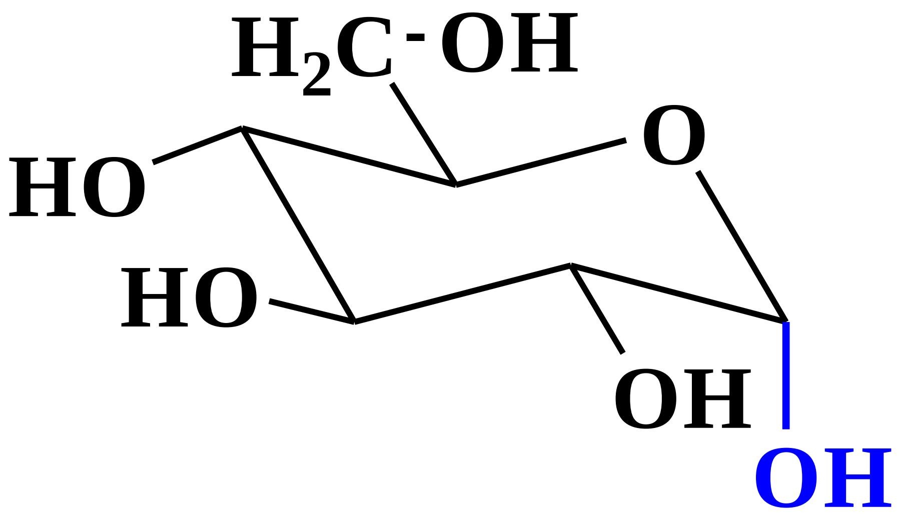


Haworth formulas   Fisher projection formulas



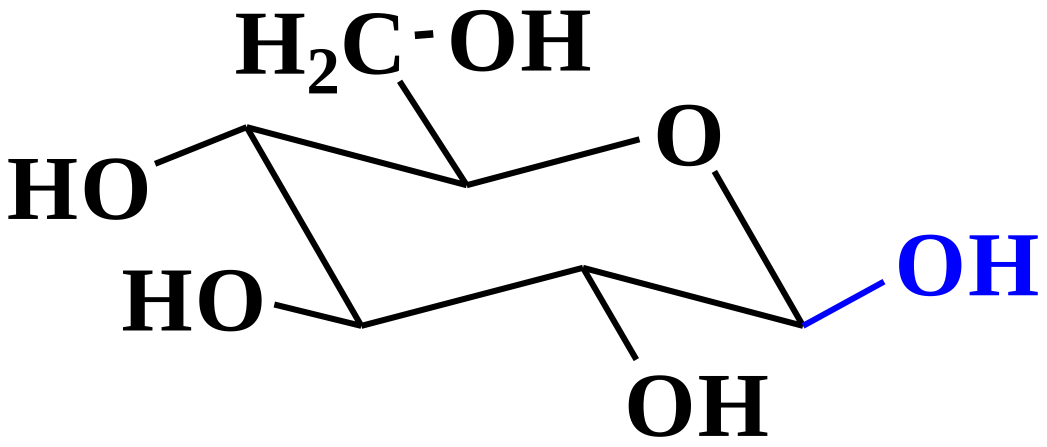
CHAIR CONFORMATIONS OF D-GLUCOPYRANOSES

Glicosidic OH-axial
(36% at equilibrium)



α-D-(+)-Glucopyranose

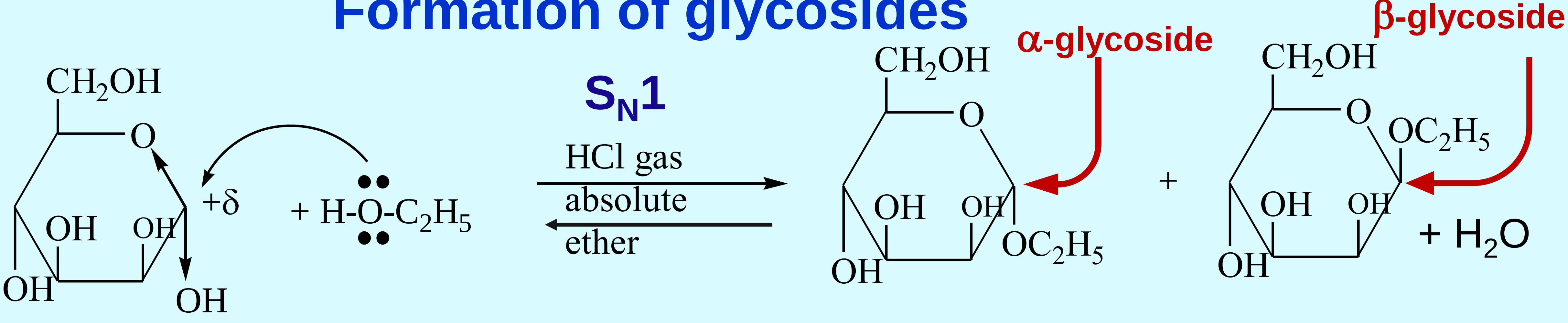
Glicosidic OH-equatorial
(64% at equilibrium)



β-D-(+)-Glucopyranose

REACTIVITY OF MONOSACCHARIDES.

Formation of glycosides



substrate

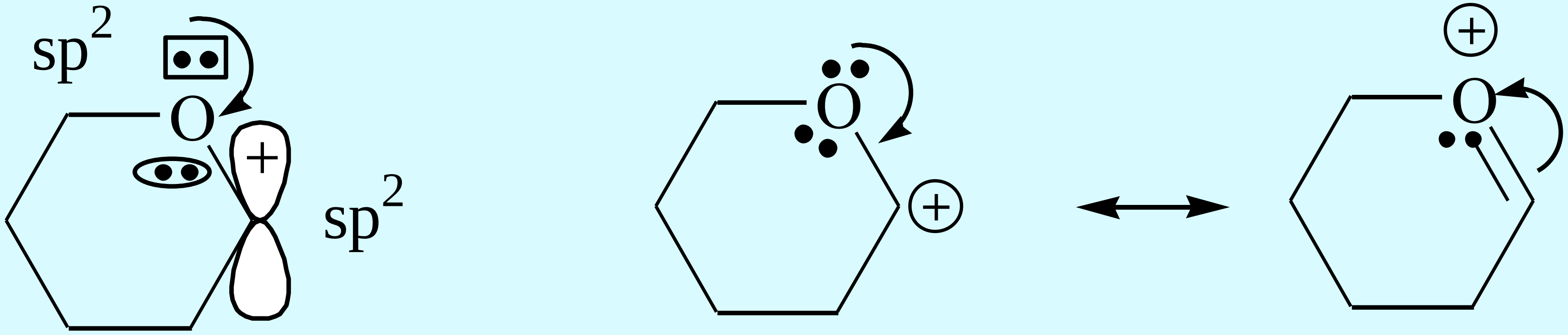
nucleophilic reagent

o-ethyl-α–D-manno-pyranoside

o-ethyl-β–D-manno-pyranoside

O-glycosides

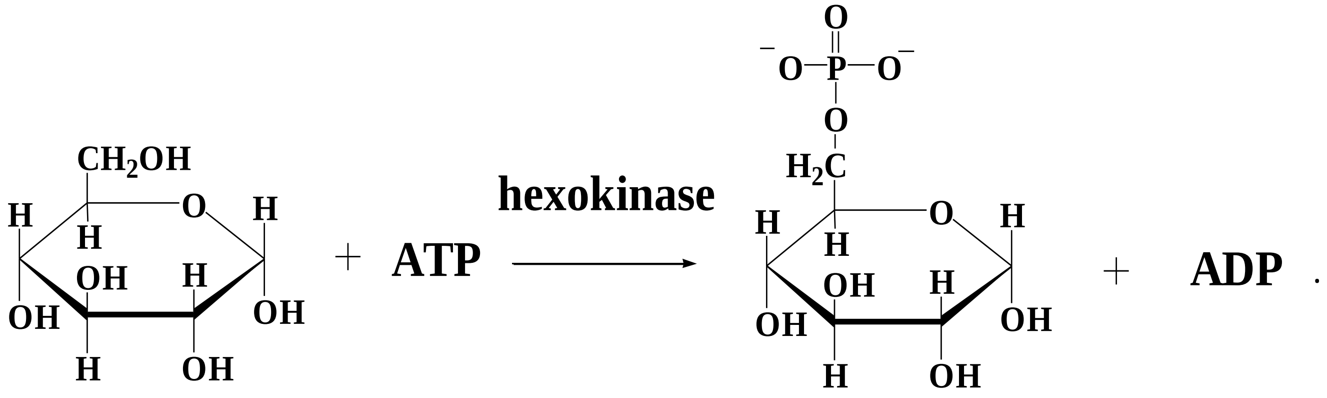
The structure of carbocation:



delocalization of the positive charge increase stability of carbocation

PHOSPHORILATION OF MONOSACCHARIDES.

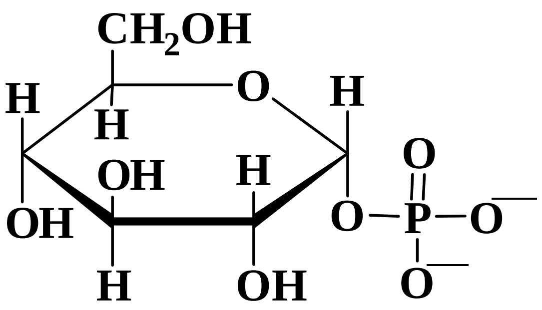
Phosphorilation is a reaction of activation of monosaccharides in a biological proceses. The first reaction of glycolysis is the enzyme-catalyzed transfer of a phosphoryl group from ATP to the hydroxyl group on C6 of D-glucopyranose to form glucose-6-phosphate.



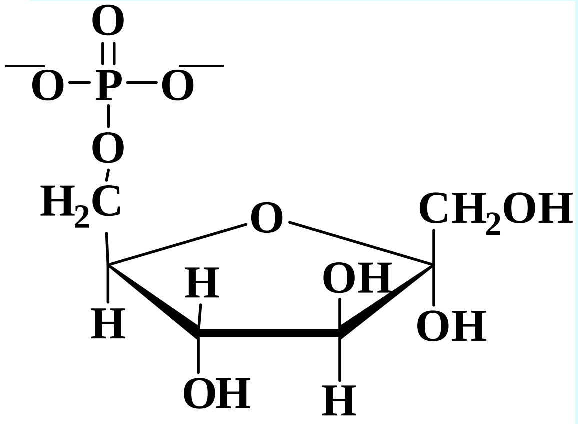
α-D-glucopyranose

α-D-glucopyranose -6-phosphate

Glucose-1-phosphate is also the first product obtained by hydrolysis of glycogen when the body needs to obtain energy from its stored glycogen. Fructose-6-phosphate is also the entry point for glycolysis that converts glucose to energy.

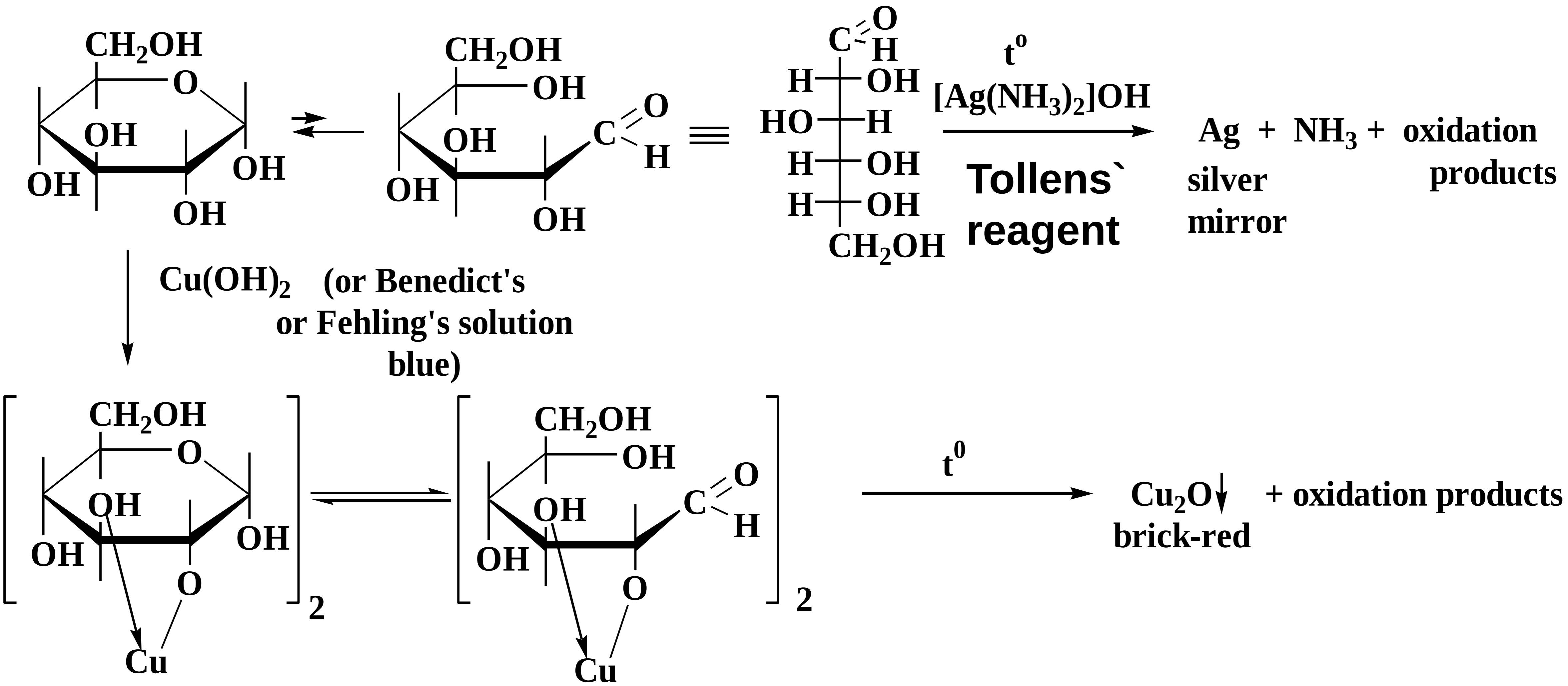


D-glucose -1-phosphate



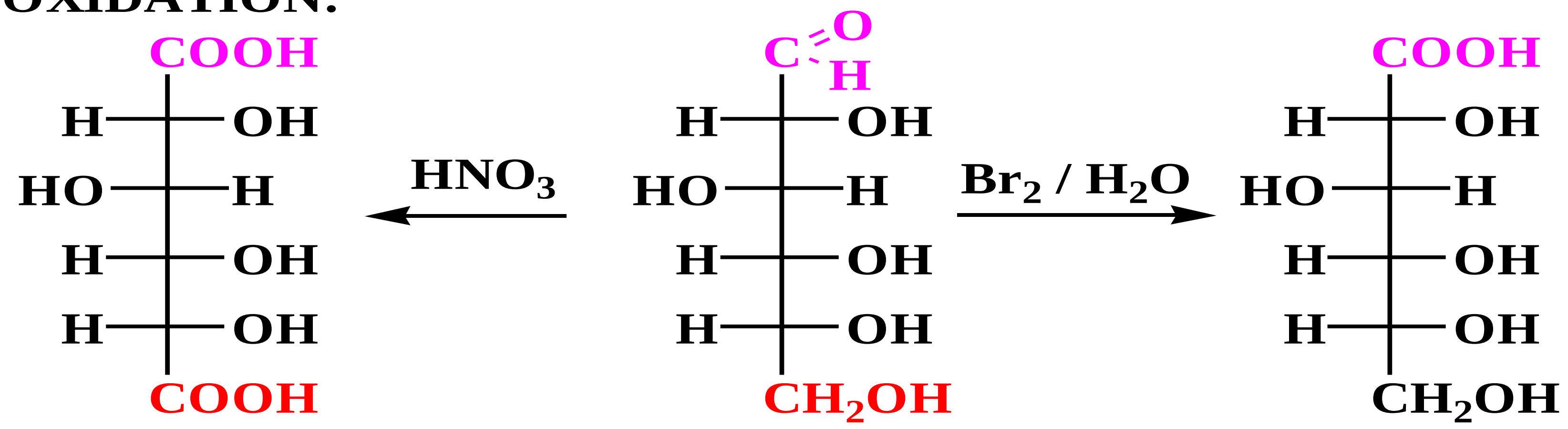
D-fructose -6-phosphate

OXIDATION REACTIONS OF MONOSACCHARIDES. BENEDICT'S OR TOLLENS' REAGENTS. REDUCING SUGARS



OXIDATION AND REDUCTION OF MONOSACCHARIDES.

OXIDATION:

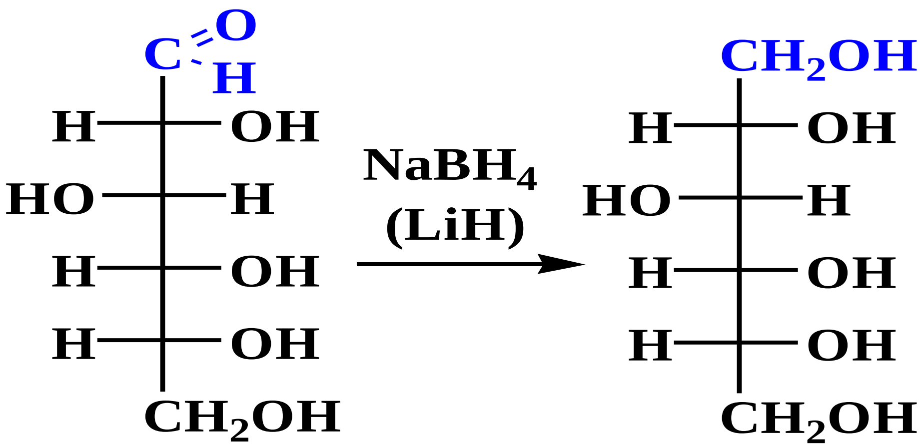


D-glucaric acid
Aldaric acid

D-glucose

D-gluconic acid
Aldonic acid

REDUCTION:

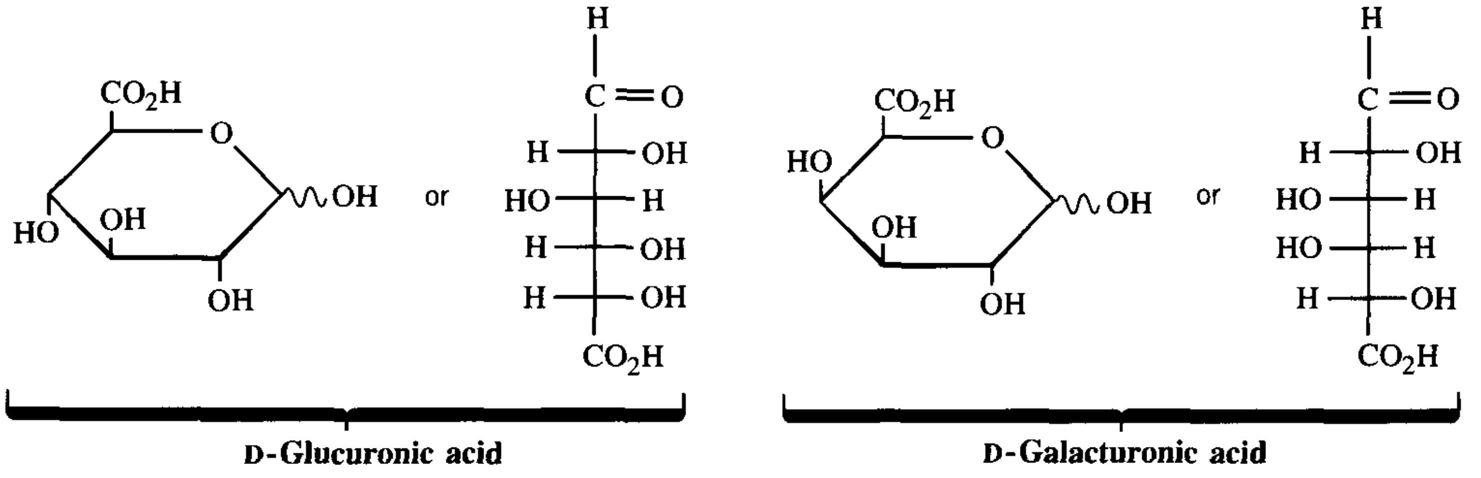


D-glucose

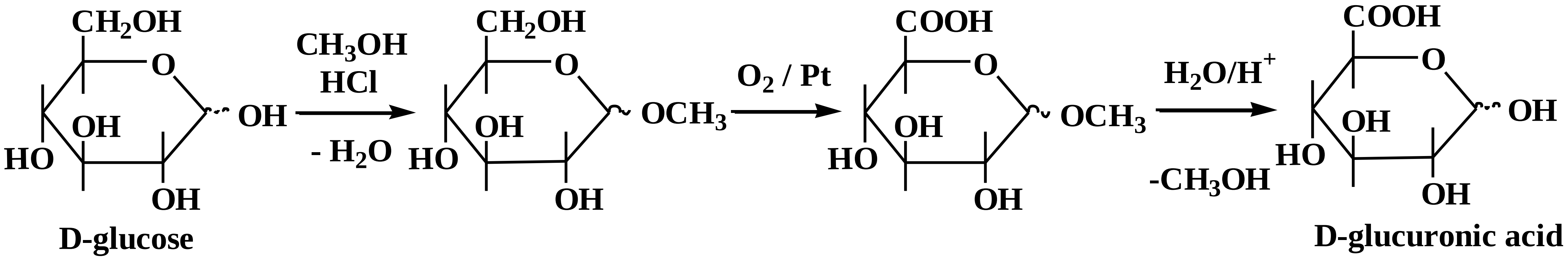
D-glucitol (D-sorbitol)
Alditol

BIOLOGICALLY IMPORTANT SUGARS.

