NUCLEIC ACIDS. LIPIDS. LOW-MOLECULAR WEIGHT BIOREGULATORS

1. The structure and hydrolysis of nucleotides of DNA and RNA.
2. Other nucleotides: NAD+, ATP, ADP, c-AMP
3. Structure of nucleic acids. DNA: primary structure.
4. Lipids: fatty acids and triacylglycerols; phospholipids of cell membranes.
5. Steroids
6. Alkaloids

Self-directed learning

1. Rancidness of fats that is free radical chain process as the model of the peroxidation of polyunsaturated fatty acids in the cell membranes, its mechanism and its biological role.

2. The significance of the spatial structure and physical-chemical properties of bioregulators in their interaction with receptors and the implementation of action at the molecular level.

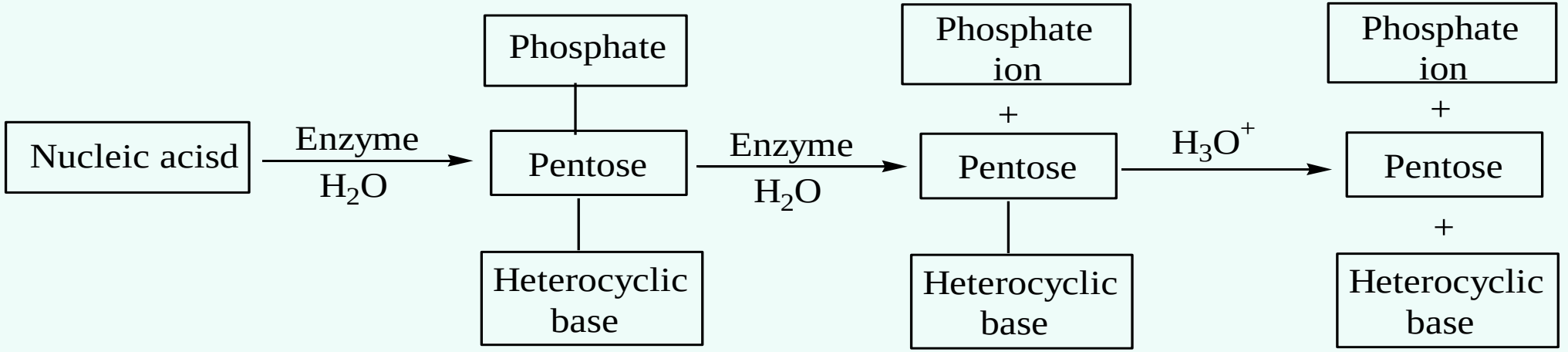
3. The concept of the secondary structure of DNA. The role of hydrogen bonds in the formation of the DNA secondary structure. Complementarity of heterocyclic bases

COMPOSITION OF NUCLEIC ACIDS

The essential property of all living systems is the ability to reproduce or replicate themselves. Macromolecules called **nucleic acids** save and transmit this information.

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** to proteins.

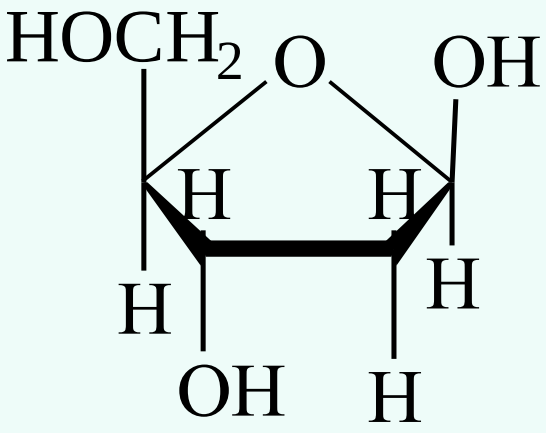


Nucleotide **Nucleoside**

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.**
- The pentose portions:

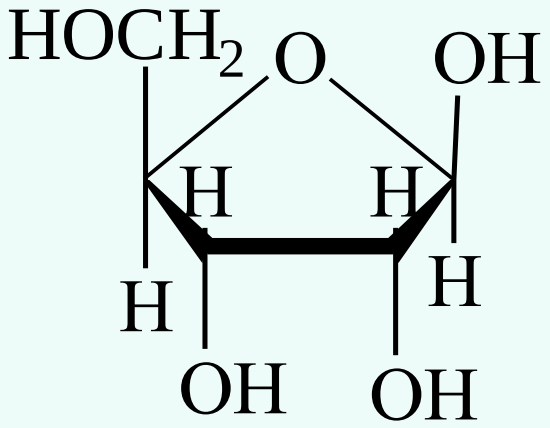
in DNA



2-deoxy-D-ribose

2-deoxy-β-D-ribofuranose

in RNA

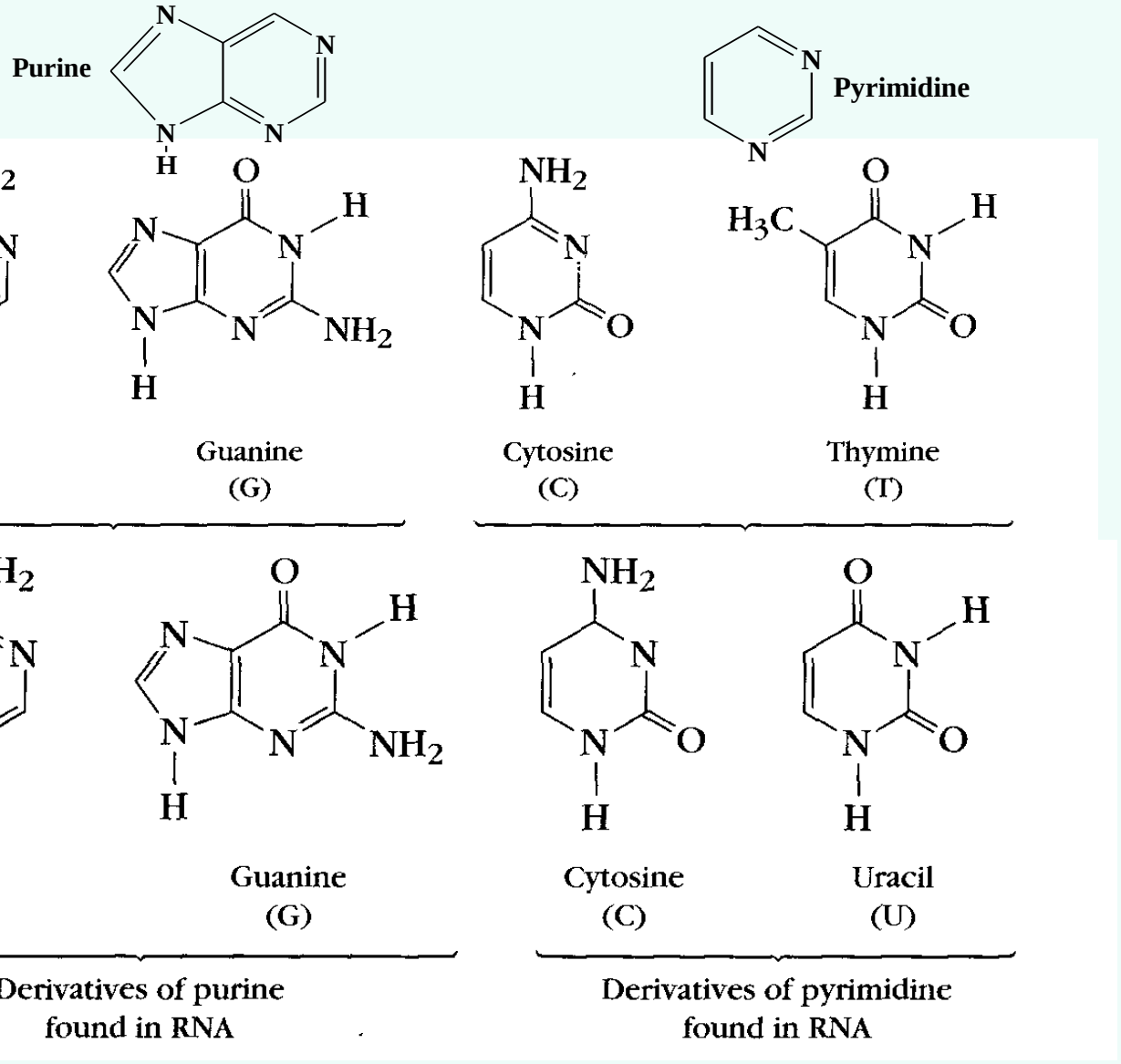


D-ribose

β-D-ribofuranose

HETEROCYCLIC BASES OF NUCLEIC ACIDS

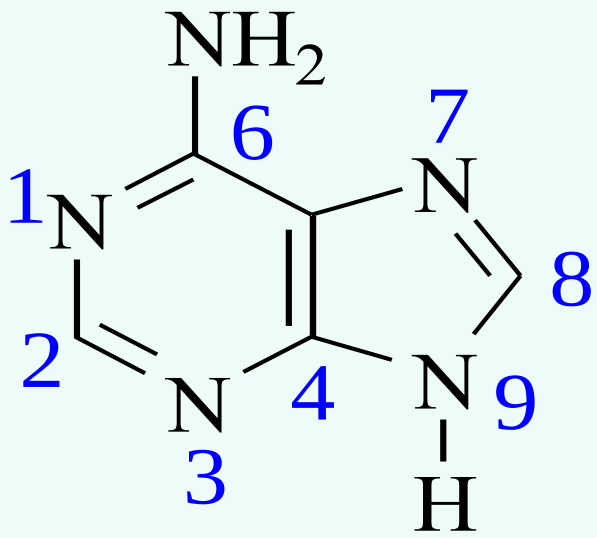
The heterocyclic bases in DNA and **RNA** are derivatives of purine and pyrimidine.



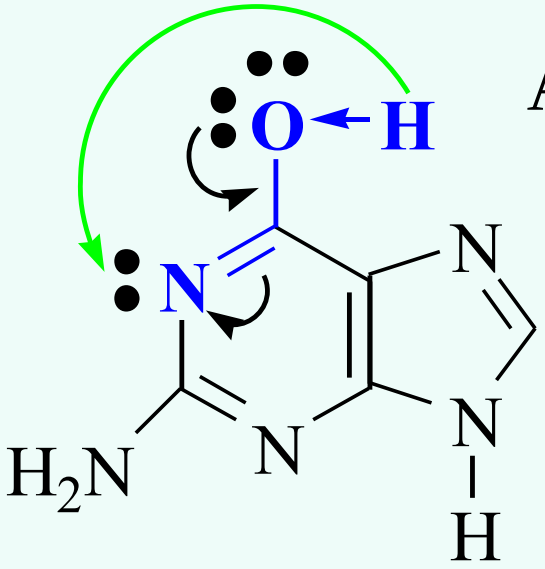
TAUTOMERIC FORMS OF HETEROCYCLIC BASES

ADENINE

6-aminopurine



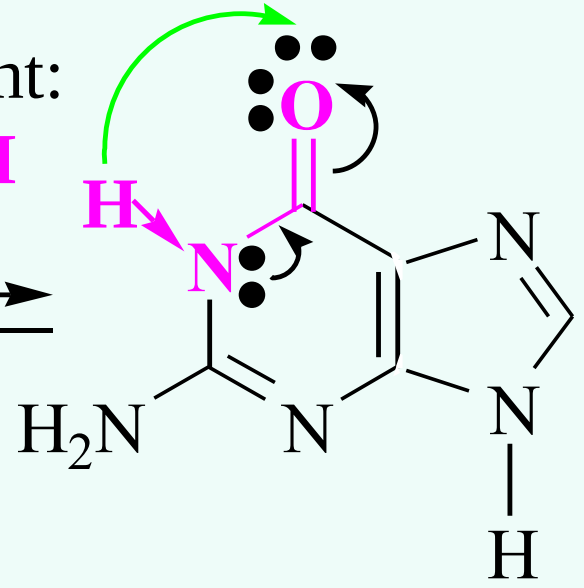
GUANINE 2-amino-6-hydroxypurine



Lactim

Acid strenght:

OH > **NH**

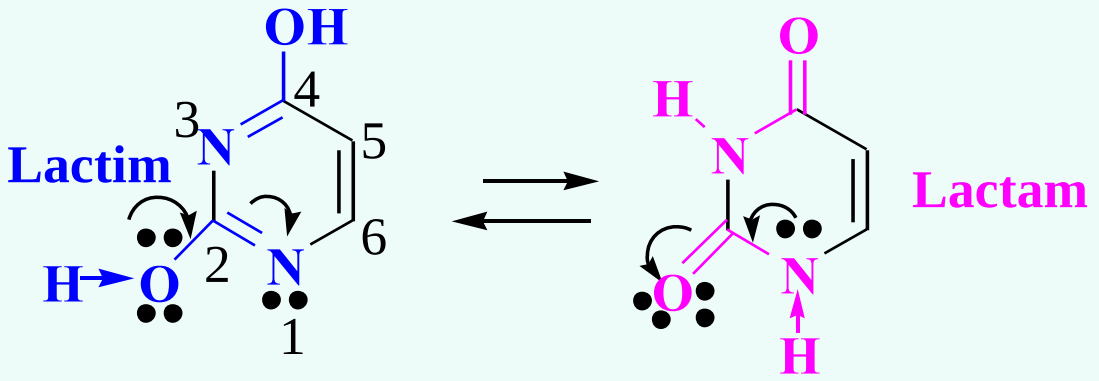


Lactam

Lactam is predominant form

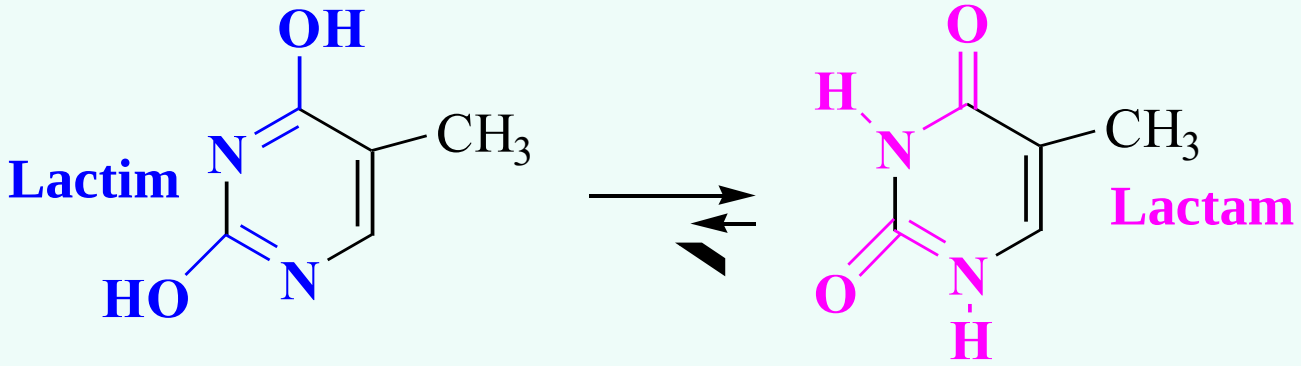
TAUTOMERIC FORMS OF HETEROCYCLIC BASES.

Uracil — **2,4-dihydroxy pyrimidine**

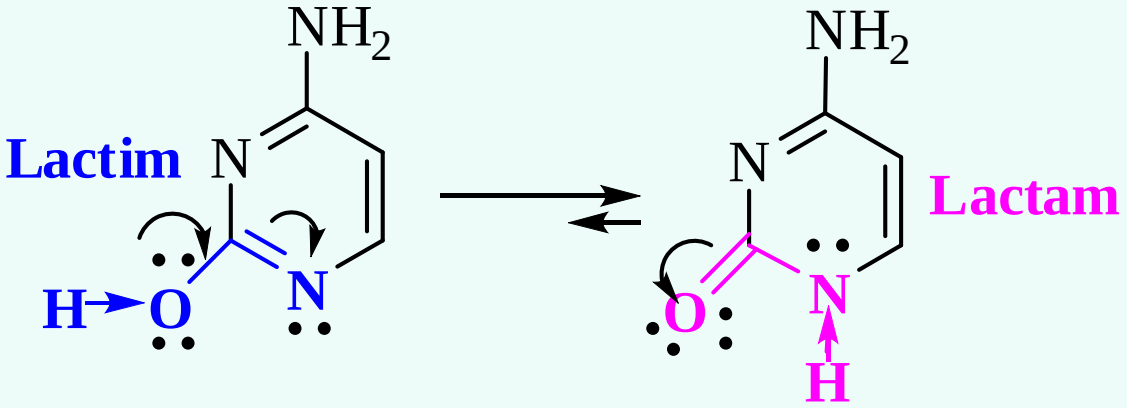


Lactames are predominant forms

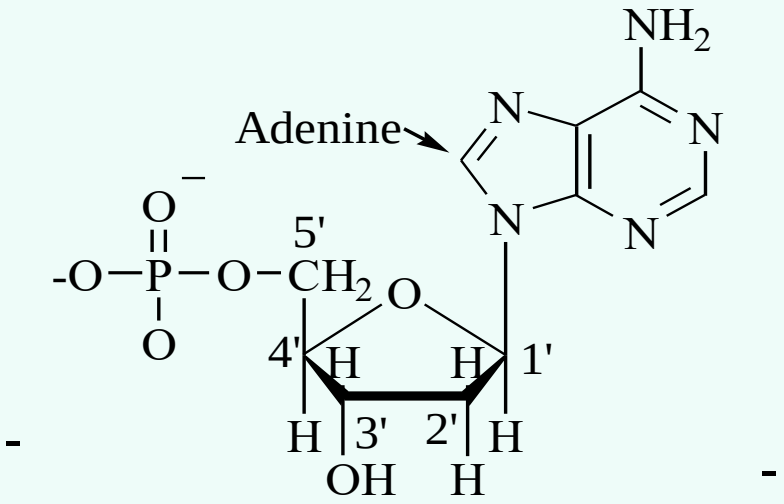
Thymine — **2,4-dihydroxy-5-methyl-pyrimidine**



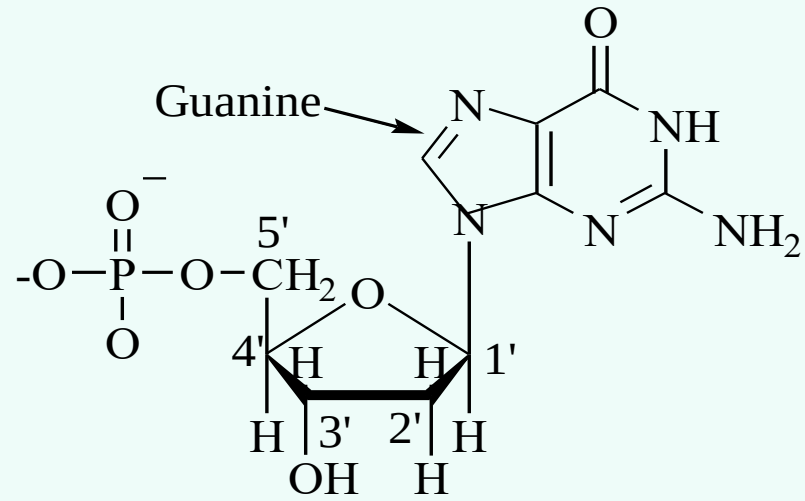
Cytosine — **4-amino-2-hydroxy pyrimidine**



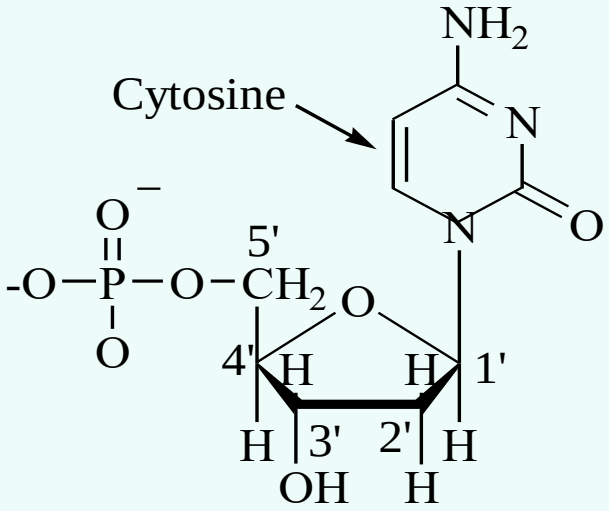
THE FOUR NUCLEOTIDES FOUND IN DNA:



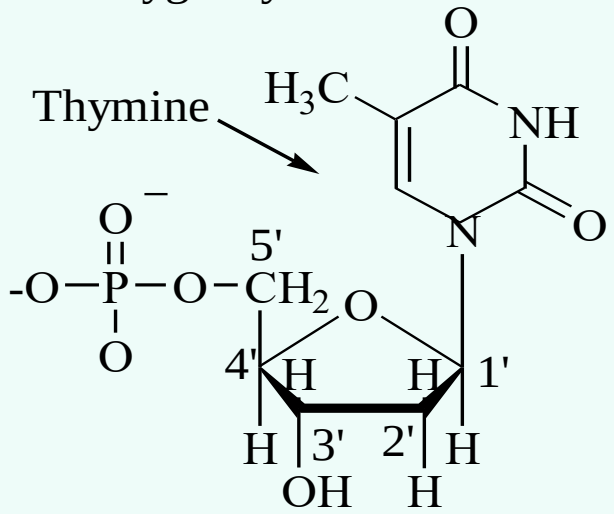
2'-Deoxyadenosine 5'-monophosphate
5'-deoxyadenylic acid



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

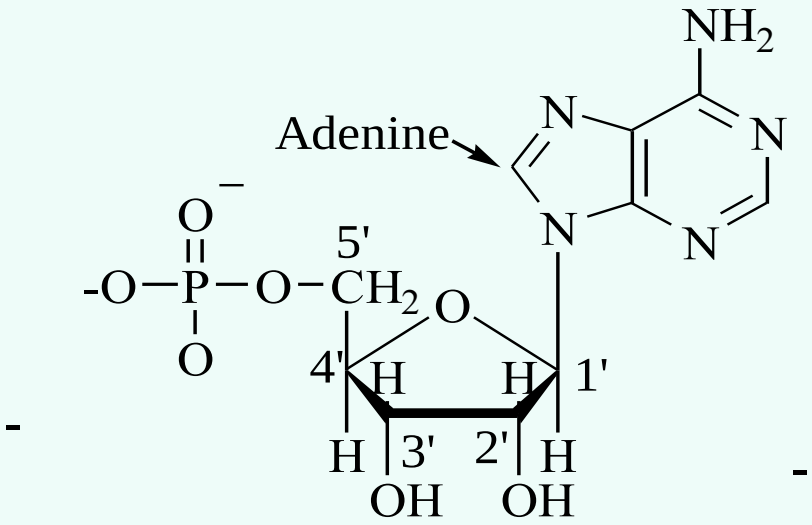


2'-Deoxycytidine 5'-monophosphate
5'-deoxycitidylic acid

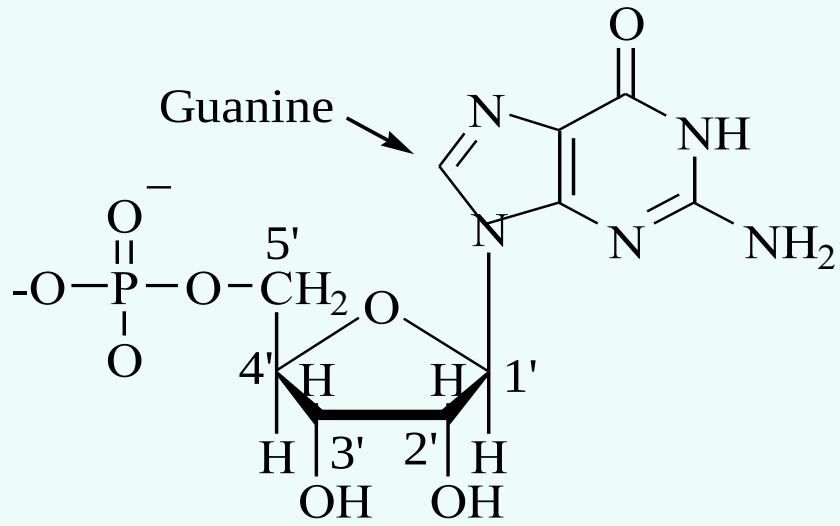


2'-Deoxythymidine 5'-monophosphate
5'-deoxythymidylic acid

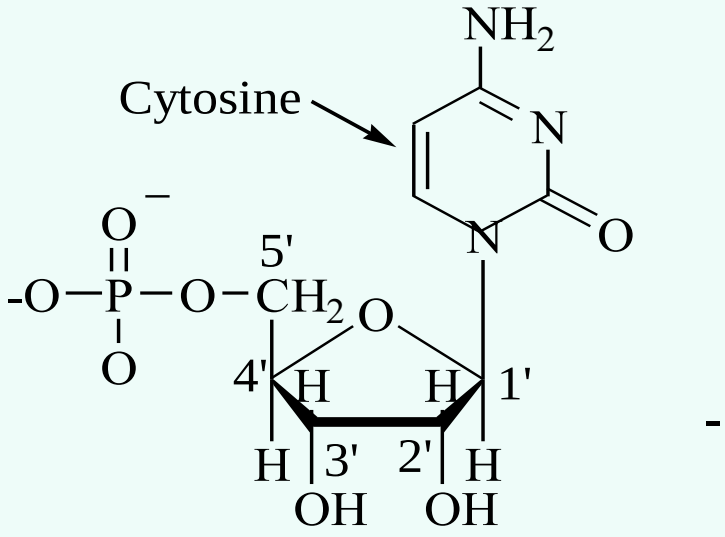
THE FOUR NUCLEOTIDES FOUND IN RNA:



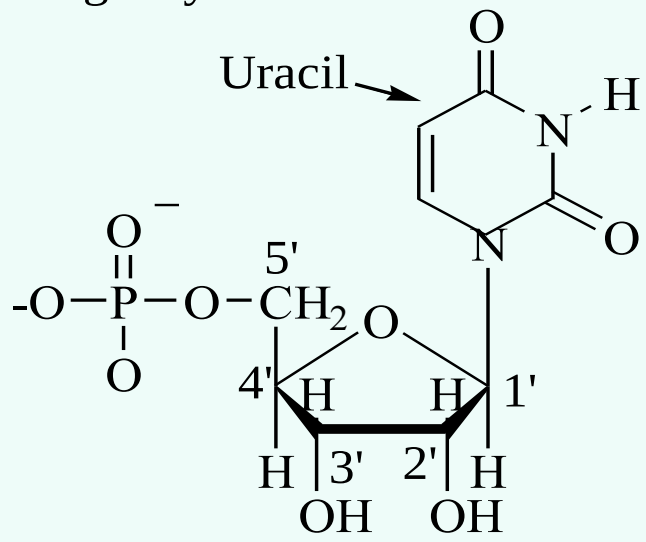
Adenosine 5'-monophosphate
5'-adenylic acid



Guanosine 5'-monophosphate
5'-guanylic acid



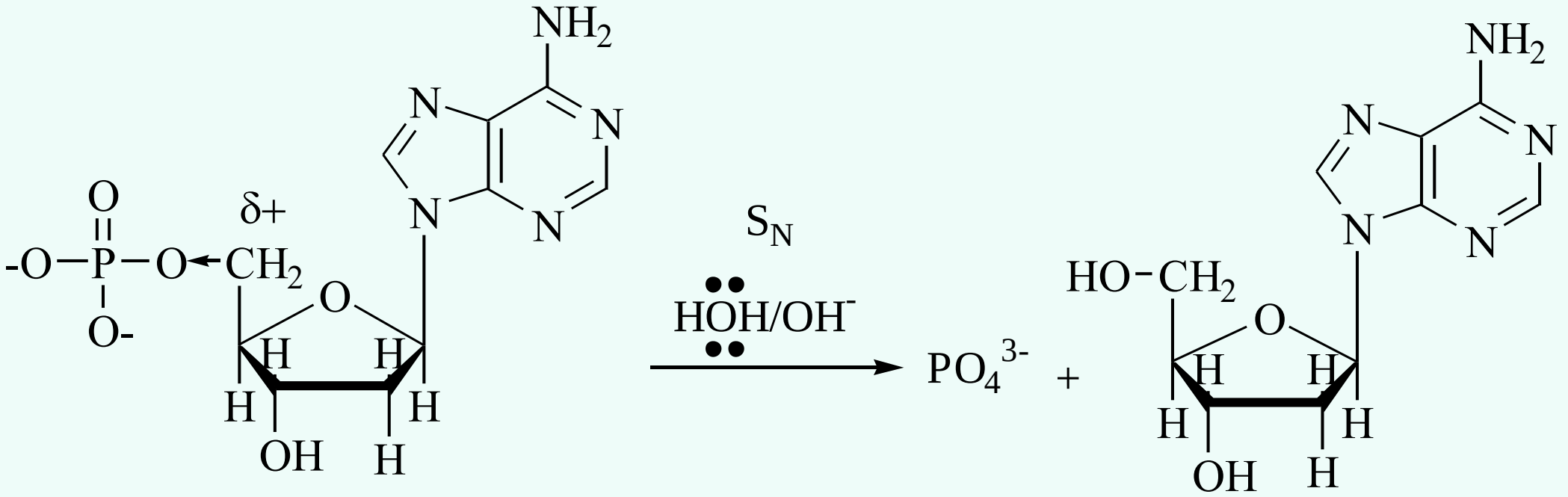
Cytidine 5'-monophosphate
5'-cytidylic acid



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

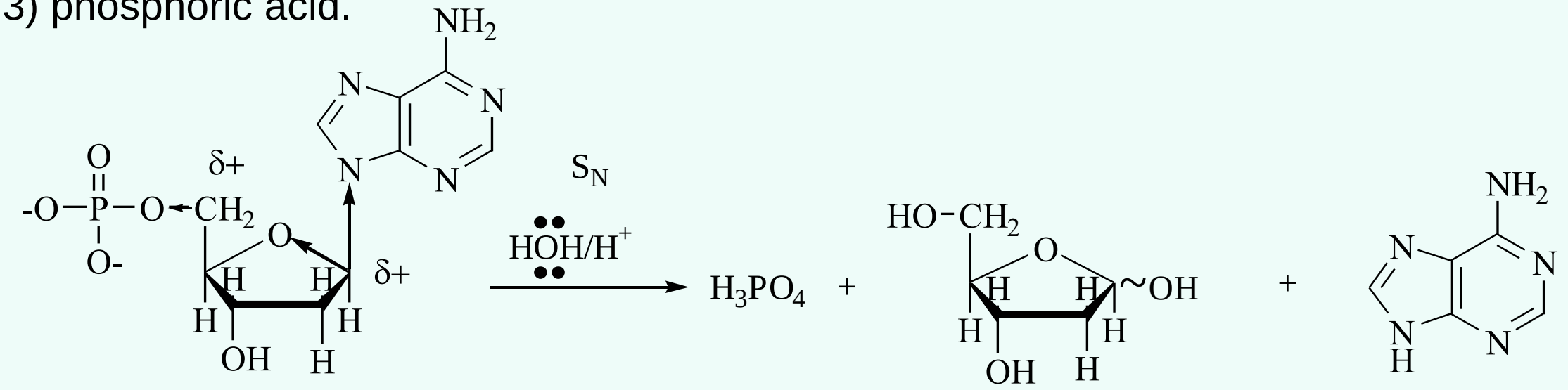
HYDROLYSIS IN ACIDIC SOLUTION

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.

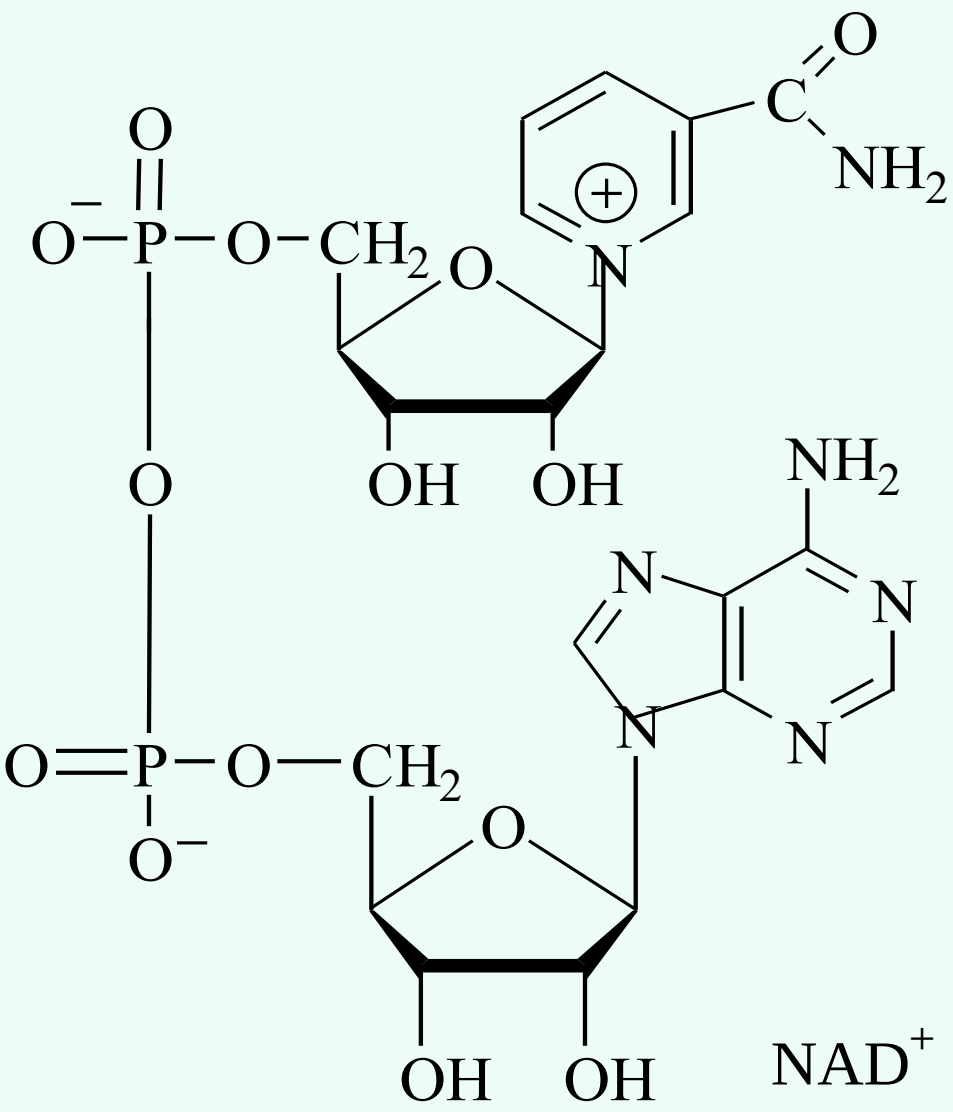


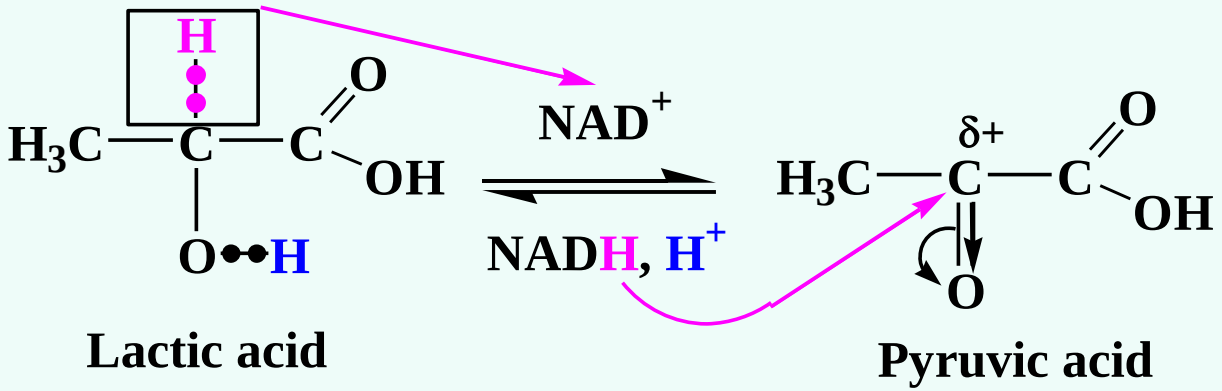
2'-Deoxyadenosine 5'-monophosphate
the nucleotide

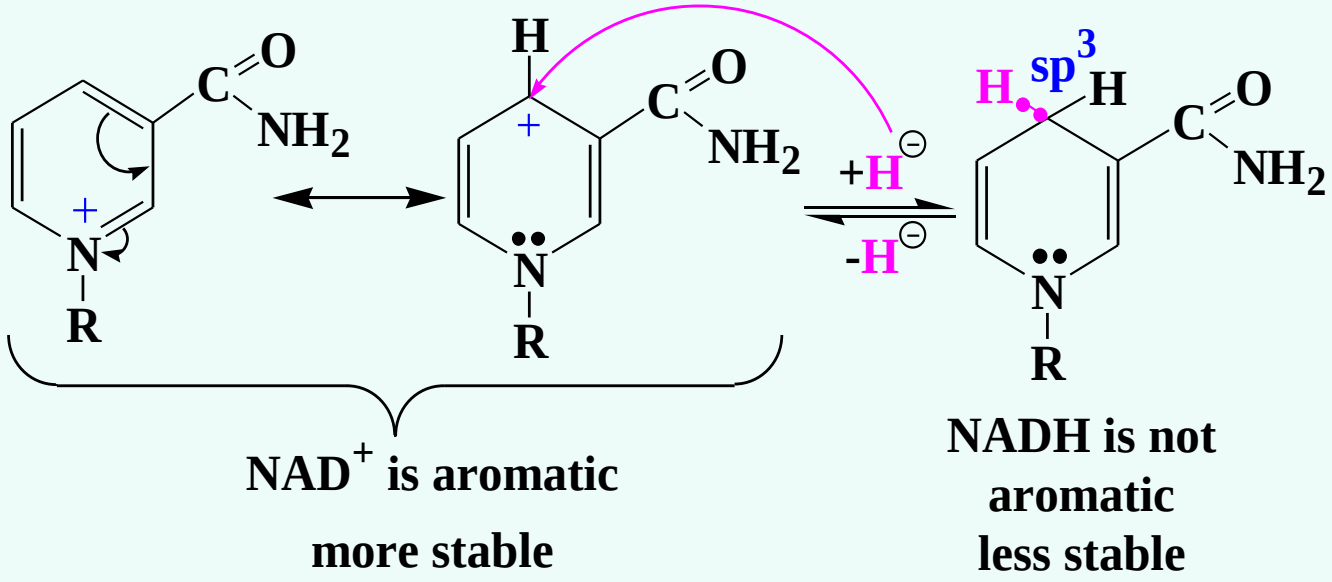
2-deoxy-D-ribose
the monosaccharide

Adenine
the heterocyclic base

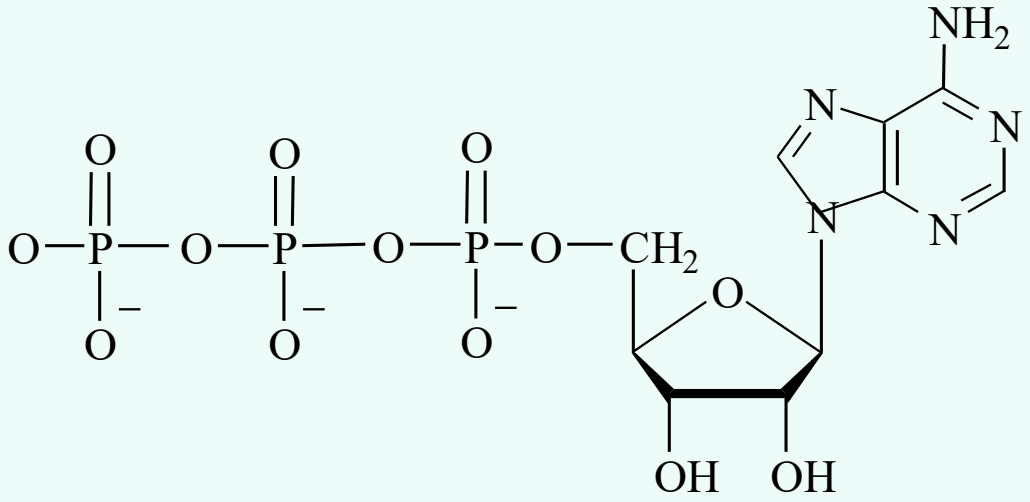
Coenzyme NAD$^+$.







