# 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.

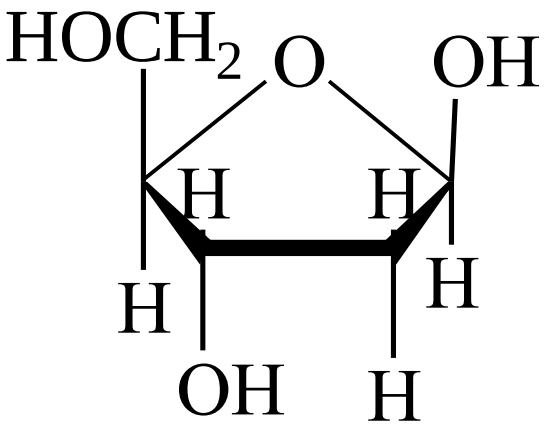
2. The significance of the spatial structure and physical-chemical properties of bioregulators in their interaction with receptors and the implementation of action at the molecular level.

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

# 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:

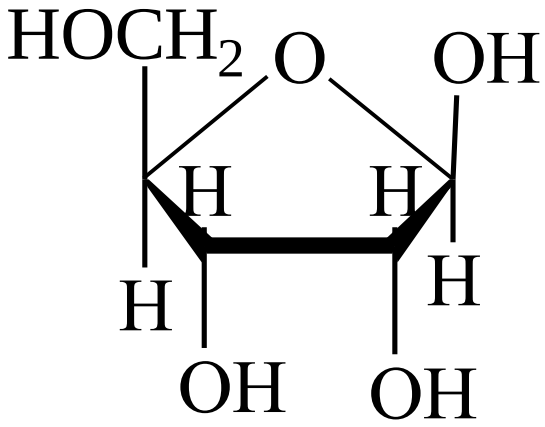
**in DNA**




**2-deoxy-D-ribose**

**2-deoxy-β-D-ribofuranose**

**in RNA**




**D-ribose**

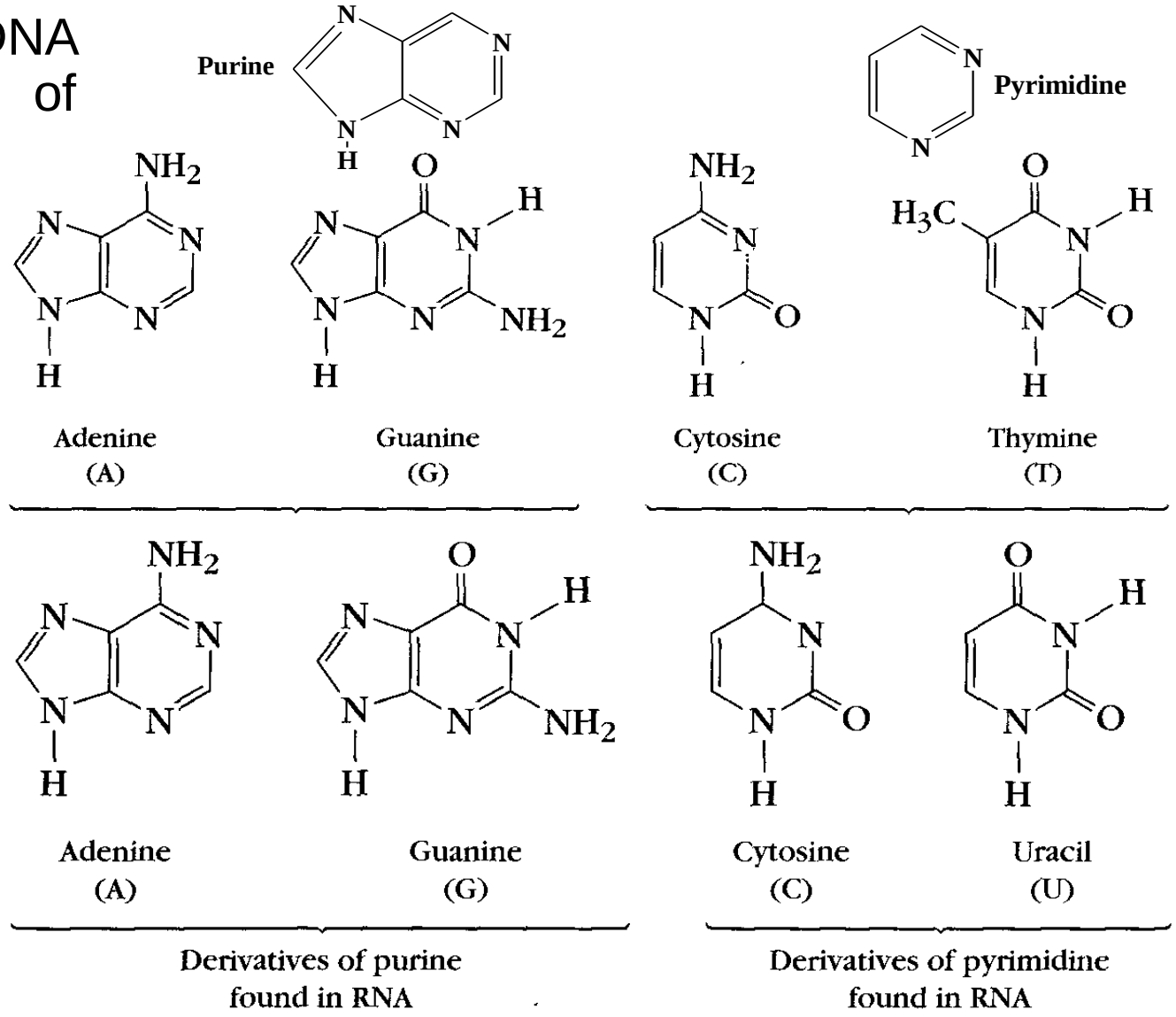
**β-D-ribofuranose**

# HETEROCYCLIC BASES OF NUCLEIC ACIDS

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

## DNA

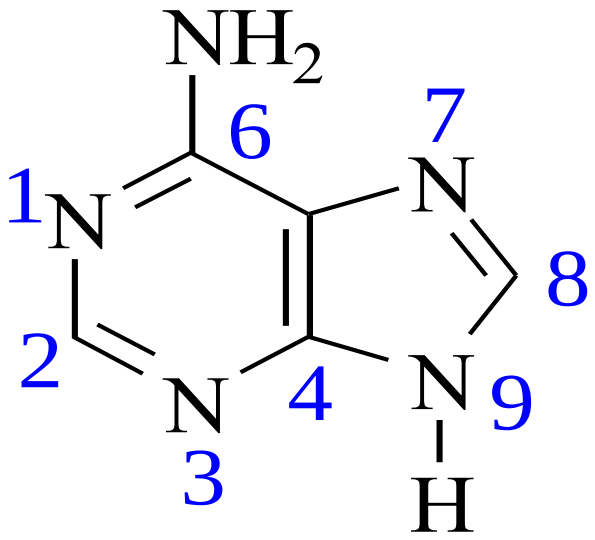
## RNA



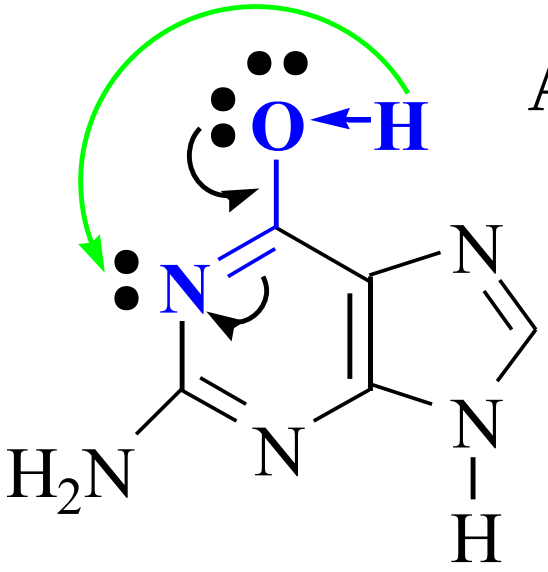
# TAUTOMERIC FORMS OF HETEROCYCLIC BASES

## ADENINE

## 6-aminopurine



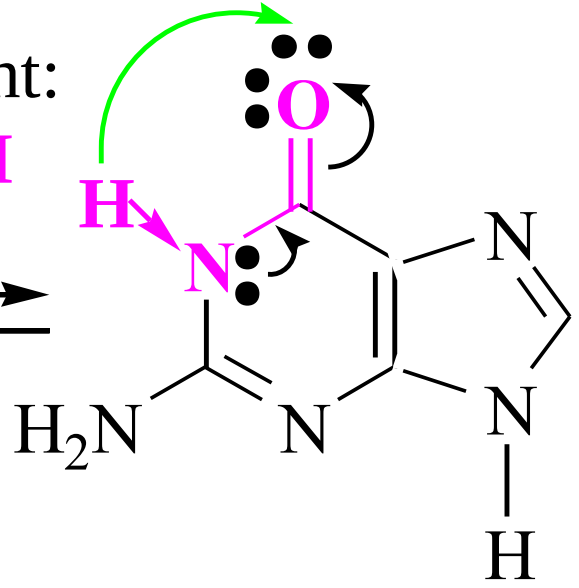

## GUANINE 2-amino-6-hydroxypurine




**Lactim**

Acid strenght:

**OH** > **NH**

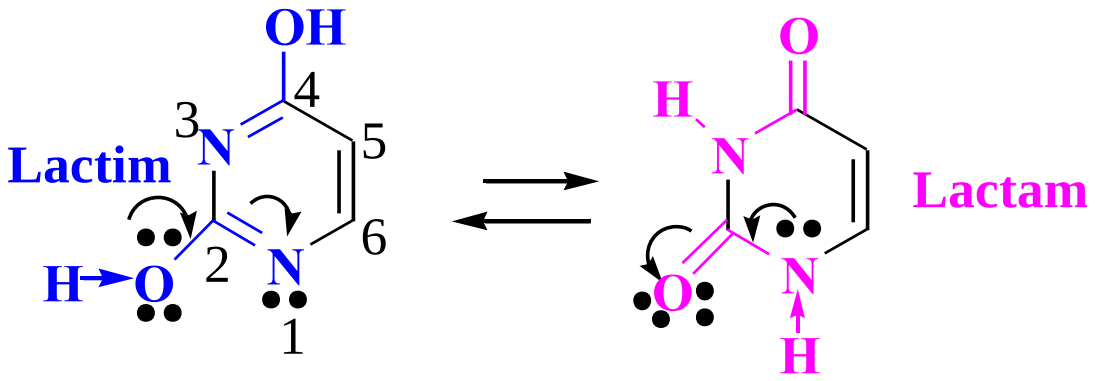



**Lactam**

**Lactam** is predominant form

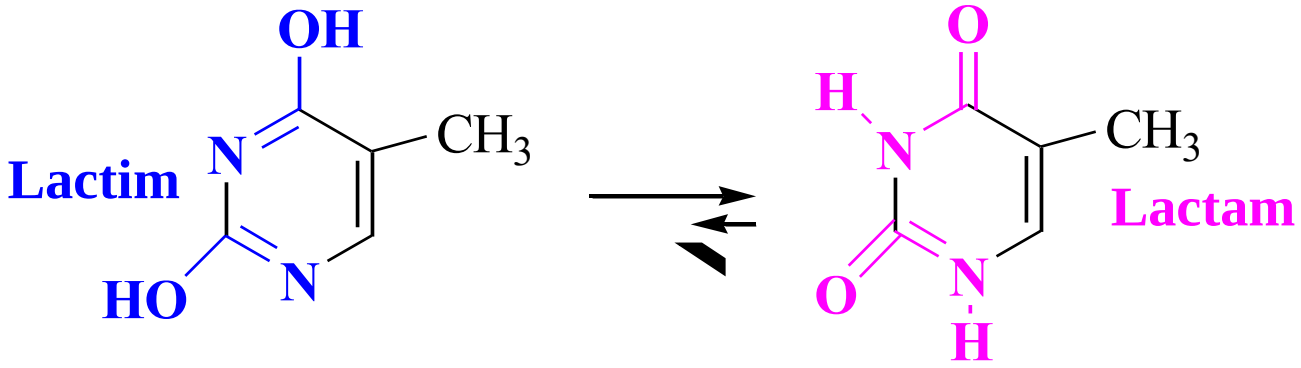
# TAUTOMERIC FORMS OF HETEROCYCLIC BASES.

**Uracil** — **2,4-dihydroxy pyrimidine**

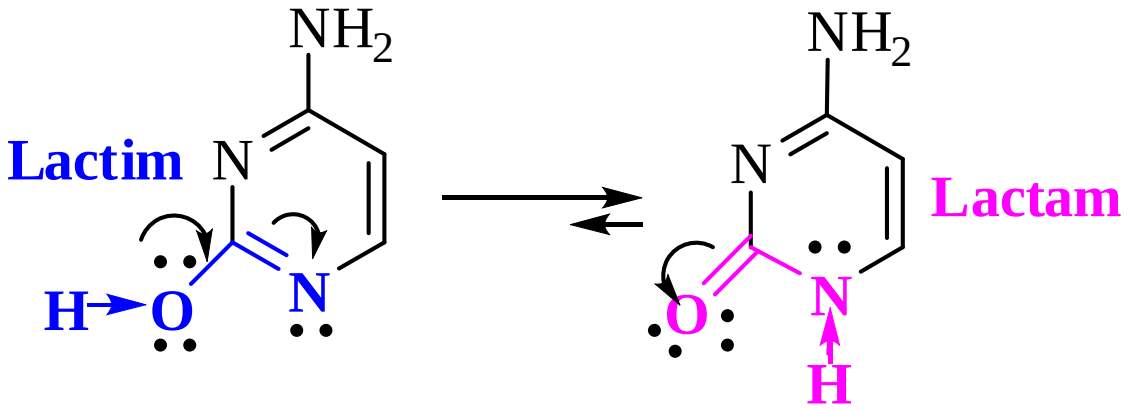



Lactames are predominant forms

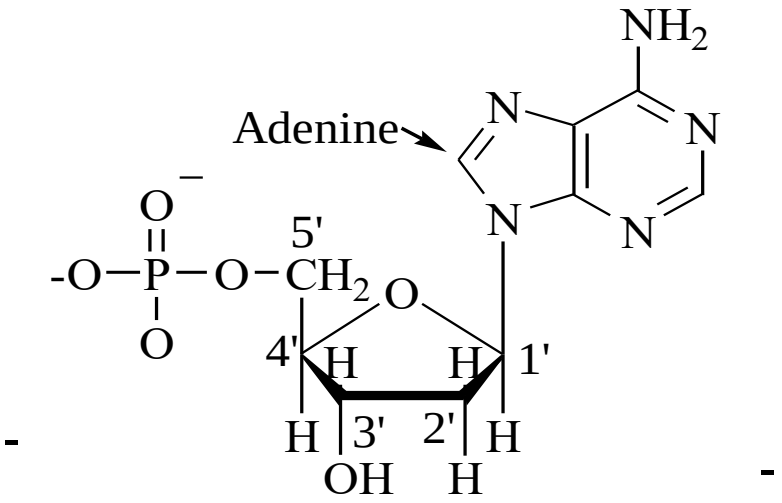
**Thymine** — **2,4-dihydroxy-5-methyl-pyrimidine**



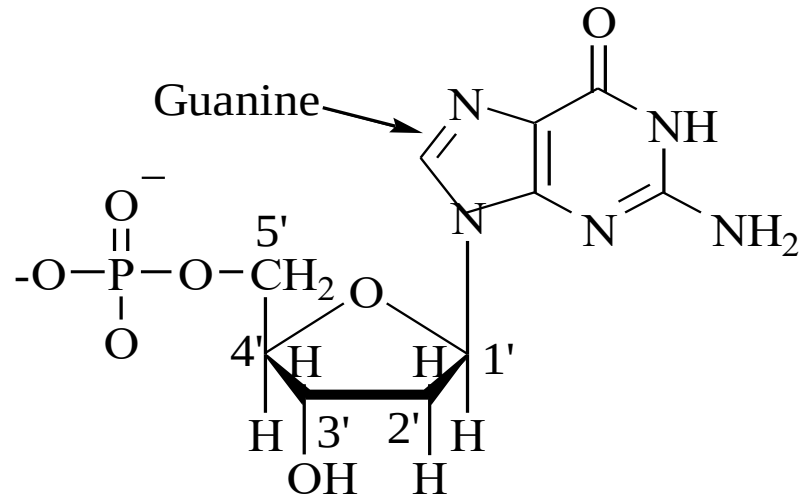

**Cytosine** — **4-amino-2-hydroxy pyrimidine**



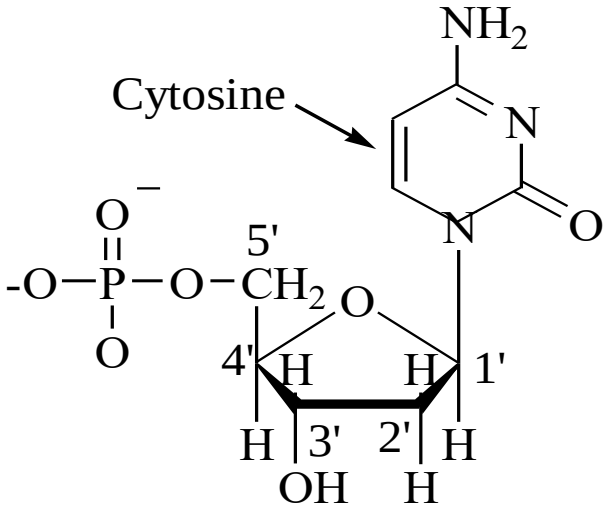
# THE FOUR NUCLEOTIDES FOUND IN DNA:



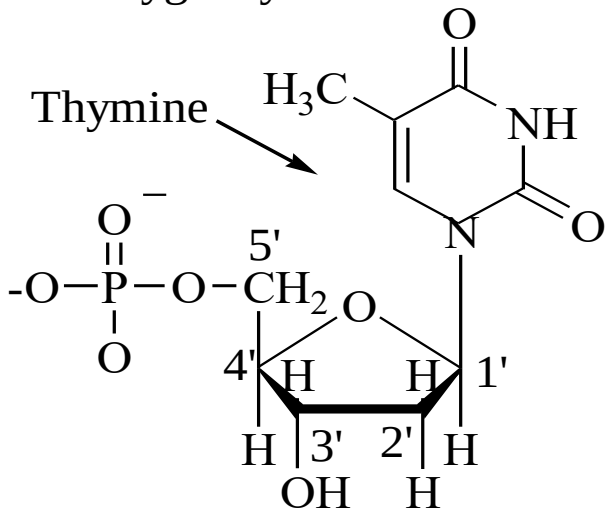

2'-Deoxyadenosine 5'-monophosphate
5'-deoxyadenylic acid




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

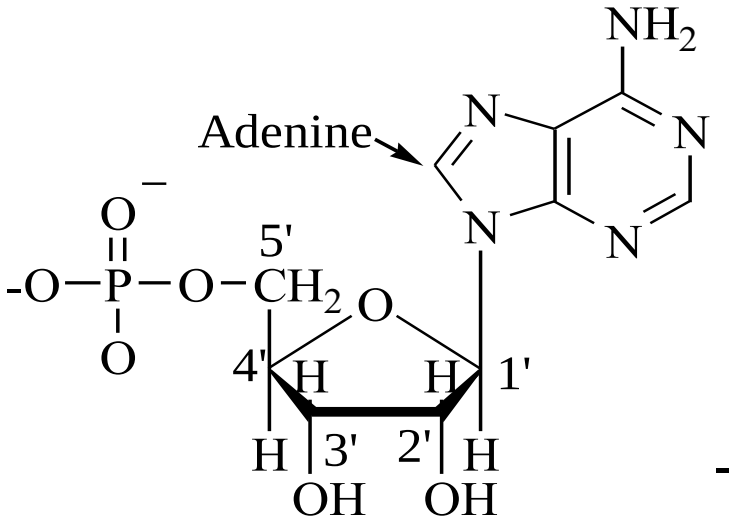



2'-Deoxycytidine 5'-monophosphate
5'-deoxycitidylic acid

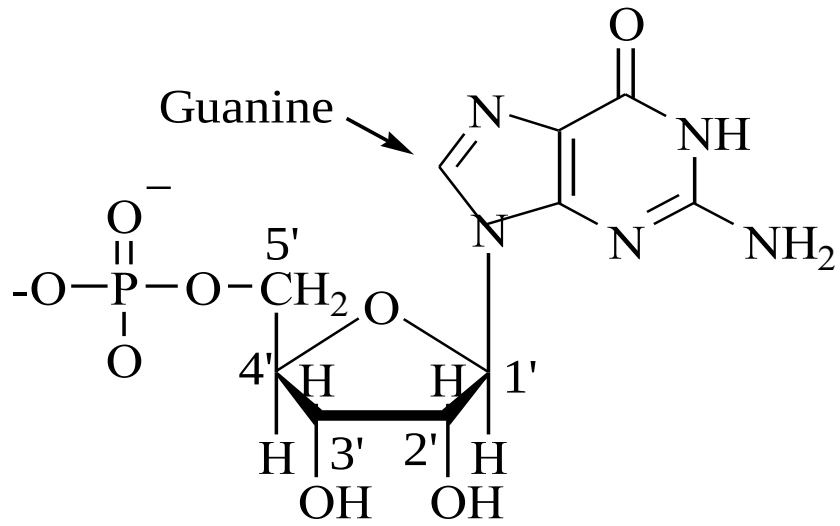



2'-Deoxythymidine 5'-monophosphate
5'-deoxythymidylic acid

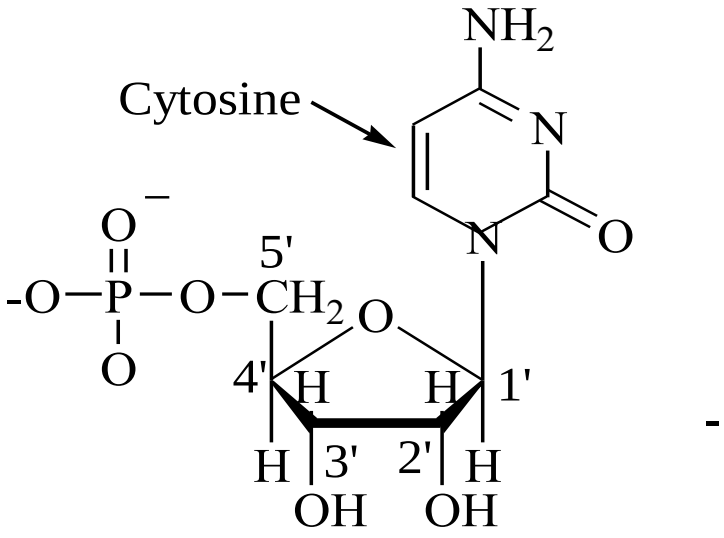
# THE FOUR NUCLEOTIDES FOUND IN RNA:



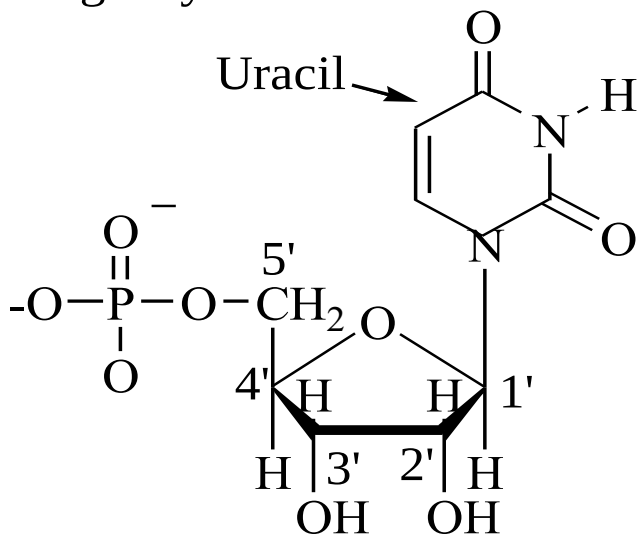

Adenosine 5'-monophosphate
5'-adenylic acid




Guanosine 5'-monophosphate
5'-guanylic acid



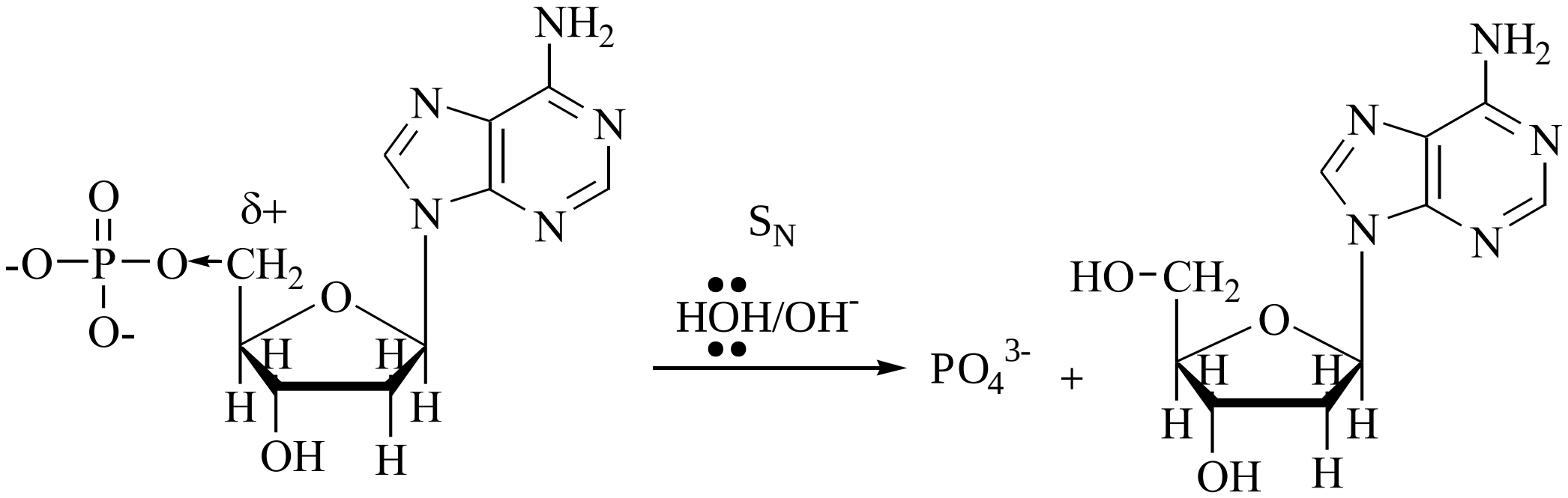

Cytidine 5'-monophosphate
5'-cytidylic acid




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**

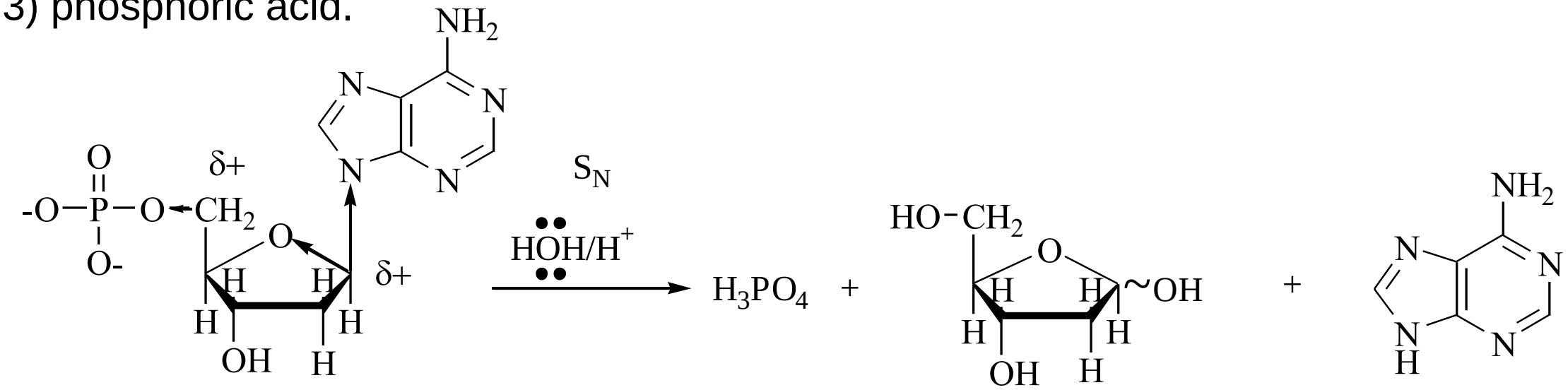
# HYDROLYSIS IN ACIDIC SOLUTION

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.

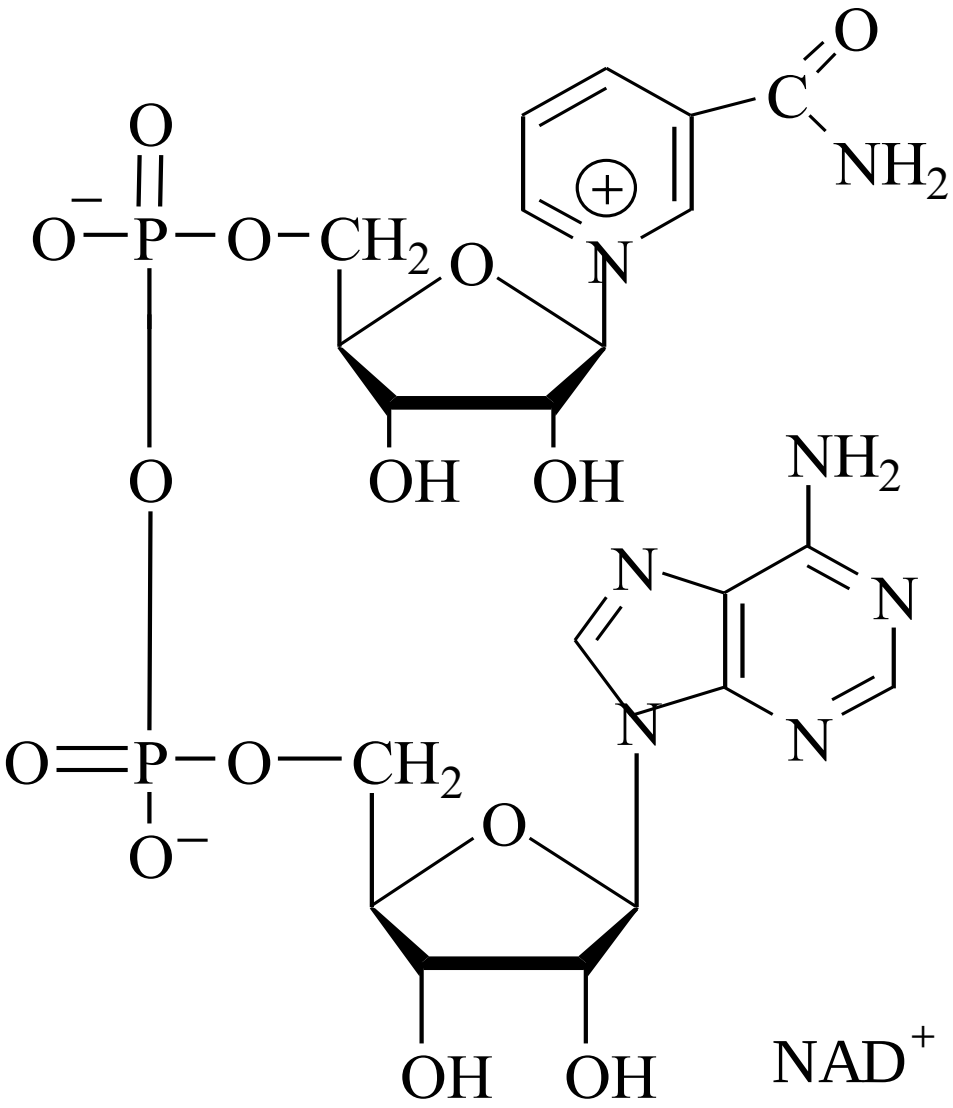


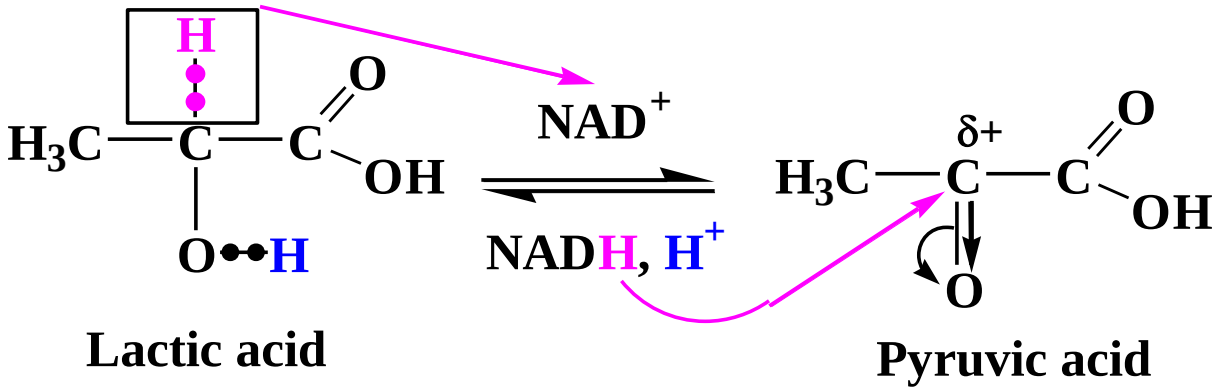

**2'-Deoxyadenosine 5'-monophosphate**
**the nucleotide**

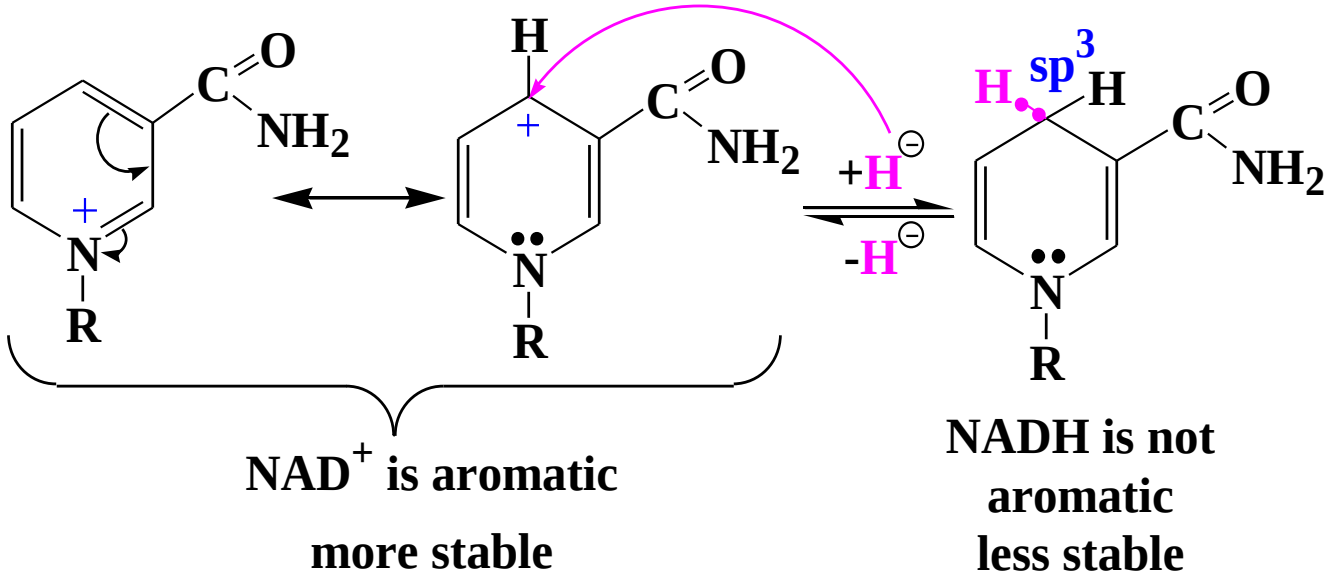
**2-deoxy-D-ribose**
**the monosaccharide**

**Adenine**
**the heterocyclic base**

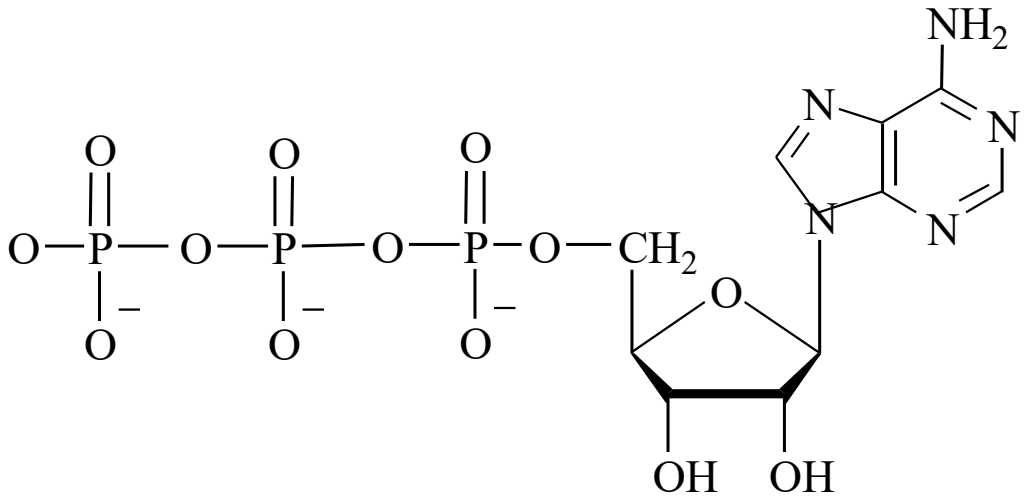
# Coenzyme $NAD^+$.