Alduronic acids.

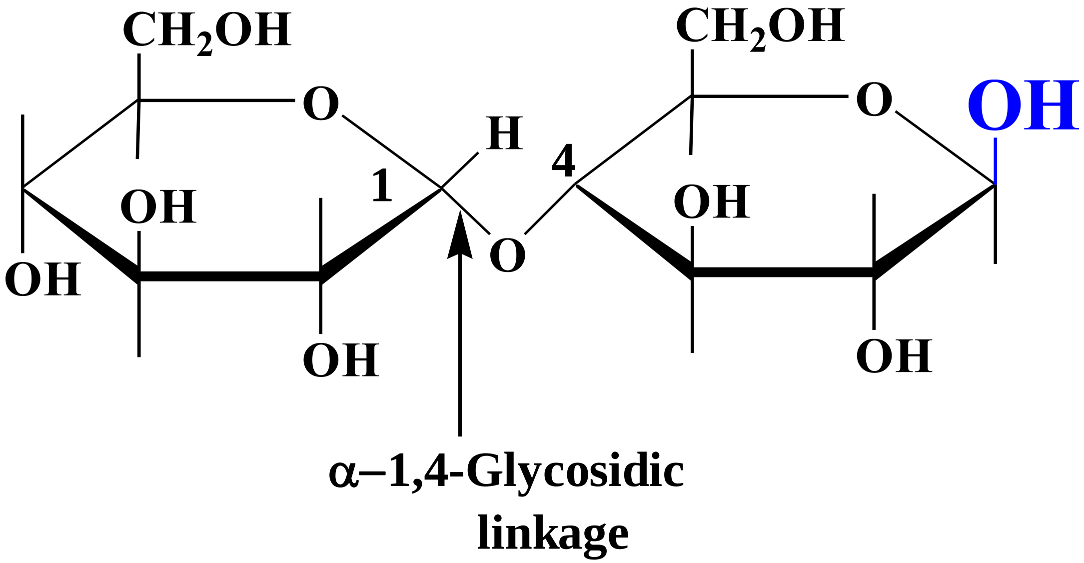


Synthesis of D-glucuronic acid:



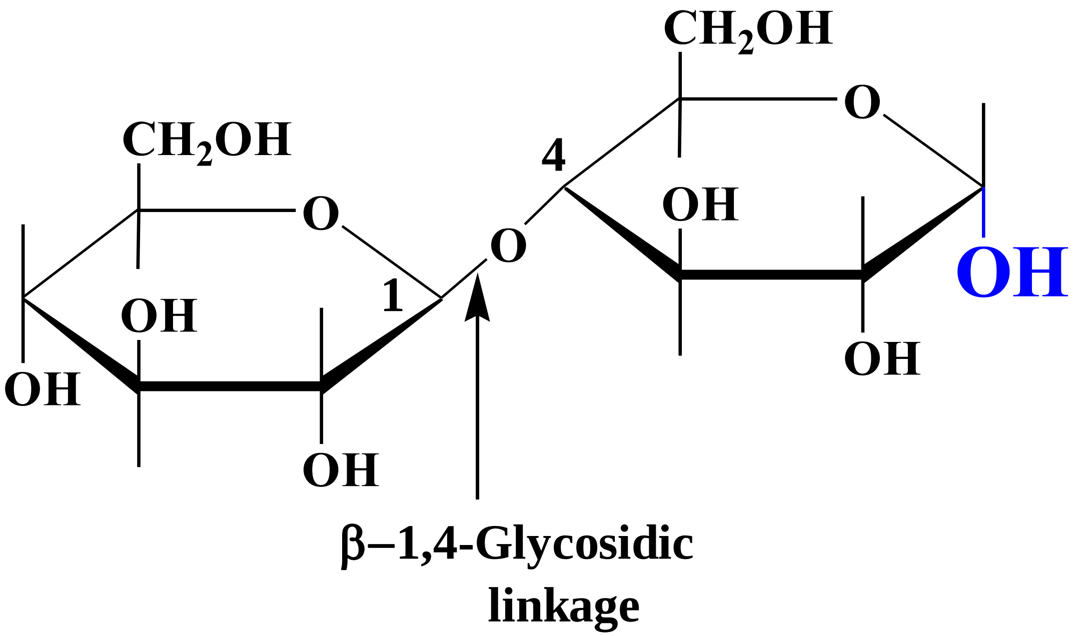
DISACCHARIDES. REDUCING SUGARS.

- Disaccharides are the dimers made up of two monosaccharide molecules, for example, of D-(+)-glucopyranose:



β-maltose

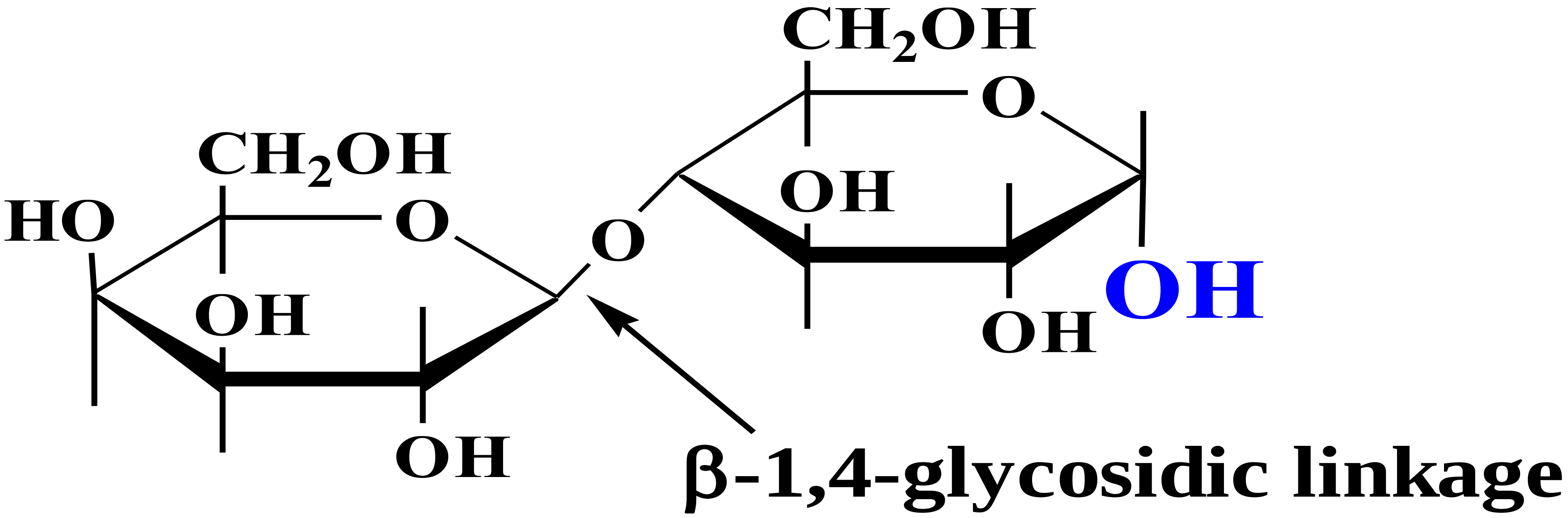
4-O-(α-D-glucopyranosyl)-β-D-glucopyranose



α-cellobiose

4-O-(β-D-glucopyranosyl)-α-D-glucopyranose

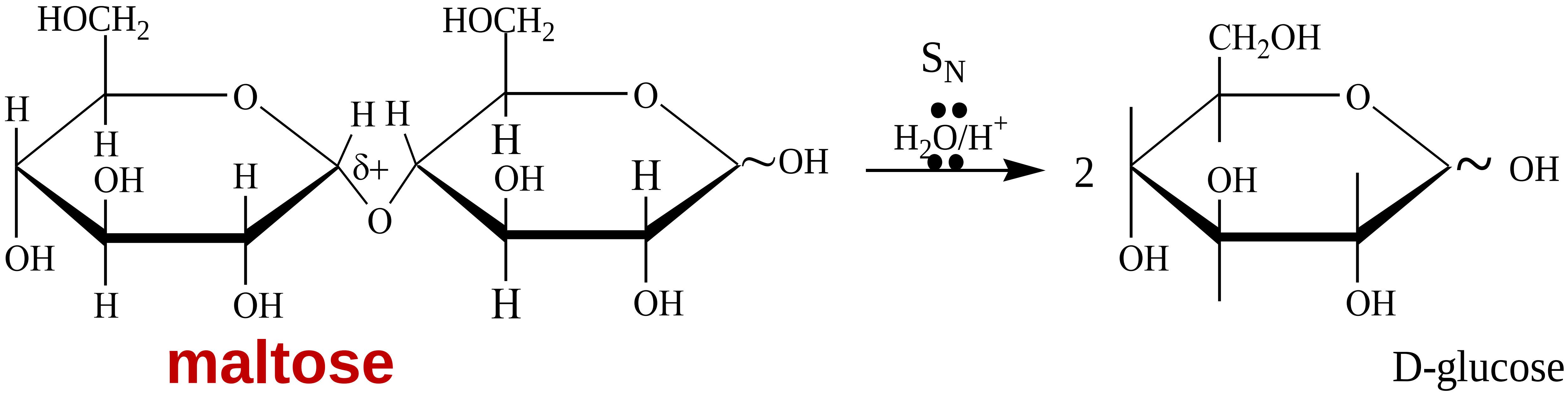
DISACCHARIDES. REDUCING SUGARS.



α–lactose

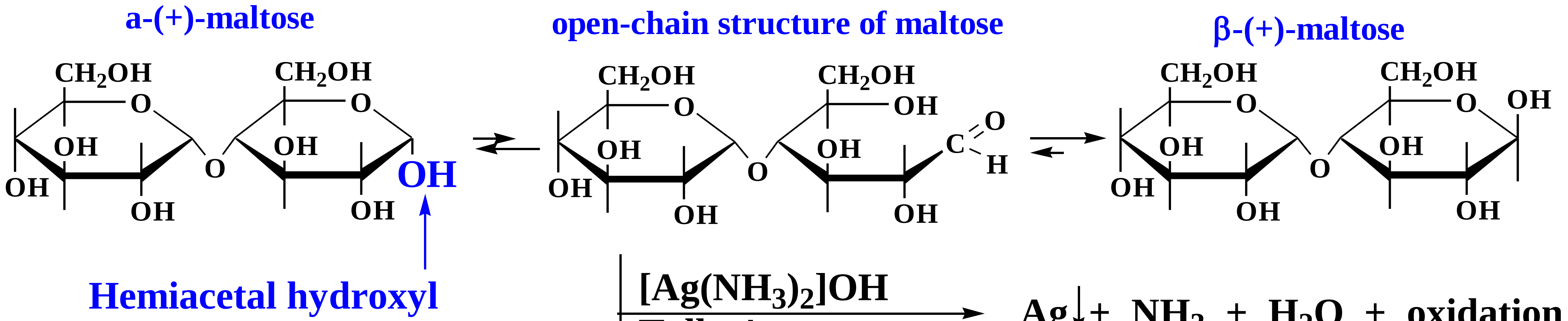
4-O-(β-D-galactopyranosyl)-α-D-glucopyranose

HYDROLYSIS


HOCH2
H
O
H
OH
H
OH
H
OH
H H
δ+
O
HOCH2
O
H
OH
H
~OH
H
OH
SN
H2O/H+
2
CH2OH
O
OH
~ OH
OH
OH
maltose
D-glucose

REDUCING PROPERTIES.

Maltose exists as an equilibrium mixture of the α-anomer, β-anomer and a small amount of the open chain form in solution. Maltose is a reducing sugar, it gives positive tests with Fehling’s, Benedict’s and Tollen’s solutions:

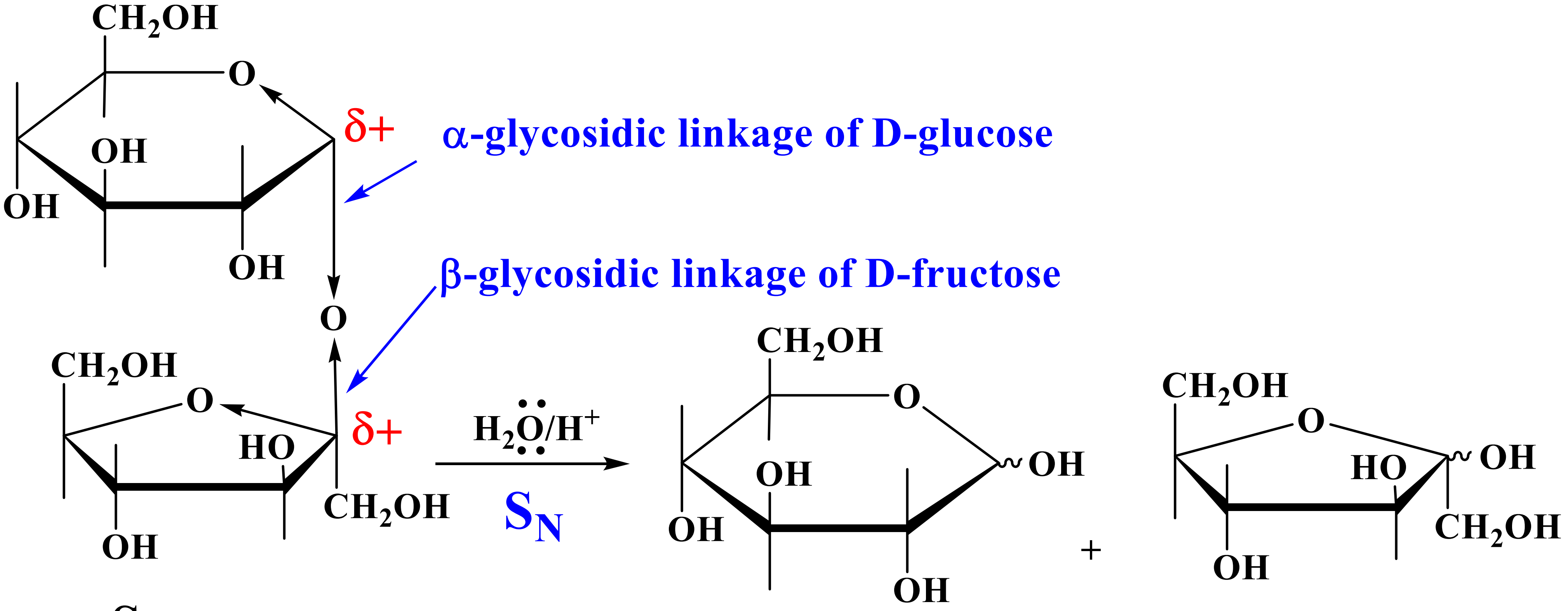


$$\xrightarrow[\text{Tollen's reagent}]{[Ag(NH_3)_2]OH} \underset{\text{silver coating}}{Ag\downarrow} + NH_3 + H_2O + \underset{\text{products}}{\text{oxidation}}$$

$$\xrightarrow[\text{Benedict's solution}]{Cu^{2+}\text{ complex}} \underset{\text{brick red}}{Cu_2O\downarrow} + \text{oxidation products}$$

NONREDUCING SUGAR. SUCROSE.

(+)-sucrose 2-(α-D-glucopyranosyl)-β-D-fructofuranoside



Sucrose
1 mol

D-(+)-glucose
1 mol

D-(+)-fructose
1 mol

POLYSACCHARIDES. CLASSIFICATION.

- Polysaccharides, also known as **glycans,** consist of monosaccharides joined together by glycosidic linkages.
- **Polysaccharides** are classified to:

  1) **homopolysaccharides** are polymers of a single monosaccharide;

  2) **heteropolysaccharides** made up of more than one type of monosaccharide.

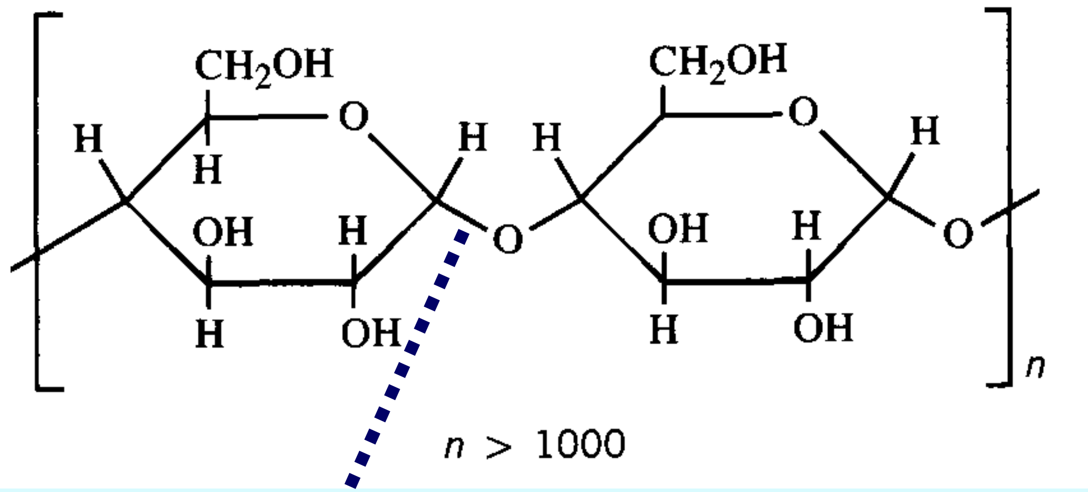
- Homopolysaccharides are also classified on the basis of their monosaccharide units:

  1) a homopolysaccharide consisting of glucose monomeric units is called a **glucan;**

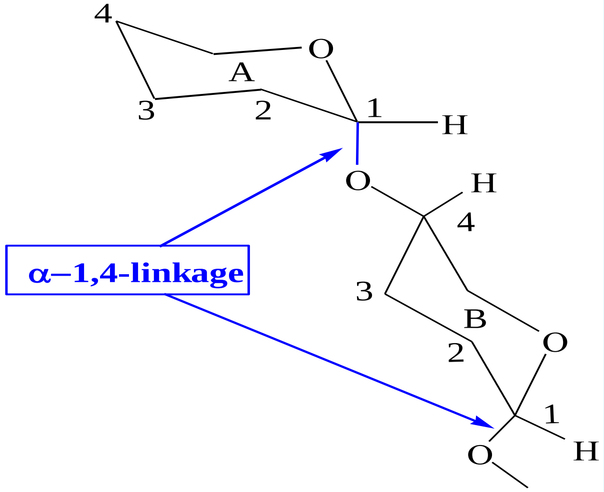
  2) one consisting of galactose units is a **galactan**, and so on.

HOMOPOLYSACCHARIDES. STARCH.