5’-Triphosphate of adenosine (ATP).

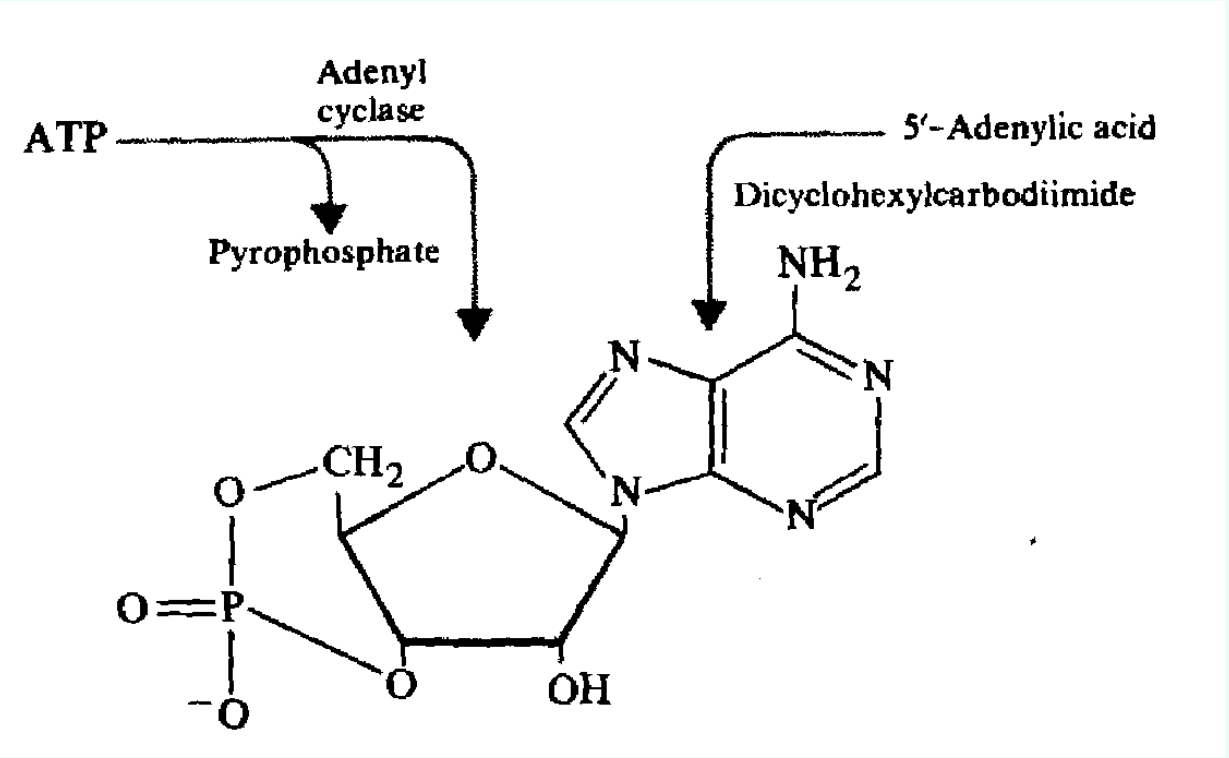


The 5'-triphosphate of adenosine is the important energy source, ATP.

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.*



DEOXYRIBONUCLEIC ACID: DNA PRIMARY STRUCTURE

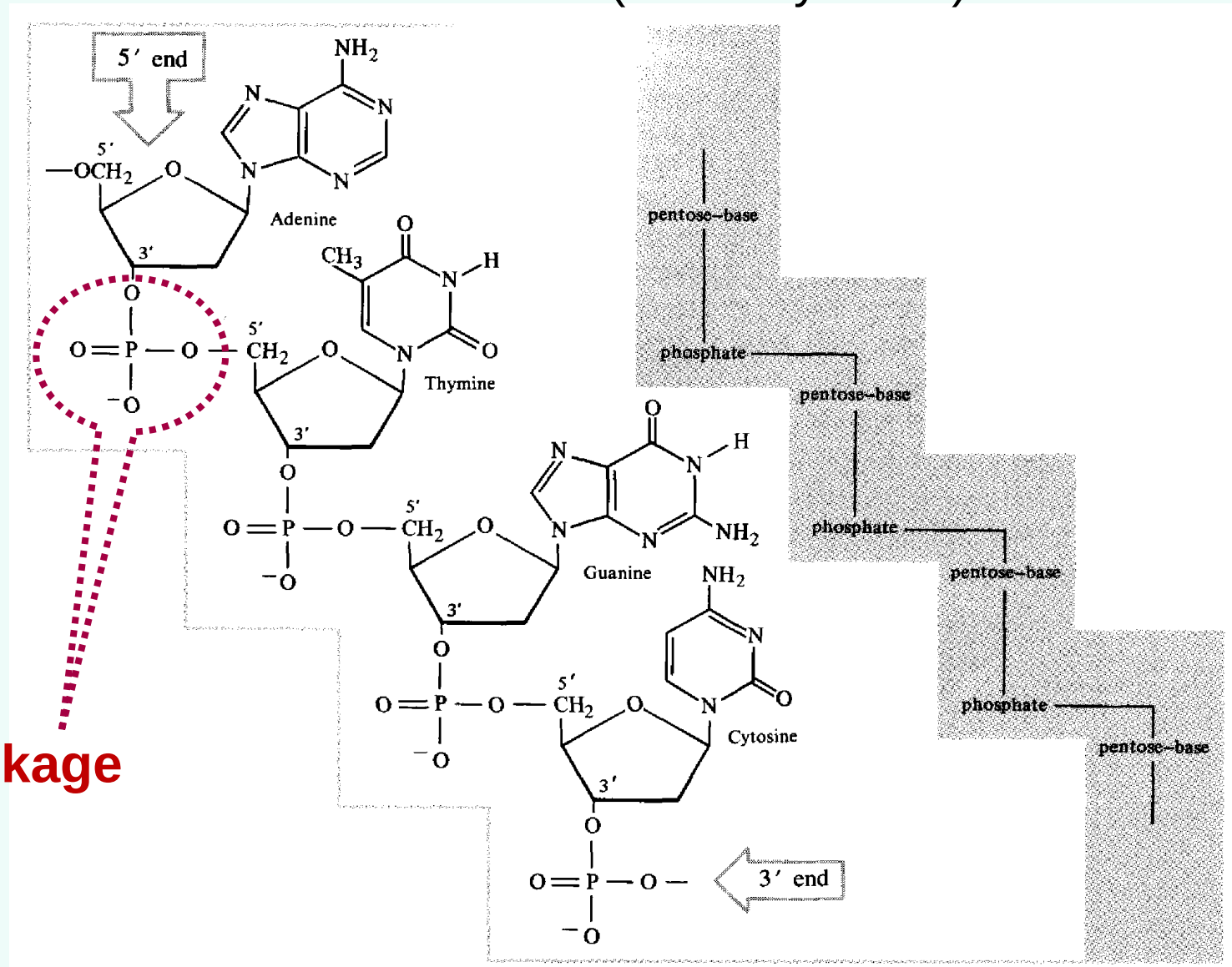
Nucleotides are the monomeric units of nucleic acids. Their connecting links are phosphate ester linkages. Phosphate esters link the 3'-OH of one ribose (or deoxyribose) with the 5'-OH of another.

The DNA contains the encoded genetic information.

RNA has a similar structure with two exceptions:

A hydroxyl replaces a hydrogen atom at the 2'-position of each ribose unit and uracil replaces thymine.

3`-5` Phosphate diester linkage



SECONDARY STRUCTURE OF DNA

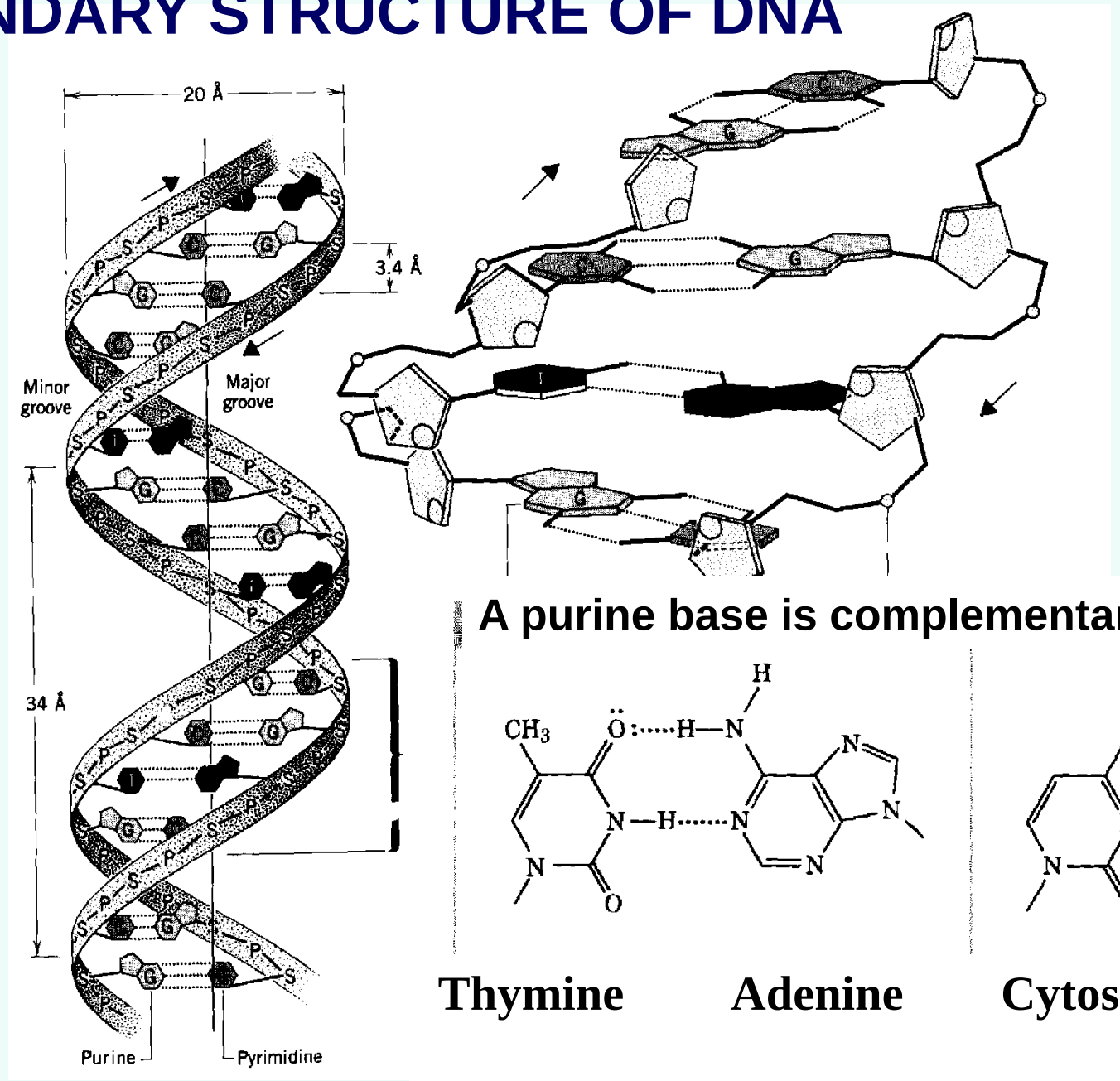


Diagram of the DNA double helix showing complementary base pairing. The arrows indicate the 3' →5' direction.

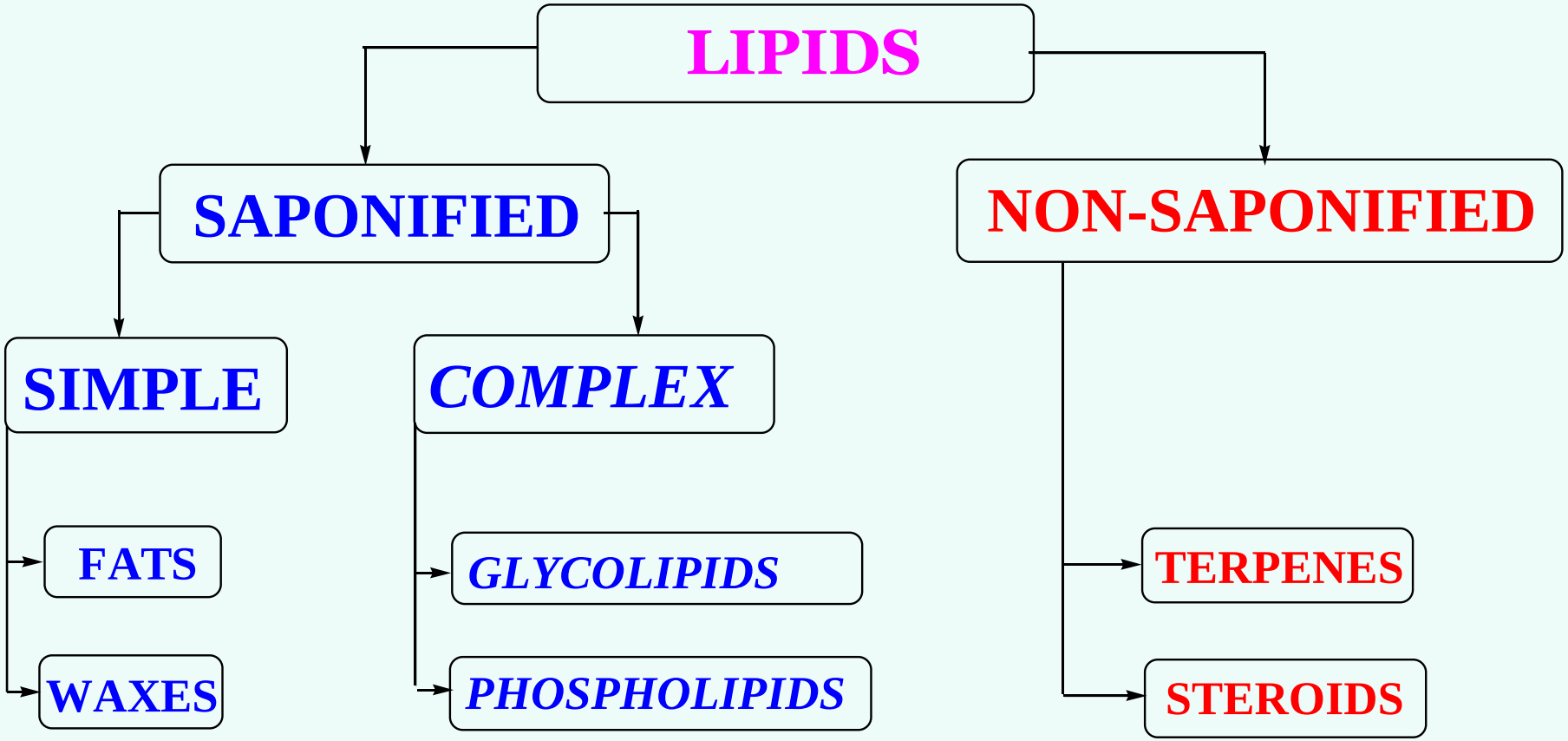
The repeat distance
10 nucleotide pair

A purine base is complementary for pyrimidine base:

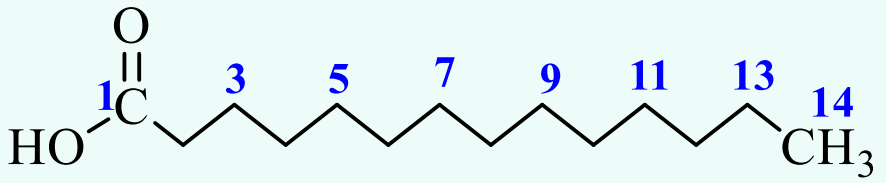
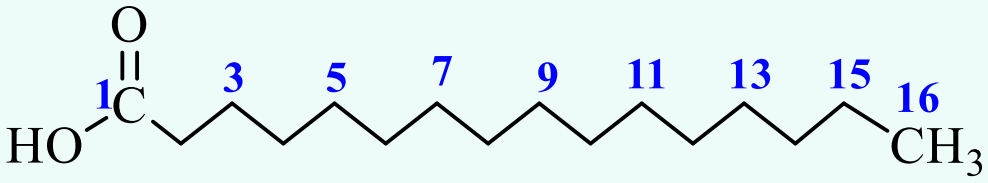
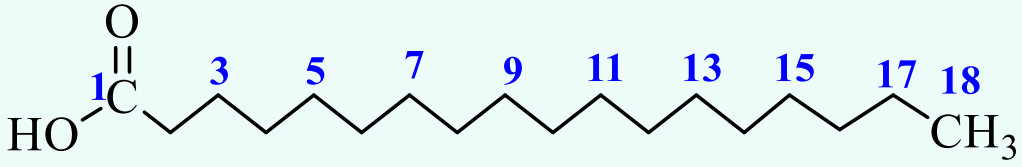
Thymine **Adenine** **Cytosine** **Guanine**

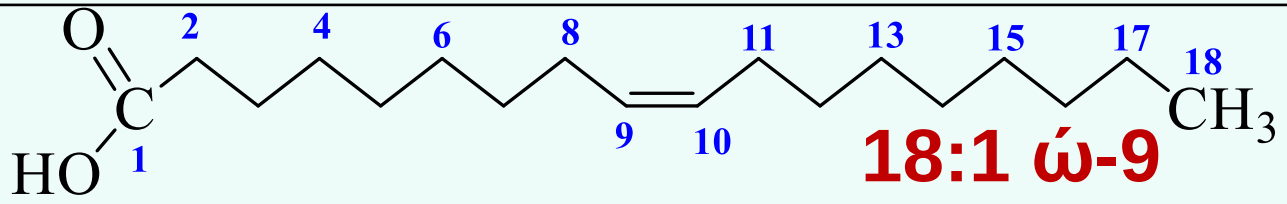
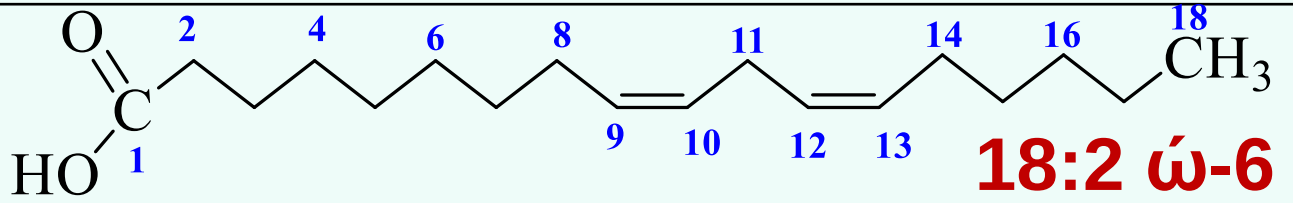
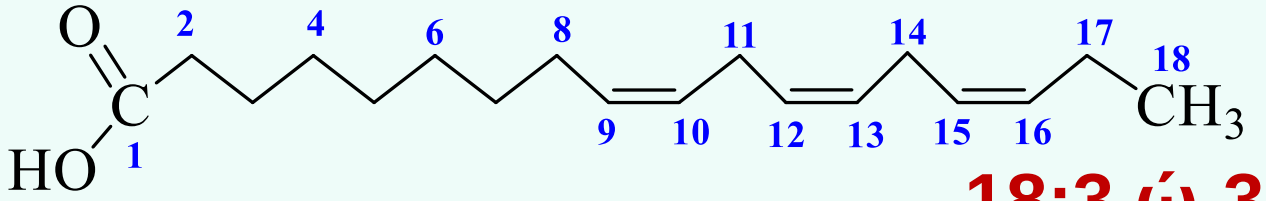
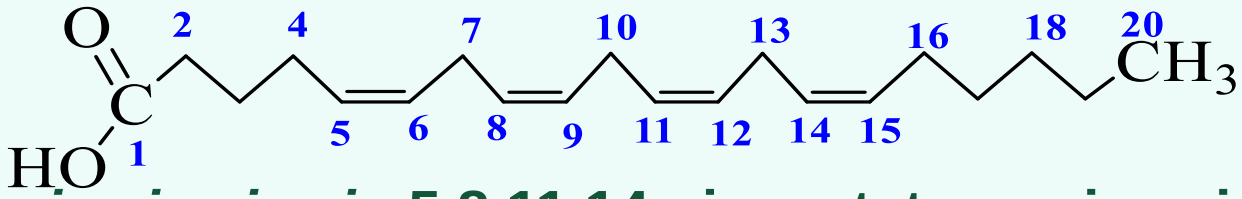
CLASSIFICATION OF LIPIDS

Lipids are compounds of biological origin that dissolve in nonpolar solvents, such as chloroform or diethyl ether. Lipids are classified according to hydrolyzation in basic solution. Thus, a lipids hydrolyzed in basic solution are called saponified lipids, and ones nonhydrolized are called non-saponified.