# *5’-Triphosphate of adenosine (ATP).*

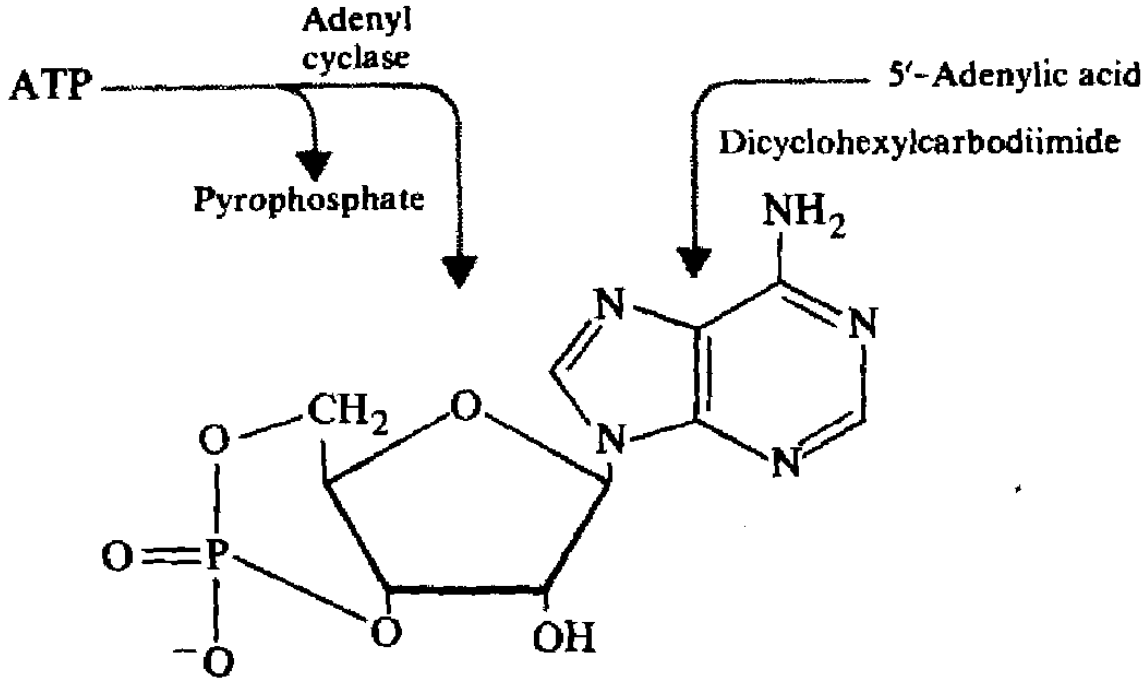


The 5'-triphosphate of adenosine is the important energy source, ATP.

## *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.*



# SECONDARY STRUCTURE OF DNA

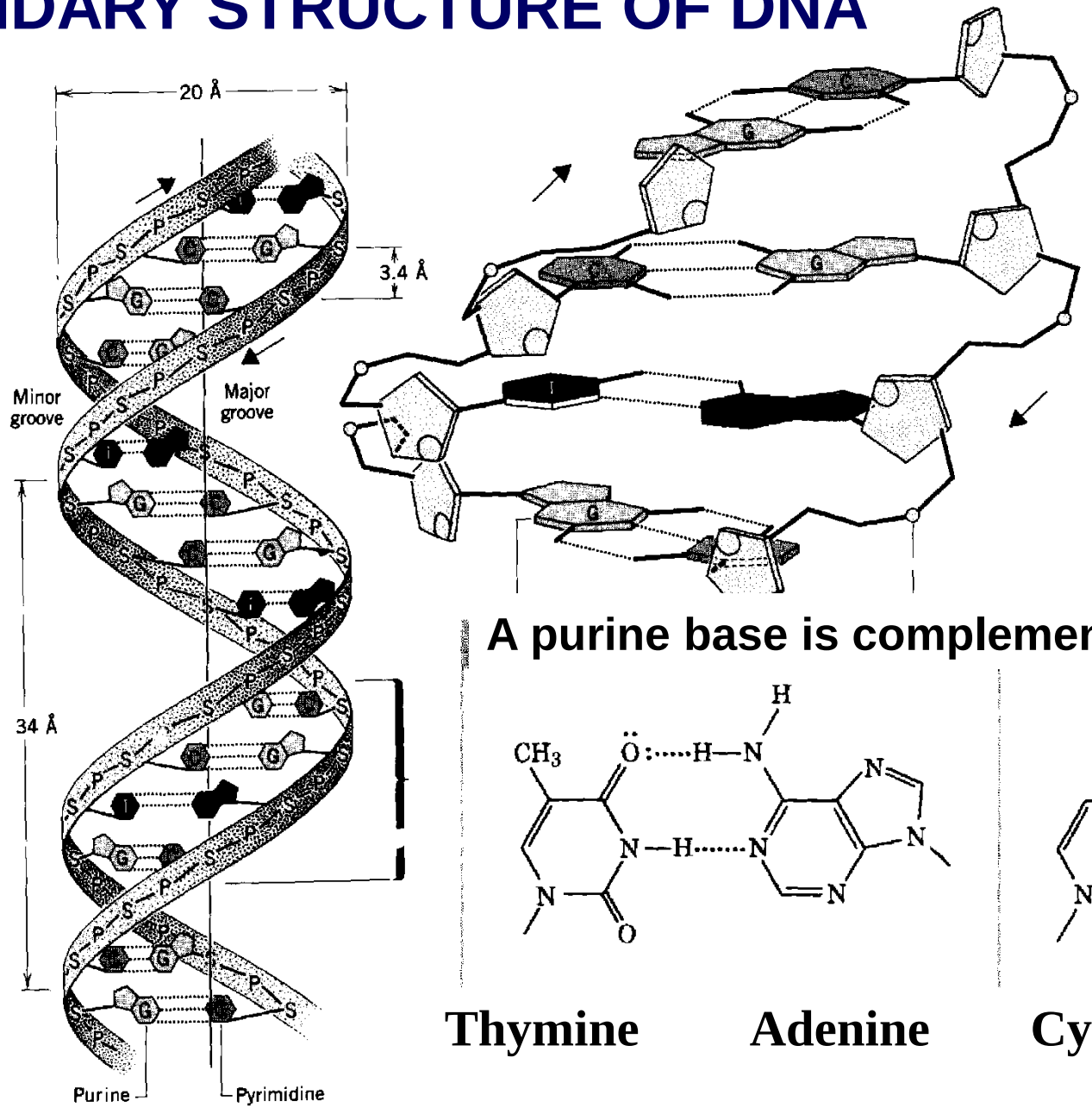



***Diagram of the DNA double helix showing complementary base pairing. The arrows indicate the 3' →5' direction.***

*The repeat distance*
*10 nucleotide pair*

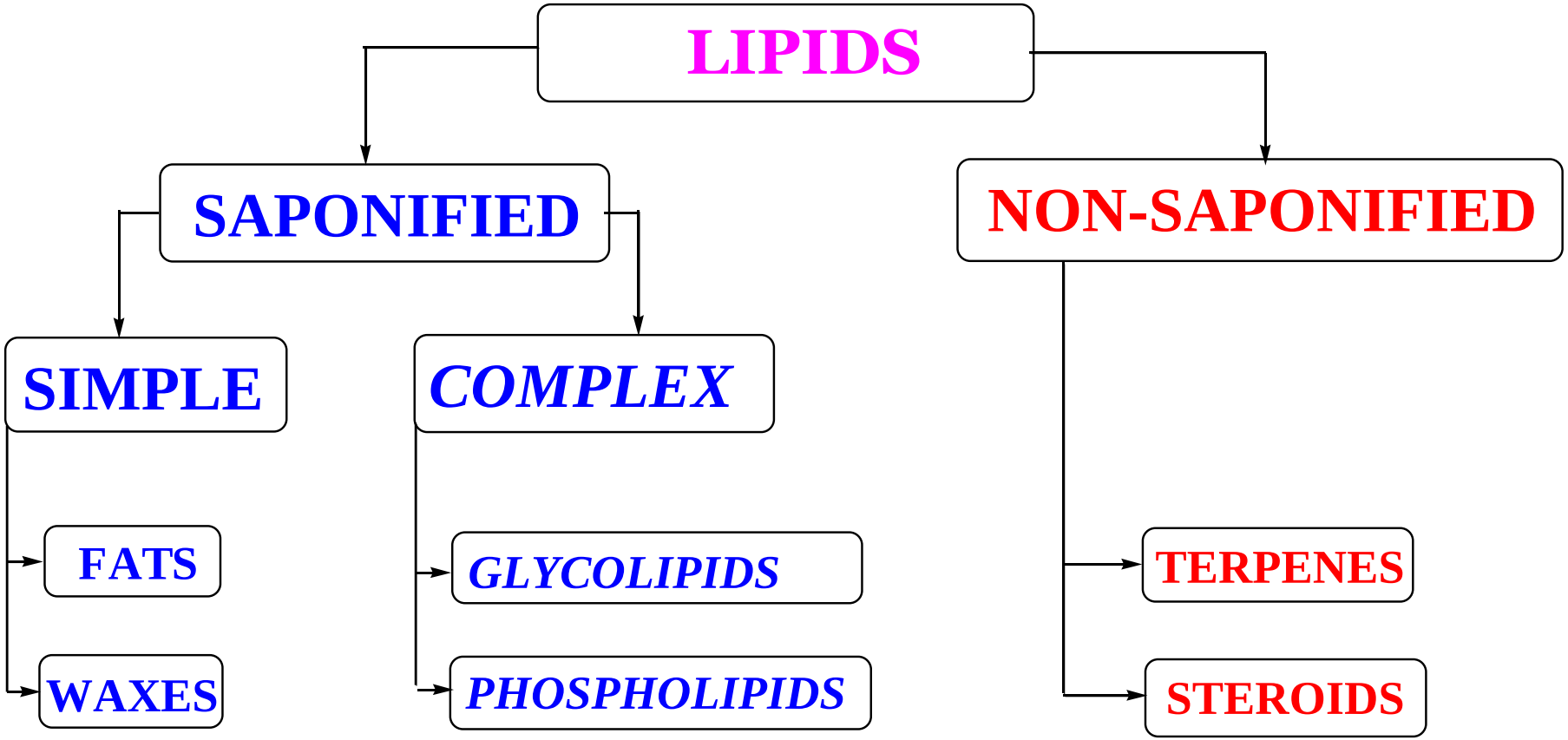
**A purine base is complementary for pyrimidine base:**



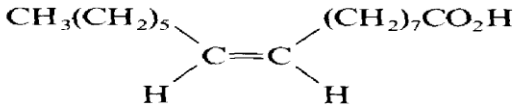
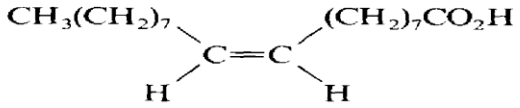
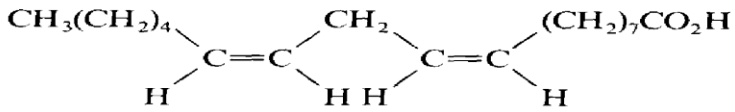
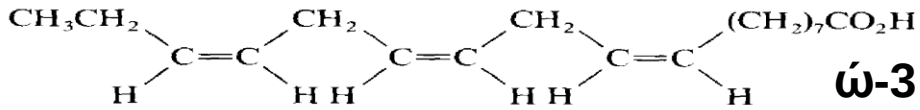
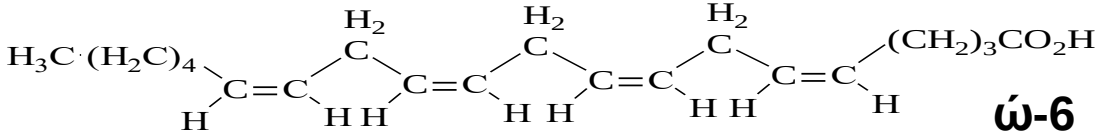
**Thymine** **Adenine** **Cytosine** **Guanine**

# 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

| | | | Example of occurrence |
|---|---|---|---|
| | **Saturated Carboxylic Acids** | | |
| $(C_{14})$; $C_{13}H_{27}COOH$ | $CH_3(CH_2)_{12}CO_2H$<br>**Myristic acid**<br>**(tetradecanoic acid)** | | **Natural fats and oils, especially palm oil** |
| $(C_{16})$; $C_{15}H_{31}COOH$ | $CH_3(CH_2)_{14}CO_2H$<br>**Palmitic acid**<br>**(hexadecanoic acid)** | | **Natural fats and oils, especially beef fat** |
| $(C_{18})$; $C_{17}H_{35}COOH$ | $CH_3(CH_2)_{16}CO_2H$<br>**Stearic acid**<br>**(octadecanoic acid)** | | |
| | **Unsaturated Carboxylic Acids** | | |
| $(C_{16})$; $(\Delta 9)$; $C_{15}H_{29}COOH$ |  <br>**Palmitoleic acid**<br>**(*cis*-9-hexadecenoic acid)** | | **Natural fats and oils, especially olive oil** |
| $(C_{18})$; $(\Delta 9)$ $C_{17}H_{33}COOH$ |  <br>**Oleic acid**<br>**(*cis*-9-octadecenoic acid)** | | **Widespread, many seed oils** |
| $(C_{18})$; $(\Delta 9,12)$ $C_{17}H_{31}COOH$ |  <br>**Linoleic acid**<br>**(*cis,cis*-9,12-octadecadienoic acid)** | **ώ-6** | **All plant leaves, some seed oils, e.g. soybean, rapeseed, linseed oils** |
| $(C_{18})$; $(\Delta 9,12,15)$ $C_{17}H_{29}COOH$ |  <br>**Linolenic acid**<br>**(*cis,cis,cis*-9,12,15-octadecatrienoic acid)** | **ώ-3** | **Animal cell membrans.** |
| $(C_{20})$; $(\Delta 5,8,11,14)$ $C_{19}H_{31}COOH$ |  <br>**Arachidonic acid**<br>**(cis,cis,cis,cis-5,8,11,14-eicosatetraenoic acid)** | **ώ-6** | |

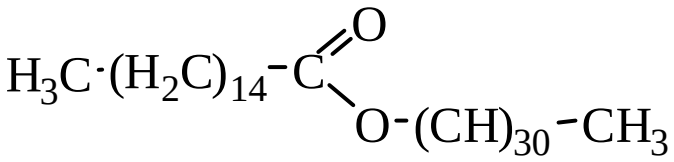
# WAXES

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%).

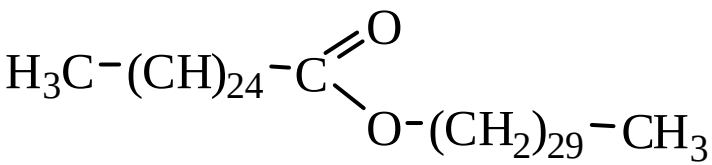
**Carnauba wax** is vegetable wax; it is found as protecting coating on leaves of palm-tree Copernicia cerifera.