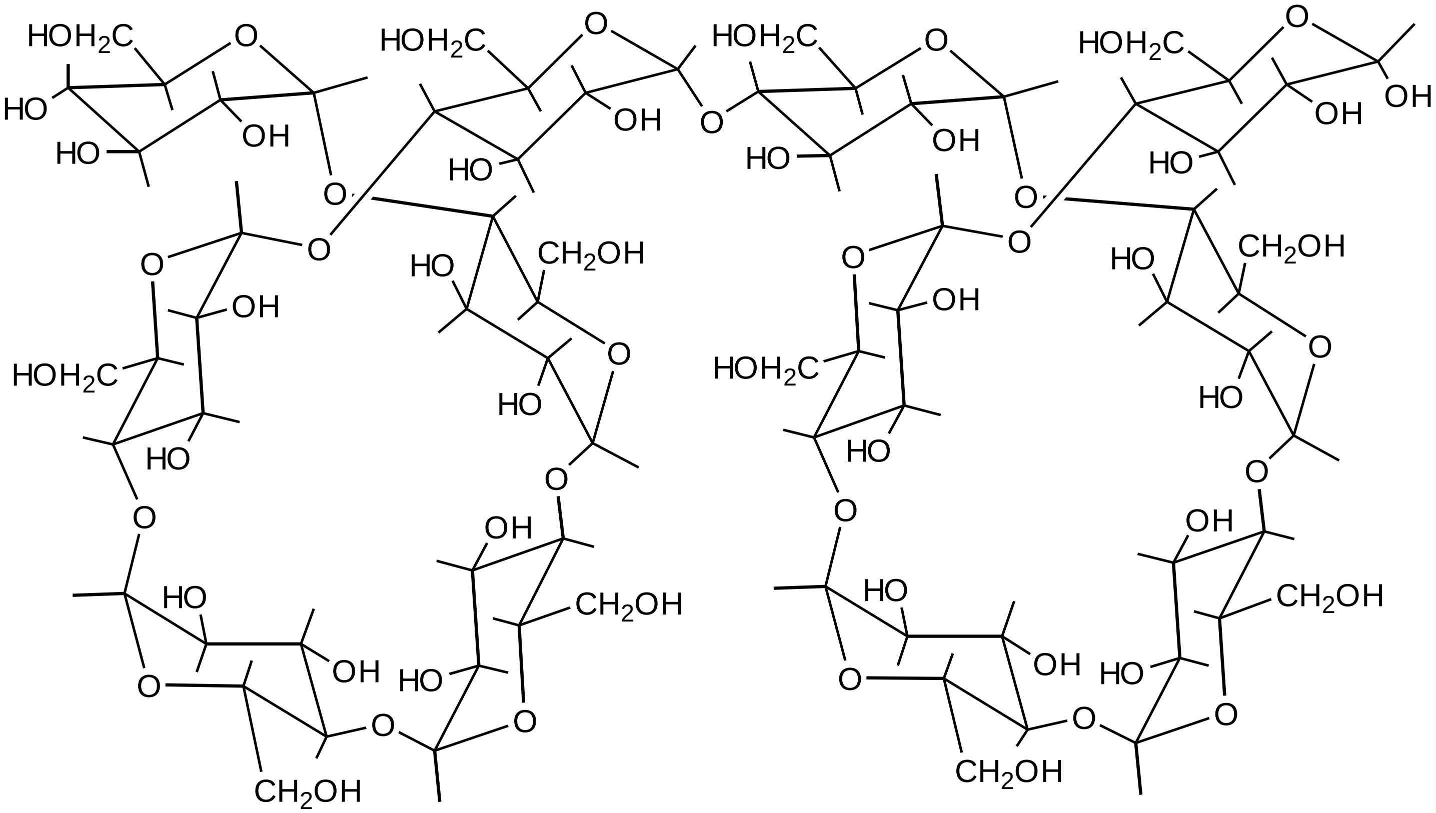
Starch is a mixture of about 10-20% amylose and 80-90% amylopectin. Amylose is an unbranched polymer of D-glucose connected in a-1,4-glycosidic linkages.



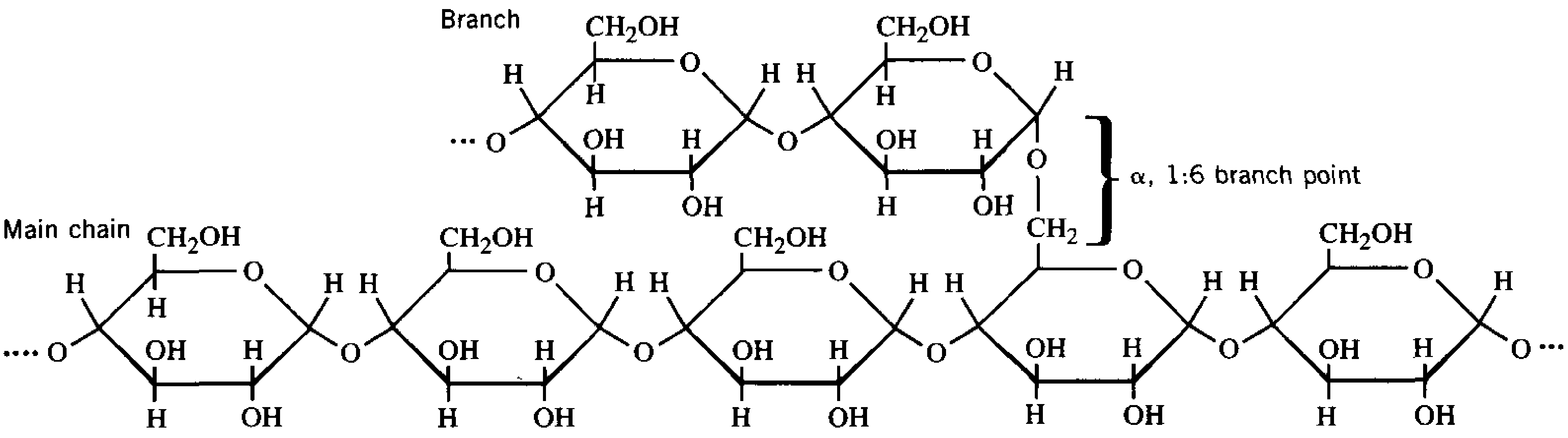
α-1,4-glycoside linkage



The α-1,4 linkages cause it to assume the shape of left handed helix



HOMOPOLYSACCHARIDES.
STARCH, AMYLOPECTIN. GLYCOGEN.

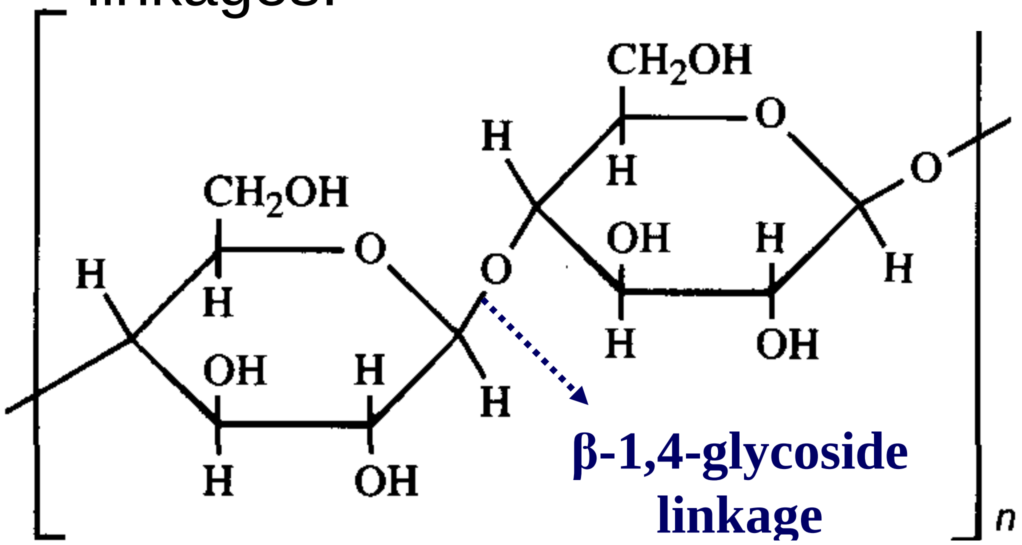


Amylopectin (plants). Molecular weight of 1-6 million. Interval between branching is 20-25 glucose units.

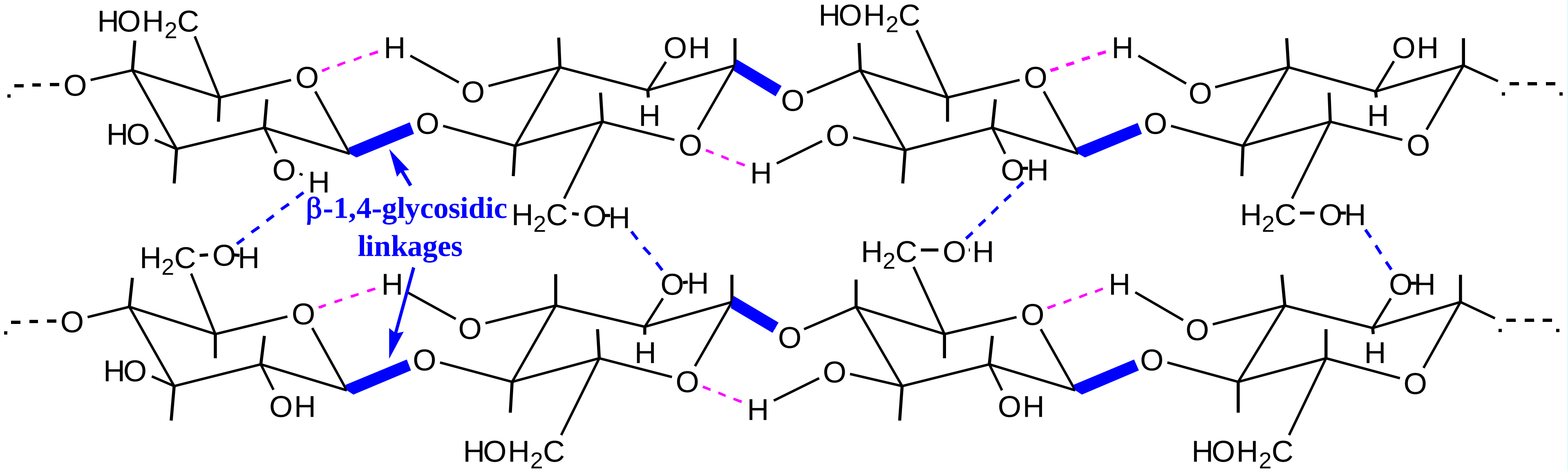
Glycogen (animals). Molecular weight of 100 million. Interval between branching is 10-12 glucose units, in internal parts one is 3-4 glucose units.

HOMOPOLYSACCHARIDES. CELLULOSE.

Cellulose is an unbranched polymer of D-glucose connected in β-1,4-glycosidic linkages:



A fiber of cellulose may consist of about 40 parallel strands of glucose molecules linked in a β, 1: 4 fashion. Each glucose unit in a chain is turned over with respect to the preceding glucose unit, and is held in this position by hydrogen bonds between the chains. The glucan chains line up laterally to form sheets and these sheets stack vertically so that they are staggered by one half of a glucose unit.

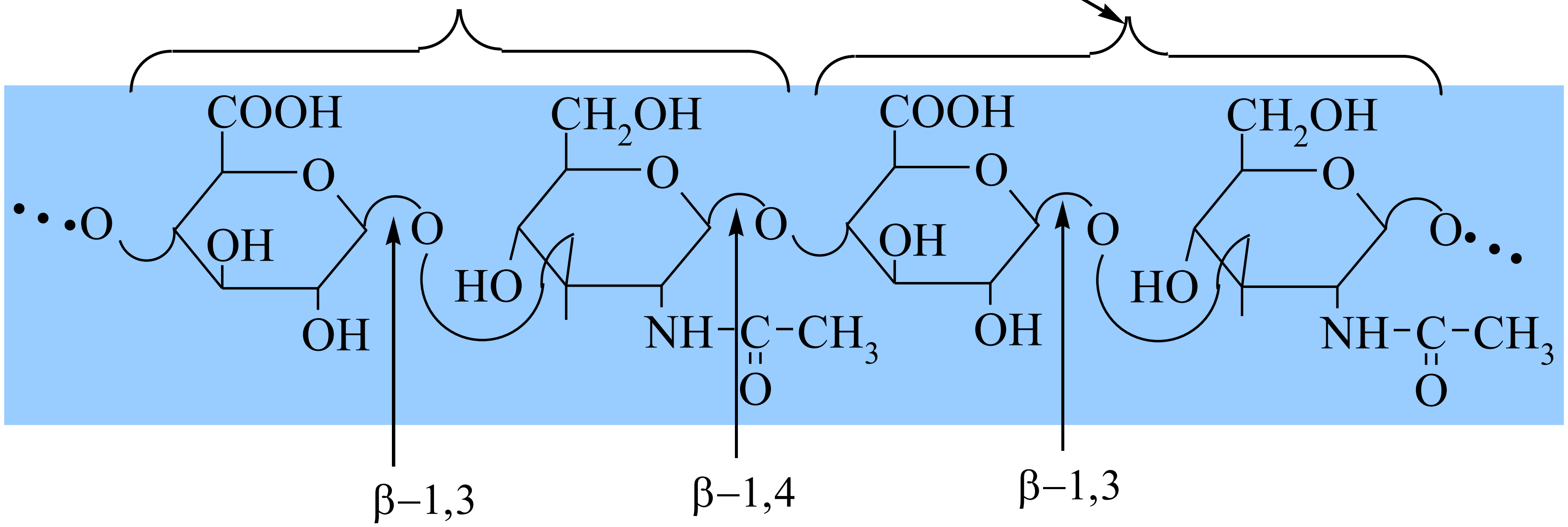


GLYCOSAMINOGLYCANS. HYALURONIC ACID

Glycosaminoglycans are highly negatively charged because of the presence of carboxyl or sulfate groups on many of the sugar residues. The high negative charge causes the polymeric chains to adopt a stretched or extended conformation. It gives a high viscosity to the surrounding region and produce a viscous extracellular matrix that resist compression in living organism. Hyaluronic acid help maintain certain structural shapes such as the ball of the eye.

….D-glucuronic acid - β-1,3 - N-acetyl-D-Glucosamine - β-1,4….

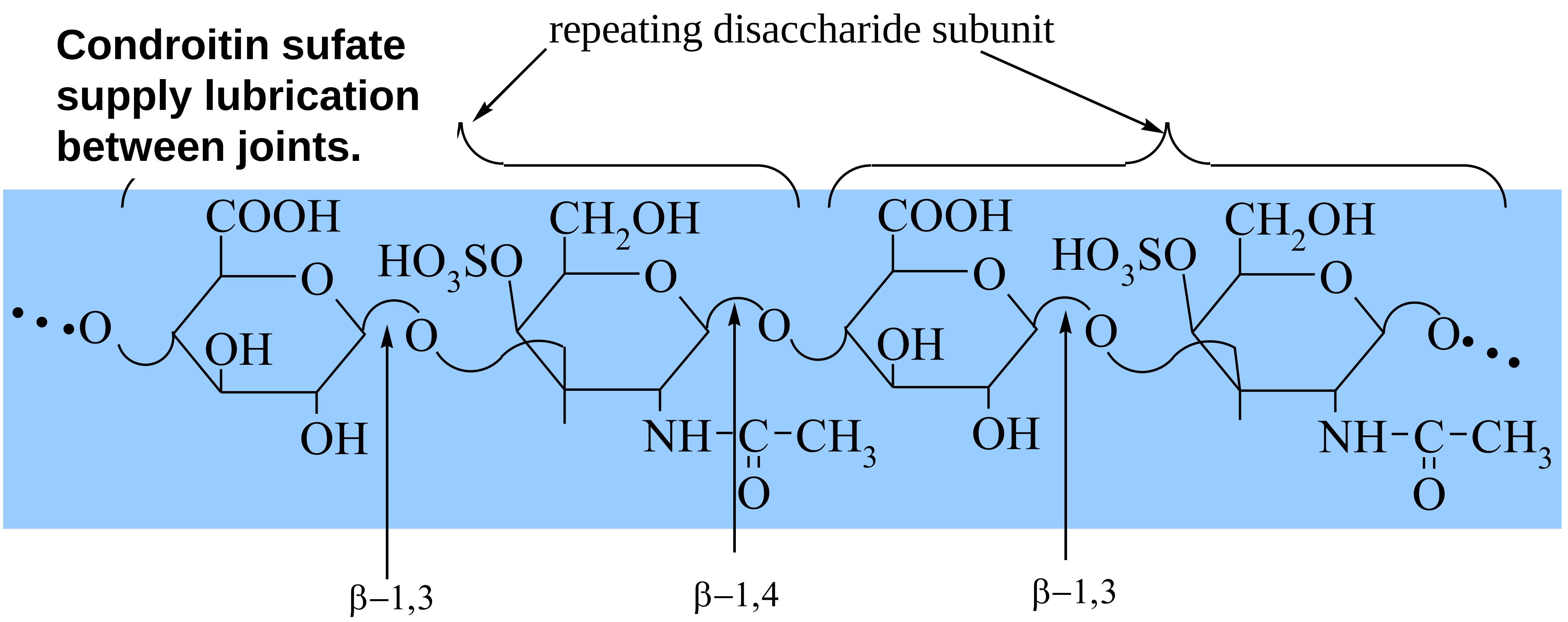
repeating disaccharide subunit



GLYCOSAMINOGLYCANS. CHONDROITIN SULFATE

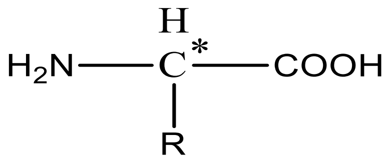
….D-glucuronic acid - β-1,3 - N-acetyl-D-galactosamine-4-sulfate - β-1,4….

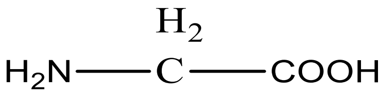
Condroitin sufate supply lubrication between joints.



STRUCTURE AND STEREOCHEMISTRY OF α-AMINO ACIDS

Hydrolysis of proteins with acid or base gives a mixture of 20 different amino acids. The structure of α-amino acid can be represented by the next structural formula





Glycine

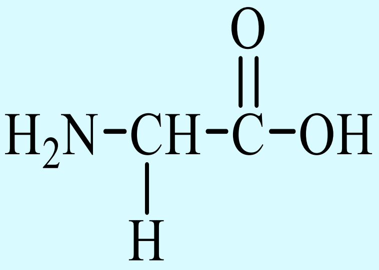
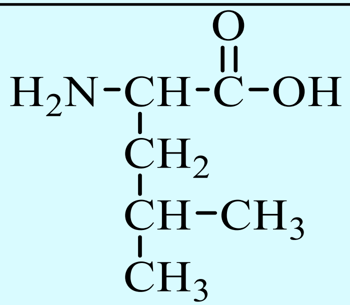
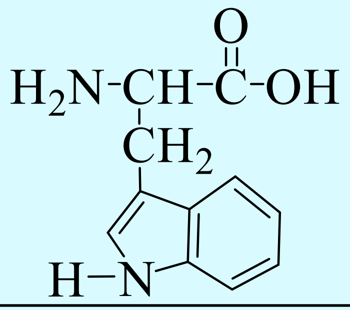
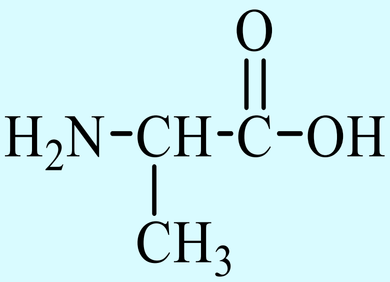
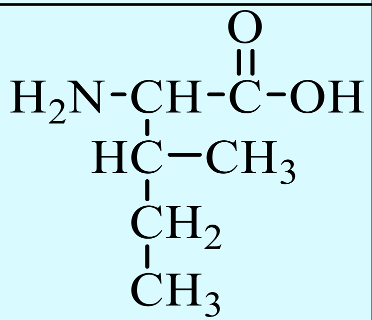
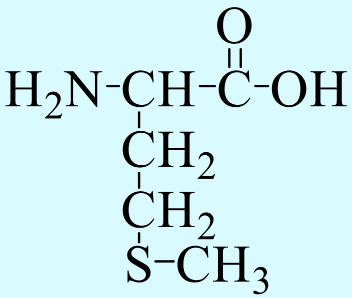
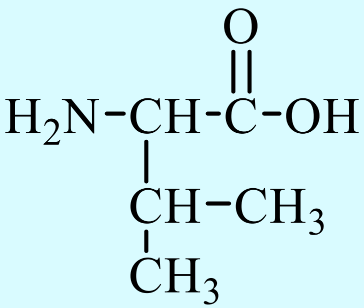
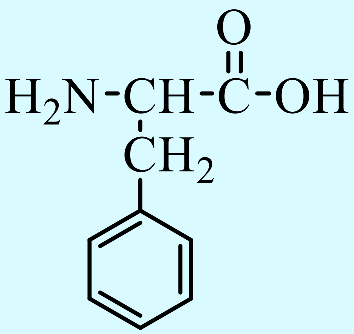
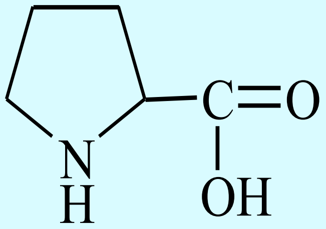
α-Amino acids has COOH and NH_2 groups bonded to the α-carbon. This α-carbon is stereocenter, it bonded to 4 different groups. Molecules of α-amino acids are chiral and can exist as enantiomers. Almost all naturally occurring amino acids have the L configuration at the α-carbon except glycine.