COMMON FATTY ACIDS

Saturated fatty carboxylic acid		Occurrence
(C_{14}); $C_{13}H_{27}COOH$ **Myristic acid**	 ***Tetradecanoic acid***	
(C_{16}); $C_{15}H_{31}COOH$ **Palmitic acid**	 ***Hexadecanoic acid***	Natural fats and oils, especially palm oil
(C_{18}); $C_{17}H_{35}COOH$ **Stearic acid**	 ***Octadecanoic acid***	Natural fats and oils, especially palm oil

Unsaturated fatty carboxylic acid		Occurrence
(C_{18}); $(\Delta 9)$ **$C_{17}H_{33}COOH$** **Oleic acid**	 **18:1 ώ-9** ***cis*-9-octadecenoic acid**	Natural fats and oils, especially olive oil
(C_{18}); $(\Delta 9,12)$ **$C_{17}H_{31}COOH$** **Linoleic acid**	 **18:2 ώ-6** ***cis,cis*-9,12-octadecadienoic acid**	Widespread, many seed oils
(C_{18}); $(\Delta 9,12,15)$ **$C_{17}H_{29}COOH$** **Linolenic acid**	 **18:3 ώ-3** ***cis,cis,cis*-9,12,15-octadecatrienoic acid**	All plant leaves, seed, soybean, rapeseed, linseed oils
(C_{20}); $(\Delta 5,8,11,14)$ **$C_{19}H_{31}COOH$** **Arachidonic acid**	 ***cis,cis,cis,cis*-5,8,11,14-eicosatetraenoic acid**	Animal cell membranes **20:4 ώ-6**

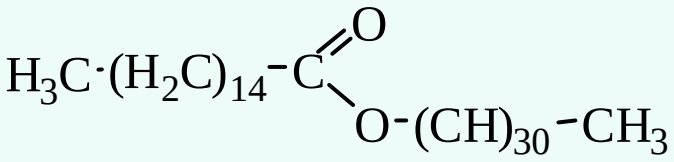
WAXES

Most waxes are esters of long-chain fatty acids and long chain alcohols. Beside of this, waxes always contain free fatty acids, free long-chain alcohols and long-chain hydrocarbons.

Beeswax is animal wax; it is produced by specific bee's glands and obtained from honeycomb and wax growths in hives. Beeswax is mixture of esters (72%), saturated unbranched alkanes C_{21}-C_{35} (12-15%) and fatty acids C_{16}-C_{36} (15%).

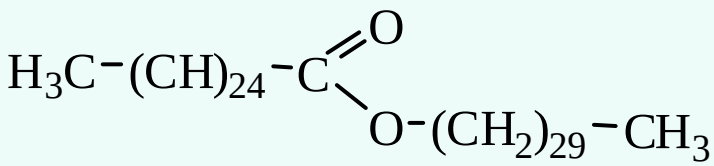
Carnauba wax is vegetable wax; it is found as protecting coating on leaves of palm-tree Copernicia cerifera.

Beeswax

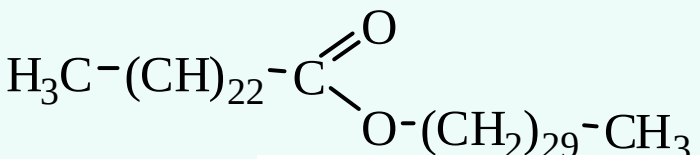


myricyl palmitate

Carnauba wax



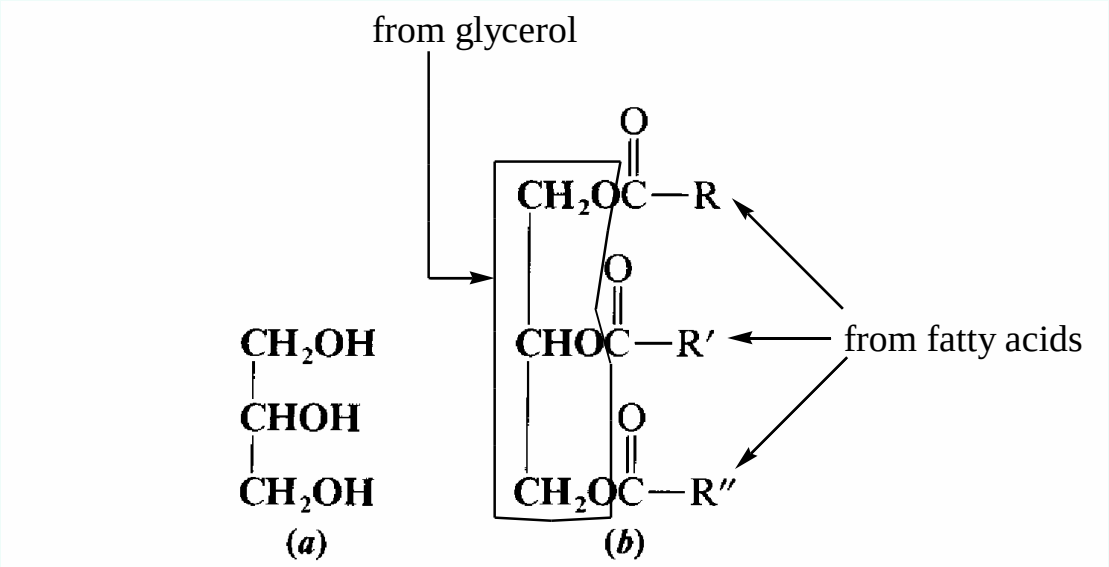
myricyl cerotate

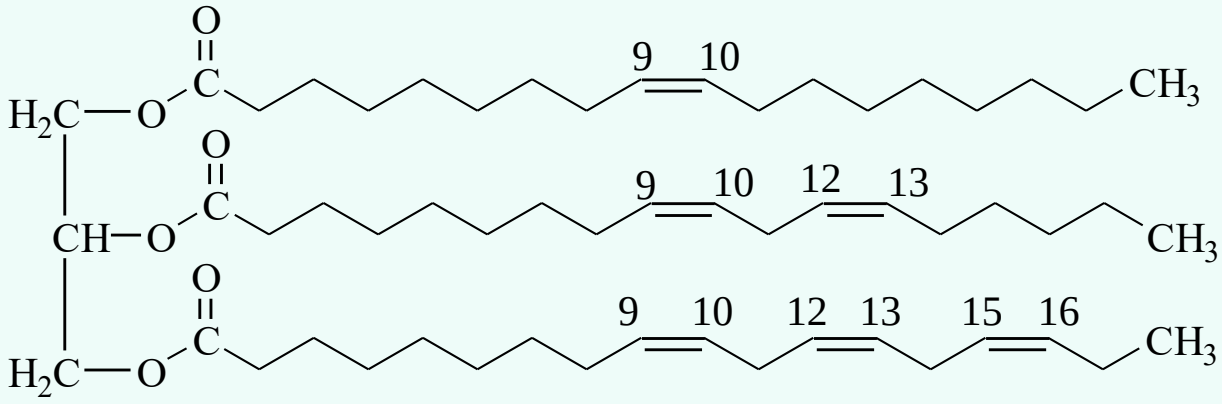


myricyl lignocerate

TRIACYLGLYCEROLS

- Only a small portion of the total lipid fraction consists of long-chain carboxylic acids. Most of the carboxylic acids of biological origin are found as *esters of glycerol,* that is, as triacylglycerols.





1-O-oleoyl-2-O-linoleoyl-3-O-linolenoylglycerol

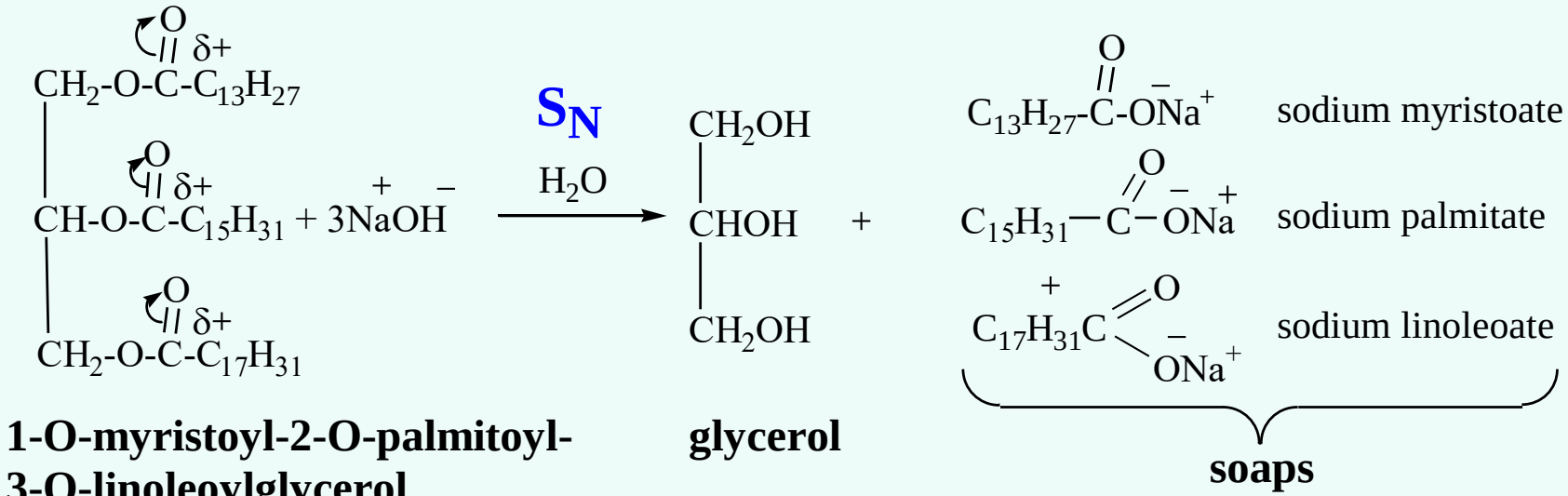
Triacylglycerols:

1. oils – triacylglycerols with a high proportion of unsaturated and polyunsaturated fatty acids, that a liquids at room temperature.

2. ***fats*** –triacylglycerols made up of saturated fatty acids, that a solids at room temperature.

HYDROLYSIS OF TRIACYLGLYCFROLS

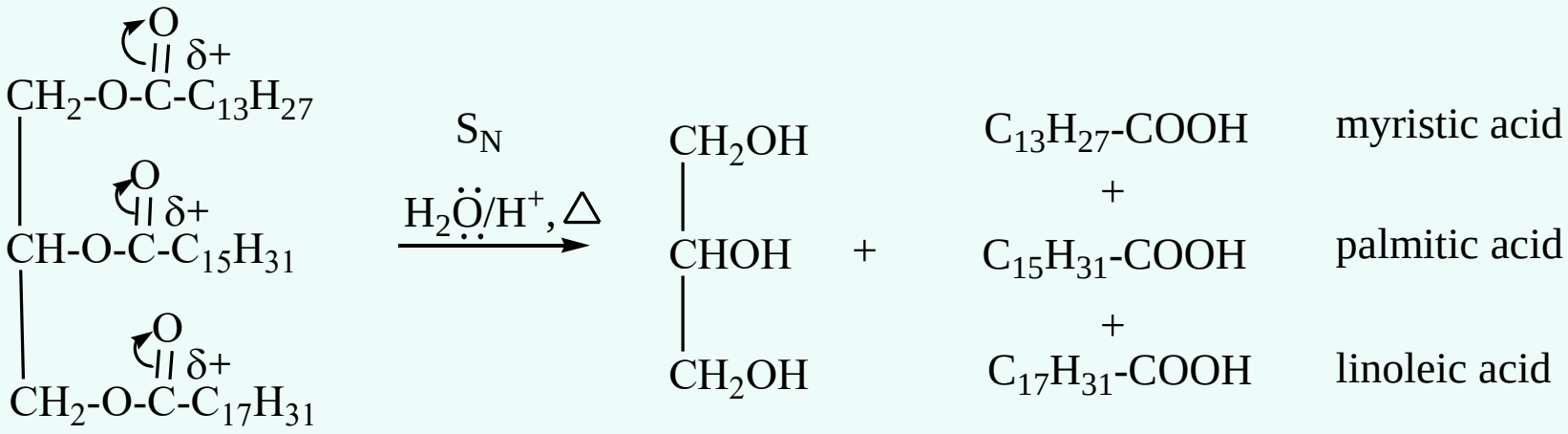
Alkaline hydrolysis (i.e., saponification) of triacylglycerols produces glycerol and a mixture of salts of long-chain carboxylic acids



1-O-myristoyl-2-O-palmitoyl-3-O-linoleoylglycerol

glycerol

Hydrolysis in acidic solution of a fat or oil produces a mixture of fatty acids



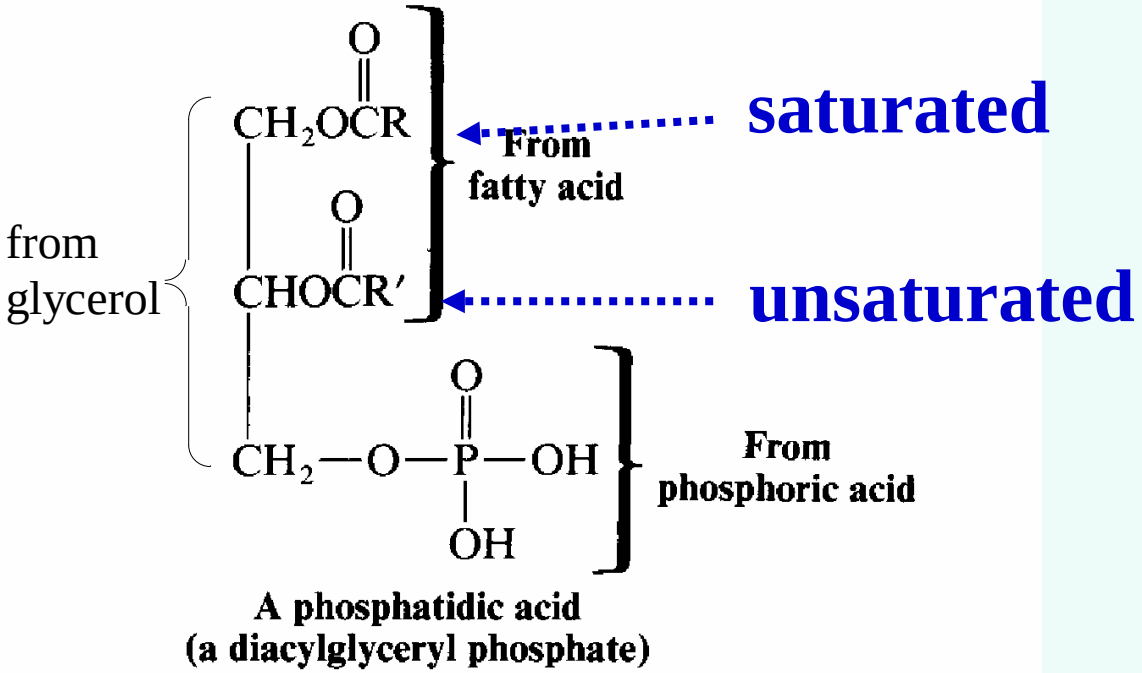
1-O-myristoyl-2-O-palmitoyl-3-O-linoleoylglycerol

glycerol

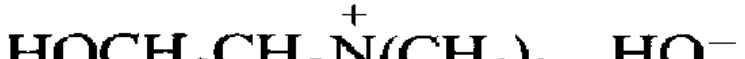
PHOSPHOLIPIDS AND CELL MEMBRANES

- Another large class of lipids are those *called* ***phospholipids***, *which are* ***complex saponified lipids***.

- **In *phosphatides***, the phosphate group of a phosphatidic acid is bound through another phosphate ester linkage to one of the following nitrogen-containing compounds.