Beeswax

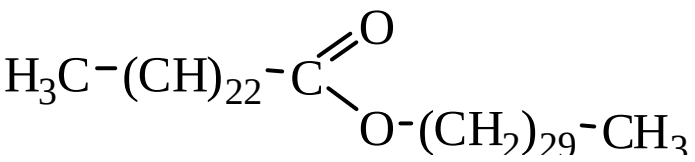


myricyl palmitate

Carnauba wax



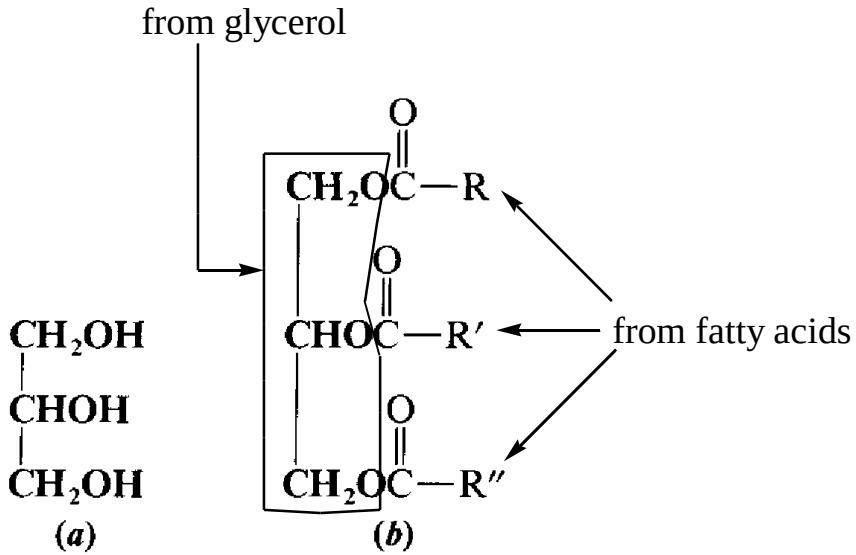
myricyl cerotate

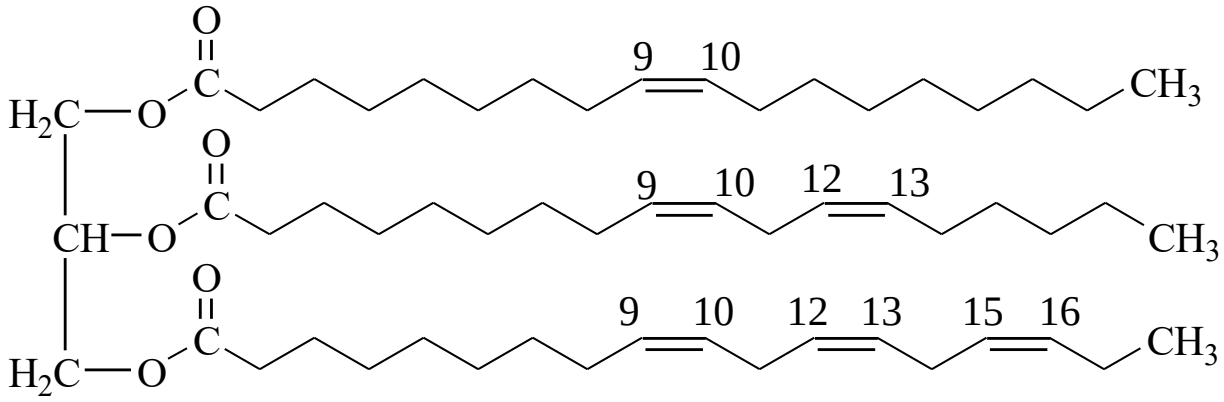


myricyl lignocerate

# 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

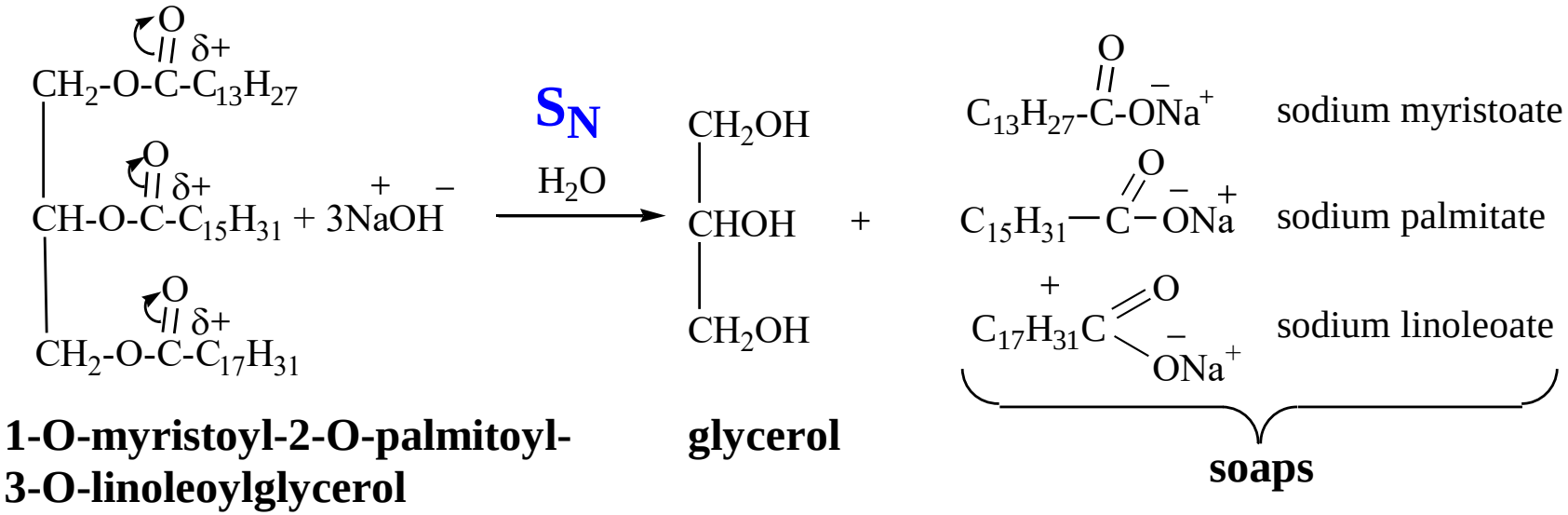
## Triacylglycerols:

***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

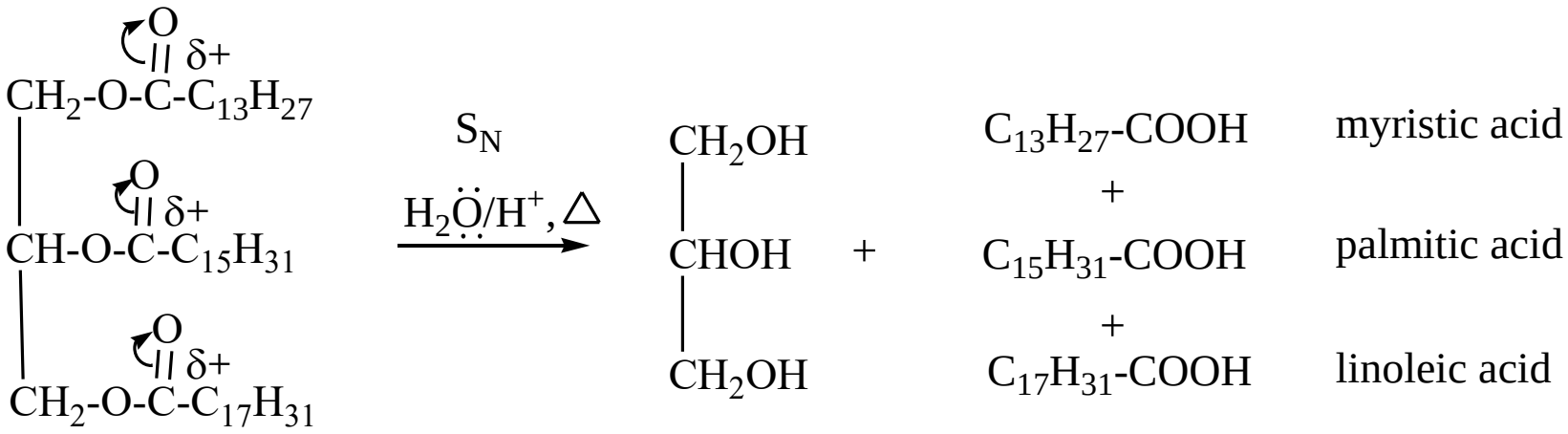
Alkaline hydrolysis (i.e., saponification) of triacylglycerols produces glycerol and a mixture of salts of long-chain carboxylic acids




**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

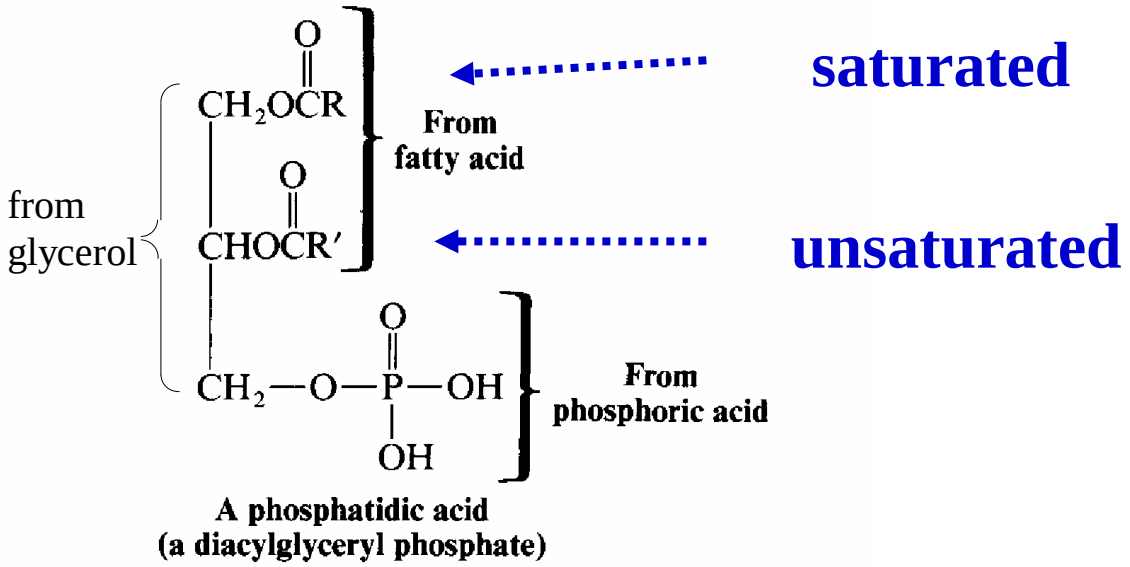



1-O-myristoyl-2-O-palmitoyl-3-O-linoleoylglycerol

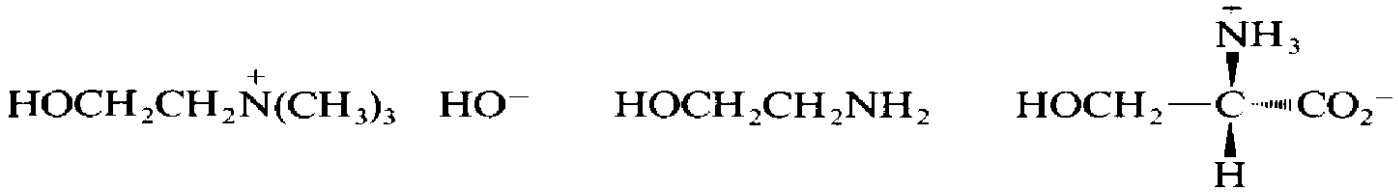
glycerol

# PHOSPHOLIPIDS AND CELL MEMBRANES

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



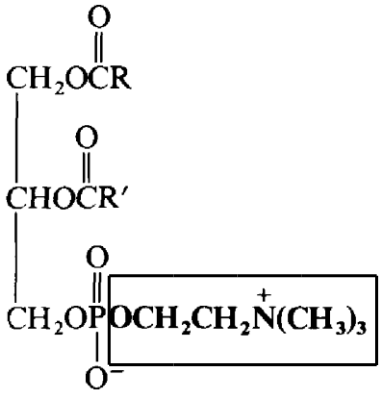

➢In *phosphatides,* the phosphate group of a phosphatidic acid is bound through another phosphate ester linkage to one of the following nitrogen-containing compounds.



**Choline** | **2-Aminoethanol (ethanolamine)** | **L-Serine**

# PHOSPHATIDES

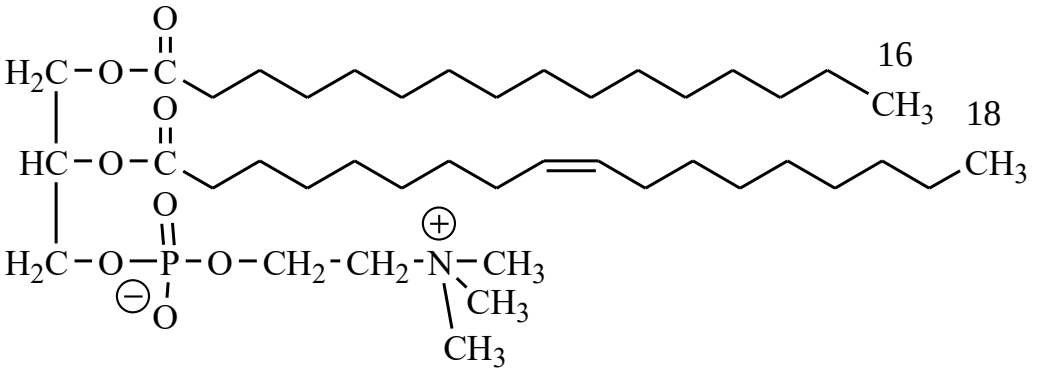
**Lecithins**



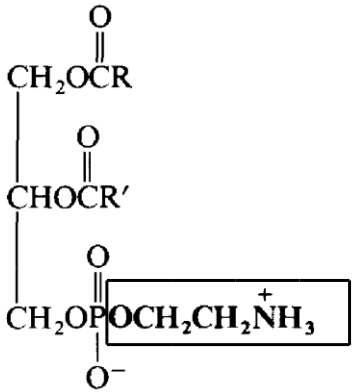
**(from choline)**

R is saturated and R′ is unsaturated

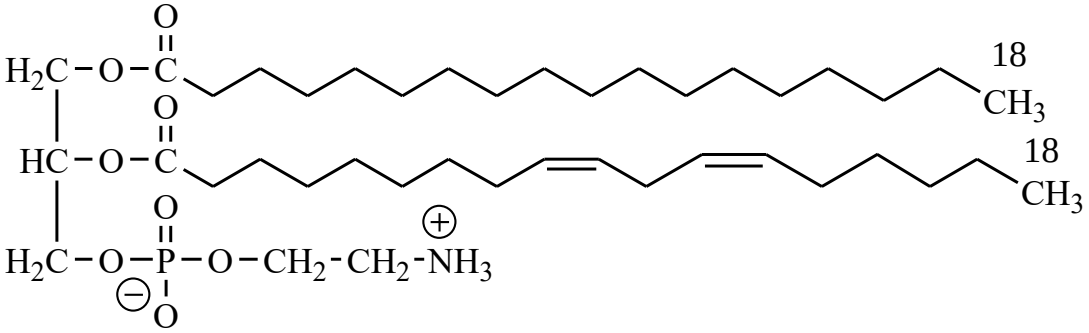
examples



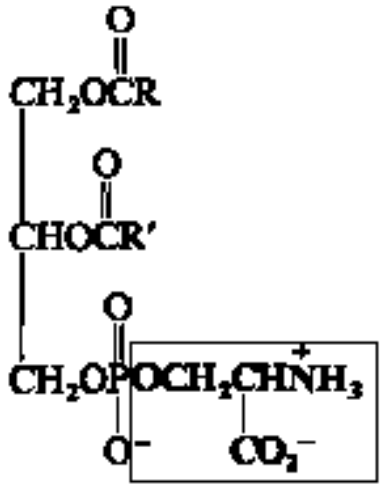

**Cephalins**



**(from 2-aminoethanol)**



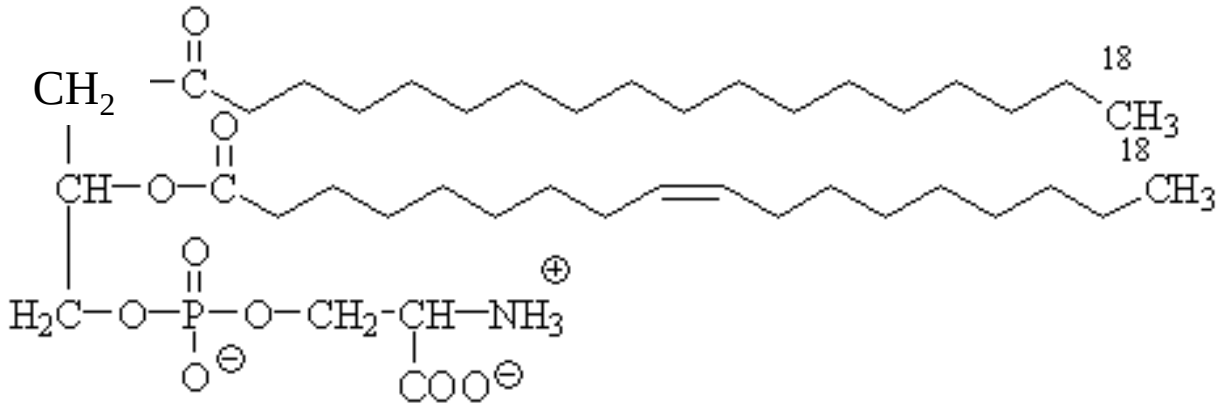
**Phosphatidyl Serines**



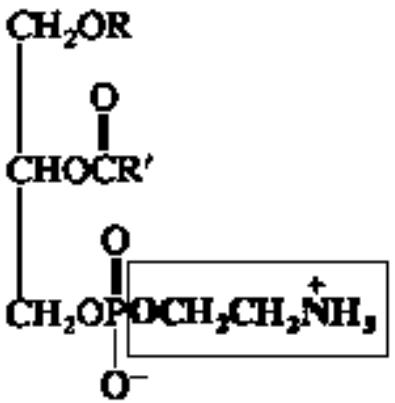
**(from L-serine)**

R is saturated and R′ is unsaturated

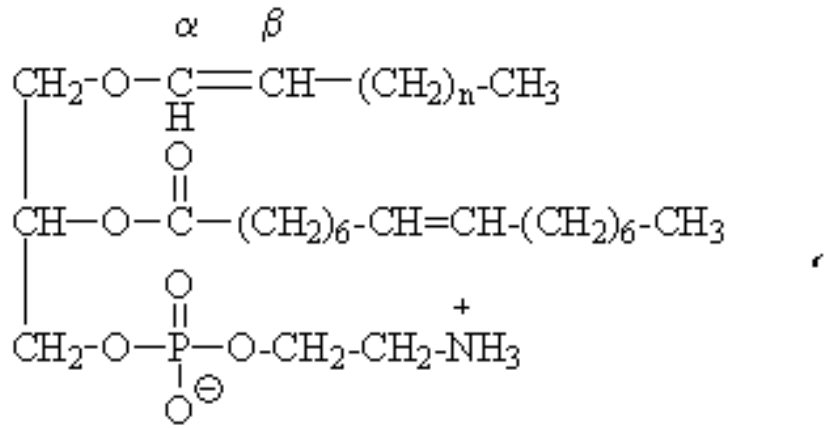
Examples:



**Plasmalogens**



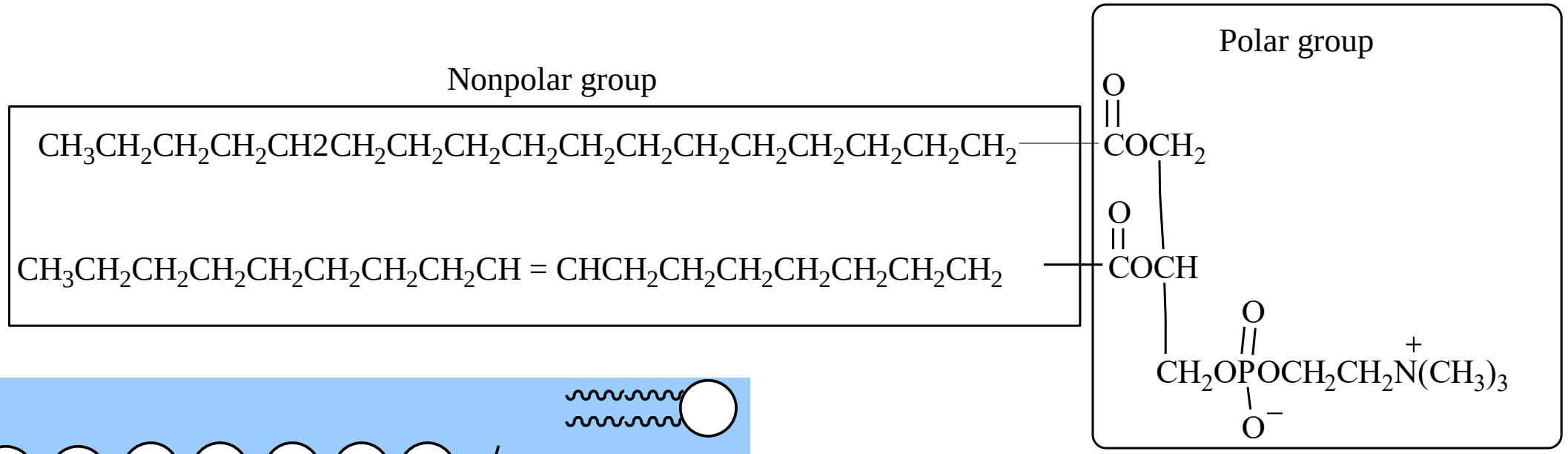
**(from 2-aminoethanol)** **or** **$OCH_2CH_2\overset{+}{N}(CH_3)_3$** **(from choline)**

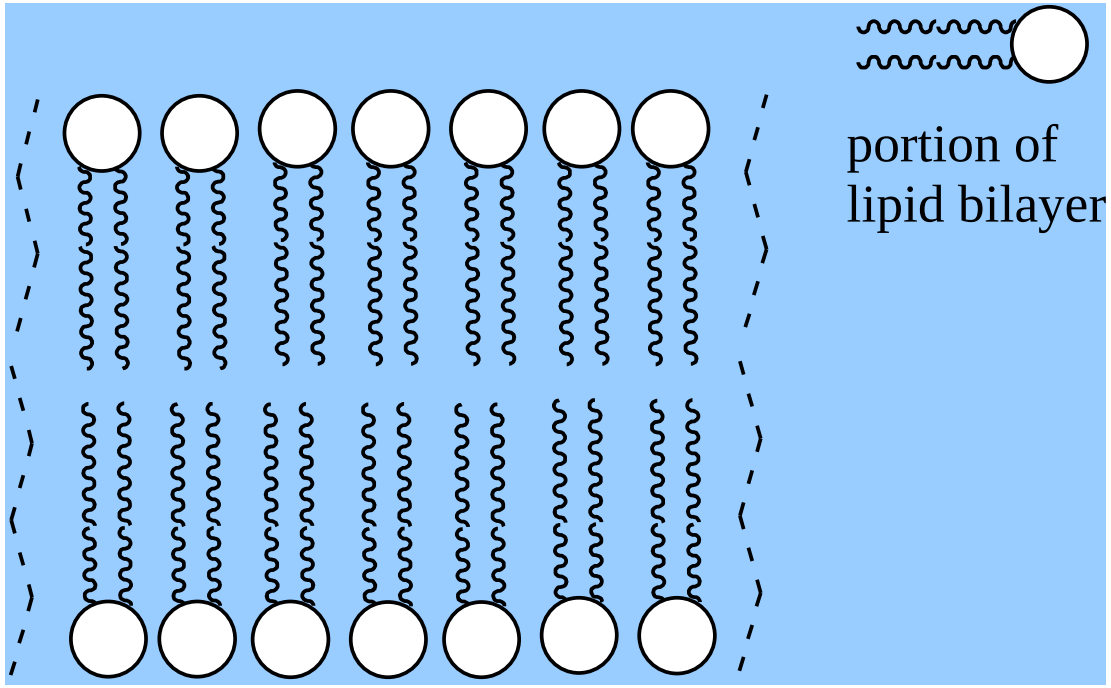


**R is —CH═CH$(CH_2)_nCH_3$ (this linkage is that of an $\alpha,\beta$-unsaturated ether)**

**R′ is that of an unsaturated fatty acid**

# POLAR AND NONPOLAR SECTIONS OF A PHOSPHATIDE.

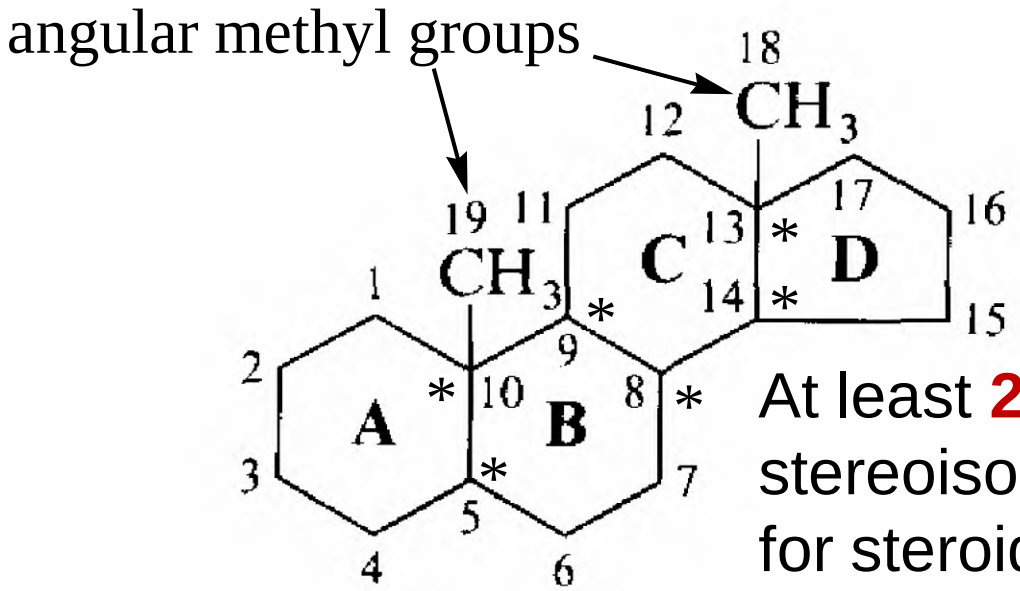


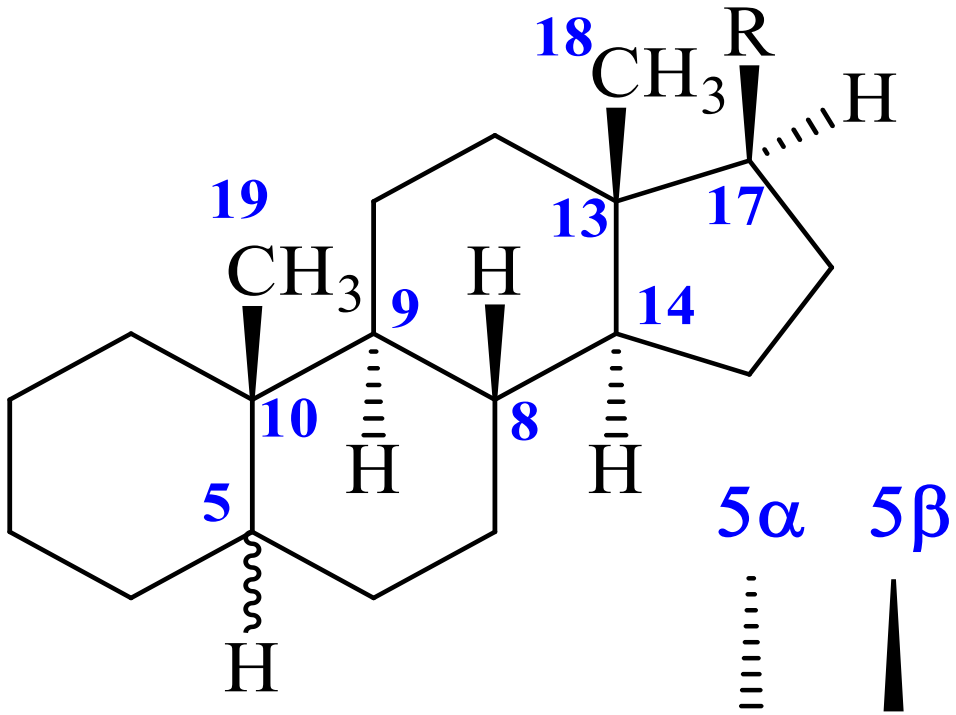

The hydrophilic and hydrophobic portions of phosphatides make them perfectly suited for one of their most important biological functions: They form a portion of a structural unit that creates an interface between an organic and an aqueous environment. This structure is found in cell walls and membranes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

# STEROIDS. STRUCTURE AND SYSTEMATIC NOMENCLATURE

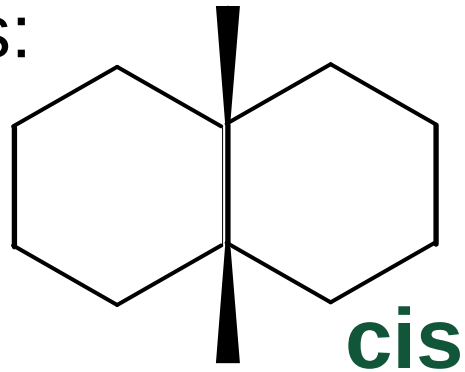
Steroids are derivatives of the perhydrocyclopentanophenanthrene ring system.



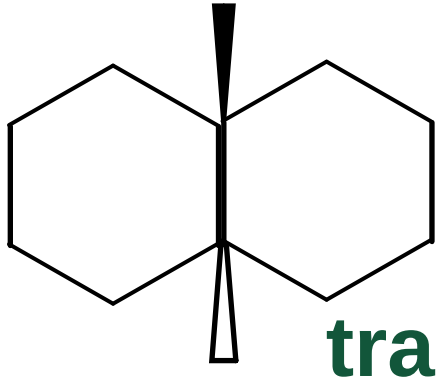

At least $2^6=64$ stereoisomers for steroids are possible




Cis- and trans joints of cycles:



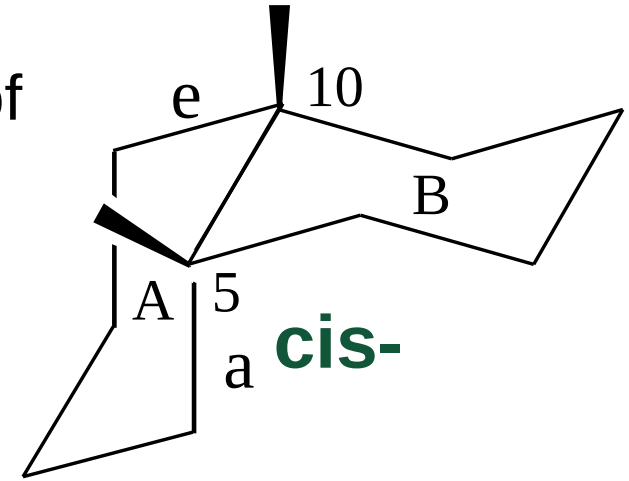
**cis-**



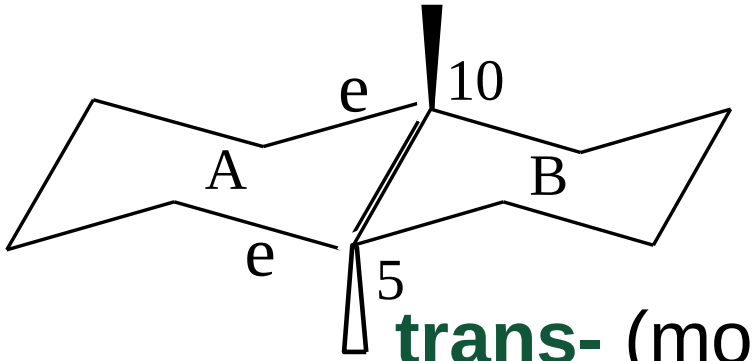
**trans-**

# CONFORMATIONS OF STEROIDS

Conformations of cycles A and B

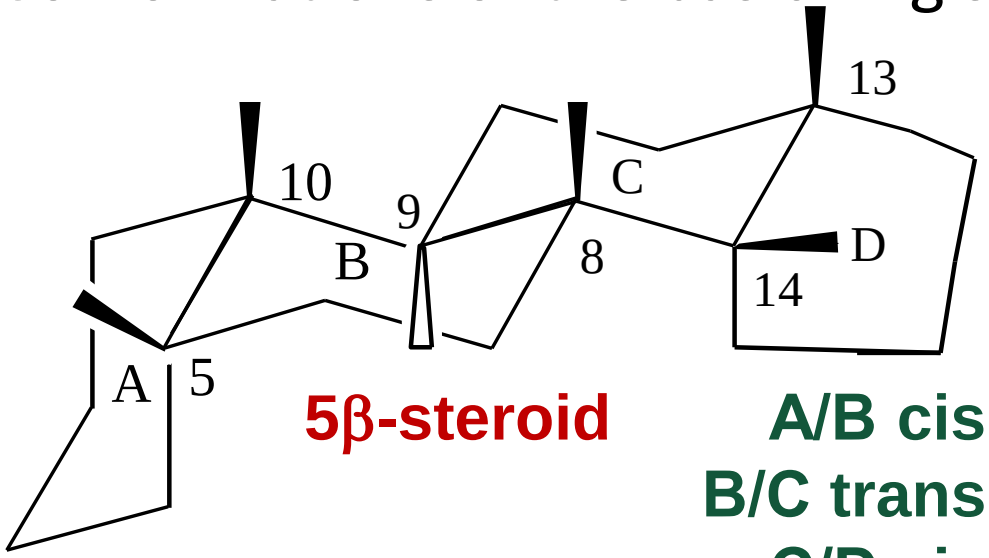



**cis-**



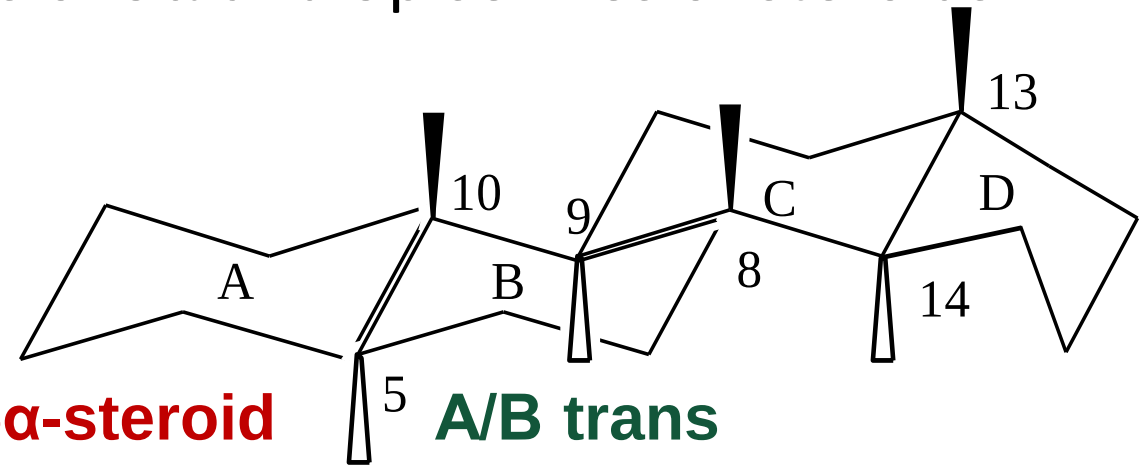

**trans-** (more stable)

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




**5β-steroid**

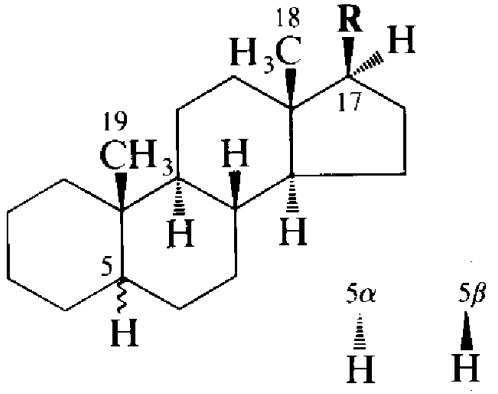
**A/B cis**
**B/C trans**
**C/D cis**




**5α-steroid**

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

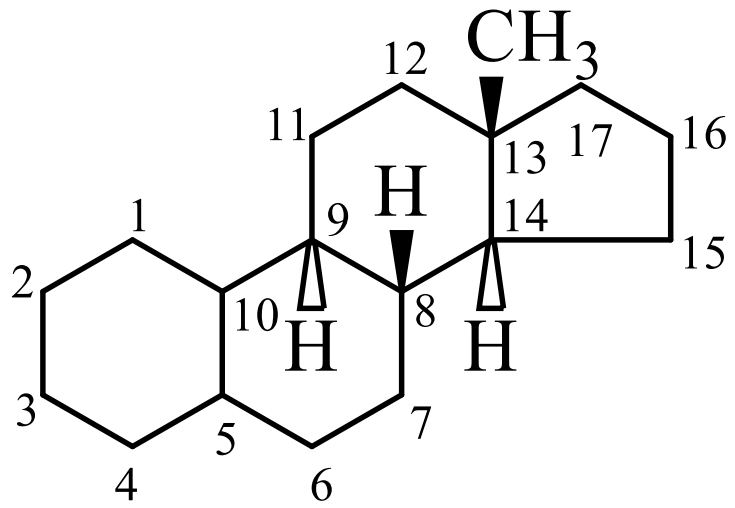
# Nomenclature of steroids



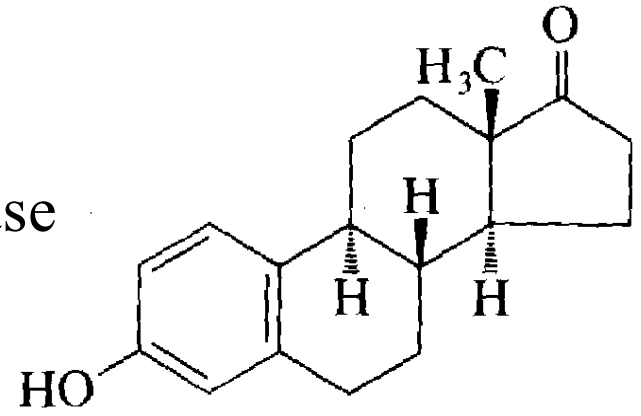

| R | NAME |
|---|---|
| —H | Androstane |
| —H (with —H also replacing —$^{19}CH_3$) | Estrane |
| —$^{20}CH^{21}CH_2CH_3$ | Pregnane |
| —$^{20}CH(^{21}CH_3)^{22}CH_2^{23}CH_2^{24}CH_3$ | Cholane |
| —$^{20}CH(^{21}CH_3)^{22}CH_2^{23}CH_2^{24}CH_2^{25}CH(^{27}CH_3)^{26}CH_3$ | Cholestane |