The 20 α-amino acids are classified according to the polarities of their side chains:

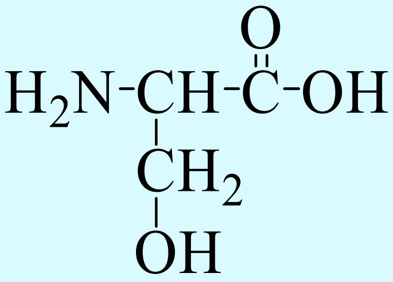
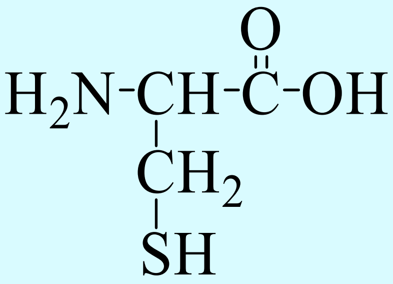
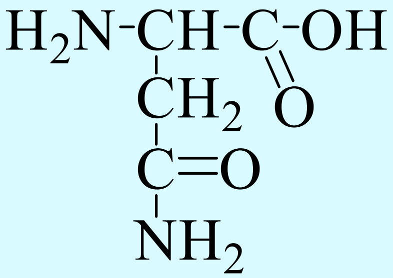
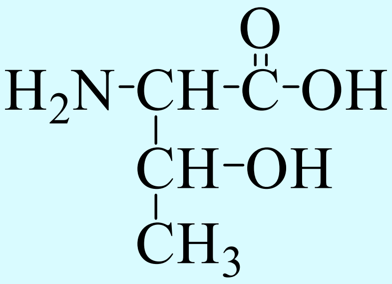
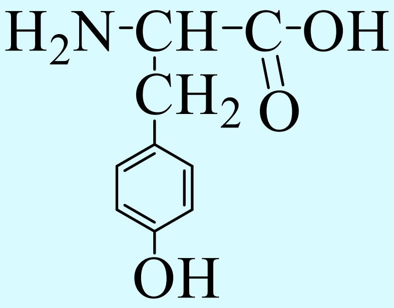
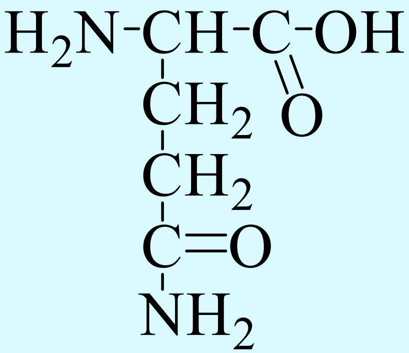
1. Nonpolar α-amino acids.
2. Polar α-amino acids.
3. Charged α-amino acids:
    - negative charged;
    - positive charged.

Amino acids can be synthesized by all living organisms, plants and animals. Many higher animals, however, are deficient in their ability to synthesize all of the amino acids they need for their proteins. Thus, these higher animals require certain amino acids as a part of their diet. For adult humans there are eight essential amino acids: ***Valine, Leucine, Isoleucine, Phenylalanine, Tryptophan, Methionine, Threonine, Lysine.***

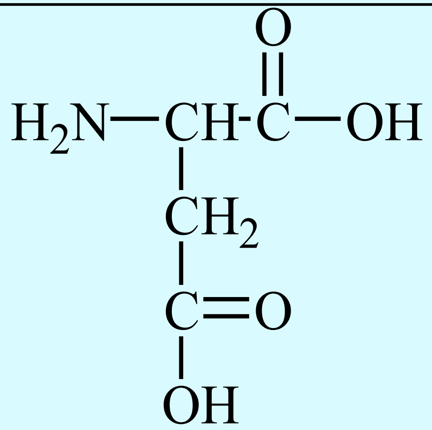
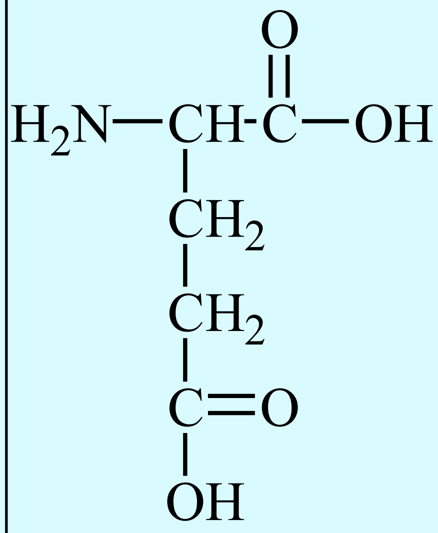
Structure of nonpolar L-α-amino acids

№	Name Abbreviation	Structure	№	Name Abbreviation	Structure	№	Name Abbreviation	Structure
1	**Glycine** **Gly**		4	**Leucine*** **Leu**		7	**Tryp-tophan*** **Trp**	
2	**Alanine** **Ala**		5	**Isoleu-cine*** **Ile**		8	**Methionine*** **Met**	
3	**Valine*** **Val**		6	**Phenyl alanine*** **Phe**		9	**Proline** **Pro**	

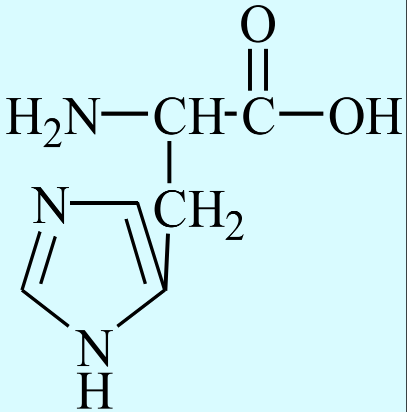
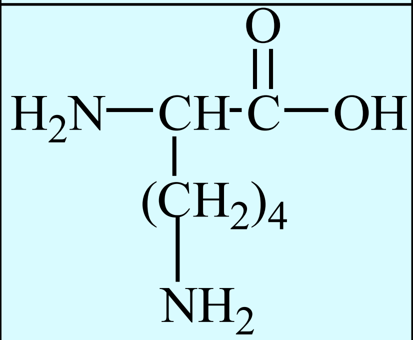
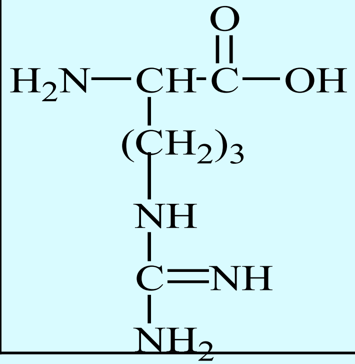
Structure of polar L-α-amino acids

№	Name Abbreviation	Structure	№	Name Abbreviation	Structure	№	Name Abbreviation	Structure
1	**Serine** **Ser**		**3**	**Cysteine** **Cys**		**5**	**Asparagine** **Asn**	
2	**Threonine*** **Thr**		**4**	**Tyrosine** **Tyr**		**6**	**Glutamine** **Gln**	

Negative charged amino acids

№	Name	Structure	Abbreviation
1	**Aspartic acid**		**Asp**
2	**Glutamic acid**		**Glu**

Positive charged amino acids

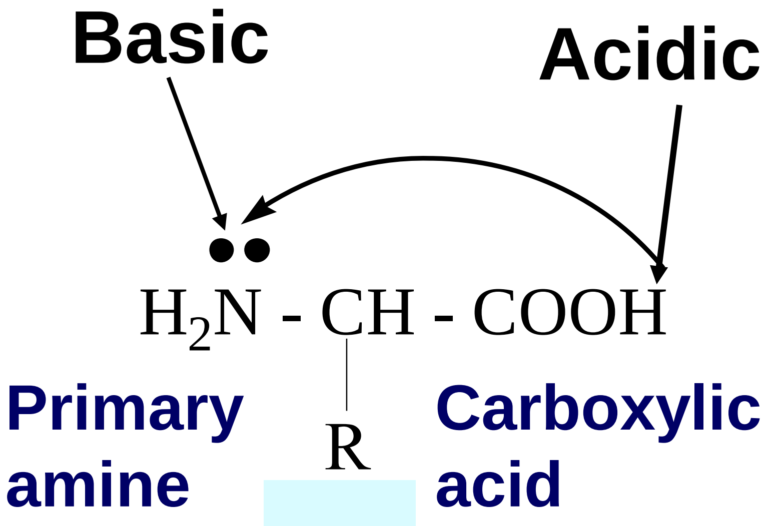
№	Name	Structure	Abbreviation
1	**Histidine**		**His**
2	**Lysine***		**Lys**
3	**Arginine**		**Arg**

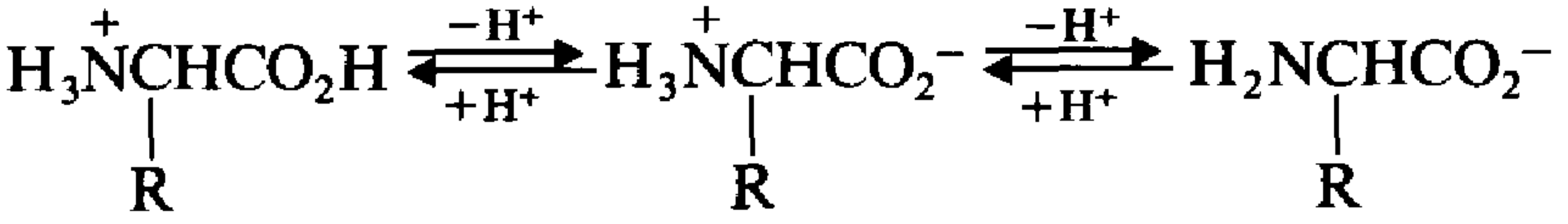
α-AMINO ACIDS AS DIPOLAR IONS

The α-amino acids are heterofunctional compounds. They develop chemical properties of:

1) Carboxilic acids; 2) primary amines; 3) α-amino acids.

Amino acid has carboxyl group COOH with OH-acidic center and amino group NH_2 with the basic center on nitrogen. So, they are amphoteric.





Cationic form (predominant in strongly acidic solutions, e.g., at pH 0)

Dipolar ion zwitterion (dry solid state)

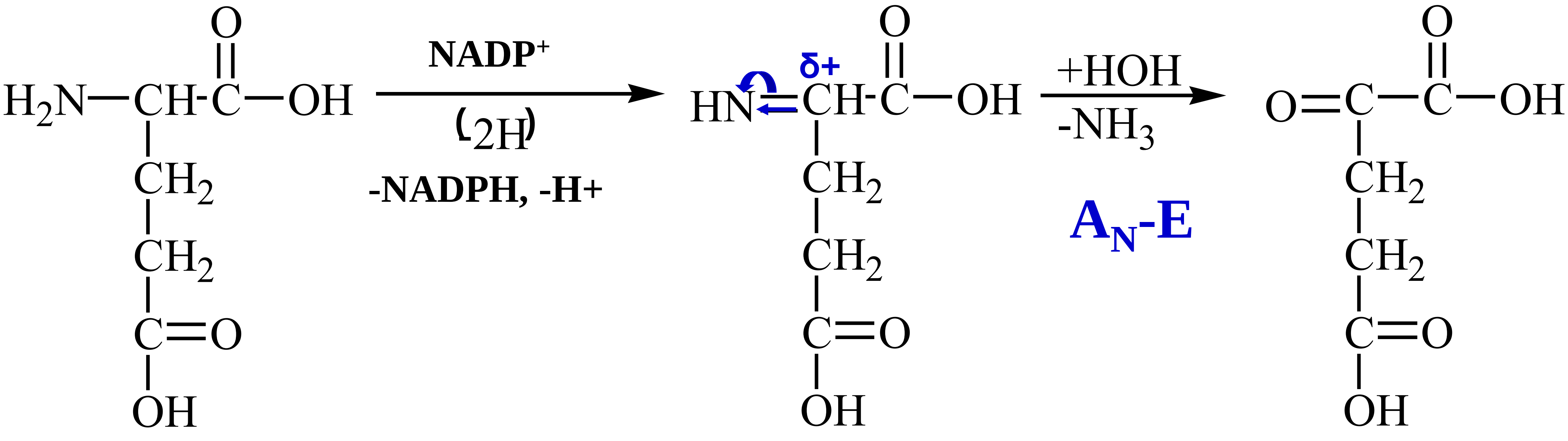
Anionic form (predominant in strongly basic solutions, e.g., at pH 14)

The **isoelectric point (pI)** is pH of solution when concentration of a dipolar ion is at its maximum and the concentrations of the anions and cations are equal.

THE BIOLOGICALLY IMPORTANT REACTIONS OF α-AMINO ACIDS

The biologically important reactions of α-amino acids are deamination, transamination, decarboxylation, hydroxylation reactions and oxydation of cysteine thiol group.

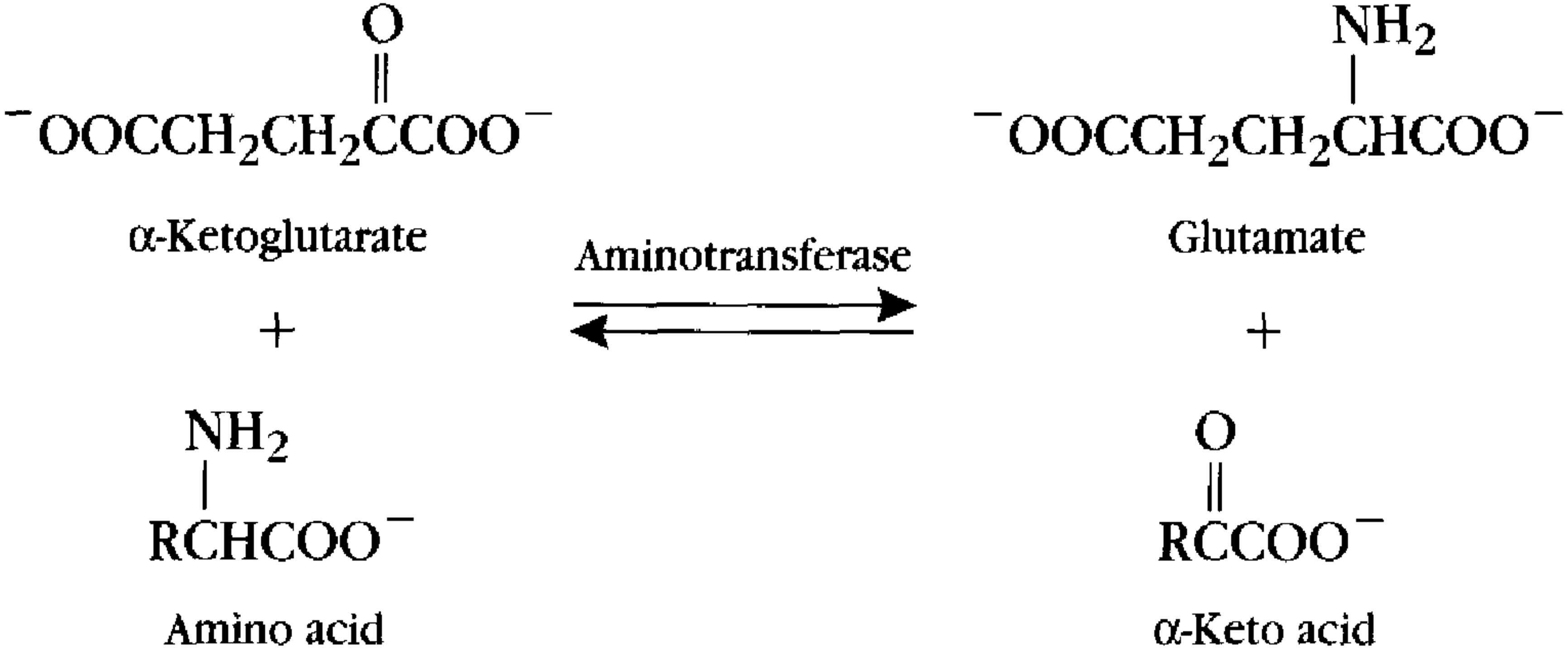
Oxidative deamination of α-amino acids

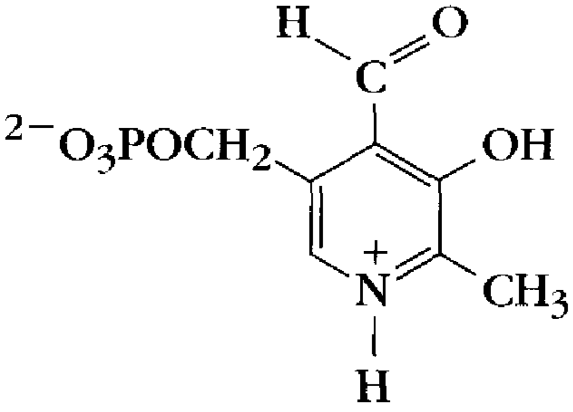


Glu imino acid

THE BIOLOGICALLY IMPORTANT REACTIONS OF α-AMINO ACIDS

Enzyme catalyzed transamination reaction

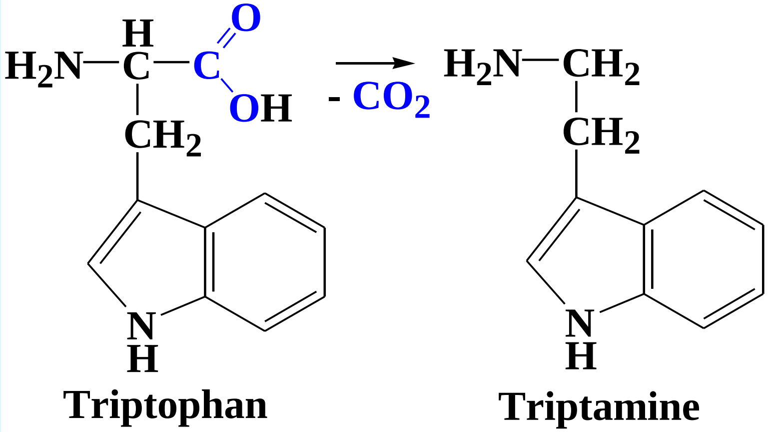


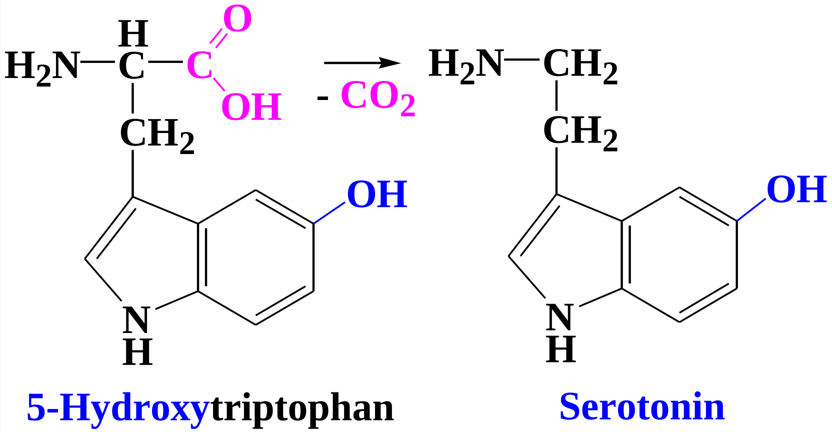


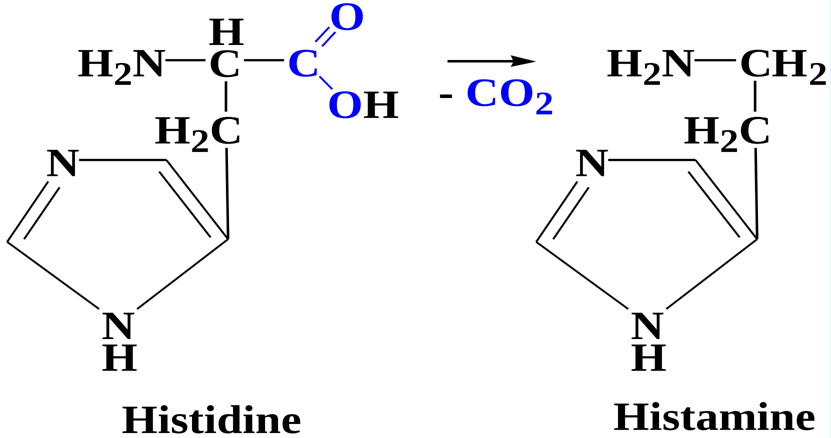
Pyridoxal phosphate (PLP)

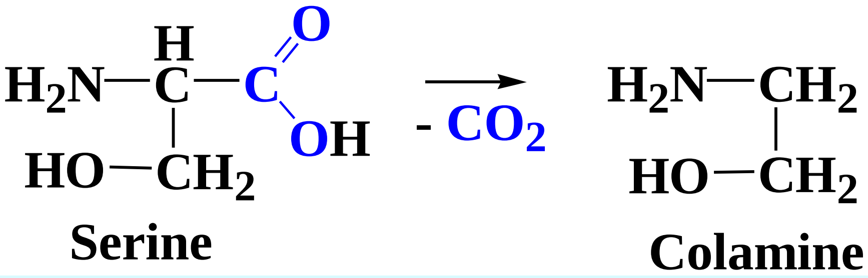
THE BIOLOGICALLY IMPORTANT REACTIONS OF α-AMINO ACIDS

Decarboxylation of **5-hydroxytriptophan** gives **serotonin**. It appears to be important in maintaining stable mental processes. It has been suggested that the mental disorder schizophrenia may be connected with abnormalities in metabolism of serotonin.