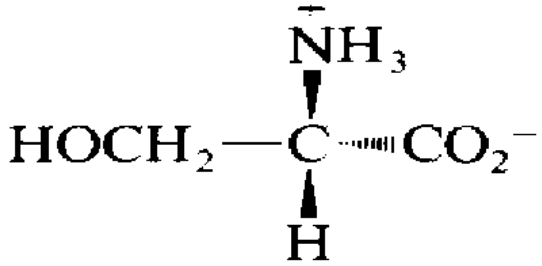


A phosphatidic acid (a diacylglyceryl phosphate)



Choline

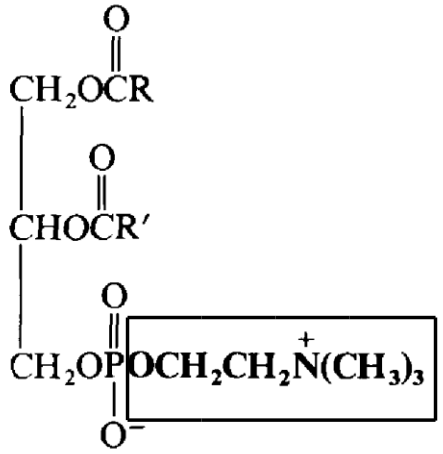
2-Aminoethanol (ethanolamine)



L-Serine

PHOSPHATIDES

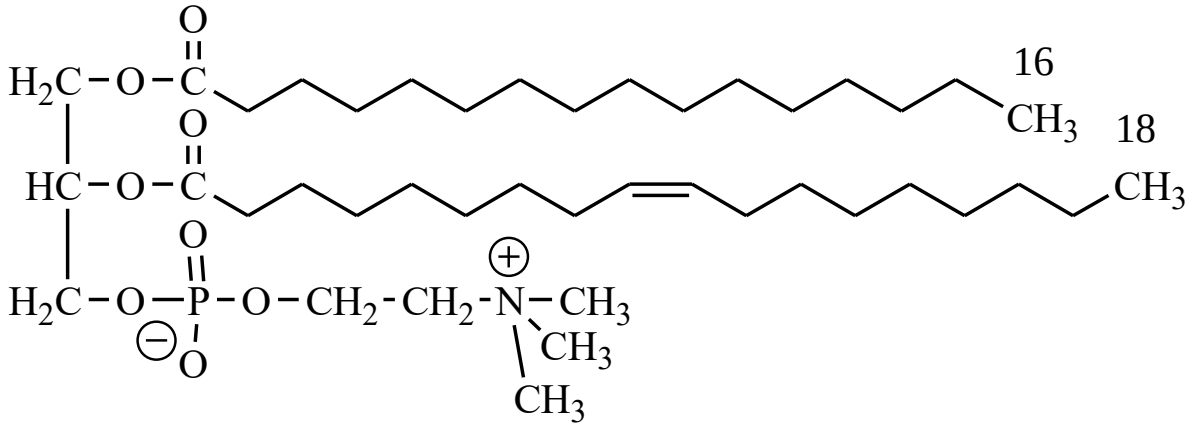
Lecithins



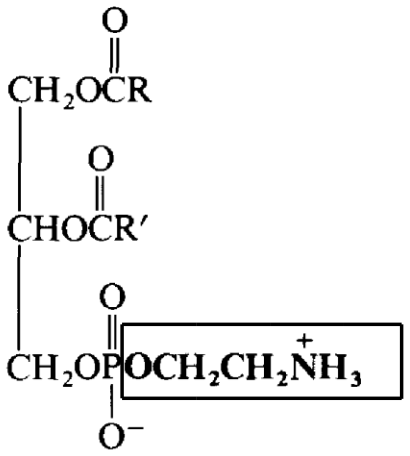
(from choline)

R is saturated and R′ is unsaturated

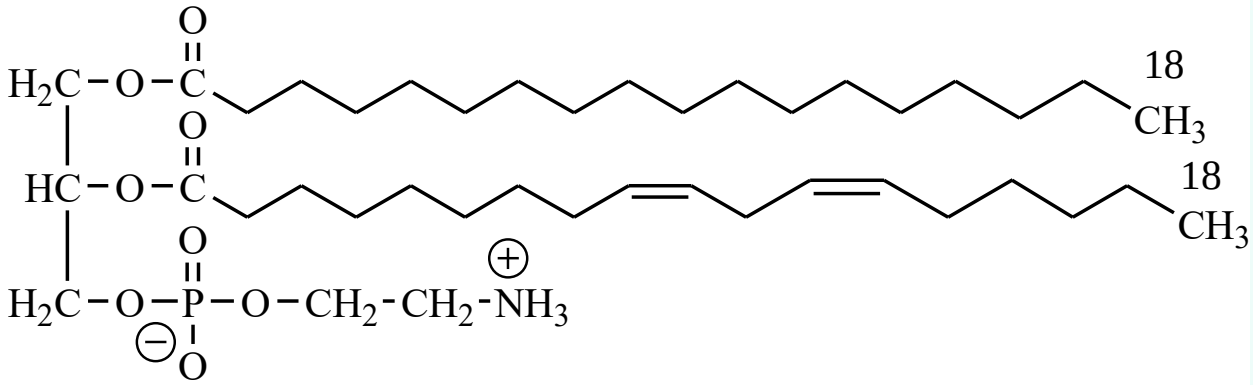
examples



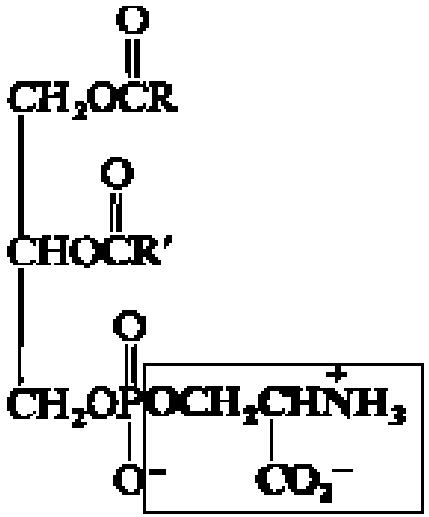
Cephalins



(from 2-aminoethanol)

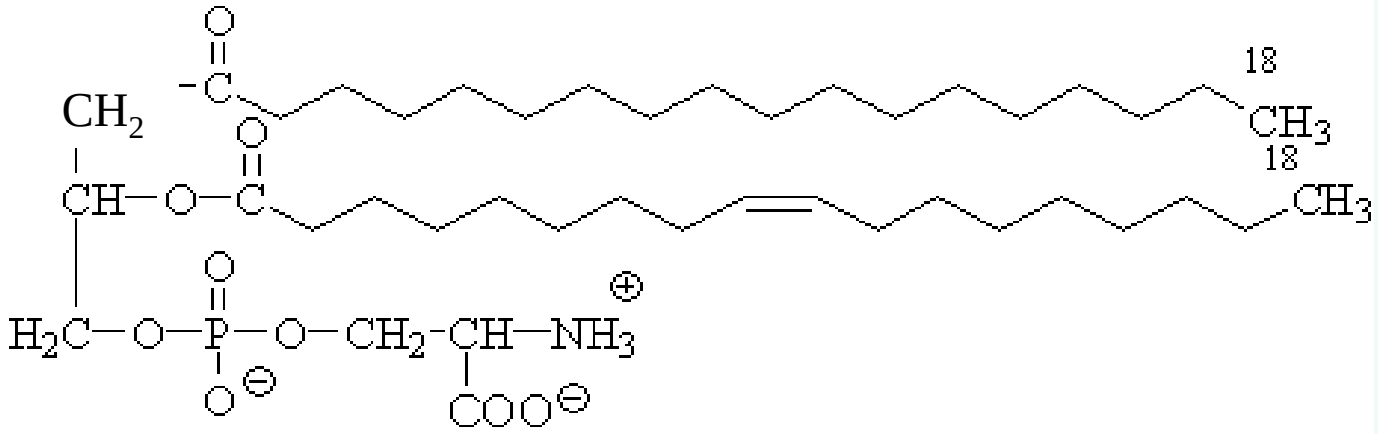


Phosphatidyl Serines



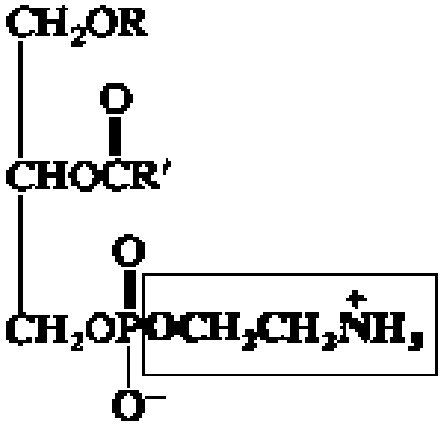
(from L-serine)

Examples:

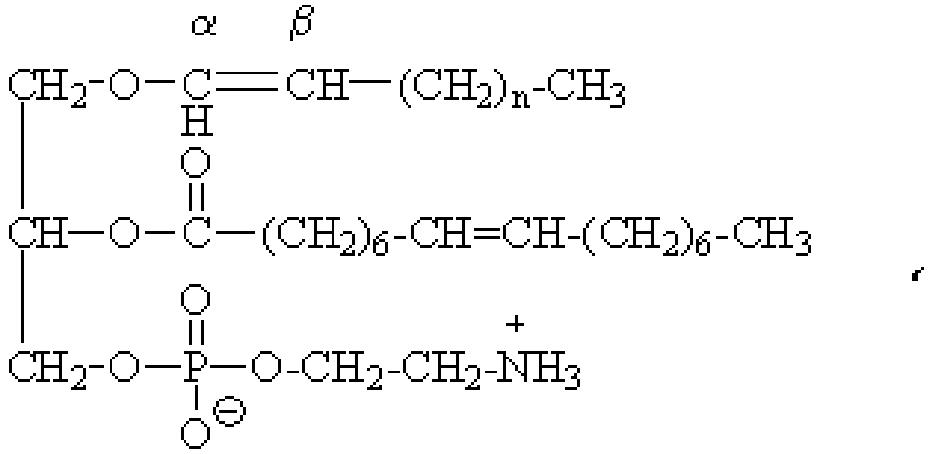


R is saturated and R′ is unsaturated

Plasmalogens



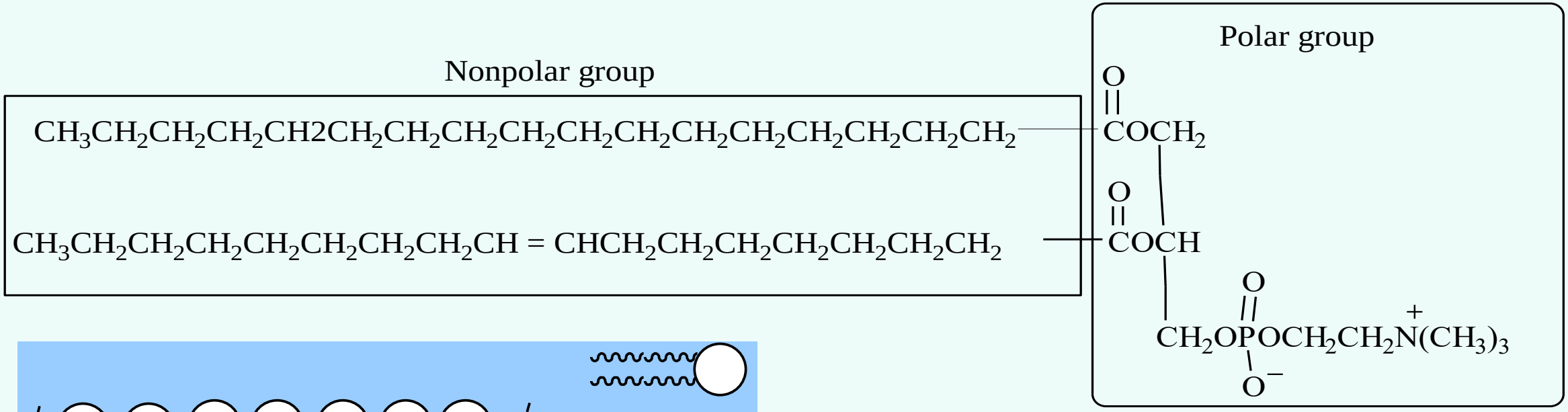
(from 2-aminoethanol) **or** **$OCH_2CH_2\overset{+}{N}(CH_3)_3$** **(from choline)**

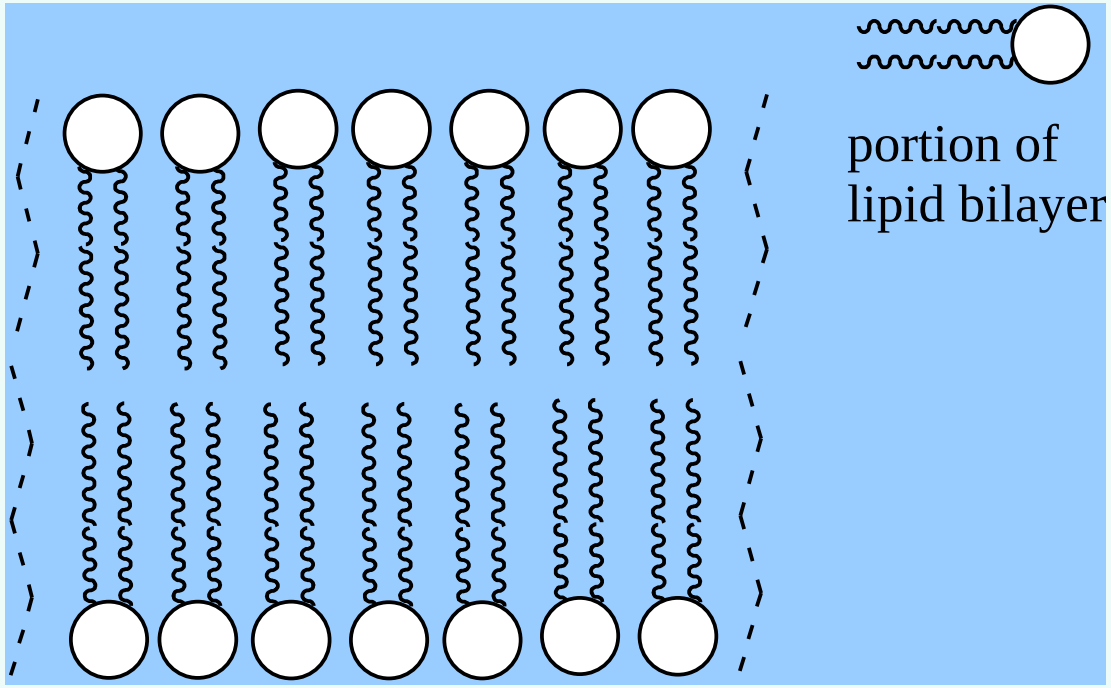


R is —CH═CH$(CH_2)_nCH_3$ (this linkage is that of an *α,β*-unsaturated ether)

R′ is that of an unsaturated fatty acid

POLAR AND NONPOLAR SECTIONS OF A PHOSPHATIDE.

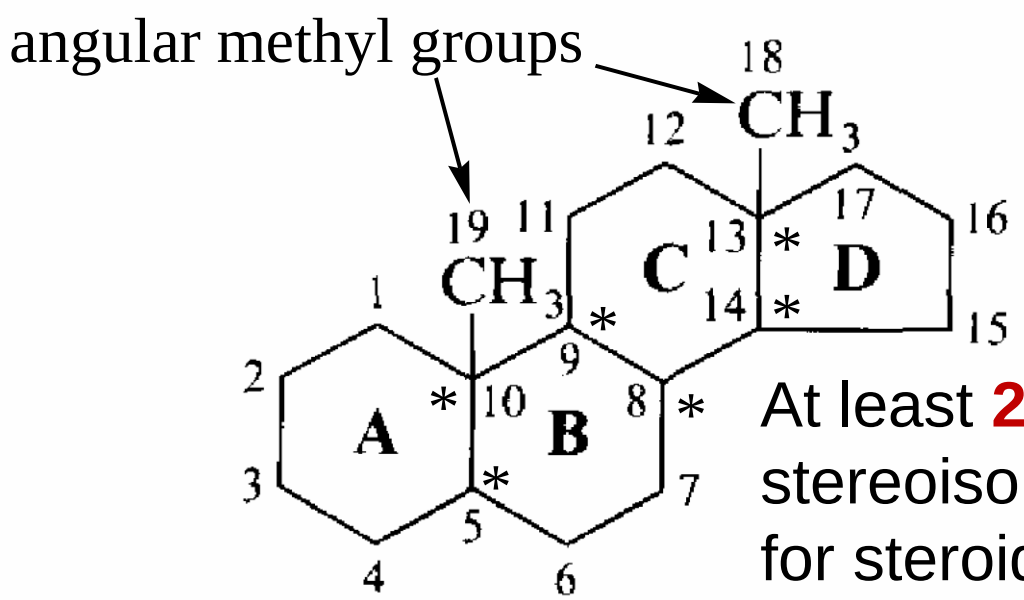




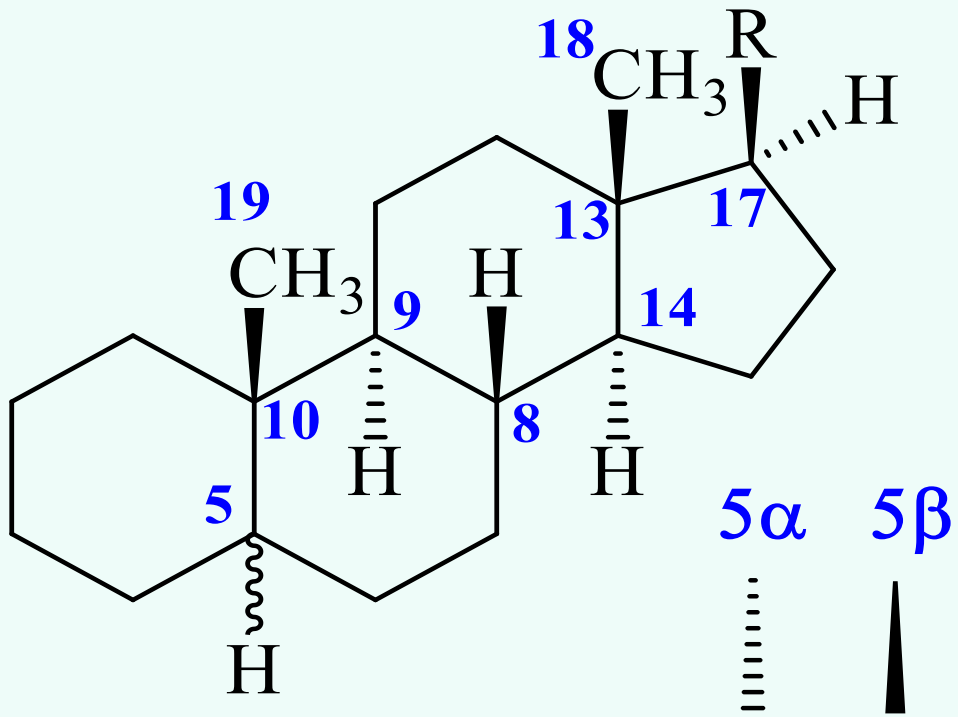
The hydrophilic and hydrophobic portions of phosphatides make them perfectly suited for one of their most important biological functions: They form a portion of a structural unit that creates an interface between an organic and an aqueous environment. This structure is found in cell walls and membranes where phosphatides are often found associated with proteins and glycolipids.

STEROIDS. STRUCTURE AND SYSTEMATIC NOMENCLATURE

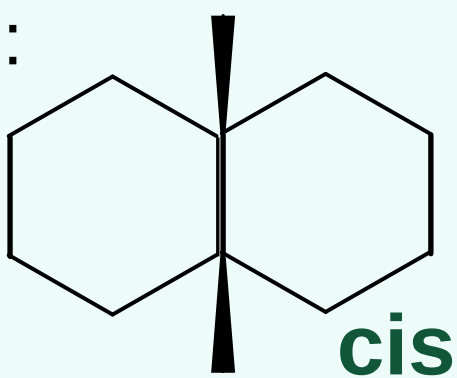
Steroids are derivatives of the perhydrocyclopentanophenanthrene ring system.