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

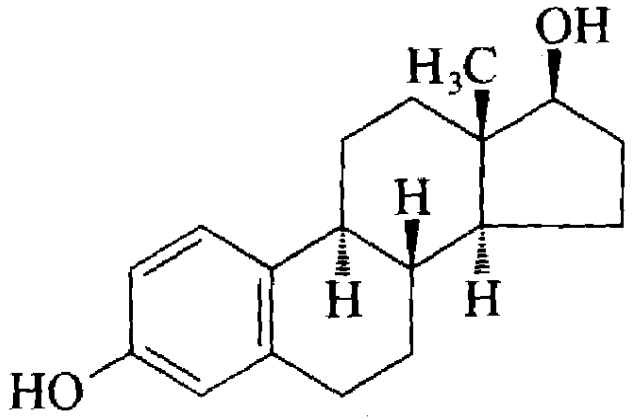
# SEX HORMONES. THE FEMALE SEX HORMONES




estrane is hydrocarbon in base of the female sex hormones

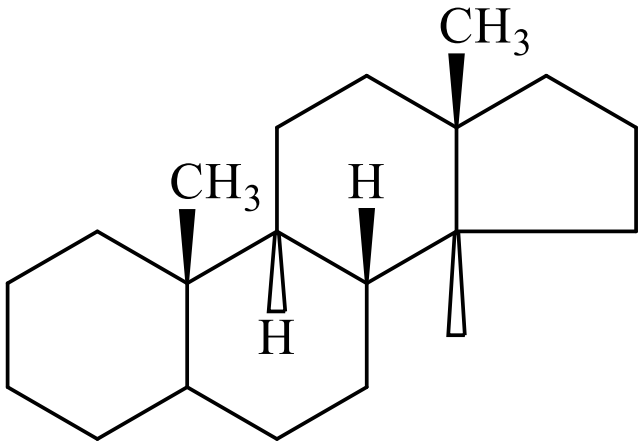



**Estrone**
**[3-hydroxy-1,3,5(10)-estratrien-17-one]**

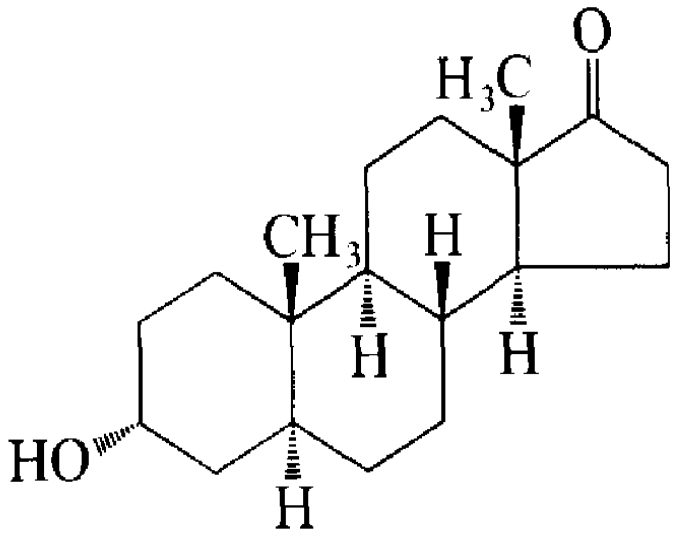



**Estradiol**
**[1,3,5(10)-estra-triene-3,17β-diol]**

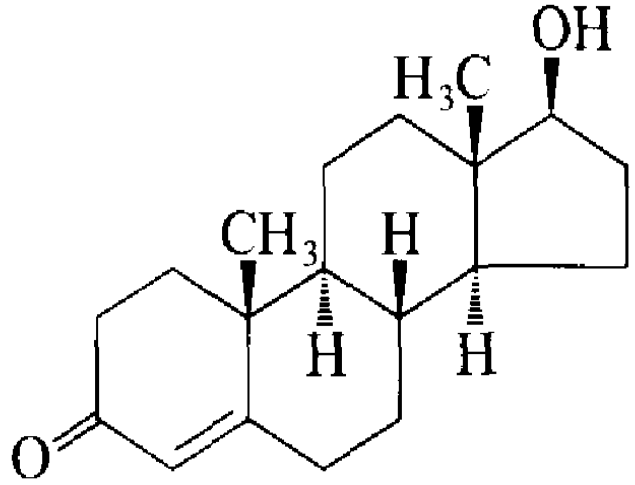
# SEX HORMONES. THE MALE SEX HORMONES




androstane is hydrocarbon in base of the male sex hormones

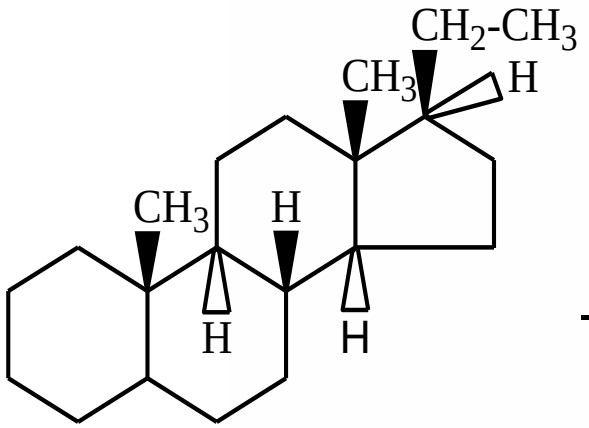



**Androsterone**
**(3α-hydroxy-5α-androstan-17-one)**

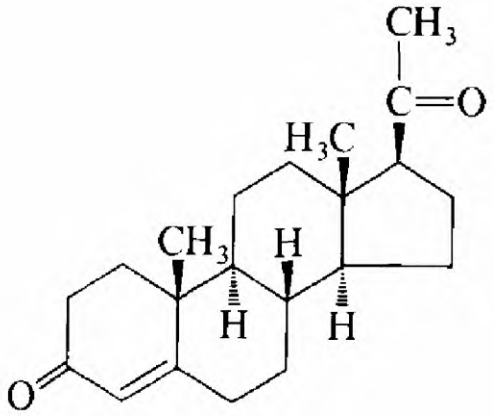



**Testosterone**
**(17β-hydroxy-4-androsten-3-one)**

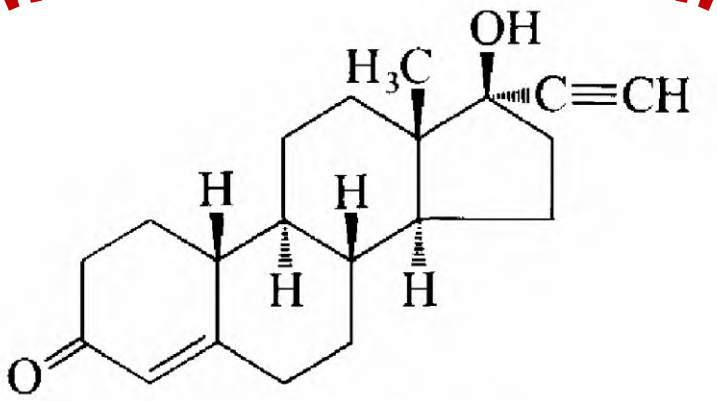
# PREGNANCY HORMONE



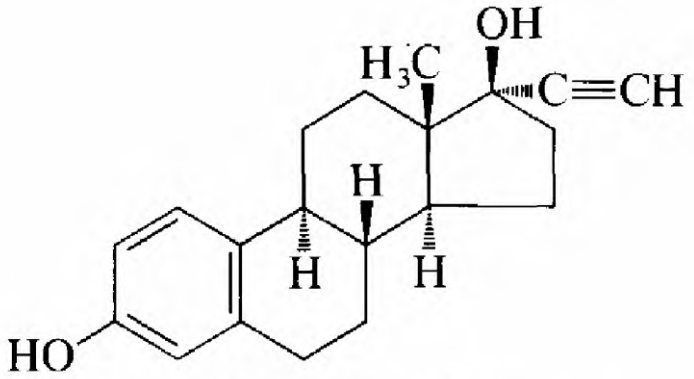

pregnane is hydrocarbon in base of progestins




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




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



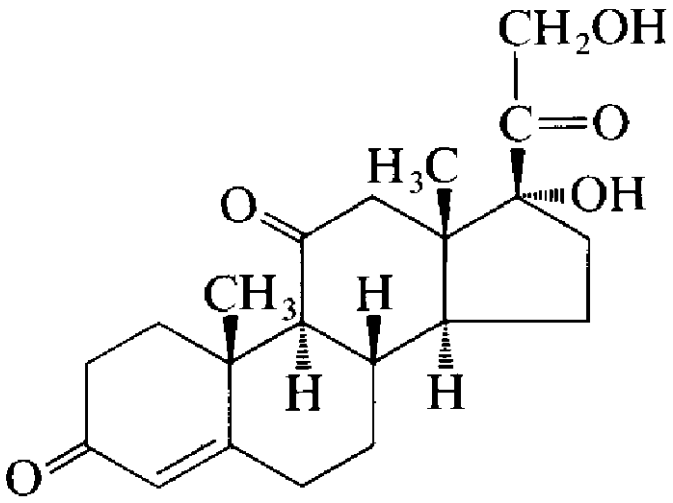

**Ethynylestradiol**
**[17α-ethynyl-1,3,5(10)-estratriene-3,17β-diol]**
sinthetic estrogen

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.*

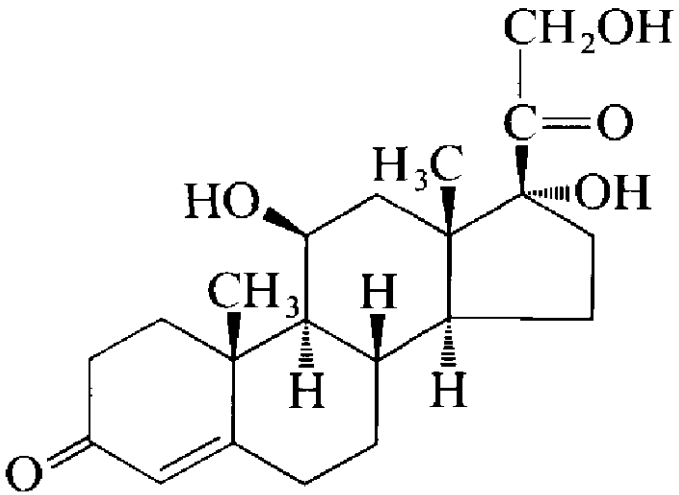
# ADRENOCORTICAL HORMONES

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

**Pregnane is a base of adrenocortical hormones:**

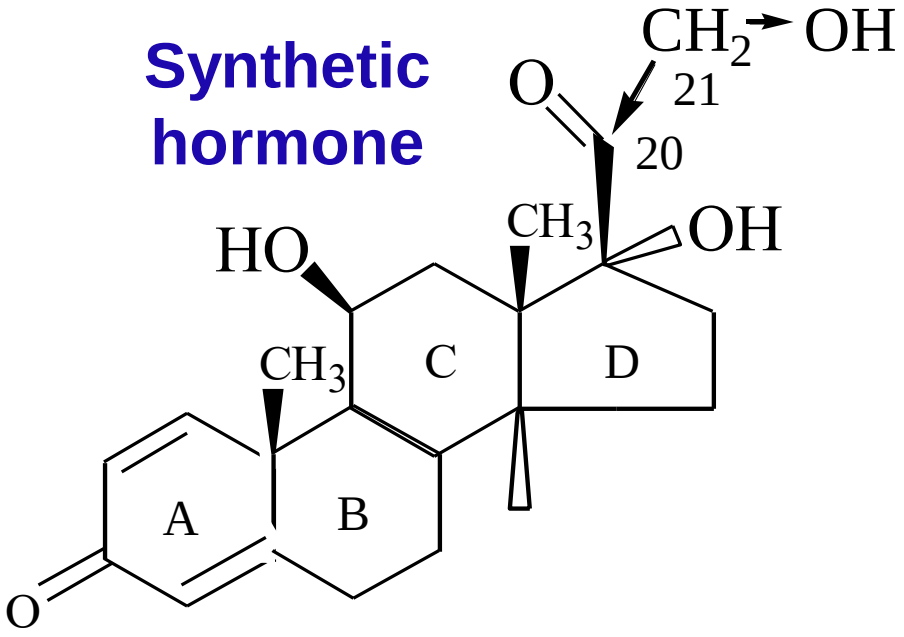



**Cortisone**
**(17α,21-dihydroxy-4-pregnene-3,11,20-trione)**




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

**Synthetic hormone**

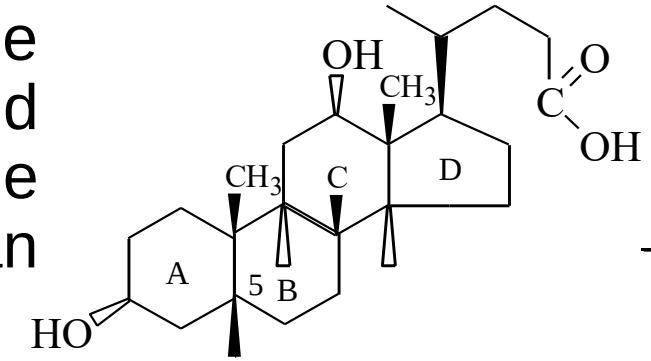



***Prednisolone:*** **11β, 17α, 21-trihydroxypregnadiene-1,4-dione-3,20**

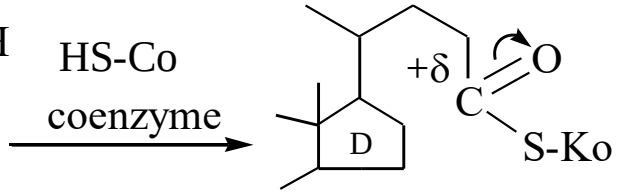
Most of the adrenocortical steroids have an oxygen function at position 11 (a keto group in cortisone, for example, and a β-hydroxyl in cortisol). Cortisol is the major hormone synthesized by the human adrenal cortex. The adrenocortical steroids are apparently involved in the regulation of a large number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

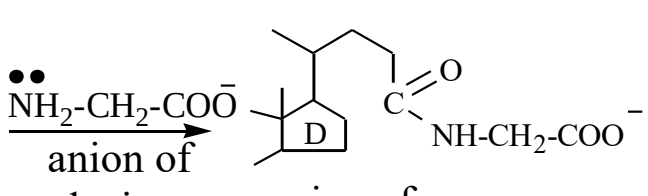
# Bile acids

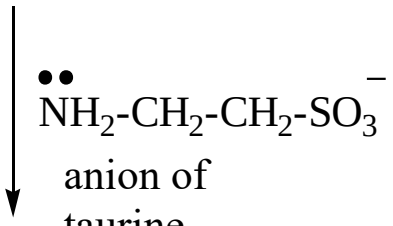
Cholic acid is the most abundant acid obtained from the hydrolysis of human or ox bile.