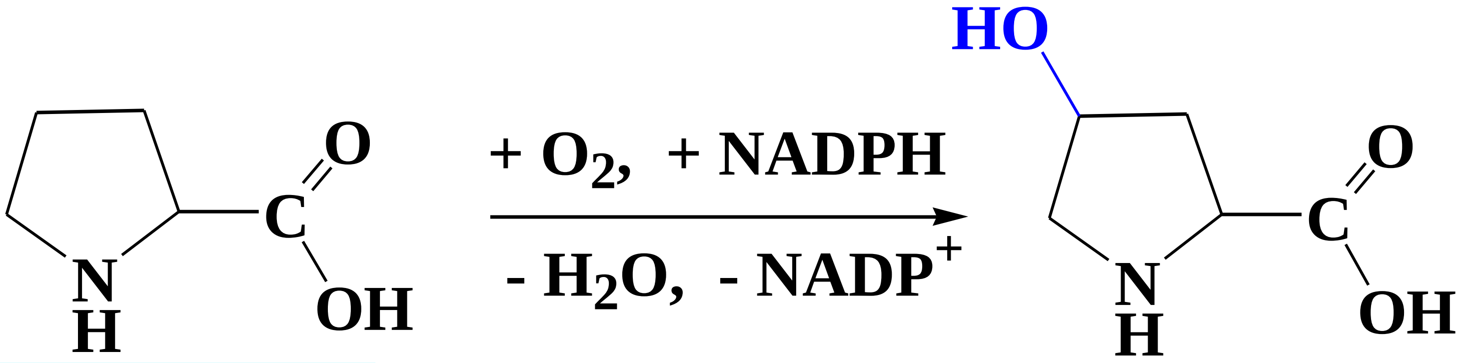


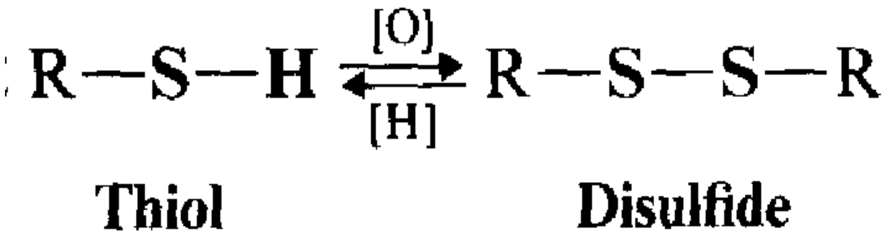
Colamine is structural part of lipids of cells membranes.

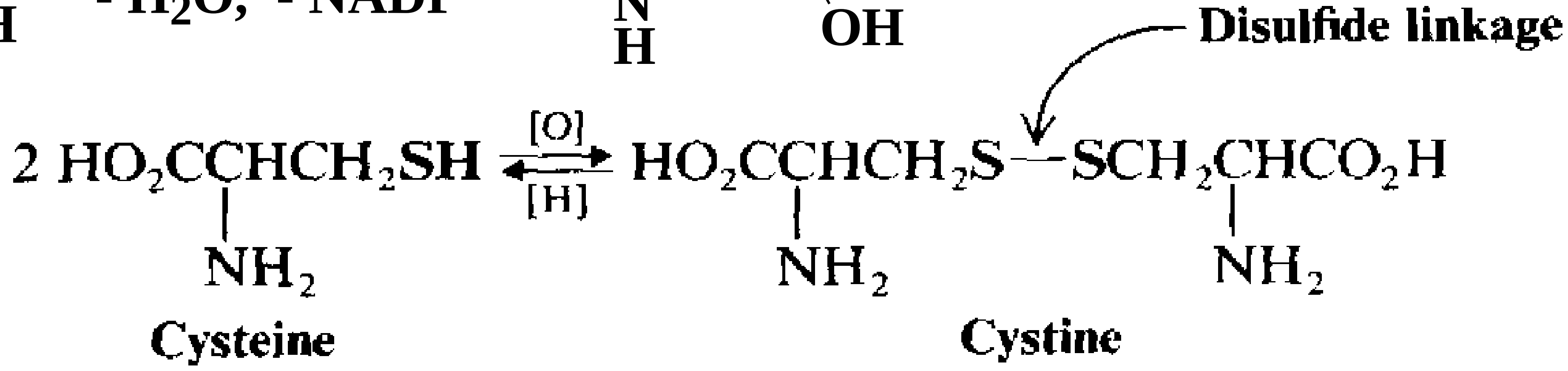
Histamine, toxic amine, is found bound to proteins in nearly all tissues of the body. Release of free histamine causes the symptoms associated with allergic reactions and the common cold.

THE BIOLOGICALLY IMPORTANT REACTIONS OF α-AMINO ACIDS. OXIDATION

- α-Amino acids of proteins sometimes are modified by hydroxylation or oxidation. Proline and lysine of collagen can be hydroxylated with enzyme to yield 4-hydroxyproline. Coenzyme of oxidation is ascorbic acid (vitamin C). The — SH group of cysteine makes cysteine a *thiol.* One property of thiols is that they can be converted to disulfides by mild oxidizing agents. This conversion can be reversed by mild reducing agents.

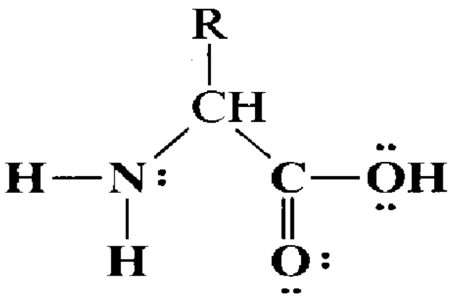




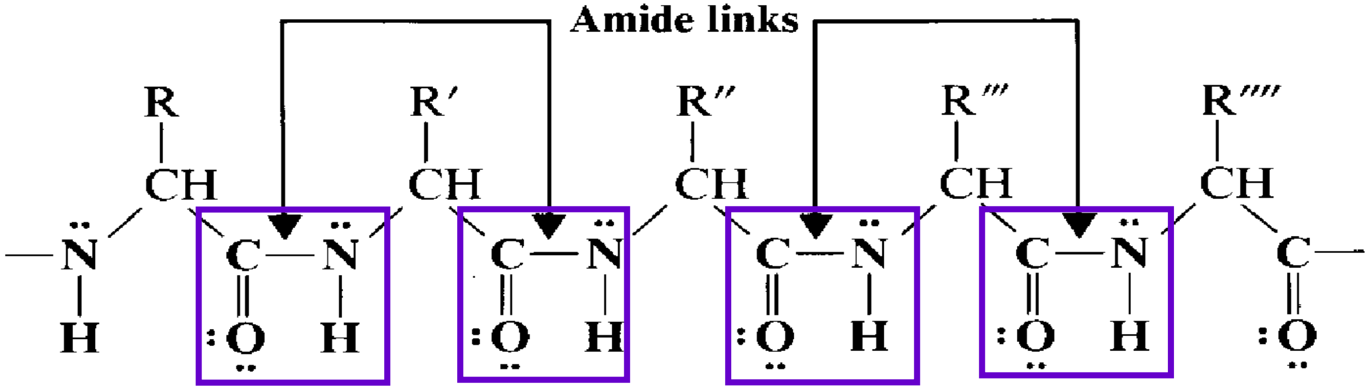


PRIMARY STRUCTURE OF THE PROTEIN

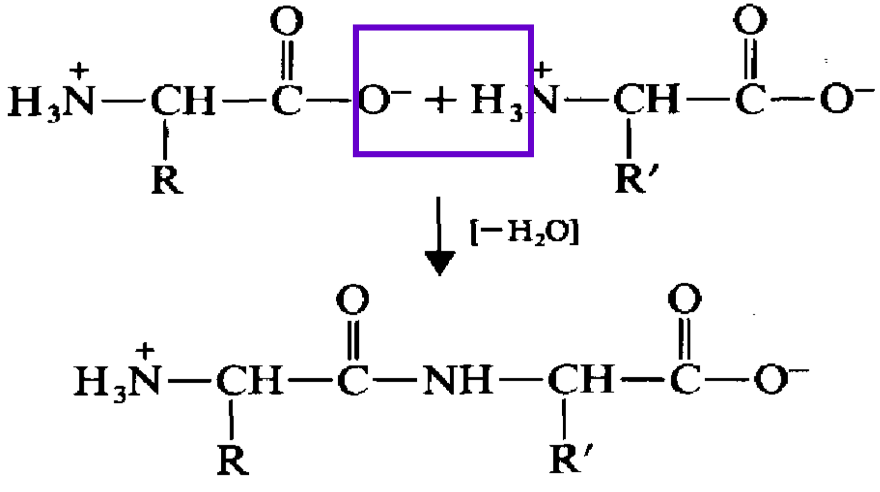
Proteins are natural polymers of α-amino acids joined by amide link. Proteins are polyamides. Their monomeric units are about 20 different α-amino acids:



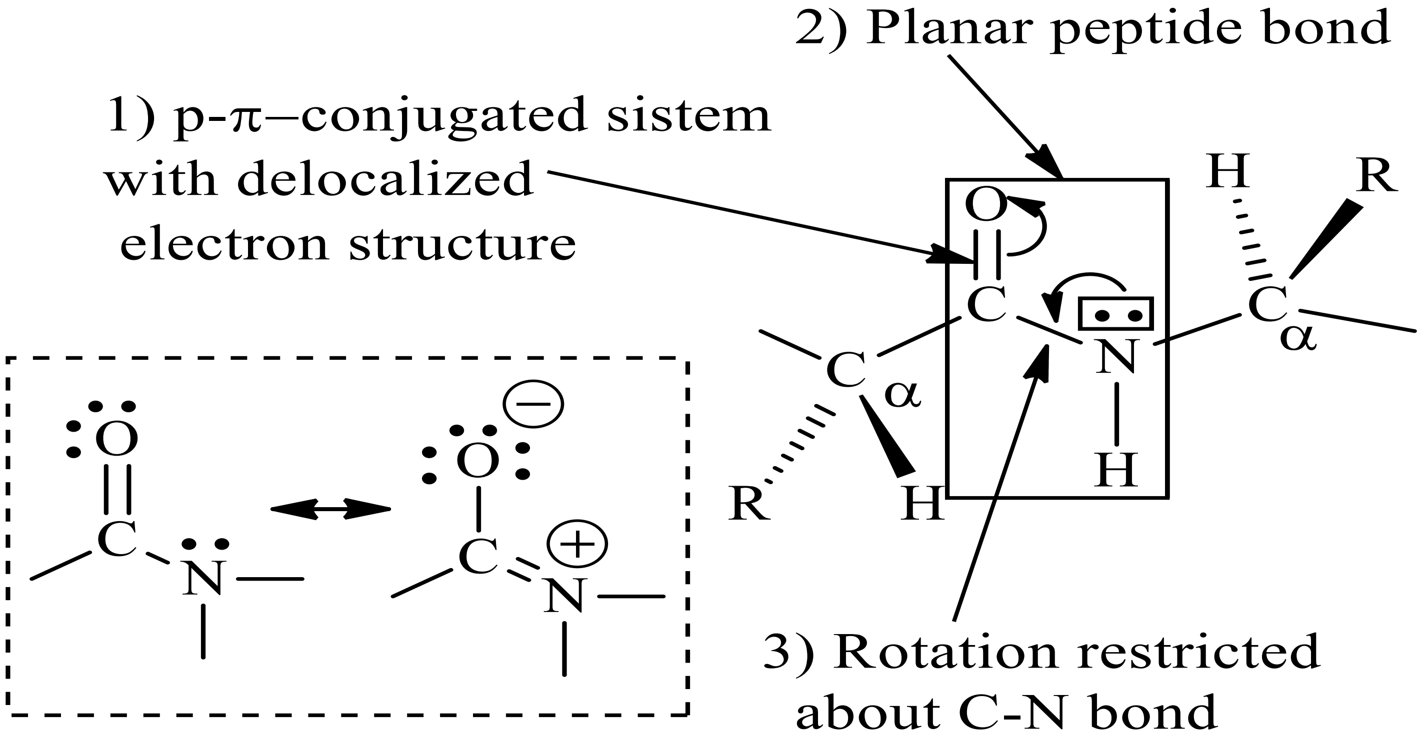
An α-amino acid



A portion of a protein molecule



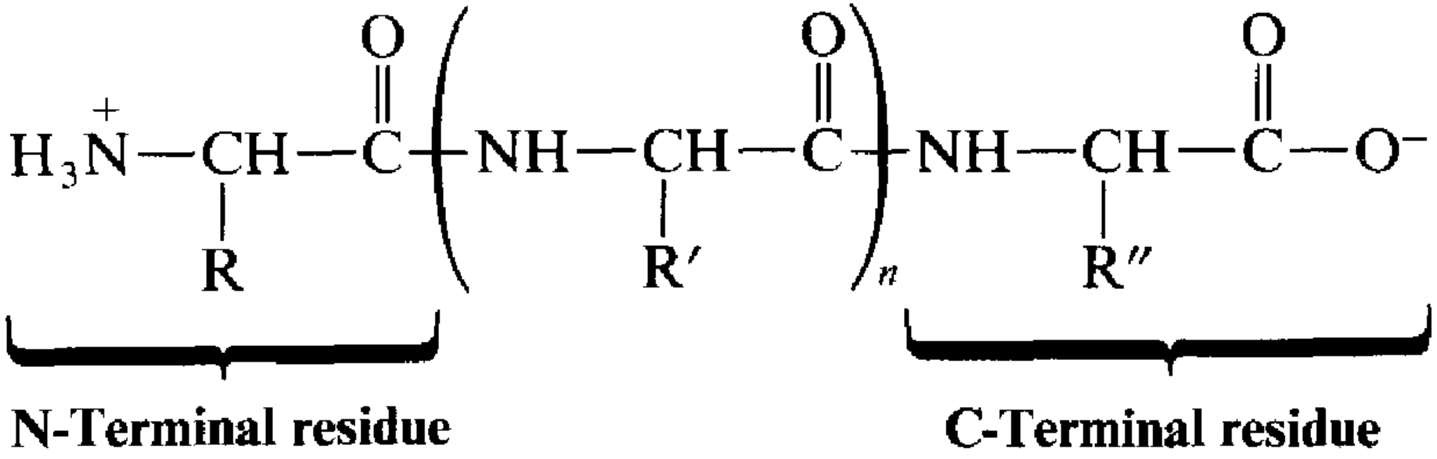
A dipeptide

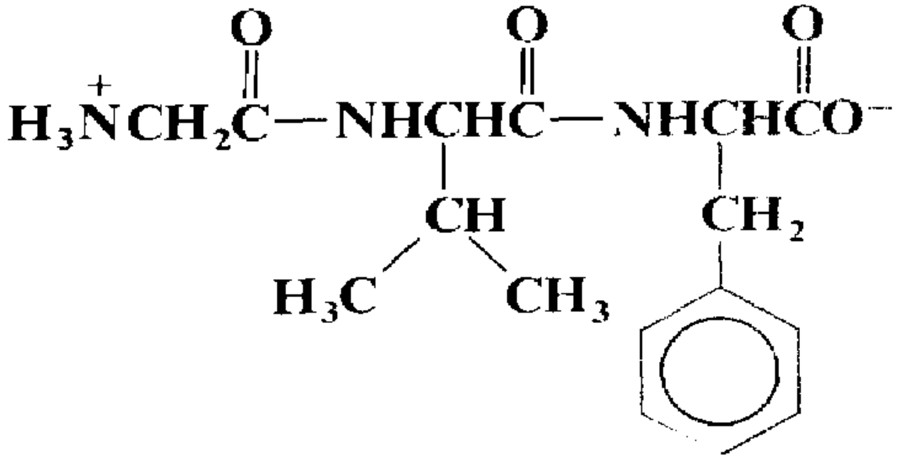


STRUCTURE OF PEPTIDES AND PROTEINS

Polypeptides are **linear polymers. One** end of a polypeptide chain terminates in an amino acid residue that has a free — NH_3^+ group; the other terminates in an amino acid residue with a free — COO^- group. These two groups are called the N-terminal and the **C-terminal residues,** respectively.

By convention, we write peptide and protein structures with the N-terminal amino acid on the left and the C-terminal residue on the right.

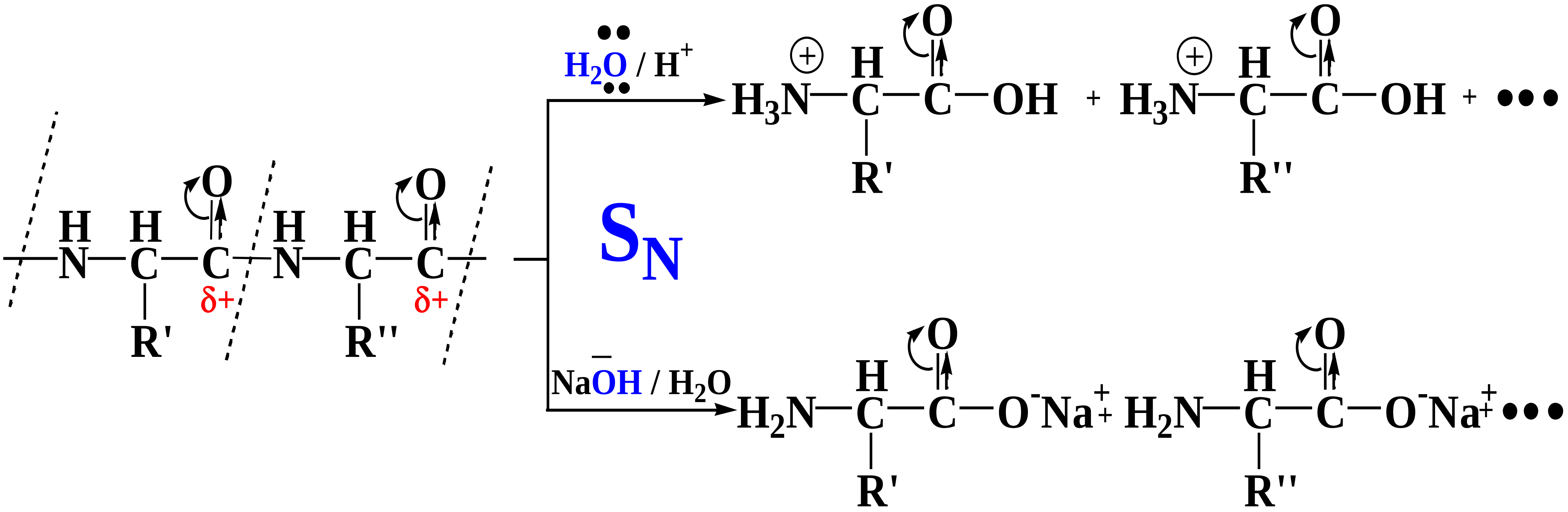




Glycylvalylphenylalanine
(Gly · Val · Phe)

HYDROLYSIS OF PEPTIDES AND PROTEINS

When a protein or polypeptide is refluxed with 6 M hydrochloric acid for 24 h, hydrolysis of all of the amide linkages usually takes place, and this produces a mixture of amino acids.