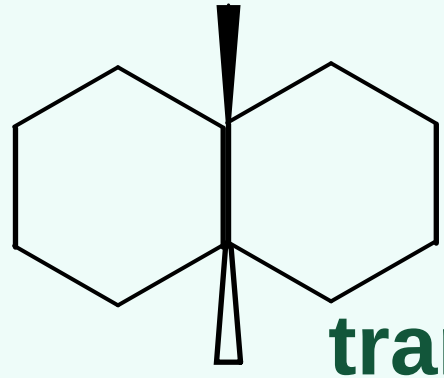
At least $2^6=64$ stereoisomers for steroids are possible



Cis- and trans joints of cycles:



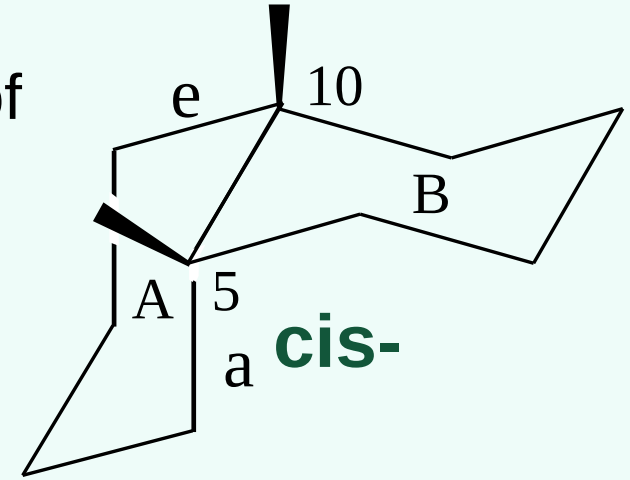
cis-



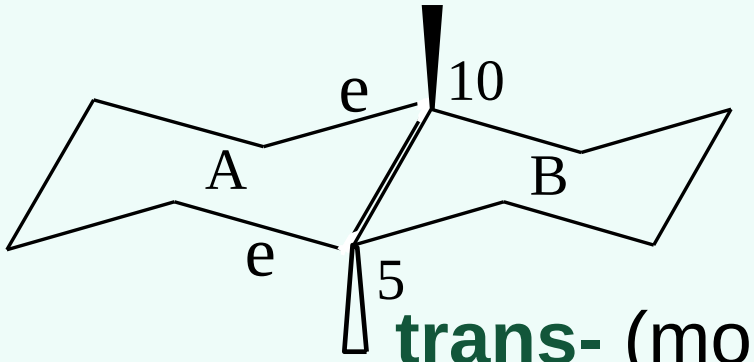
trans-

CONFORMATIONS OF STEROIDS

Conformations of cycles A and B

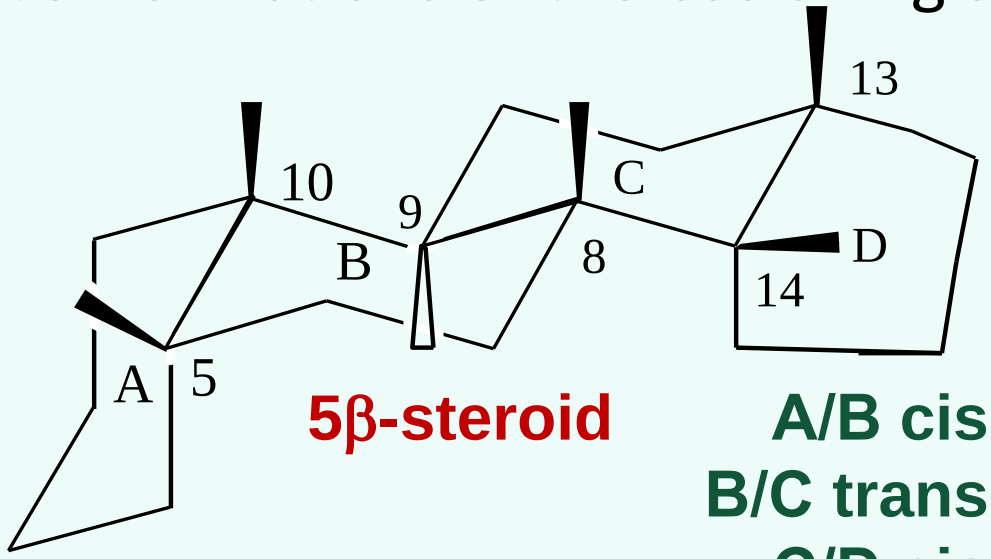


cis-



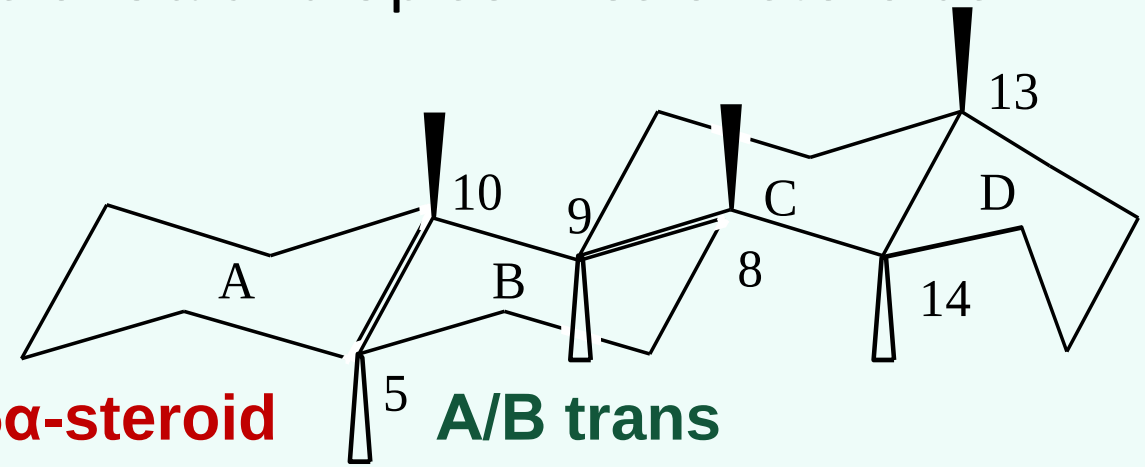
trans- (more stable)

Conformations of the basic ring systems of 5α and 5β serines of steroids



5β-steroid

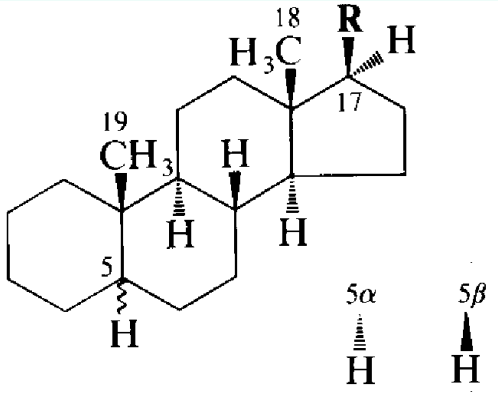
A/B cis
B/C trans
C/D cis



5α-steroid

A/B trans
B/C trans
C/D trans

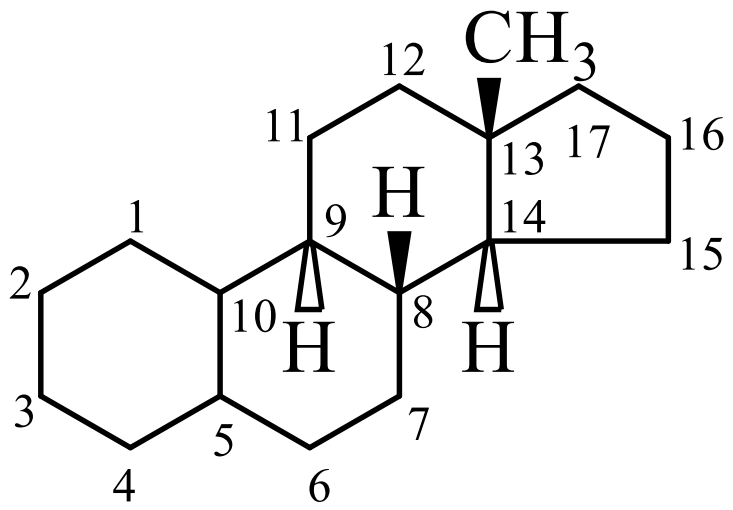
Nomenclature of steroids



R	NAME
—H	Androstane
—H (with —H also replacing —$^{19}CH_3$)	Estrane
—$^{20}CH_2{}^{21}CH_3$	Pregnane
—$^{20}CH(^{21}CH_3)^{22}CH_2{}^{23}CH_2{}^{24}CH_3$	Cholane
—$^{20}CH(^{21}CH_3)^{22}CH_2{}^{23}CH_2{}^{24}CH_2{}^{25}CH(^{27}CH_3)^{26}CH_3$	Cholestane

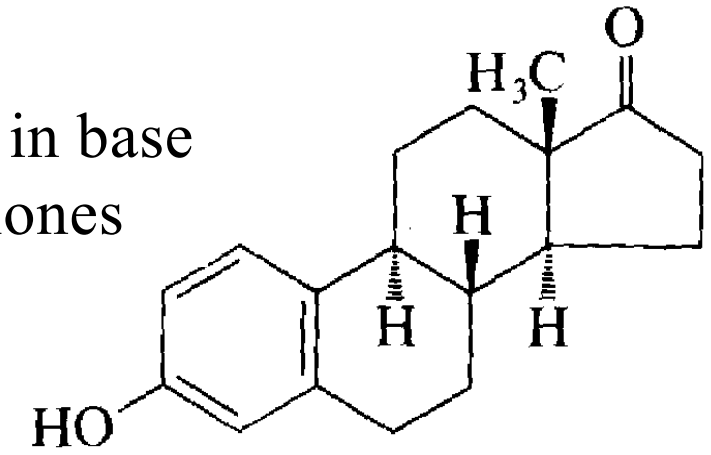
Family of steroids	Names	IUPAC names
Estrogens	Estrone Estradiol	3-hydroxy-1,3,5(10)-estratrien –17-one 1,3,5(10)-estratriene-3,17β-diol
Androgens	Androsterone Testosterone	3α-hydroxy-5α-androstan-17-one 17β- hydroxy-4-androsten-3-one
Progestin	Progesterone	4-pregnene-3,20-dione
Adrenocortical hormones	Cortisone Cortisol	17α,21-dihydroxy-4-pregnene-3,11,20-trione 17α, 11β, 21-trihydroxy-4-pregnen-3,20-dion
Bile acid	Cholic acid	3α,7α,12α-trihydroxy-5β-cholan-24-oic acid
Sterols	Cholesterol Ergosterol	5-cholesten-3β-ol 24-methyl-5,7,22-cholestatrien-3β-ol

SEX HORMONES. THE FEMALE SEX HORMONES

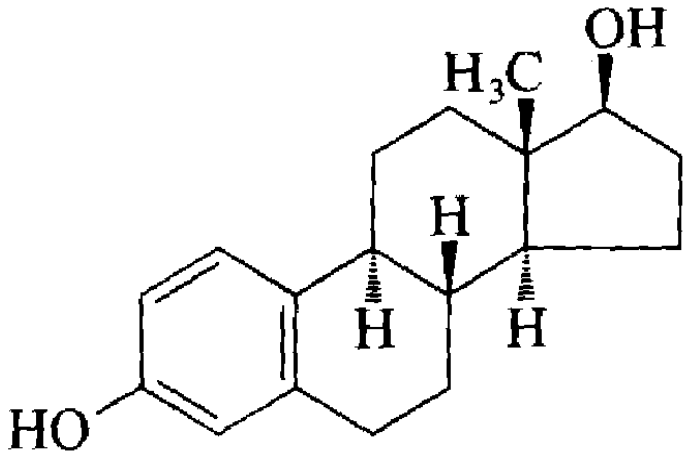


estrane is hydrocarbon in base of the female sex hormones

Estradiol is secreted by the ovaries and promotes the development of secondary female characteristics



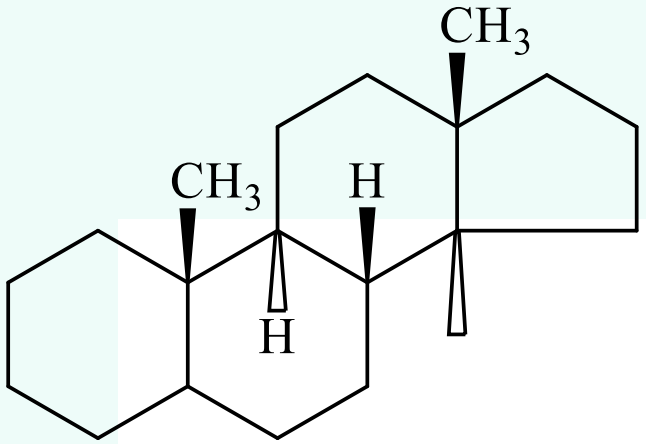
Estrone
[3-hydroxy-1,3,5(10)-estratrien-17-one]



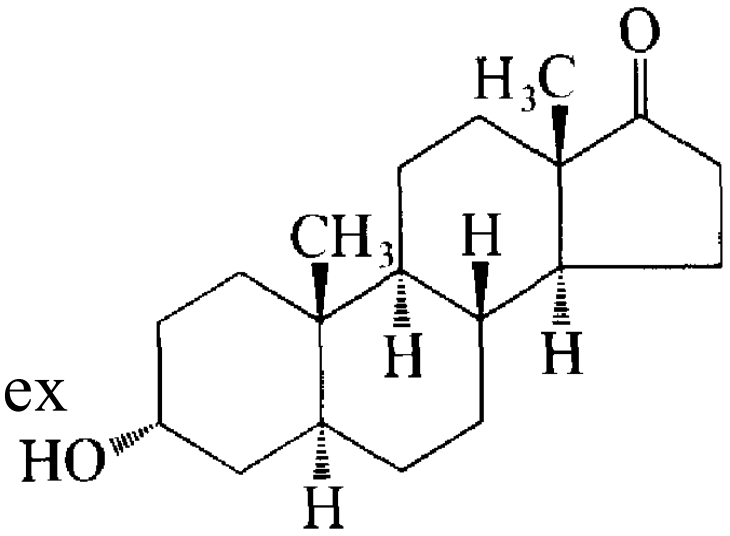
Estradiol
[1,3,5(10)-estra-triene-3,17β-diol]

SEX HORMONES. THE MALE SEX HORMONES

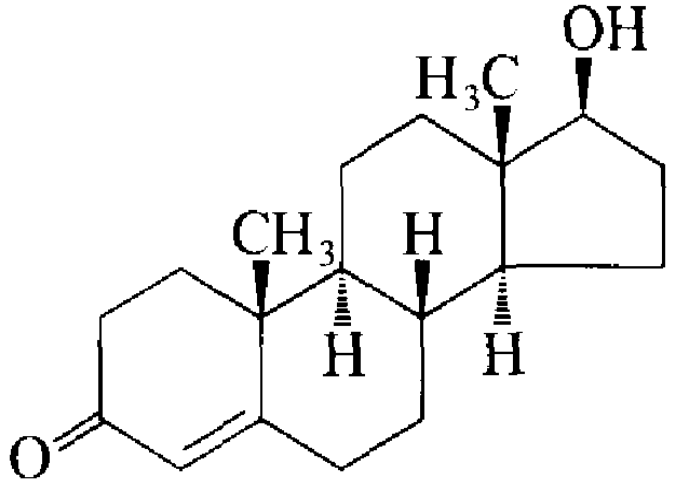
Testosterone is secreted by the testes and promotes the development of secondary male characteristics



androstane is hydrocarbon in base of the male sex hormones



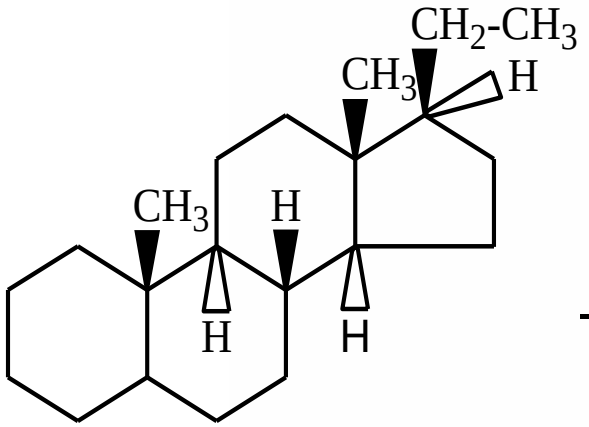
Androsterone
(3α-hydroxy-5α-androstan-17-one)



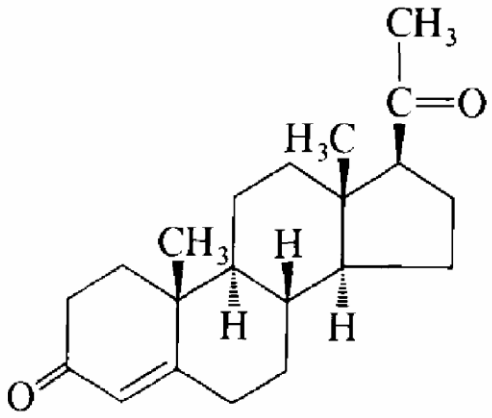
Testosterone
(17β-hydroxy-4-androsten-3-one)

PREGNANCY HORMONE

Continued secretion of progesterone is necessary for the completion of the pregnancy

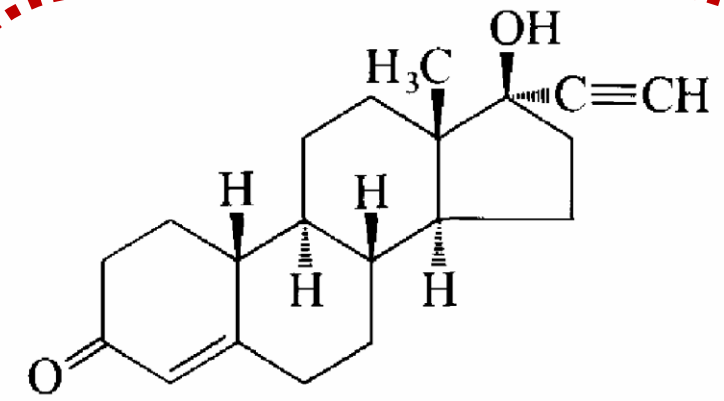


pregnane is hydrocarbon in base of progestins

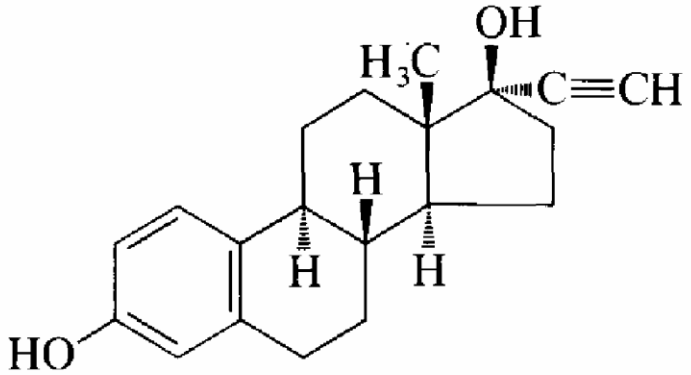


Progesterone
(4-pregnene-3,20-dione)

Synthetic estrogens are often used in oral contraceptives in combination with synthetic progestins. A very potent synthetic estrogen is the compound called *ethynylestradiol* or *novestrol.*



Norethindrone
(17α-ethynyl-17-β-hydroxy-4-estren-3-one)
sinthetic progestine

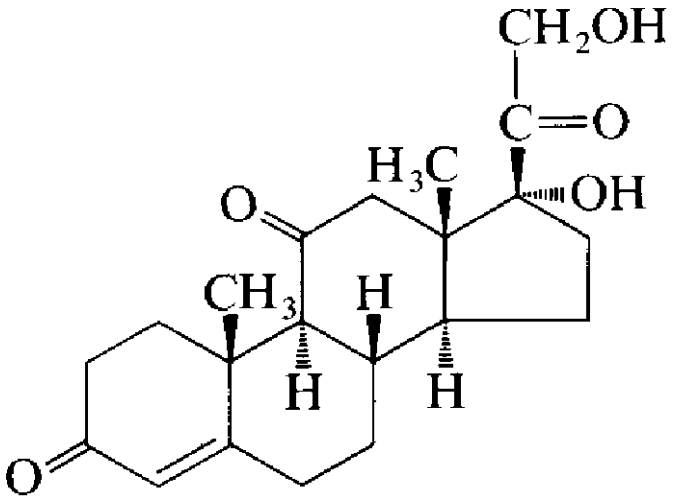


Ethynylestradiol
[17α-ethynyl-1,3,5(10)-estratriene-3,17β-diol]
sinthetic estrogen

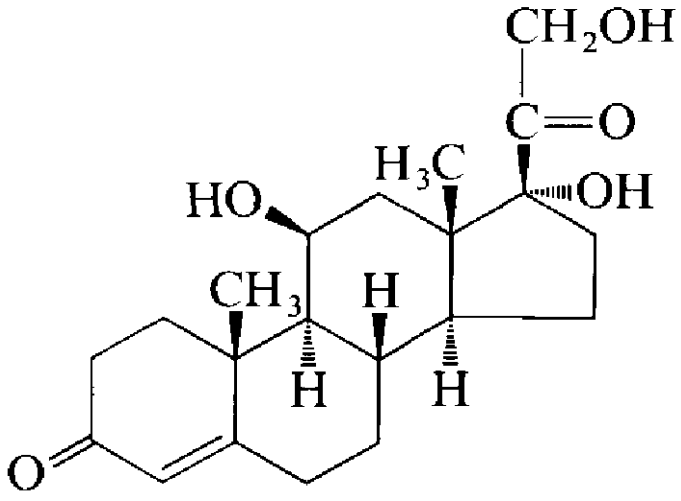
ADRENOCORTICAL HORMONES

At least 28 different hormones have been isolated from the adrenal cortex.