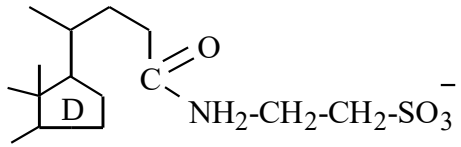


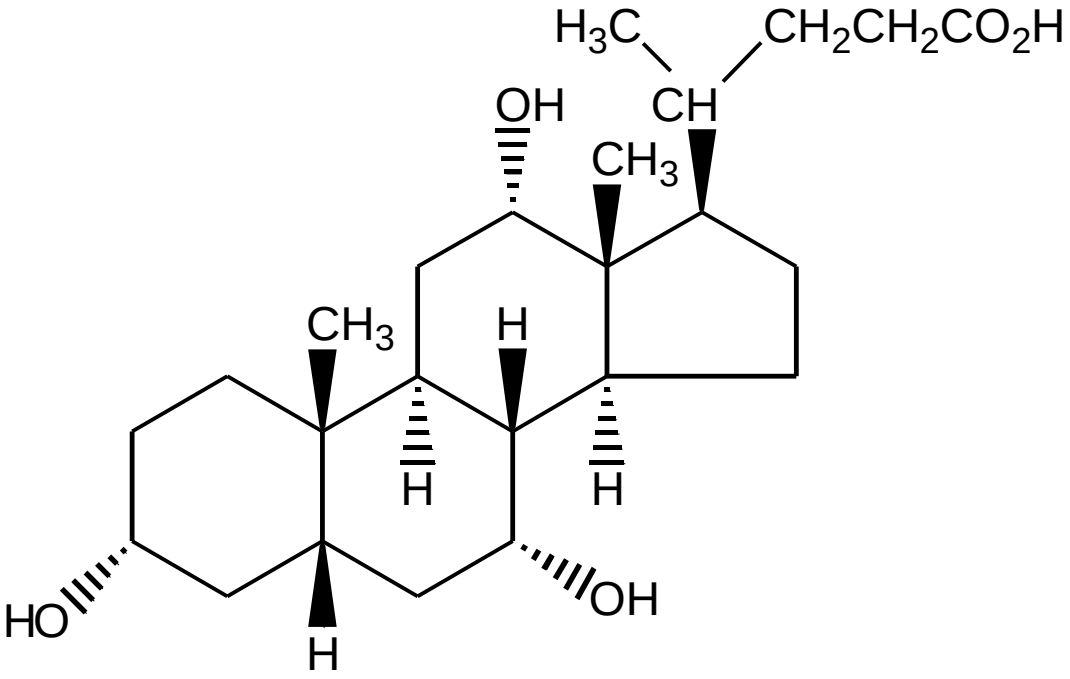

5β–steroid



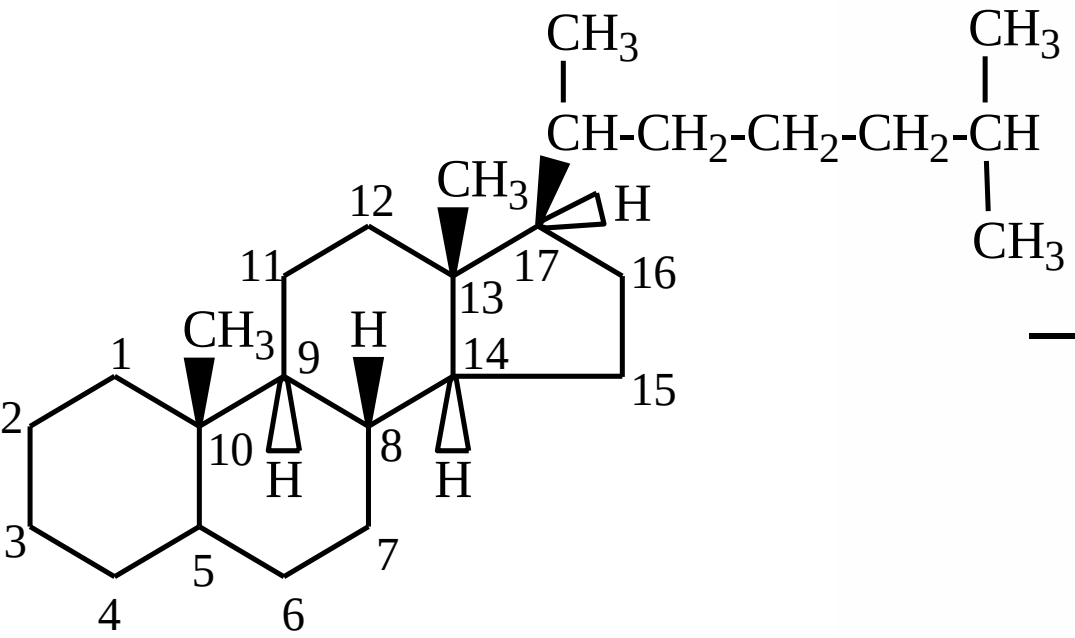



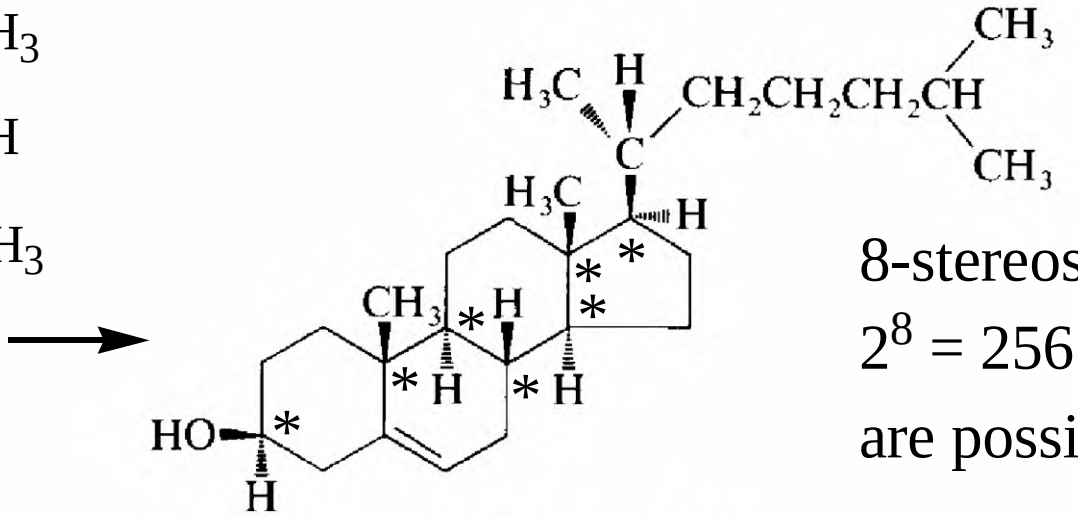

**Cholic acid**

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



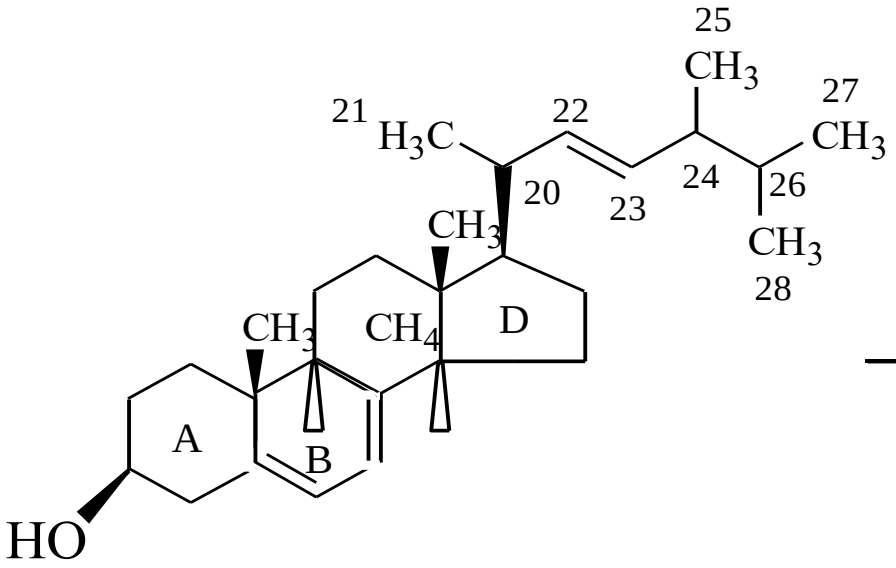

**5-Cholesten-3β-ol**
**(absolute configuration of cholesterol)**

8-stereosehters

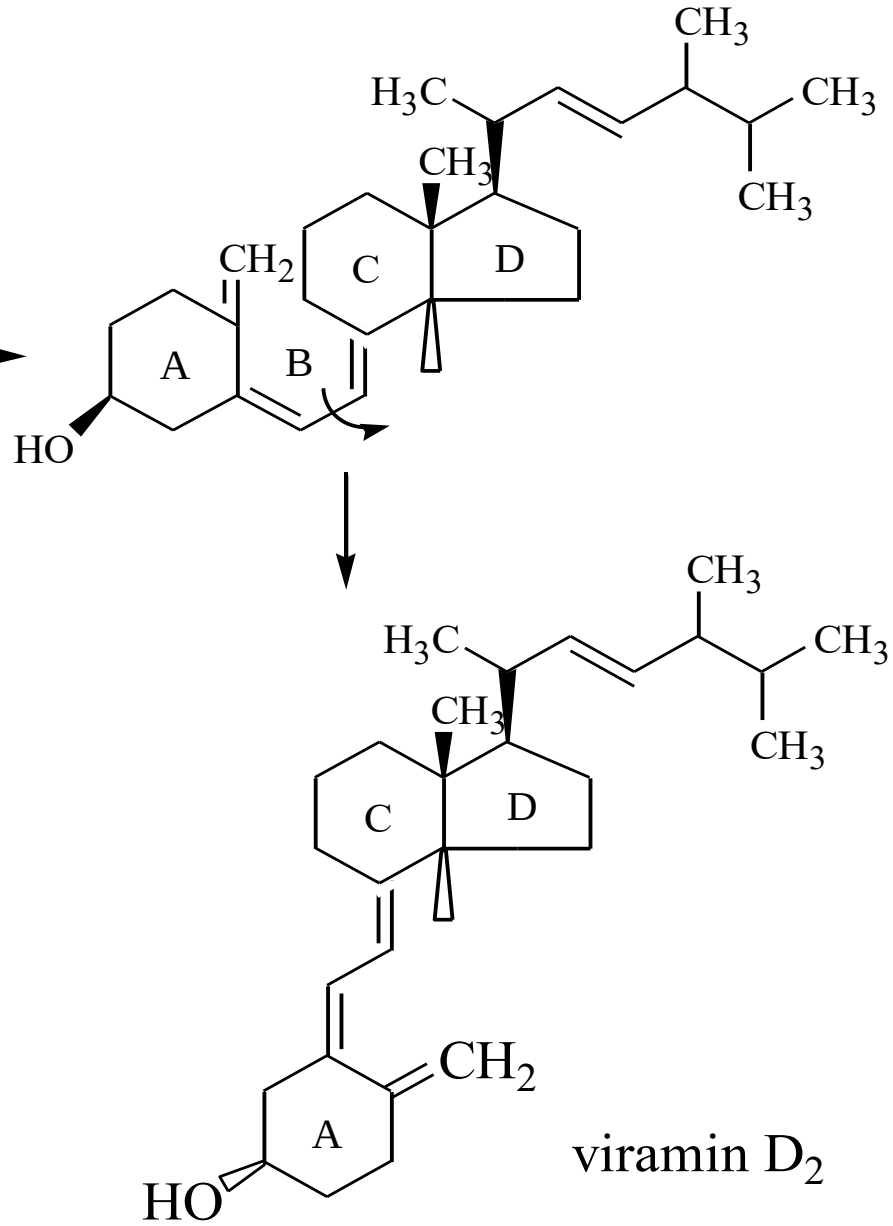
$2^8 = 256$ stereoisomers are possible

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

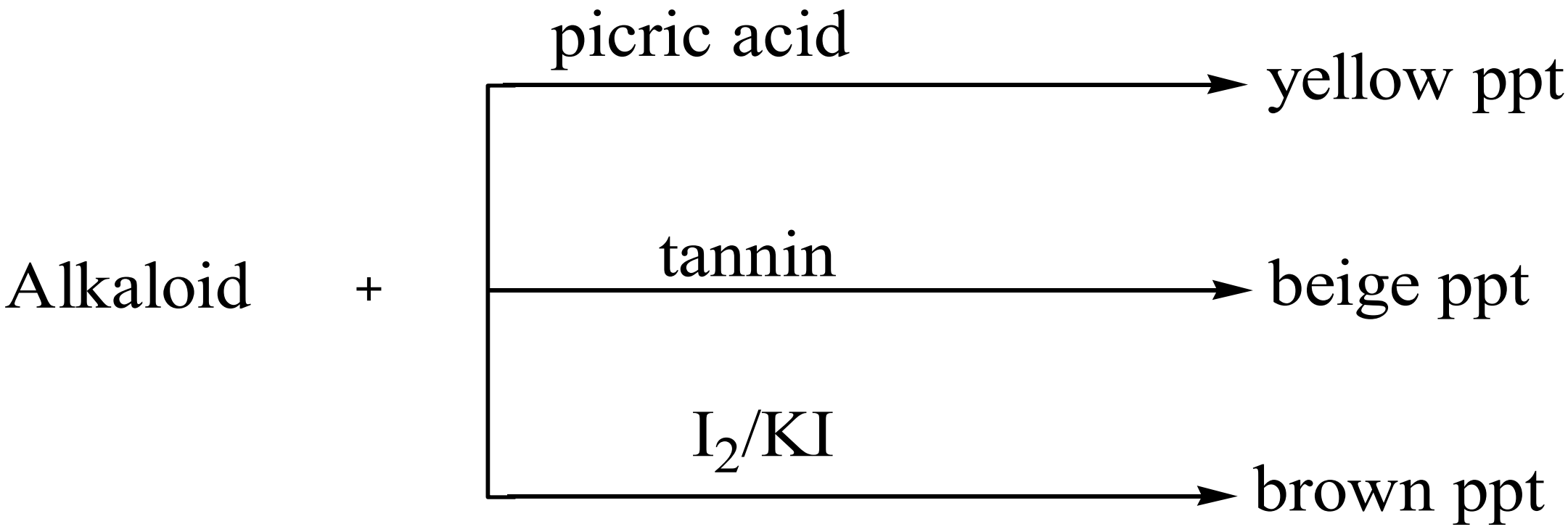
- Purine alkaloids
- Pyridine alkaloids
- Piperidine alkaloids
- Quinoline alkaloids
- Isoquinoline alkaloids
- Indole alkaloids

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.

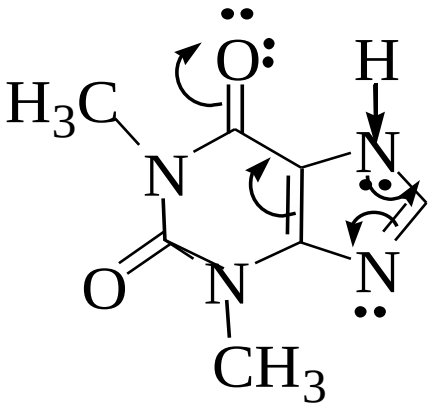
Alkaloids contain one or more nitrogen atoms. Most of alkaloids are heterocyclic compounds. **In organic chemistry alkaloids are classified according to the type of the heterocyclic ring structure.**

# IDENTIFICATION OF ALKALOIDS

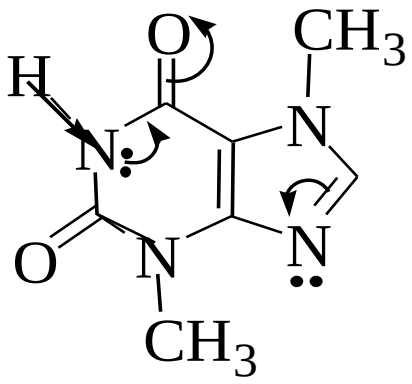
- All alkaloids are bases and they can form salts with acids. Reactions of insoluble salts formation can be used for identification



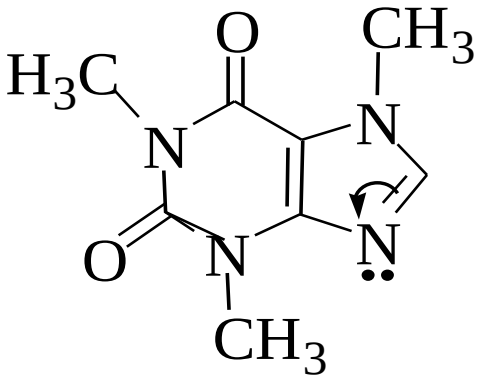
# N-METHYLXANTHINES (PURINE ALKALOIDS)



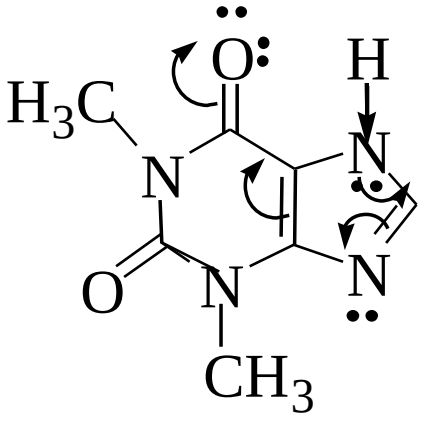
theophylline
(1,3-dimethyl
xanthine)

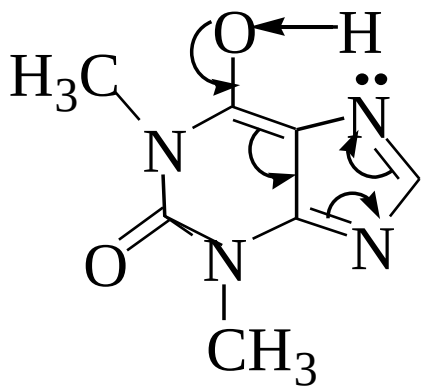


theobromine
(3,7-dimethyl
xanthine)

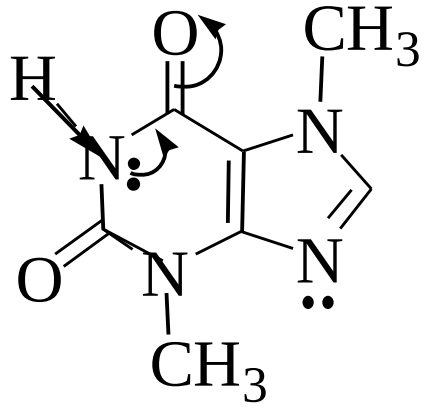


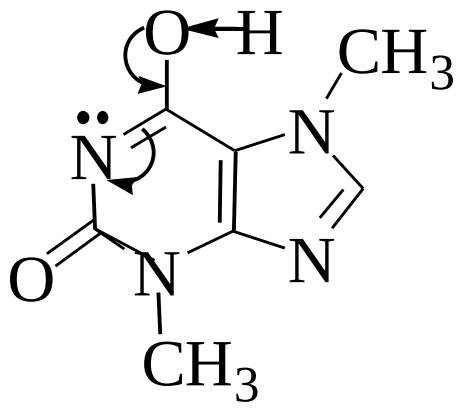
caffeine
(1,3,7-trimethyl
xanthine)





theophylline



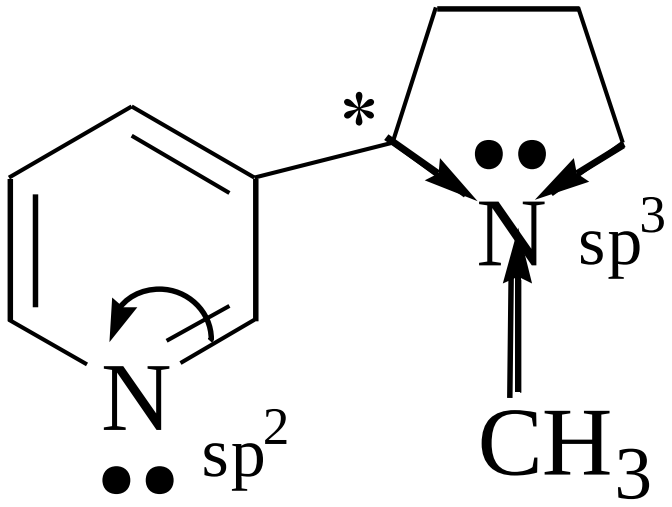


theobromine

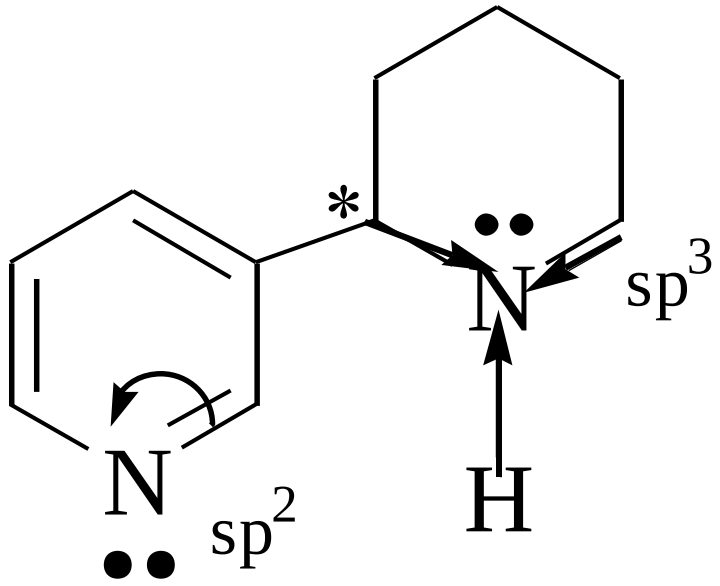
# *PYRIDINE ALKALOIDS*

Nicotine and anabasin are toxic.