SECONDARY STRUCTURE OF PROTEINS.

The secondary structure of a protein is the local conformation of its polypeptide that are repeated regularly along its main chain.

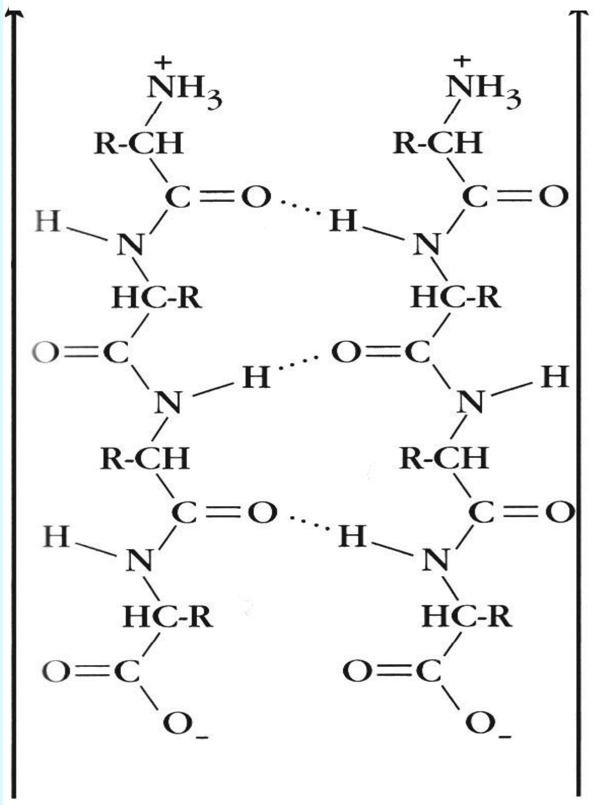
Repeat distance is 7,0 A

Types of a secondary structure:

1) β-pleated sheet:

parallel

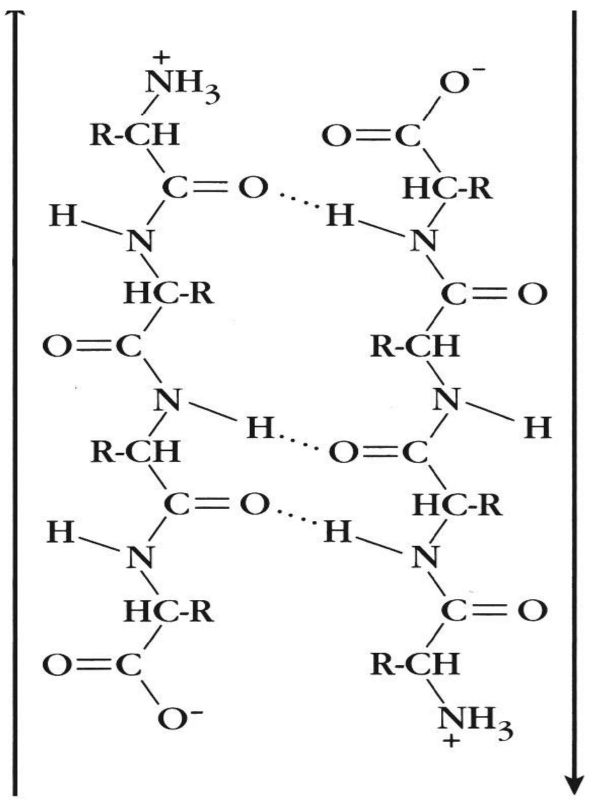
N-terminal N-terminal



C-terminal C-terminal

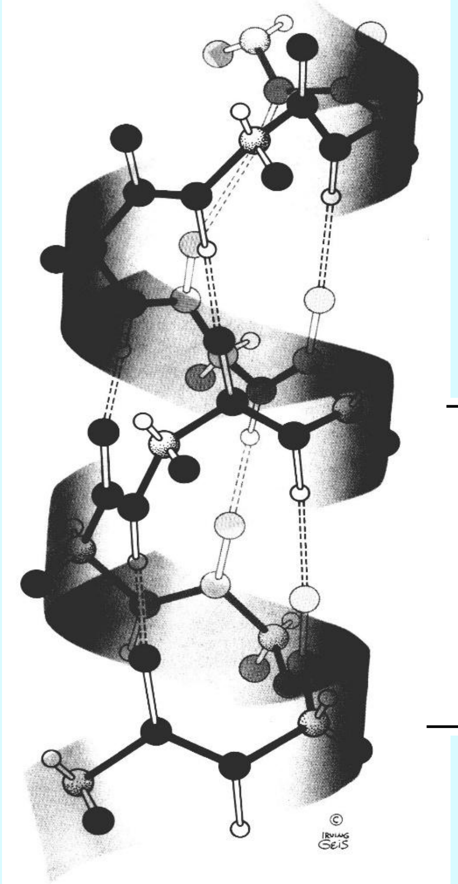
antiparallel

N-terminal C-terminal



C-terminal N-terminal

2) α-helix

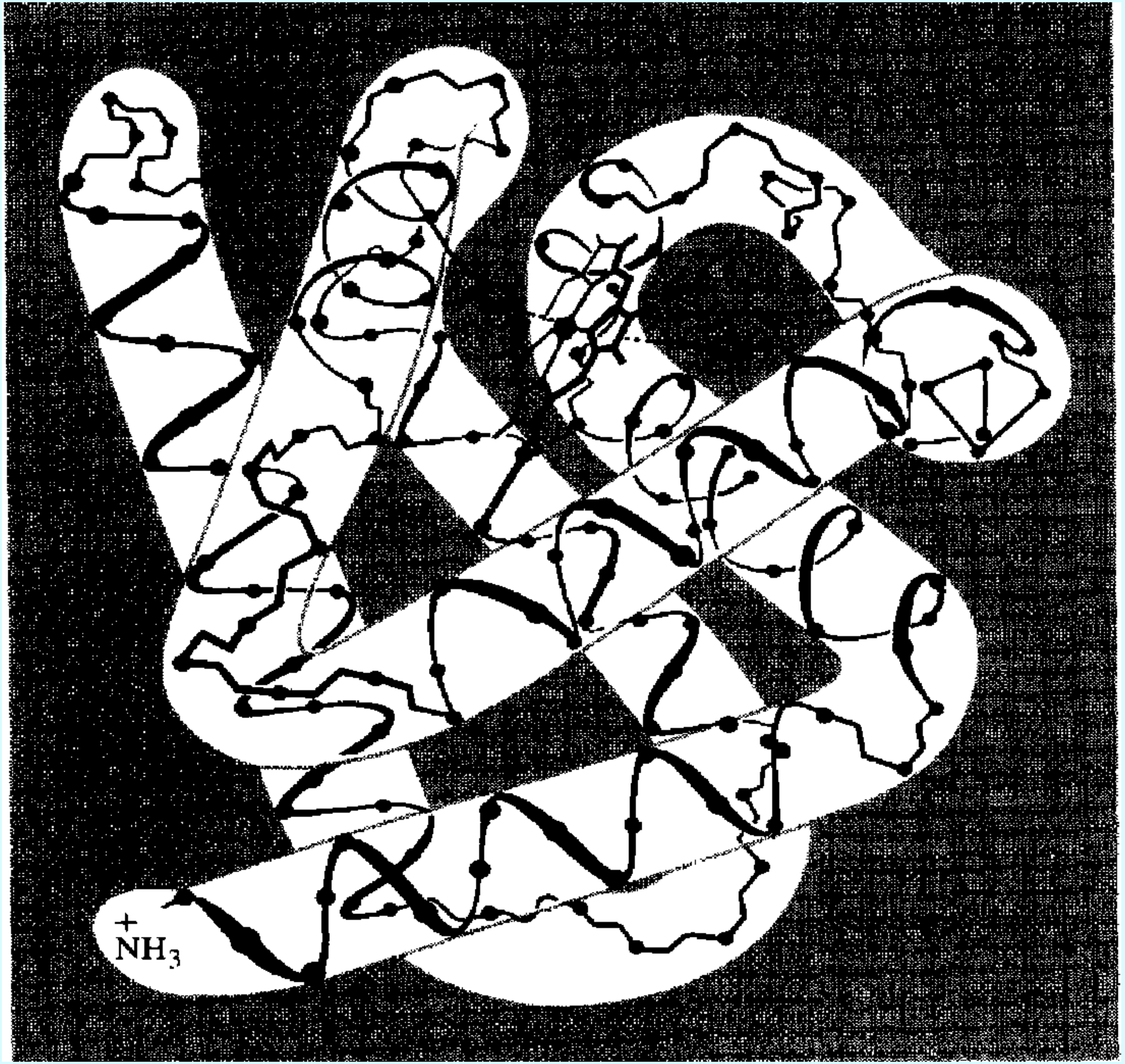


The repeat distance 3,6-α–amino-acid 1,5 A

TERTIARY STRUCTURE OF PROTEIN

The tertiary structure of a protein is its tree-dimensional shape, that arises from further folding of its secondary structures.

***The three-dimensional structure of* myoglobin.**



TERTIARY STRUCTURE OF PROTEINS.

There are fibrous and globular proteins.

The locations of the side chains of amino acids of globular proteins are usually those that we would expect from their polarities.

1. Residues with **nonpolar, hydrophobic, side chains,** such as *valine*, *leucine*, *isoleucine*, *methionine*, *and phenylalanine* are almost always found in the interior of the protein, out of contact with the aqueous solvent.

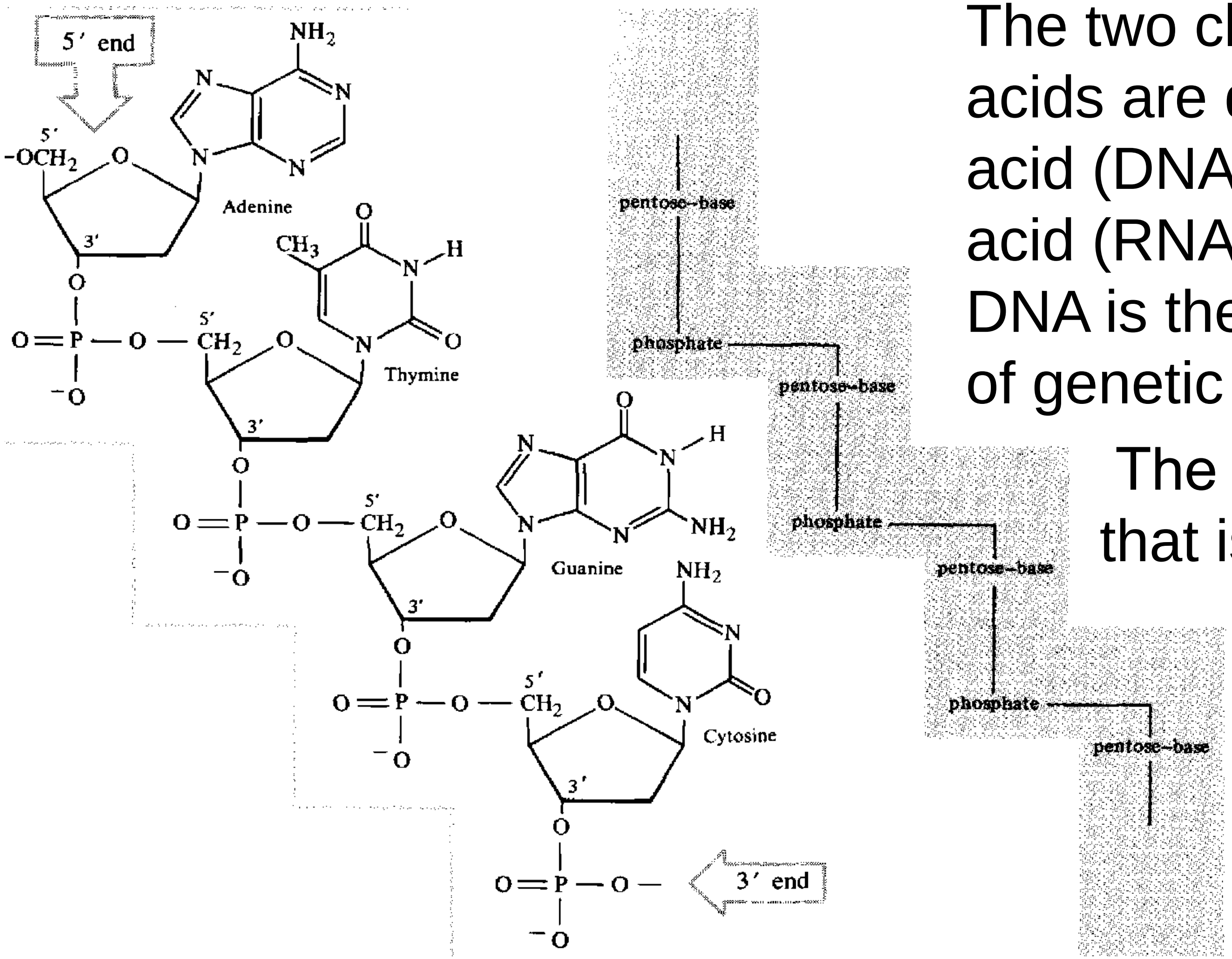
2. Side chains of **polar residues with "+" or "—" charges,** such as *arginine*, *lysine*, *aspartic acid*, and *glutamic acid*, are usually on the surface of the protein in contact with the aqueous solvent.
3. Uncharged polar side chains such as those of *serine*, *threonine*, *asparagine*, *glutamine*, *tyrosine*, *and tryptophan* are most often found on the surface, but some of these are found in the interior as well. When they are found in the interior, they are virtually all hydrogen bonded to other similar residues. Hydrogen bonding apparently helps neutralize the polarity of these groups.

<u>The quaternary structure</u> of a protein is the assembly (oligomer) of two or more individual polypeptide chains (subunits) held togethe by noncovalent forces or covalent bonds.

DEOXYRIBONUCLEIC ACID: DNA PRIMARY STRUCTURE

The essential property of all living systems is the ability to reproduce or replicate themselves.

The information required for replication of an organism is contained in molecules called nucleic acids.



The two classes of nucleic acids are deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

DNA is the master repository of genetic information in cells.

The genetic information that is stored in DNA is passed from DNA to RNA and then to proteins.

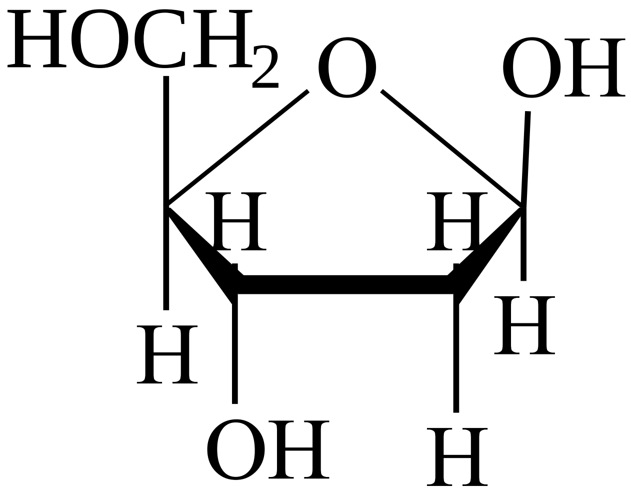
5’←A - T - G - C→3’.

A molecular model of a portion of the DNA double helix.

PENTOSES OF NUCLEIC ACIDS

- In **DNA,** the pentose portion is 2-deoxy-β- D-ribose, while in **RNA** the pentose portion is β-D-ribose. Ribose and 2-deoxyribose exist as five-membered furanose rings in both **DNA** and **RNA.**

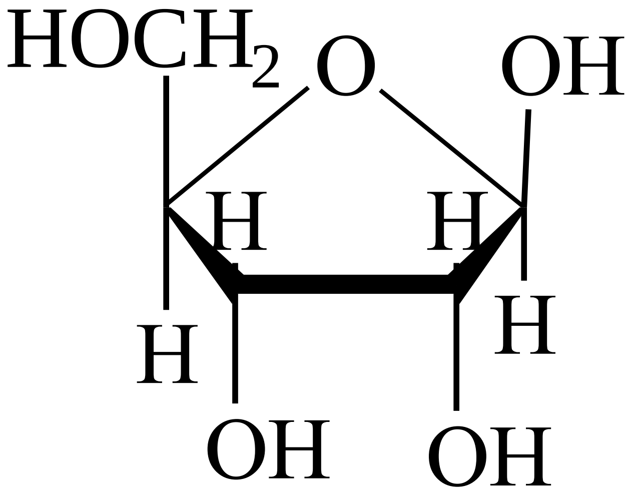
in DNA



2-deoxy-D-ribose

2-deoxy-β-D-ribofuranose

in RNA



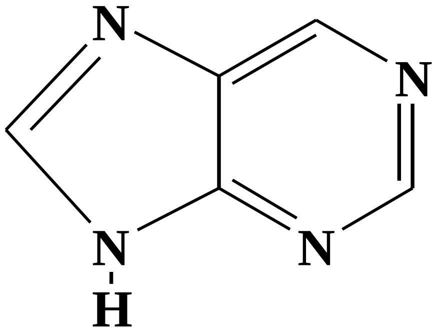
D-ribose

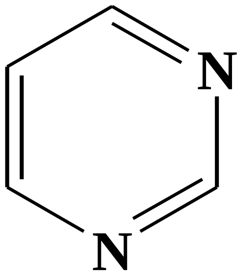
β-D-ribofuranose

HETEROCYCLIC BASES OF NUCLEIC ACIDS

The heterocyclic bases in DNA and **RNA** are derivatives of purine and pyrimidine.