Pregnane is a base of adrenocortical hormones:

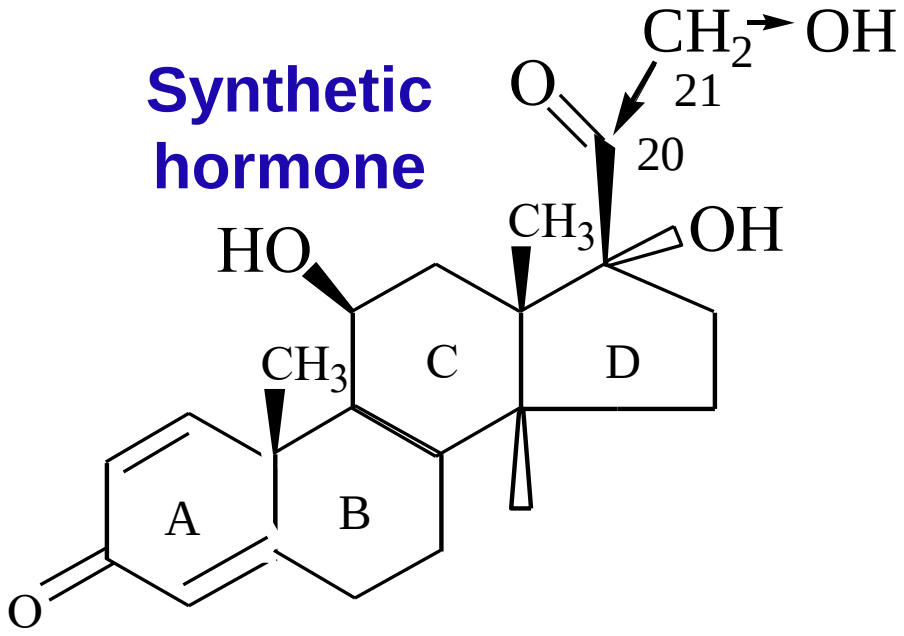


Cortisone
(17α,21-dihydroxy-4-pregnene-3,11,20-trione)



Cortisol
(11β,17α,21-trihydroxy-4-pregnene-3,20-dione)

Synthetic hormone

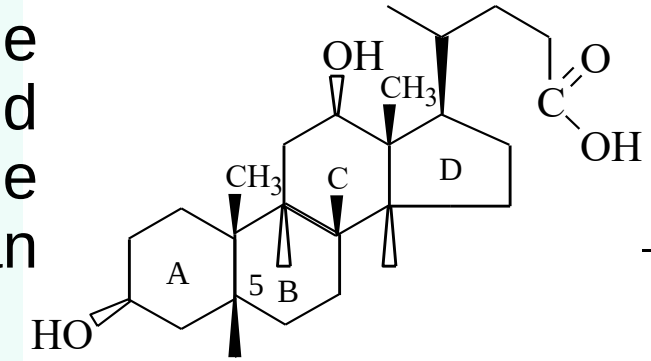


Prednisolone: **11β, 17α, 21-trihydroxypregnadiene-1,4-dione-3,20**

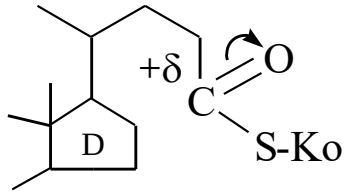
Most of the adrenocortical steroids have an oxygen function at position 11 (a keto group in cortisone, for example, and a β-hydroxyl in cortisol). **Cortisol** is the major hormone synthesized by the **human adrenal cortex**. The adrenocortical steroids are apparently involved in the regulation of a large number of biological activies including carbohydrate, protein, and lipid metabolism, water and electrolyte balance, and reactions to allergic and inflammatory phenomena.

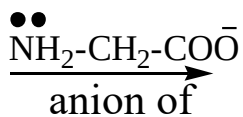
Bile acids

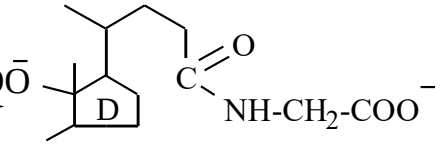
Cholic acid is the most abundant acid obtained from the hydrolysis of human or ox bile.



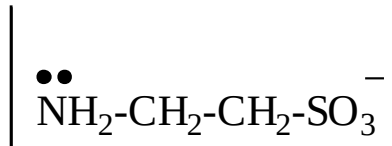
5β–steroid

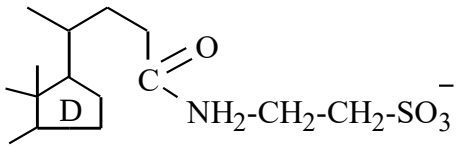




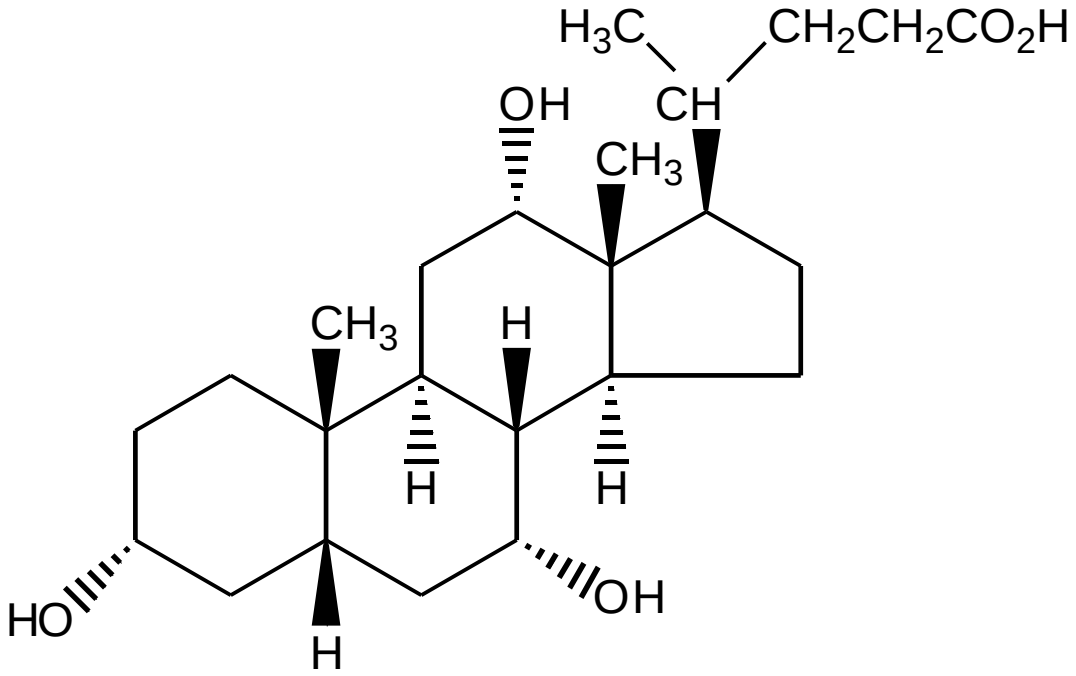


anion of glycocholic acid





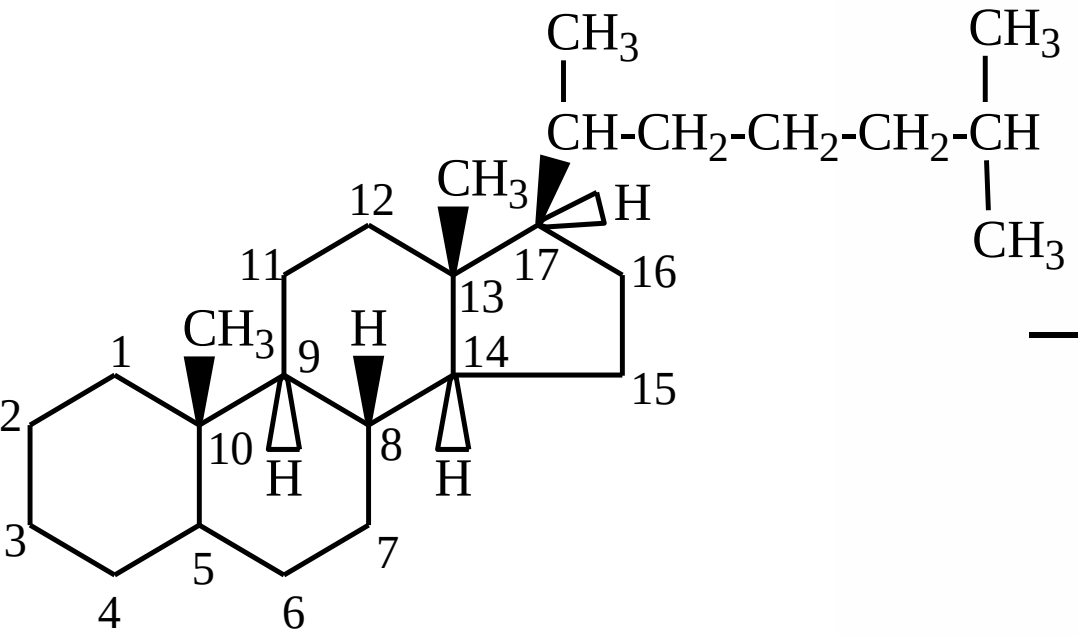
anion of taurocholic acid



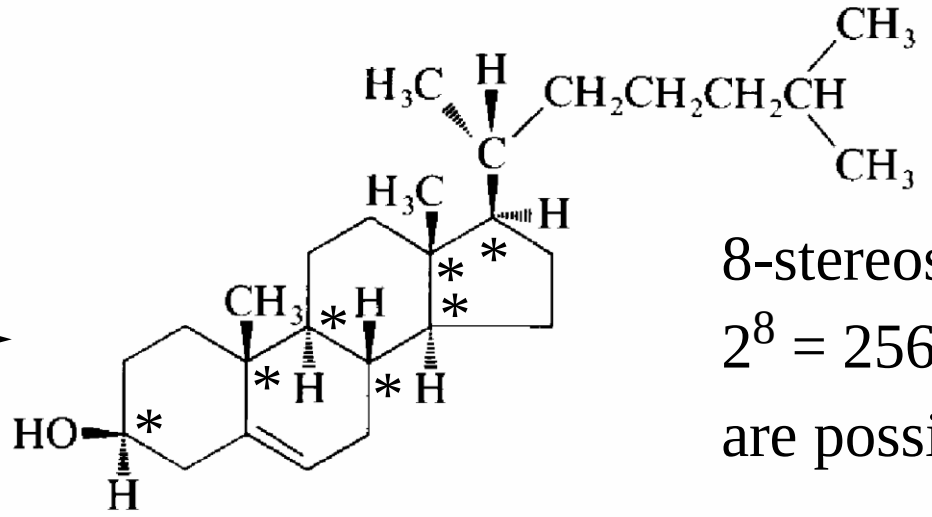
Cholic acid

Bile is produced by the liver and stored in the gall-bladder. When secreted into the small intestine, bile emulfyes lipids by acting as a soap. This action aids in the digestive process.

STEROLS. CHOLESTEROL



cholestane is hydrocarbon in base of cholesterol



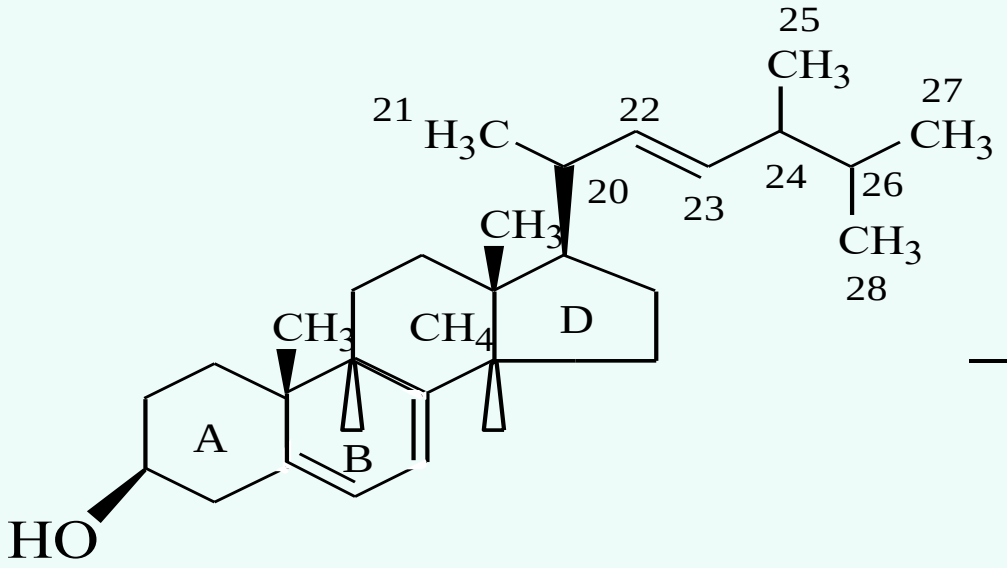
5-Cholesten-3β-ol
(absolute configuration of cholesterol)

8-stereosehters

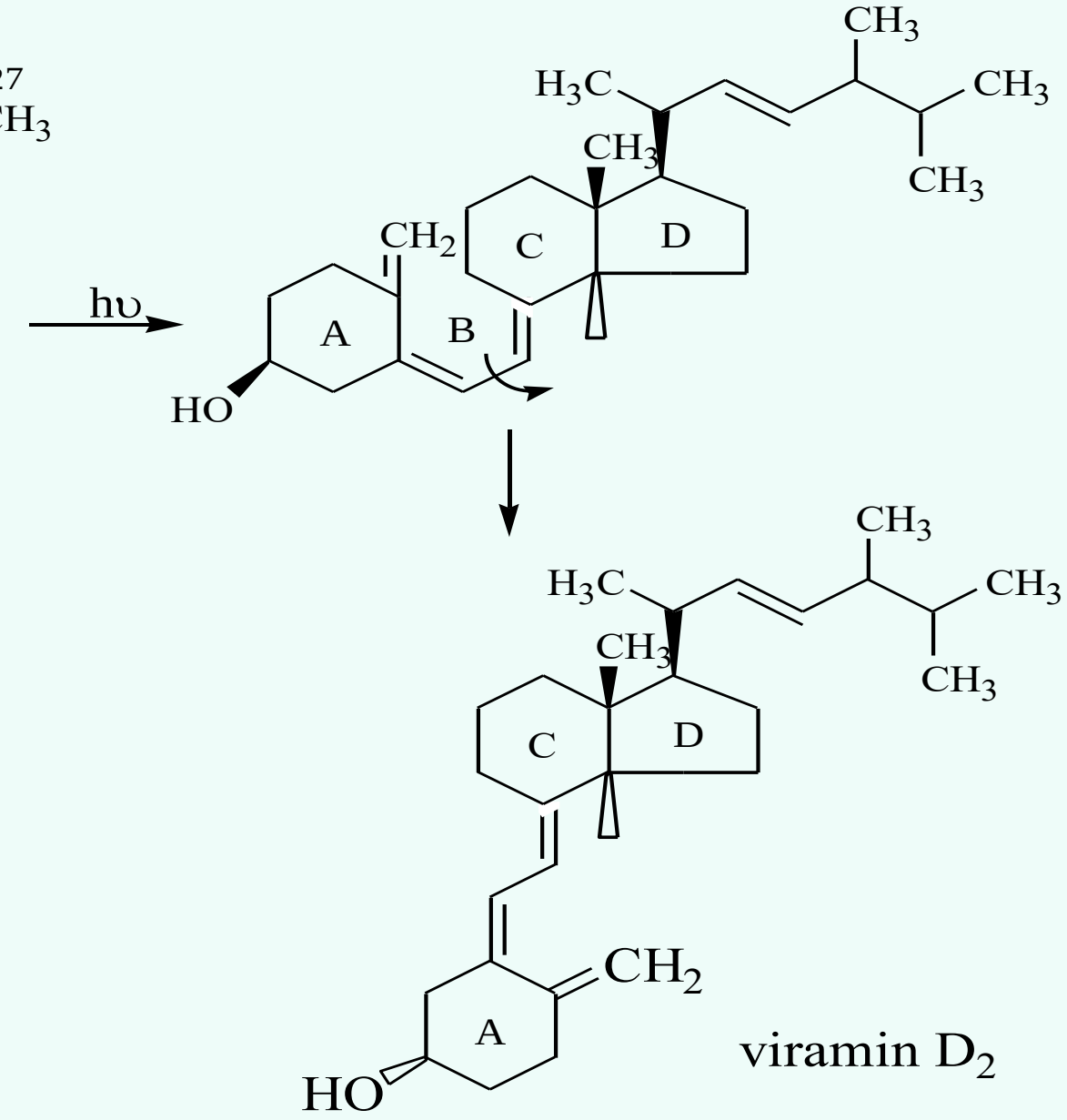
2^8 = 256 stereoisomers are possible

Cholesterol occurs widely in the human body, but not all of the biological functions of cholesterol are yet known. Cholesterol is known to serve as an intermediate in the biosynthesis of all of the steroids of the body.

ERGOSTEROL AND D VITAMINS



ergosterol
(24-methyl-5,7,22-
cholestatriene-3-β–ol).



viramin D_2

ALKALOIDS

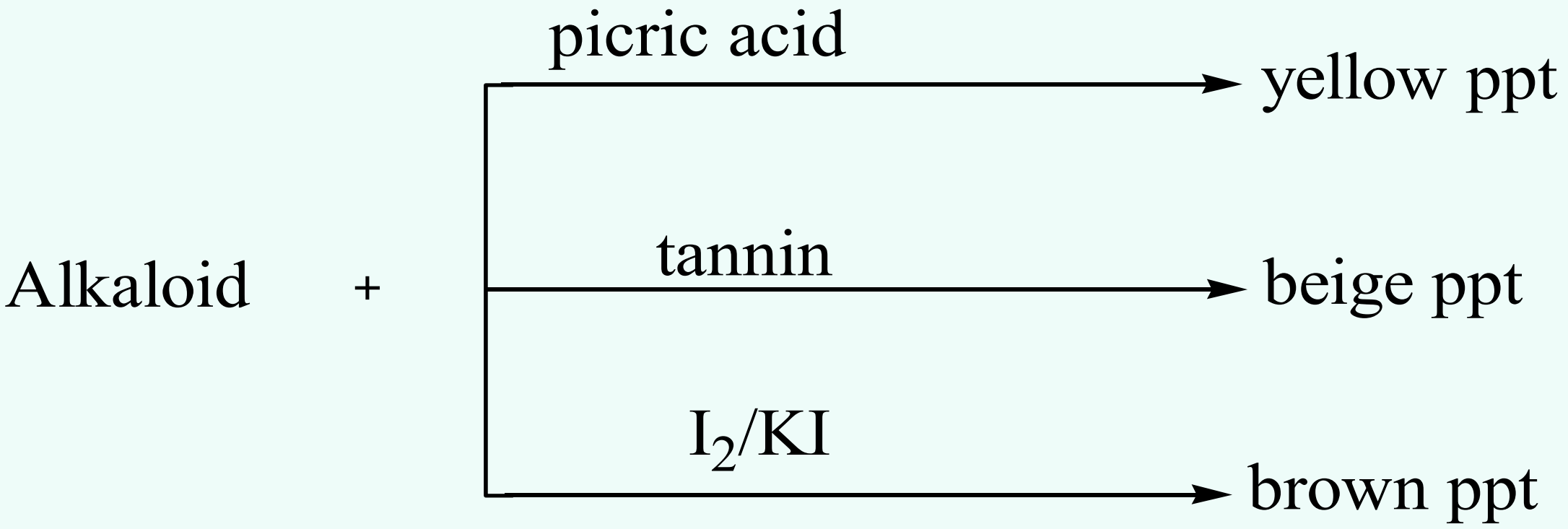
- Purine alkaloids
- Pyridine alkaloids
- Piperidine alkaloids
- Quinoline alkaloids
- Isoquinoline alkaloids
- Indole alkaloids

The name “Alkaloids” derives from the word “alkaline”. Most of alkaloids are of plant origin and present as salts of different organic acids (lactic, citric, malic, oxalic, tartaric and so on). Alkaloids are insoluble in water.