Lethal dose of nicotine for human is 30-60 mg



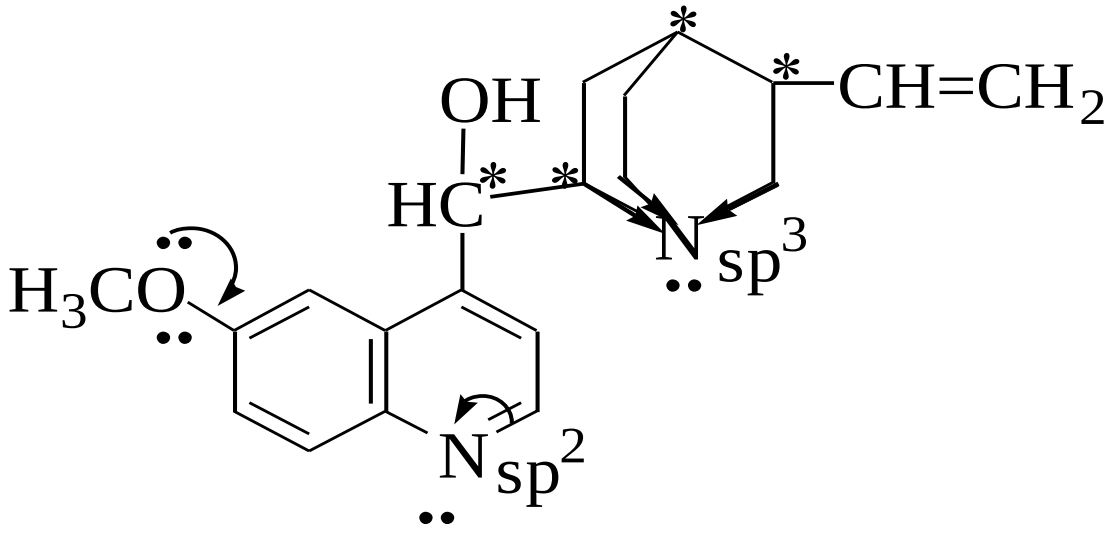

nicotine



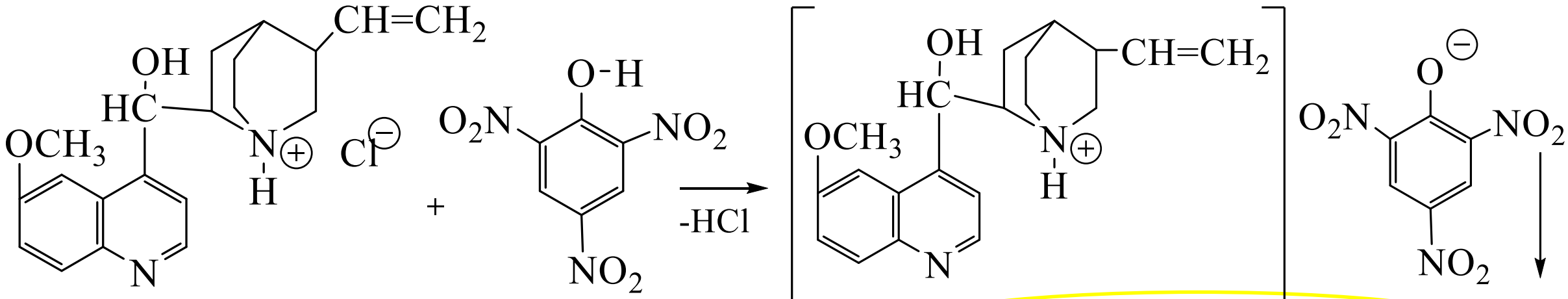

anabasin

# QUININE ALKALOIDS

***Quinine is antimalarial medicine***

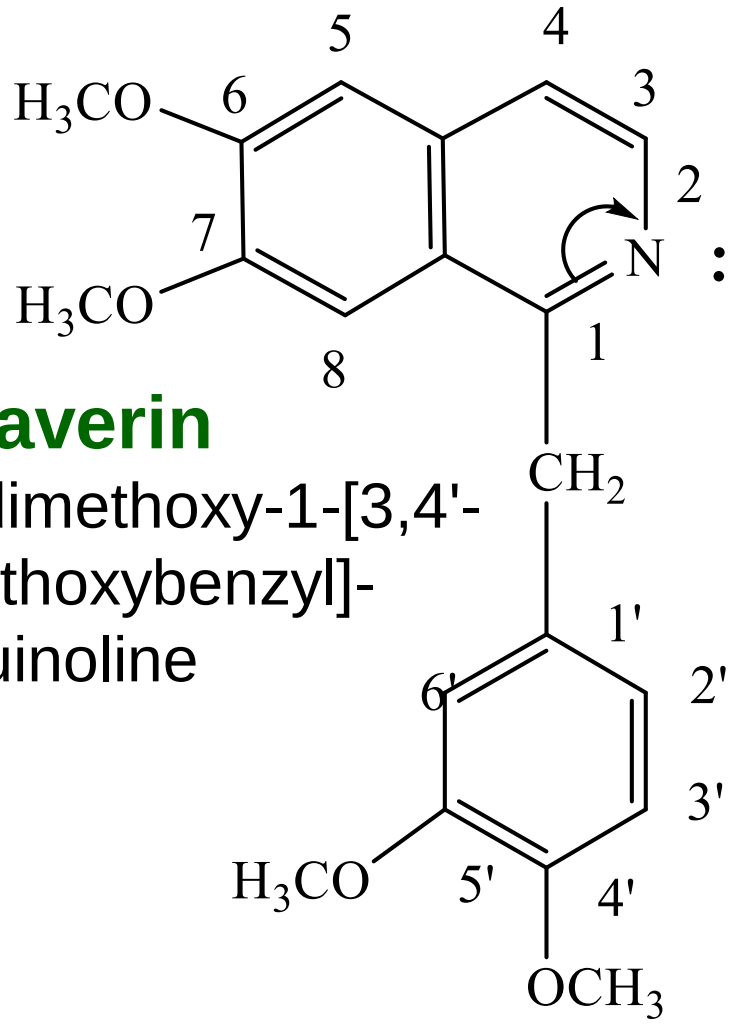



quinine



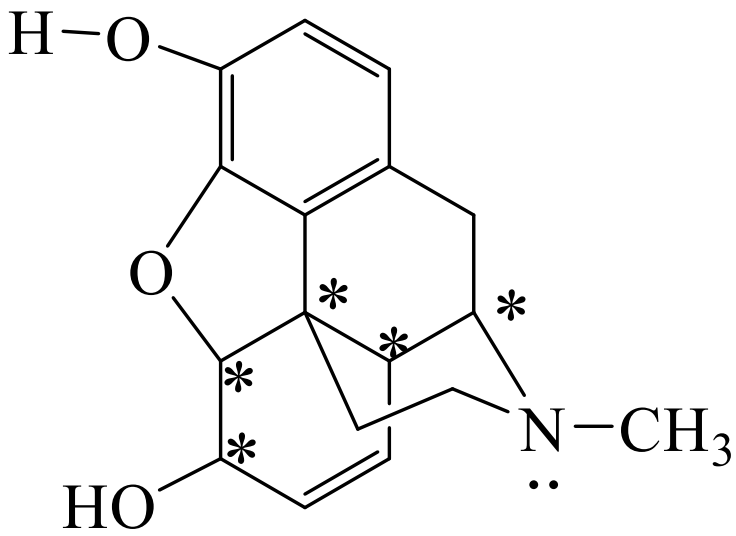

**Salt of quinine (soluble)** **picric acid** **quinine picrate (yellow ppt)**

# ISOQUINOLINE AND PHENANTHRENEISOQUINOLINE ALKALOIDS

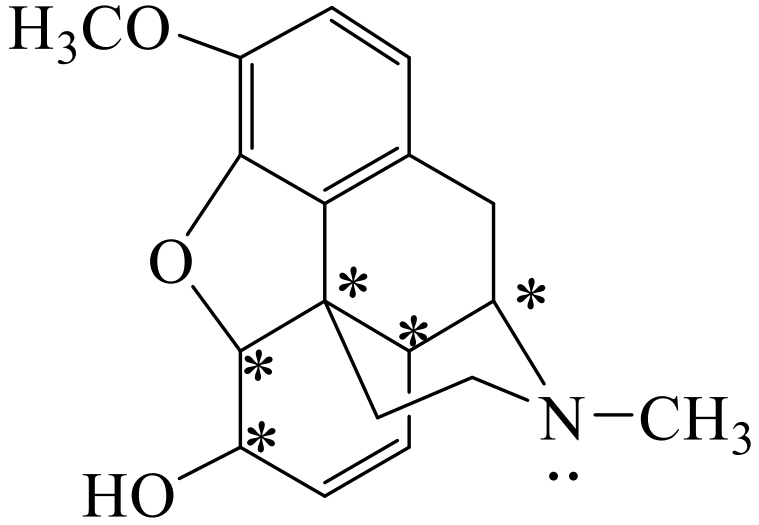



**papaverin**

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

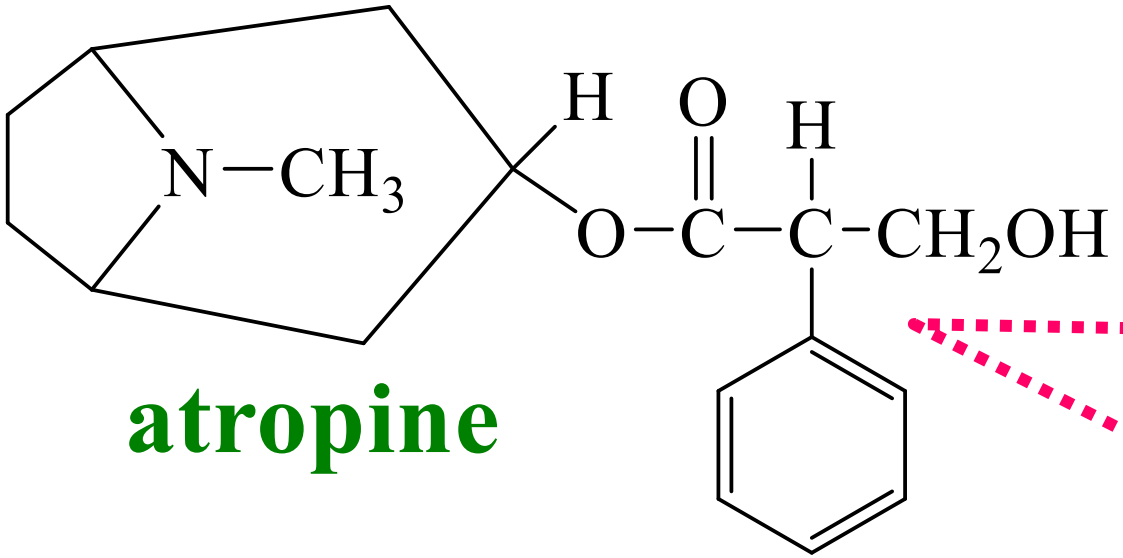



**morphine**

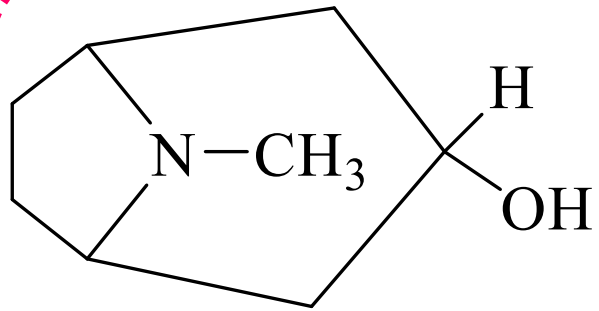



**codeine**

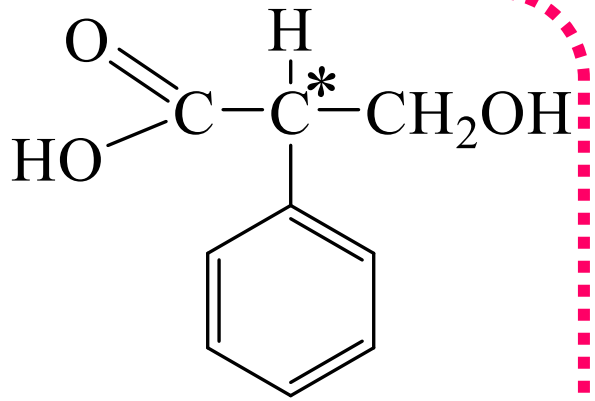
# TROPAN ALKALOIDS



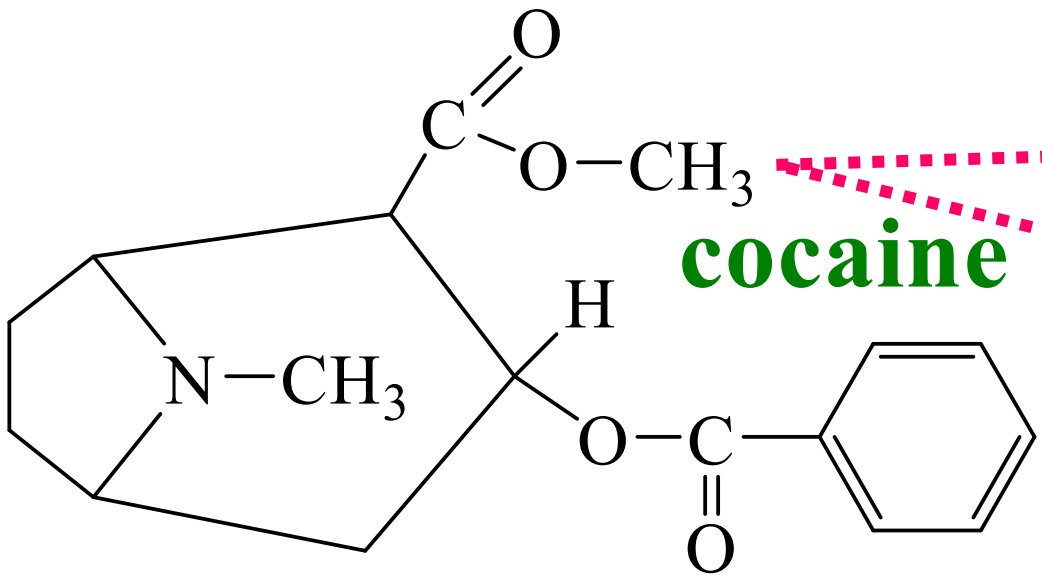

**atropine**



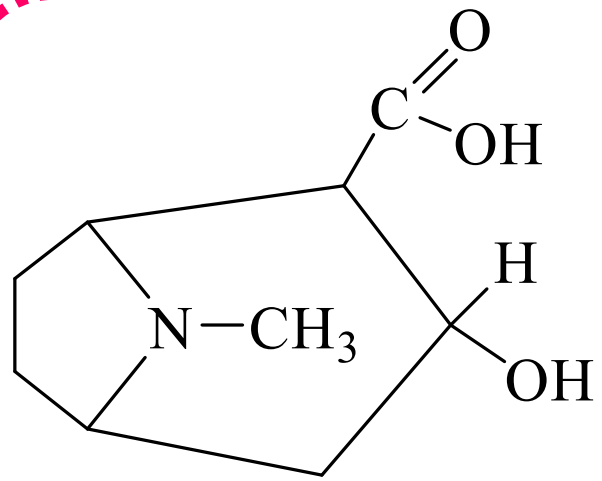

**tropin**




**tropic acid**




**cocaine**




**ekgonin (ectonin)**