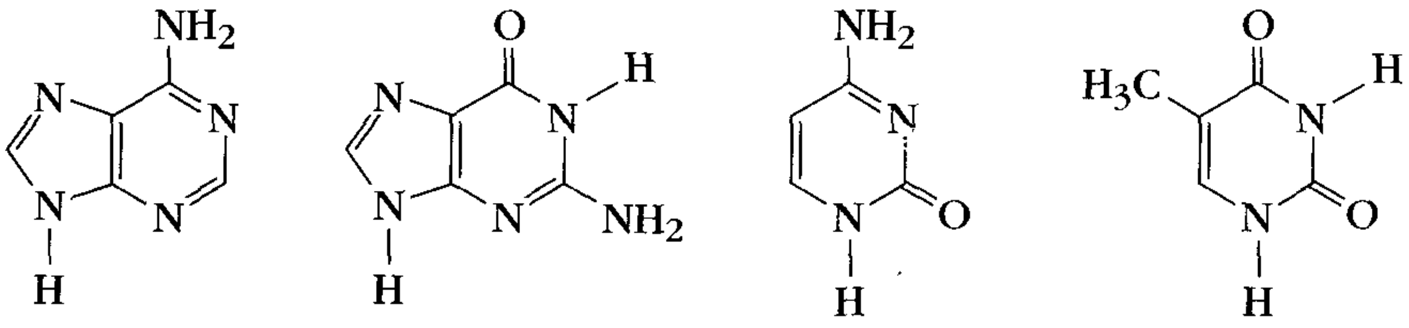
Purine





Pyrimidine

DNA

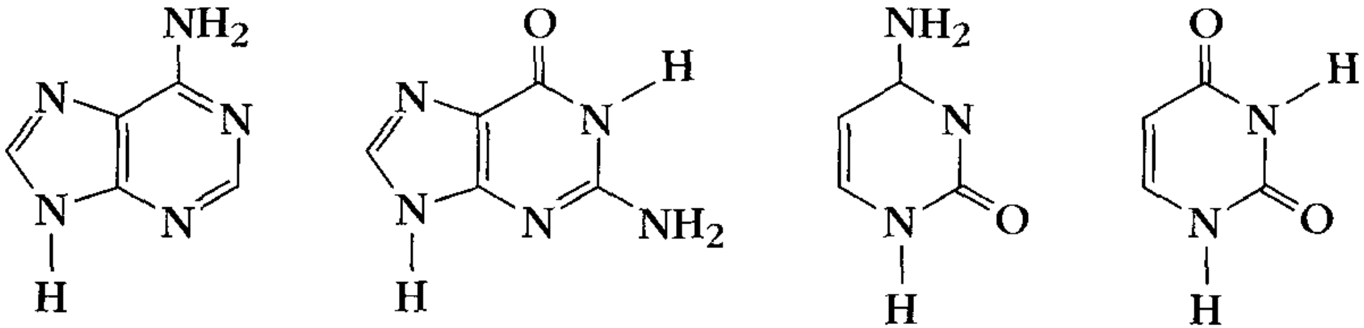


Adenine (A) | Guanine (G) | Cytosine (C) | Thymine (T)

Derivatives of purine found in DNA

Derivatives of pyrimidine found in DNA

RNA

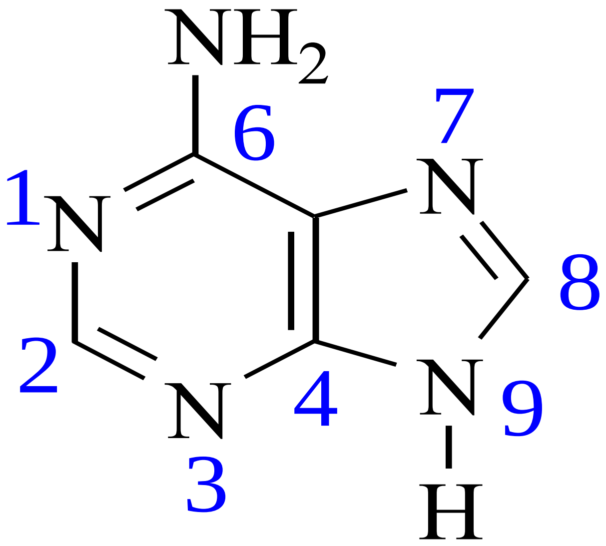


Adenine (A) | Guanine (G) | Cytosine (C) | Uracil (U)

Derivatives of purine found in RNA

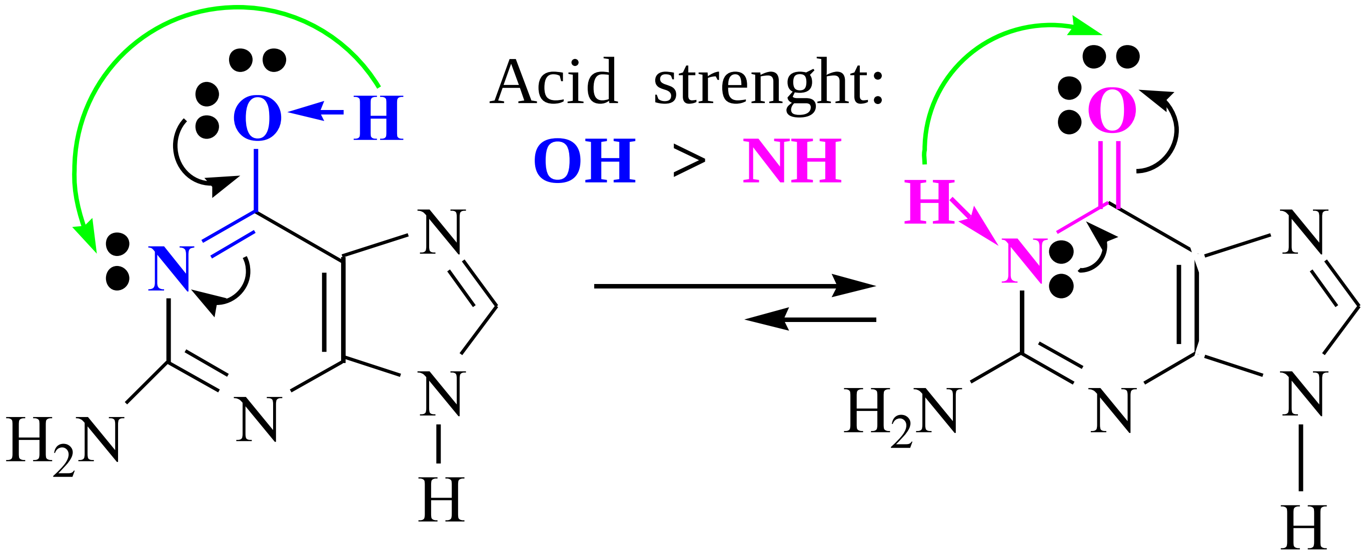
Derivatives of pyrimidine found in RNA

TAUTOMERIC FORMS OF HETEROCYCLIC BASES.



6-aminopurine
adenine

predominant form is **Lactam**

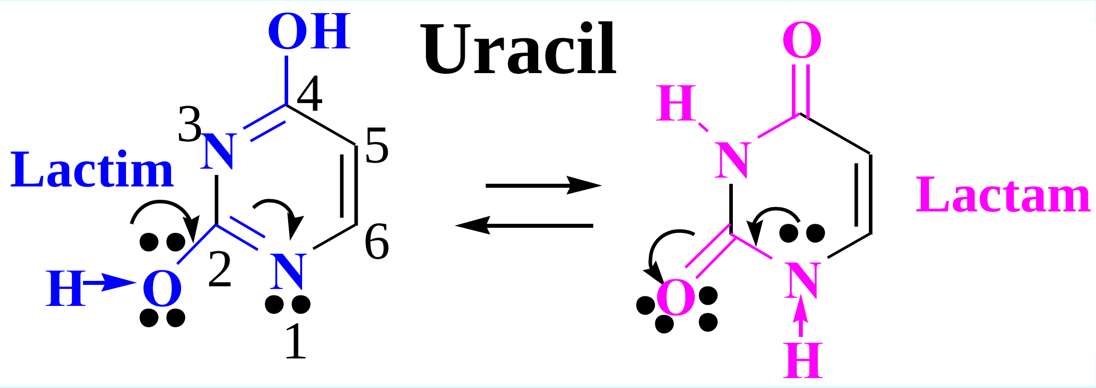


Lactim **Lactam**

2-amino-6-hydroxypurine **guanine**

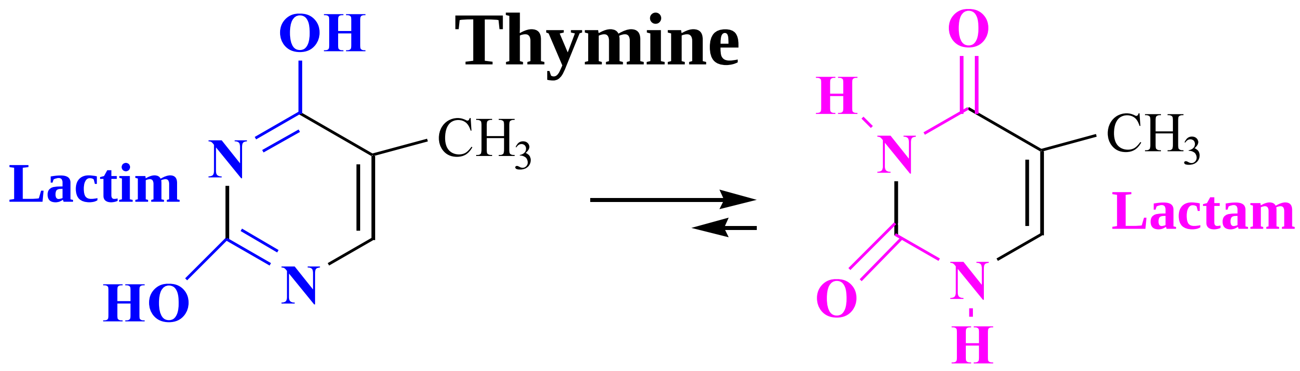
TAUTOMERIC FORMS OF HETEROCYCLIC BASES.

2,4-dihydroxy pyrimidine

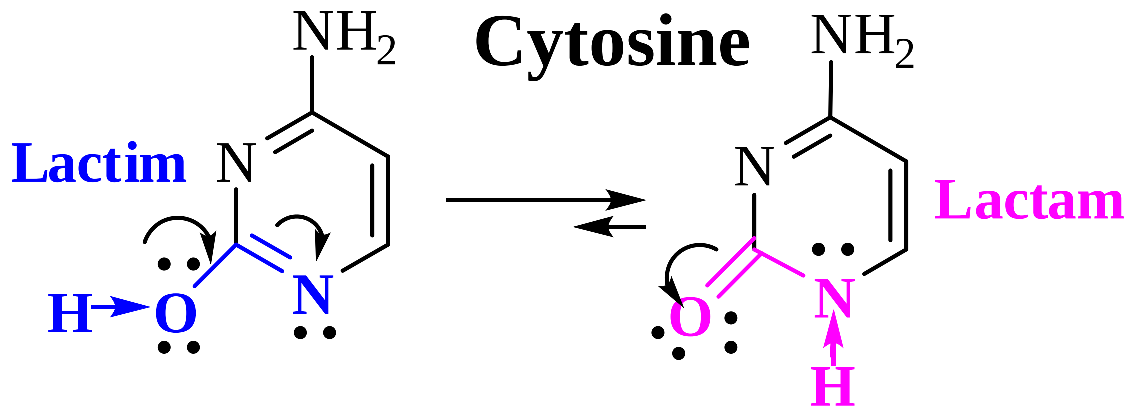


Lactames are predominant forms

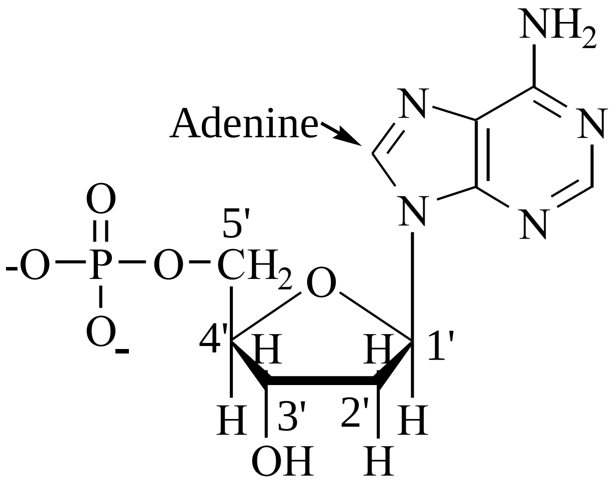
2,4-dihydroxy-5-methyl-pyrimidine



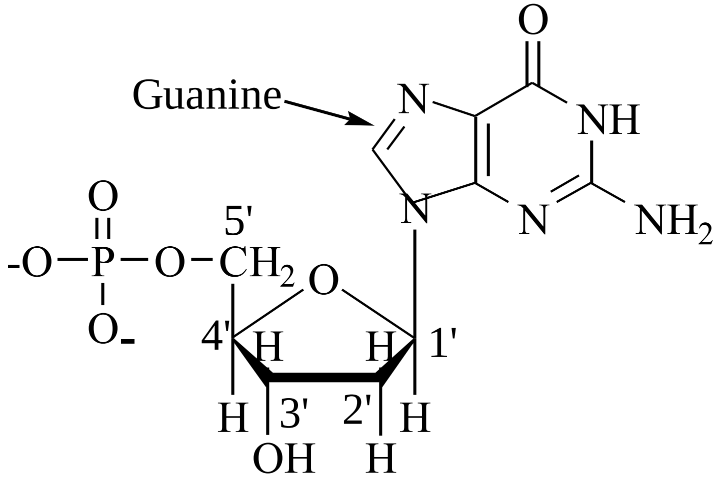
4-amino-2-hydroxy pyrimidine



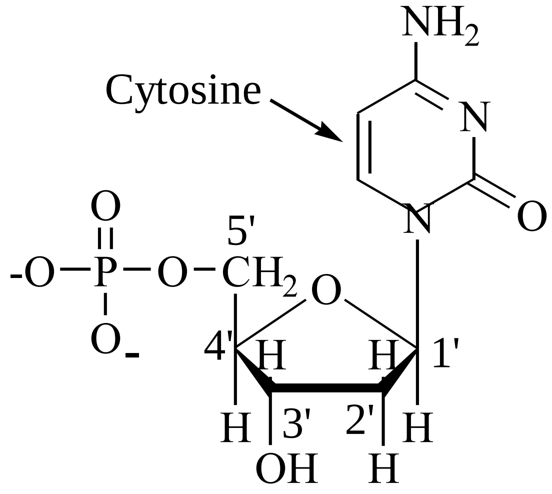
THE FOUR NUCLEOTIDES FOUND IN DNA:



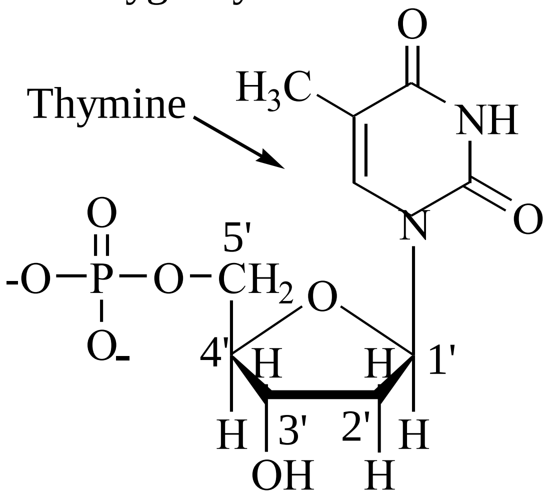
2'-Deoxyadenosine 5'-monophosphate
5'-deoxyadenylic acid



2'-Deoxyguanosine 5'-monophosphate
5'-deoxyguanylic acid

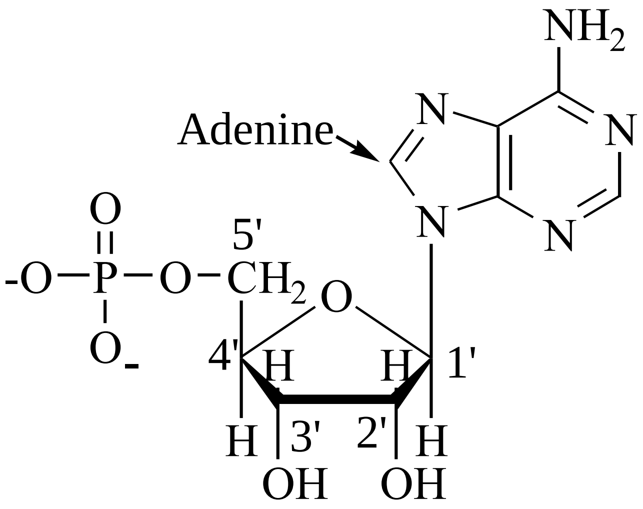


2'-Deoxycytidine 5'-monophosphate
5'-deoxycitidylic acid

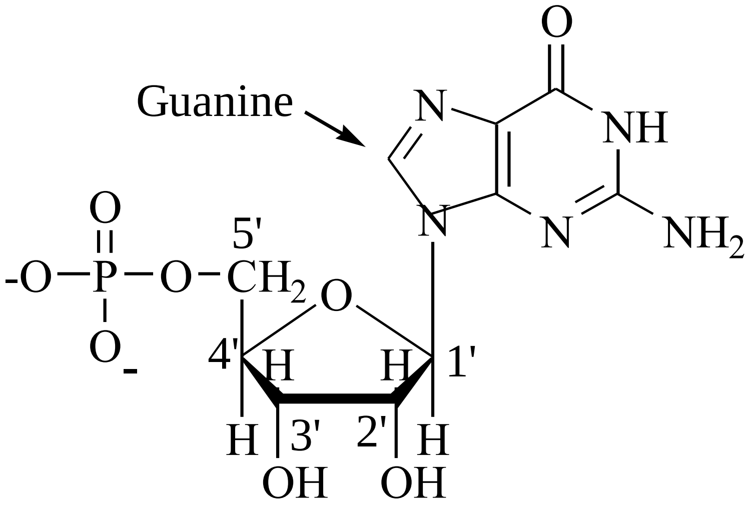


2'-Deoxythymidine 5'-monophosphate
5'-deoxythymidylic acid

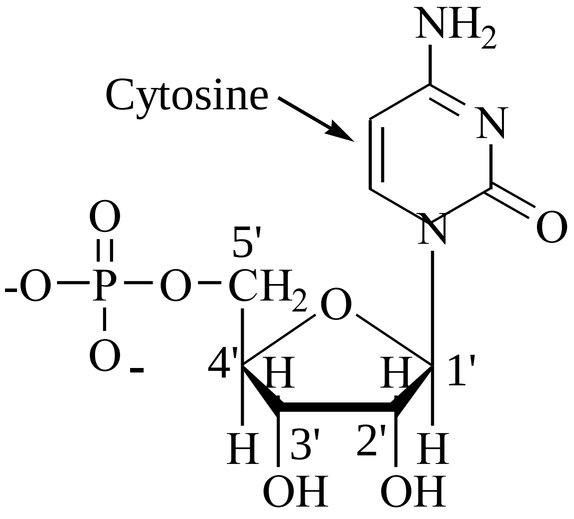
THE FOUR NUCLEOTIDES FOUND IN RNA:



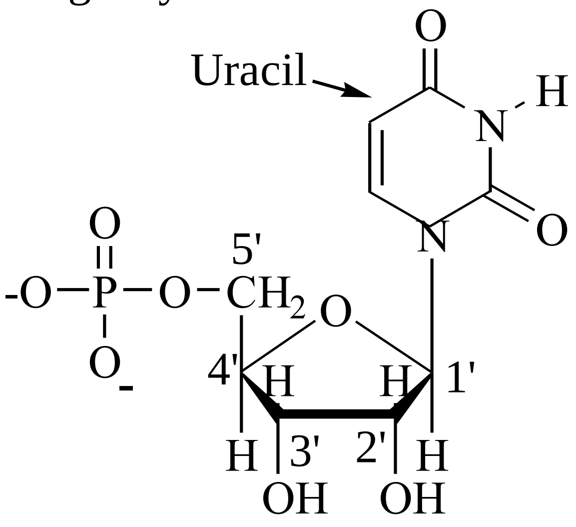
Adenosine 5'-monophosphate
5'-adenylic acid



Guanosine 5'-monophosphate
5'-guanylic acid



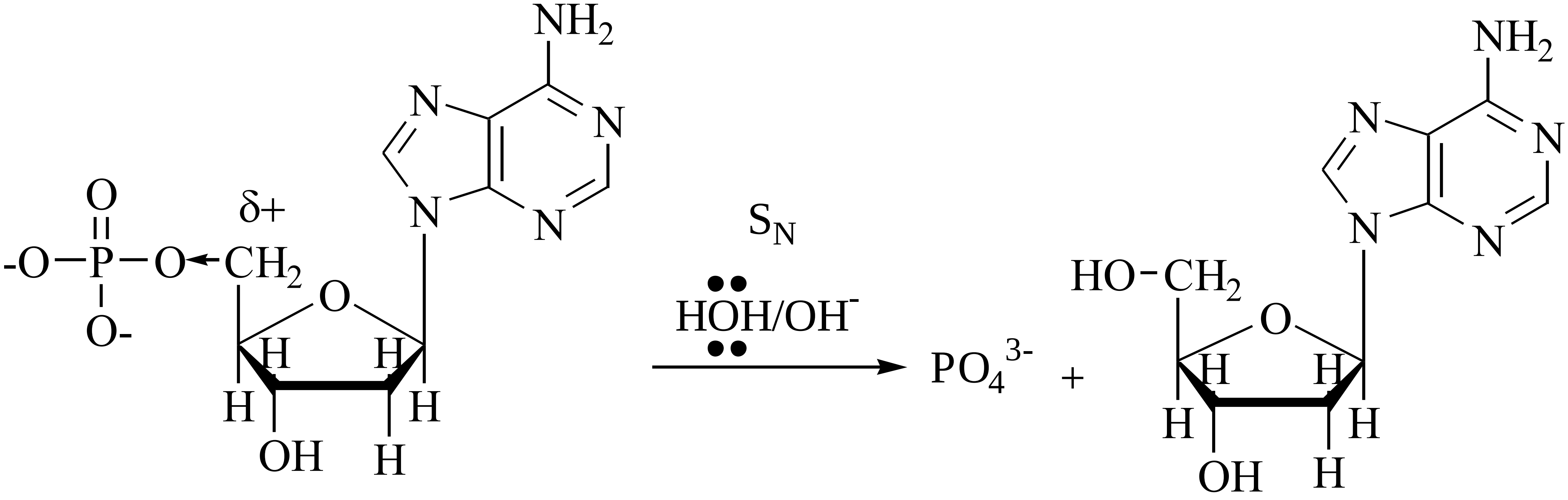
Cytidine 5'-monophosphate
5'-cytidylic acid



Uridine 5'-monophosphate
5'-uridylic acid

HYDROLYSIS OF NUCLEOTIDES IN BASIC SOLUTION

Base-catalyzed hydrolysis of nucleotides lead to break phosphate ester bond to form a nucleoside and phosphate ion.