Alkaloids contain one or more nitrogen atoms. Most of alkaloids are heterocyclic compounds. **In organic chemistry alkaloids are classified according to the type of the heterocyclic ring structure.**

IDENTIFICATION OF ALKALOIDS

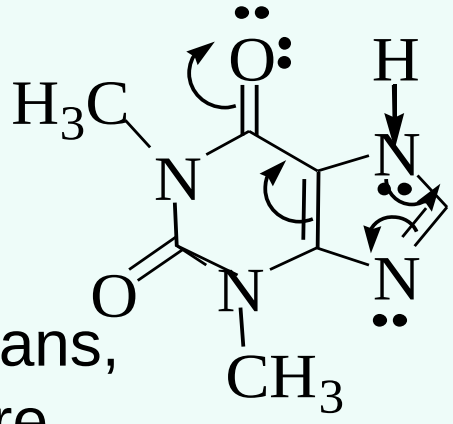
- All alkaloids are bases and they can form salts with acids. Reactions of insoluble salts formation can be used for identification



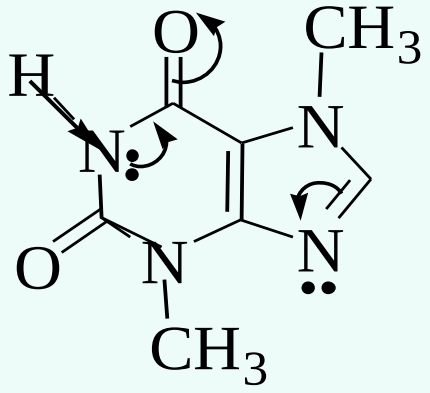
N-METHYLXANTHINES (PURINE ALKALOIDS)

Caffeine acts as psychoactive stimulant and a mild diuretic in humans.

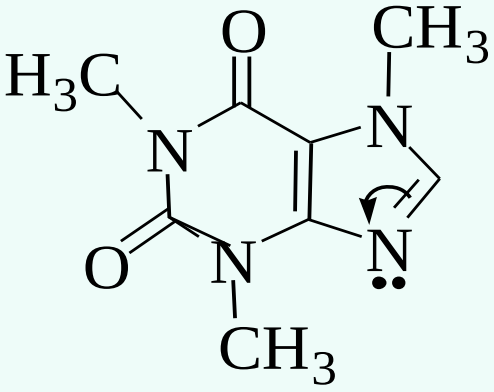
Caffeine is found in beans, leaves and fruits of more than 60 plant species – coffee, tea, cocoa.



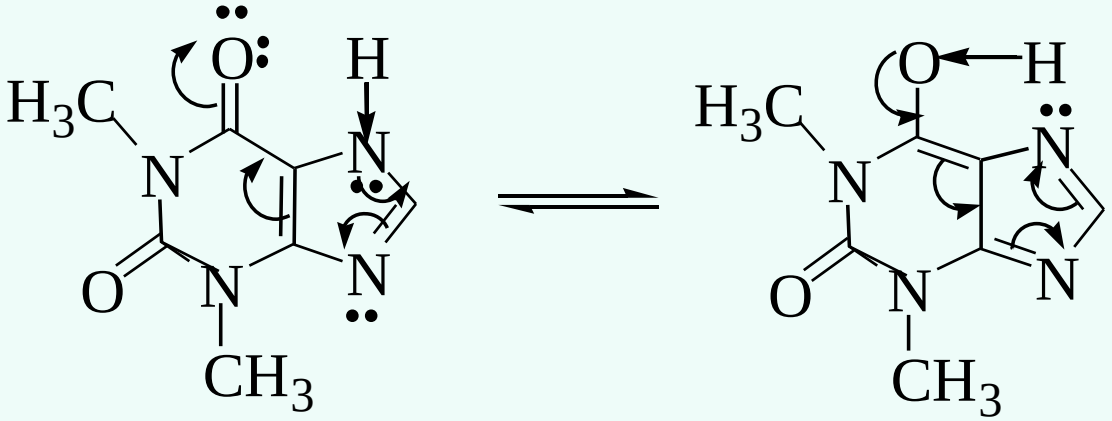
theophylline
(1,3-dimethyl xanthine)



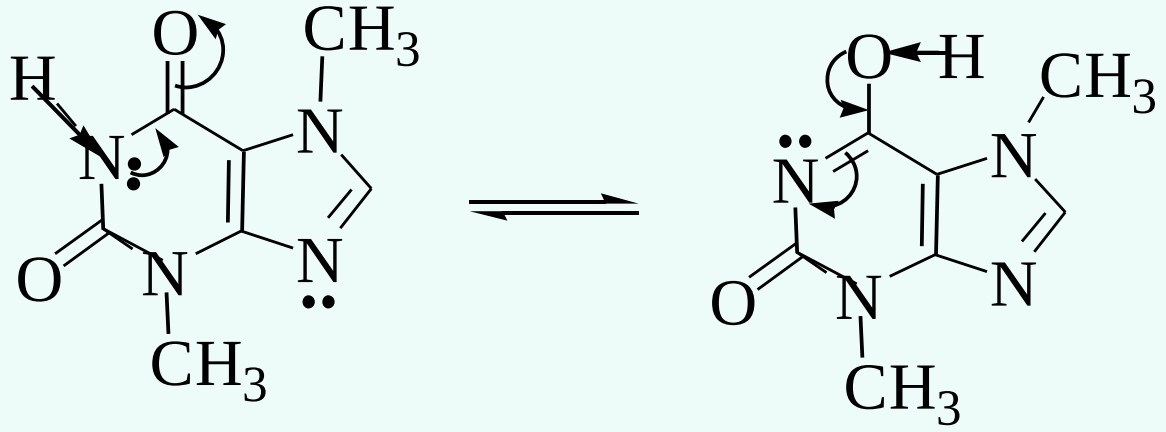
theobromine
(3,7-dimethyl xanthine)



caffeine
(1,3,7-trimethyl xanthine)



theophylline

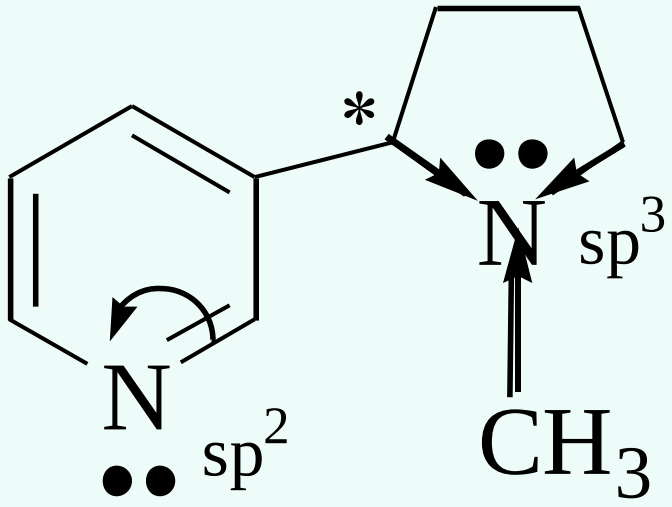


theobromine

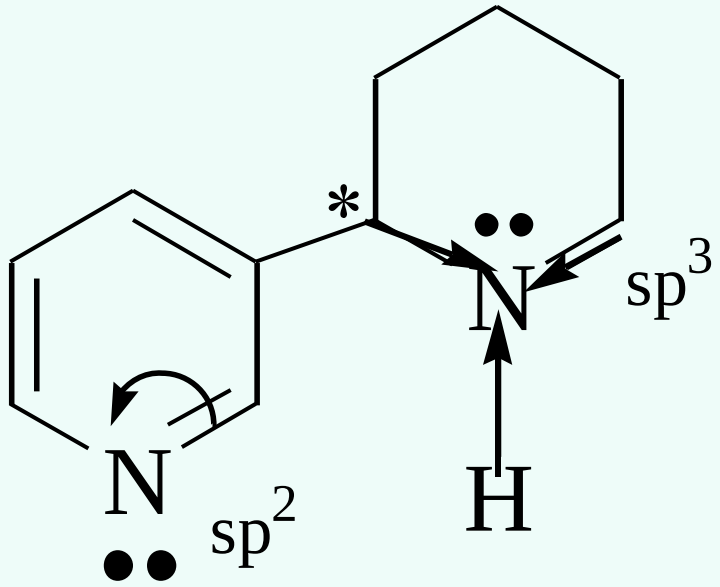
PYRIDINE ALKALOIDS

Nicotine is found in tobacco. Nicotine and anabasin are toxic.

Lethal dose of nicotine for human is 30-60 mg



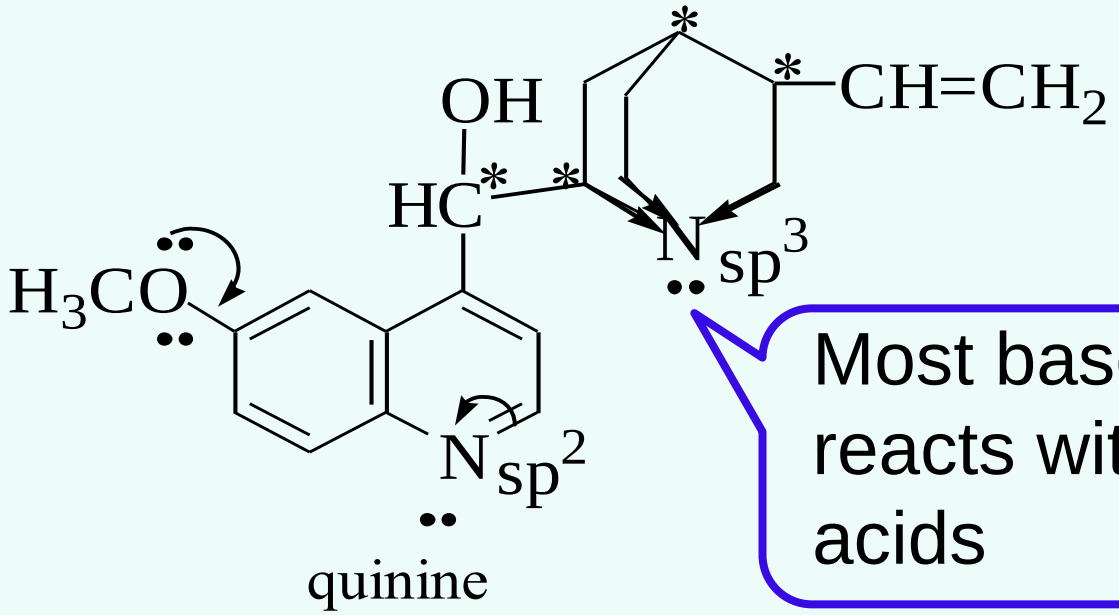
nicotine



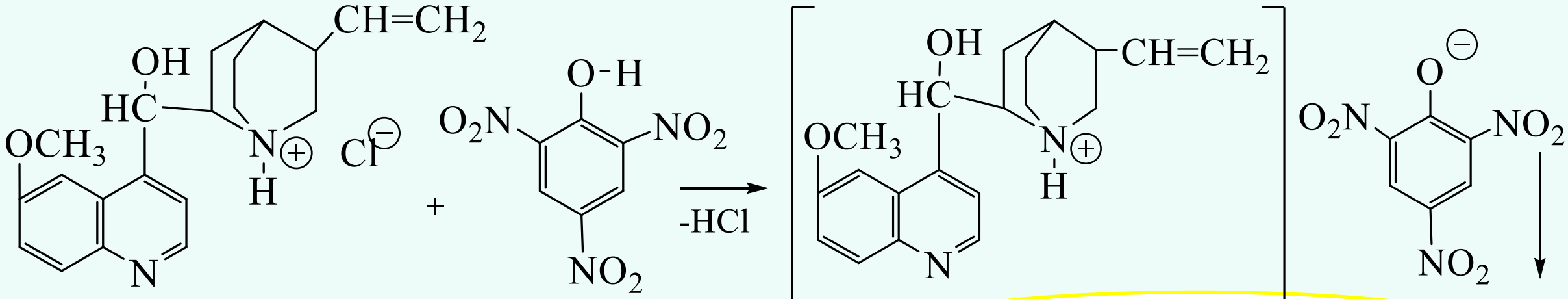
anabasin

QUININE ALKALOIDS

Quinine is antimalarial medicine

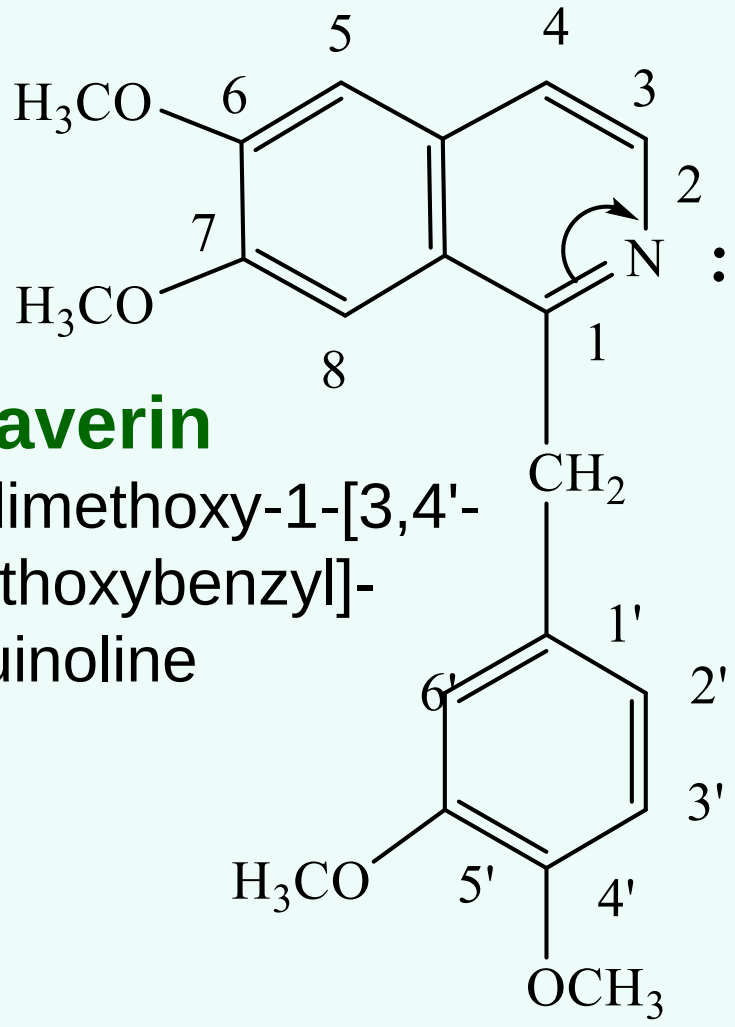


Most base – reacts with acids



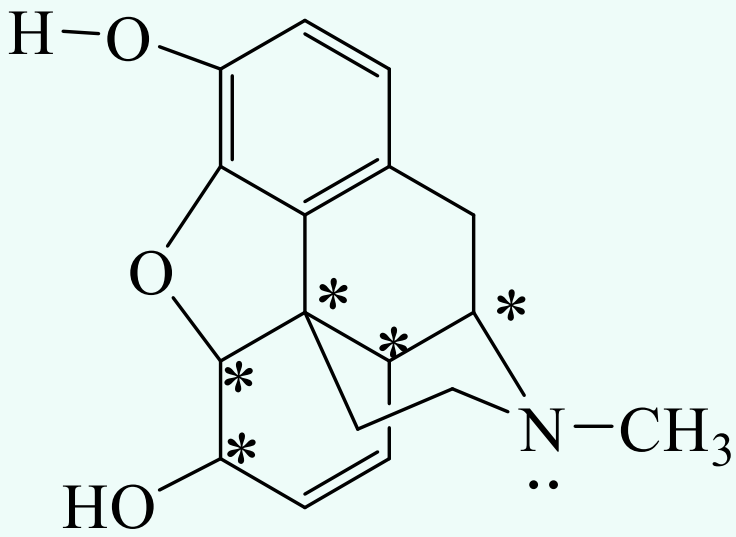
Salt of quinine (soluble) **picric acid** **quinine picrate (yellow ppt)**

ISOQUINOLINE AND PHENANTHRENEISOQUINOLINE ALKALOIDS

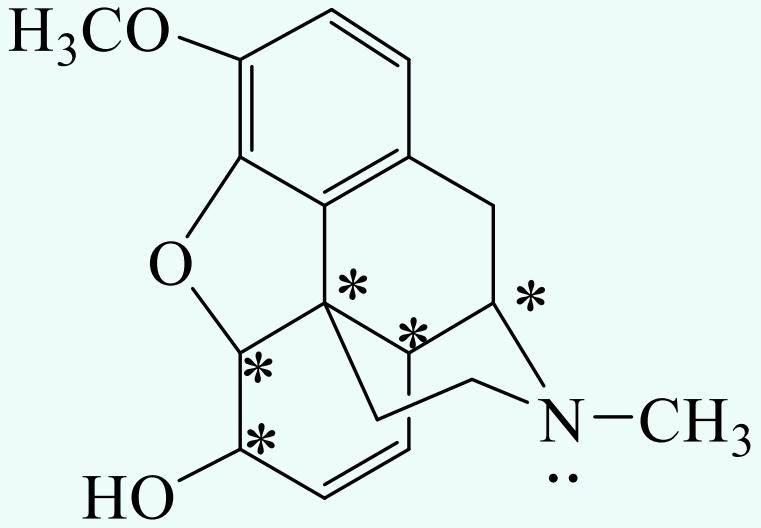


papaverin

6,7-dimethoxy-1-[3,4'-dimethoxybenzyl]-isoquinoline

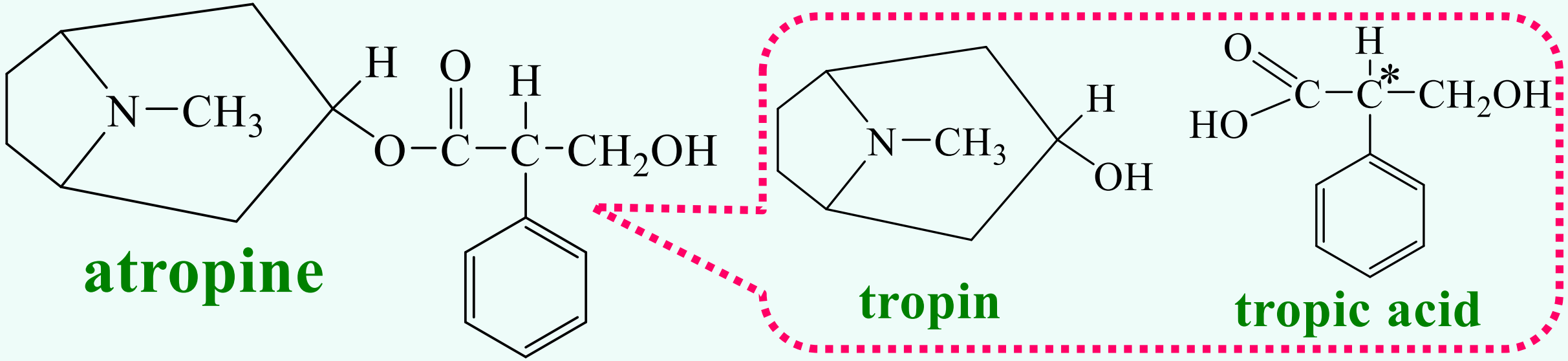


morphine



codeine

TROPAN ALKALOIDS



Atropine is plant alkaloid, it is classified as an anticholinergic agent. It is a competitive antagonist for the muscarinic acetylcholine receptor.


Thank you