2'-Deoxyadenosine 5'-monophosphate

the nucleotide

2'-Deoxyadenosine

the nucleoside

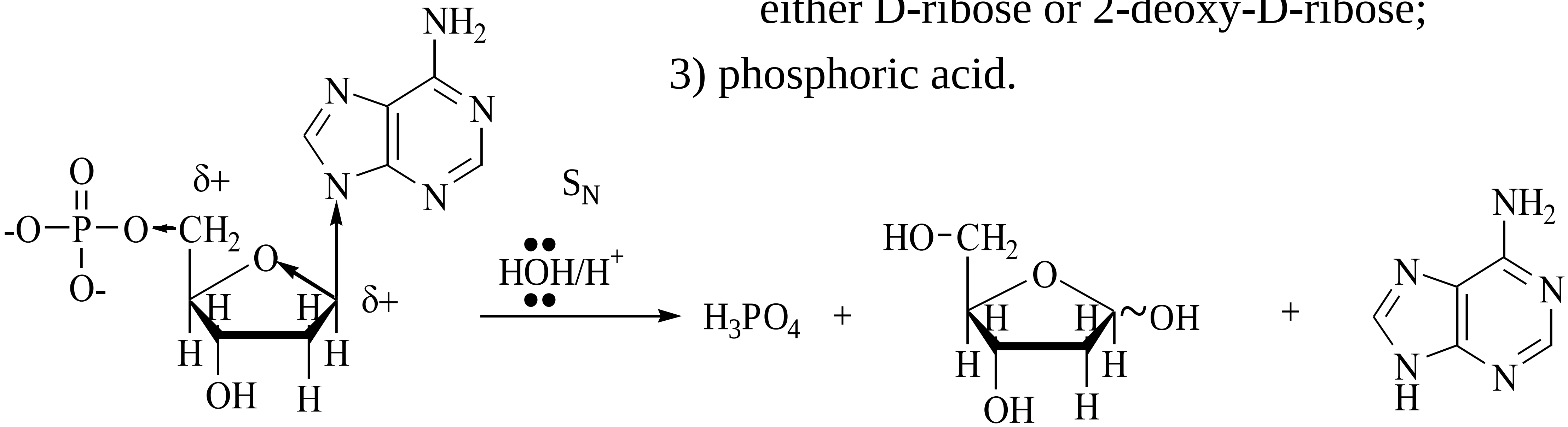
HYDROLYSIS IN ACIDIC SOLUTION

Complete hydrolysis of a nucleotides in acidic solution lead to break both phosphate ester bond and N-glycoside linkage to form: 1) a heterocyclic base, either a purine or pyrimidine;

2) a five-carbon monosaccharide,

either D-ribose or 2-deoxy-D-ribose;

3) phosphoric acid.



2'-Deoxyadenosine 5'-monophosphate

the nucleotide

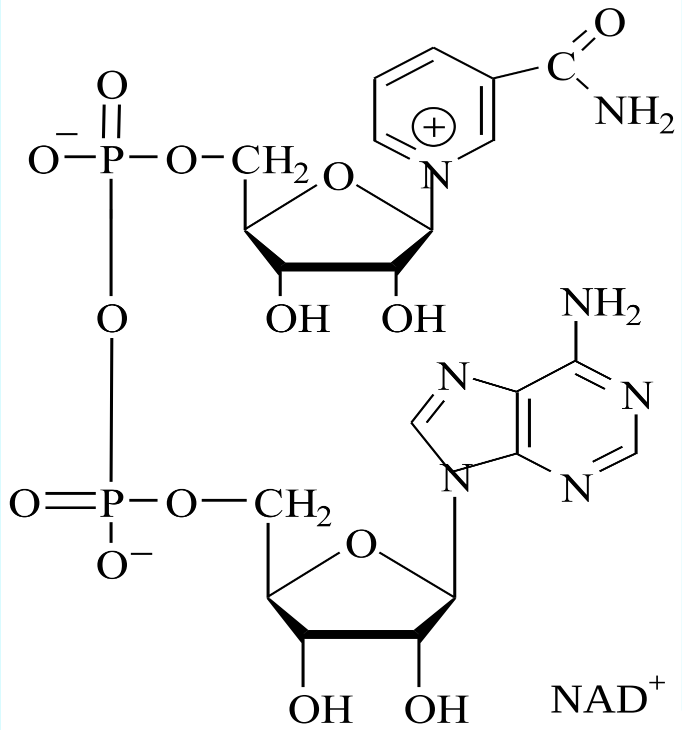
2-deoxy-D-ribose

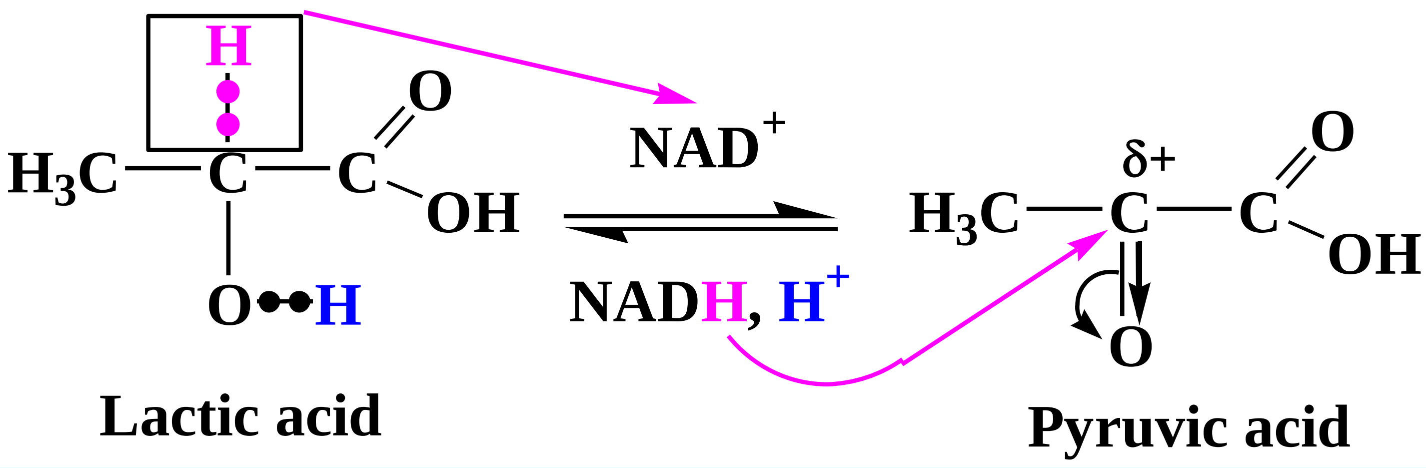
the monosaccharide

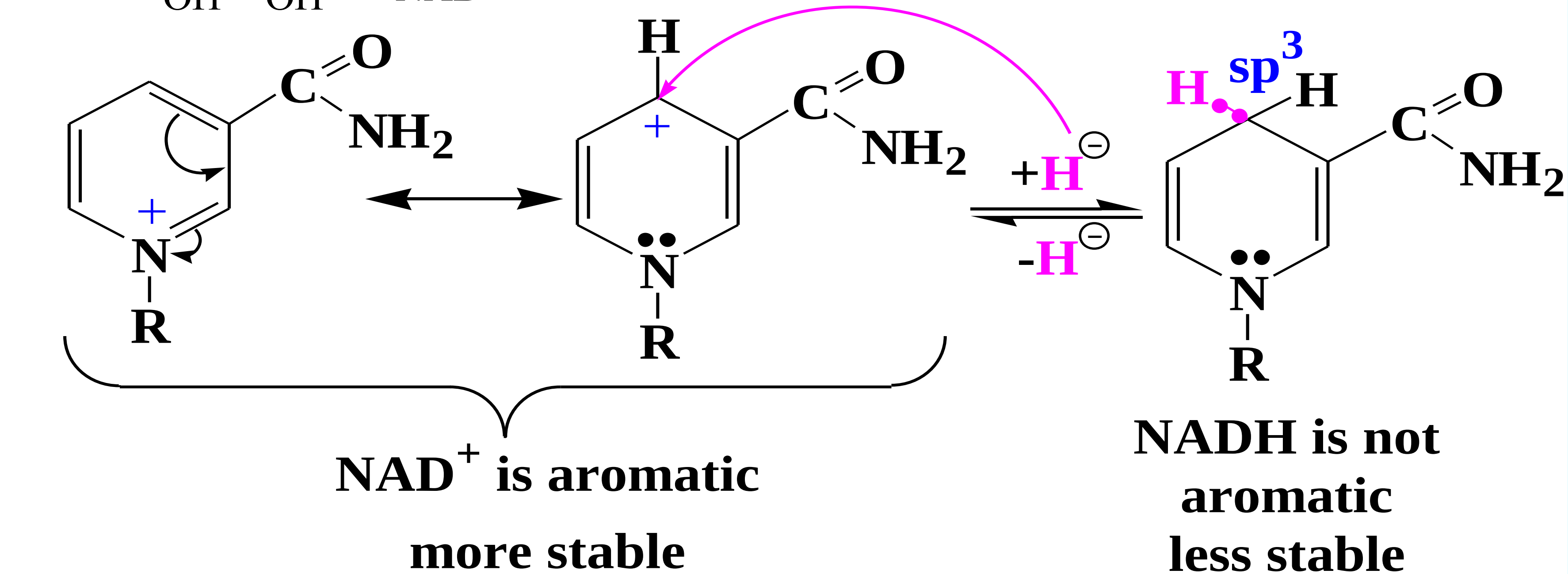
Adenine

the heterocyclic base

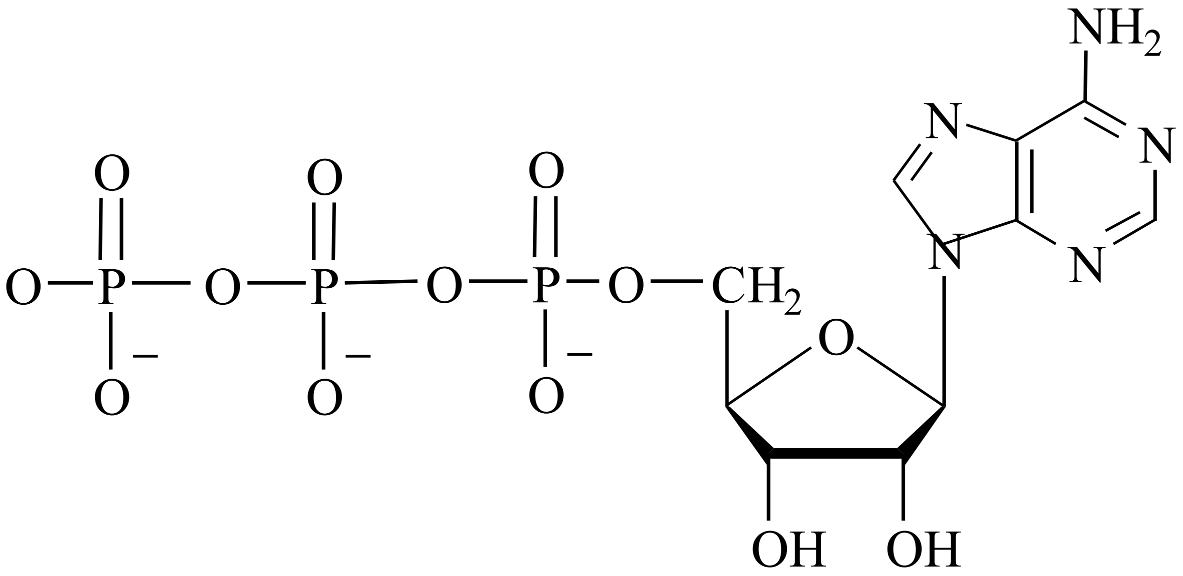
Coenzyme NAD$^+$.





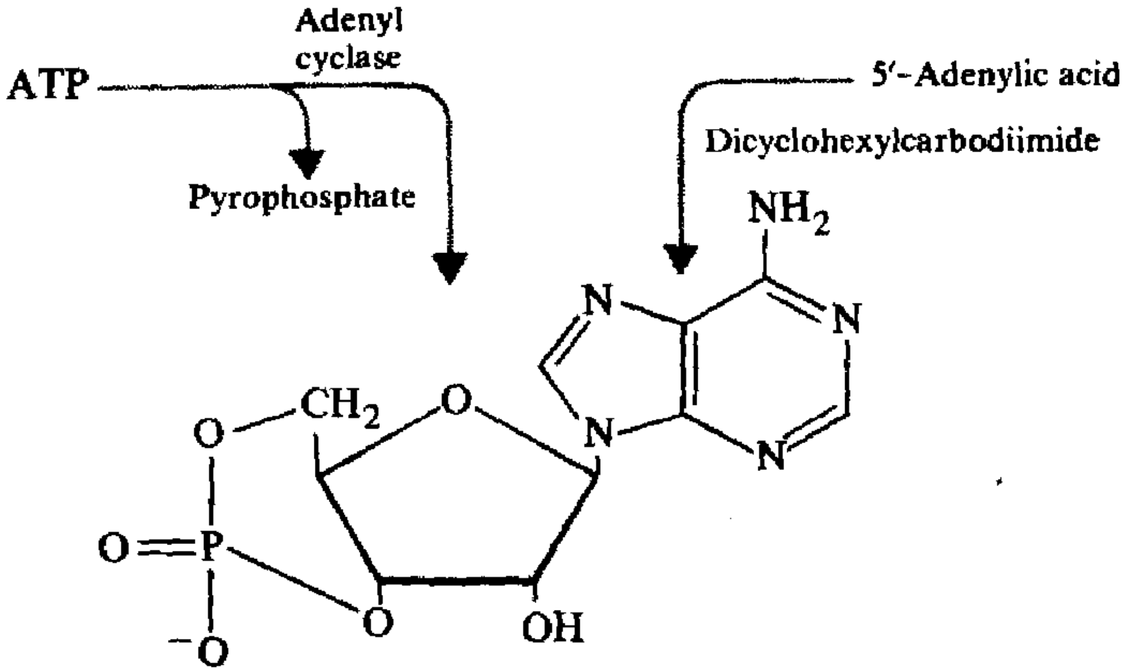


5’-Triphosphate of adenosine (ATP).



The 5'-triphosphate of adenosine is the important energy source, ATP.

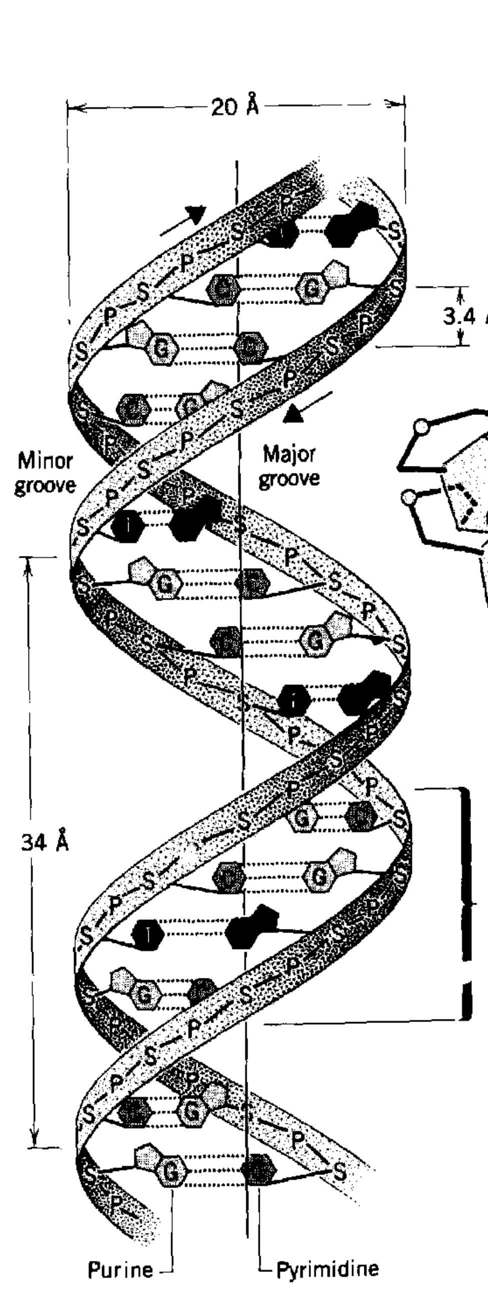
3',5'-Cyclic adenylic acid



The compound called 3',5'-cyclic adenylic acid (or cyclic AMP) is an important regulator of hormone activity.

Cells synthesize this compound from ATP through the action of an enzyme, *adenyl cyclase.*

SECONDARY STRUCTURE OF DNA



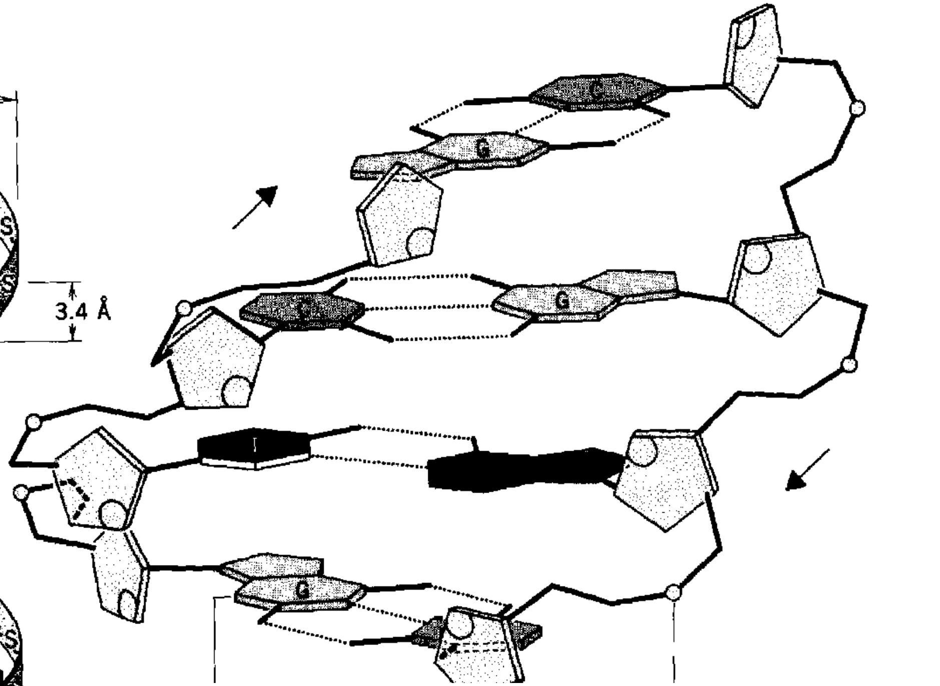
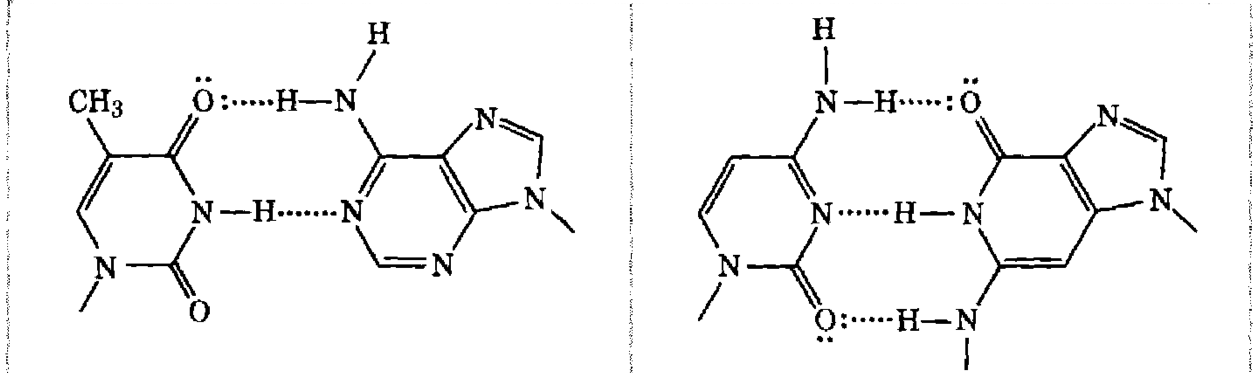


Diagram of the ***DNA*** *double helix showing complementary base pairing.*
The arrows indicate the 3′ →5′ direction.

The repeat distance 10 nucleotide pair

A purine base is complementary for pyrimidine base:



Thymine **Adenine** **Cytosine** **Guanine**

Thank you