MINISTRY OF PUBLIC HEALTH
ZAPOROZHYE STATE MEDICAL UNIVERSITY
DEPARTMENT OF ORGANIC AND BIOORGANIC CHEMISTRY

HANDBOOK
OF BIOORGANIC CHEMISTRY

LIPIDS

for medical students
specialty 222 "Medicine"

1st-year student of ___ group

____

surname, name

Zaporozhye
2016

HANDBOOK OF BIOORGANIC CHEMISTRY «LIPIDS» was approved by Zaporozhye State Medical University Scientific Council (Protocol № from . . 2016) and recommended for medical students of specialty 222 "Medicine".

Authors board:
Kovalenko S.I. – Doctor, professor.
Priimenko B.A. – Doctor, professor.
Kandybey K.I. – PhD, associate professor.
Voskoboynik A.Yu. – PhD, associate professor.
Antipenko L.N. – PhD, assistant professor.
Kazunin M.S. – PhD, assistant professor.
Bily A.K. – PhD, assistant professor.
Kholodnyak S.V. – assistant.
Antipenko A.N. - assistant

Under the general editorship of the Head of Organic and Bioorganic Chemistry Department,
doctor, professor **Kovalenko S.I.**

Reviewers:

The Head of the Biological Chemistry and Laboratory Diagnosis Department,
doctor, associate professor **Alexandrova. K.V.**

The Head of the Department of Toxicology and Inorganic Chemistry,
doctor, professor **Panasenko A.I.**

THEMATIC PLANS OF LESSONS

№	**Theme**	**Hours**
1	Classification. Principles of nomenclature. The spatial structure of organic molecules. Isomerism.	2
2	Electronic structure of chemical bonds and mutual influence of atoms in organic molecules. Acidic and basic properties. Chemical reactions mechanisms.	2
3	Aromatic and aliphatic hydrocarbons. Structure, nomenclature, chemical properties.	2
4	Halogen and hydroxy hydrocarbons, their thio analogues. Amines. Structure, nomenclature, chemical properties.	2
5	*Final submodule control I: «The theoretical basis of the structure and reactivity of organic compounds, aliphatic and aromatic, hydroxy and halogeno hydrocarbons, their thio analogues and amines."*	**2**
6	Investigation of the aldehydes and ketones' chemical properties. Biologically important reactions of carbonyl compounds.	2
7	Structure, properties and biological significance of carboxylic acids. Heterofunctional carboxylic acids' (hydroxy, oxo, phenolic) derivatives.	2
8	Polyfunctional derivatives of aliphatic and aromatic compounds.	2
9	**Saponificated lipids: fats, oils, phospholipids, waxes. Structure, nomenclature, chemical properties.**	**2**
10	**Non-saponificated lipids: prostaglandins, terpenes, steroids. Structure, nomenclature, chemical properties.**	**2**
11	***Final submodule control II: «Heterofunctional organic compounds - metabolites and basis of the most important***	2

	groups of drugs. Carbonyl compounds. Carboxylic acids and their functional derivatives".	
12	α-Amino acids. Peptides. Structure, nomenclature, chemical properties.	2
13	Structural organization, physical and chemical properties of proteins. Synthesis and analysis.	2
14	Carbohydrates. The structure, classification and chemical properties of monosaccharides.	2
15	The structure and functions of di- and polysaccharides.	2
16	Classification, structure, nomenclature, chemical properties and biological value of heterocyclic compounds.	2
17	The structure and biochemical function of nucleosides, nucleotides and nucleic acids.	2
18	*Final submodule control III: "Biologically important classes of bioorganic compounds. Heterocyclic. Biopolymers and their structural components".*	2
	Together	36
19	*FINAL MODULE CONTROL "Biologically important classes of bioorganic compounds. Biopolymers and their structural components".*	2
	Together	38

EVALUATION CRITERIA OF STUDENT ACADEMIC PROGRESS

Every lesson student gets mark: "excellent" - 5 points, "good" - 4 points, "satisfactory" - 3 points, "unsatisfactory" - 0 points.

The student is allowed to take the final module control if he scores no less than 42 mark points (18 × 5 = 90) for 18 lessons, which corresponds to maximum 110 rate points.

The final module is counted finished if the student scores no less than 50 rate points.

Characteristics	The minimum score	The maximum score
Total score for submodules.	**60**	**110**
Individual student self-work: Preparation the scientific literature review on the selected topic.	**–**	**10**
The score for final module test.	**50**	**80**
TOTAL	**110**	**200**

INTRODUCTION

Bioorganic chemistry is studied according to the approved model program in 2016 for III-IV accreditation levels students for specialty 222 "Medicine", in accordance with the educational qualification characteristics and professional training programs approved by the Zaporizhzhya State Medical University Academic Council decision of 05.30.2016, Protocol №10.

According to the plan foreign faculty English teaching students of specialty 222 “Medicine” learn bioorganic chemistry at the second semester of the first education year. The final module consists of three submodules:

Submodule 1 – "*The theoretical basis of the structure and reactivity of organic compounds, aliphatic and aromatic, hydroxy and halogeno hydrocarbons, their thio analogues and amines*".

Submodule 2 – "*Heterofunctional organic compounds - metabolites and basis of the most important groups of drugs. Carbonyl compounds. Carboxylic acids and their functional derivatives*".

Submodule 3 – " *Biologically important classes of bioorganic compounds. Heterocyclic. Biopolymers and their structural components*".

The study objectives are:

- to analyze the reactivity of lipids, ensuring their functional properties and metabolic changes in the body.

Lesson №9

Subject: SAPONIFICATED LIPIDS: FATS, OILS, PHOSPHOLIPIDS, WAXES. STRUCTURE, NOMENCLATURE, CHEMICAL PROPERTIES.

Subject motivation: Lipids are one of the major constituents of foods, and are important in our diet for a number of reasons. They are a major source of energy and provide essential lipid nutrients. They are found in cell membranes, insulating layer around nerve cells, etc. Linoleic, linolenic acid and arachidonic acids are important essential fatty acids. Humans don’t have the ability to introduce double bonds in fatty acids beyond carbon 9 and 10, because lack desaturase enzymes, required for their production. Waxes on the surface of leaves and insect cuticles, along with oils on feathers and fur, form a water-proof layer which enables the organisms to survive in their environments. Lipid-rich myelin, found wrapped around neurons, provides electrical insulation which makes rapid transmission of impulses possible.

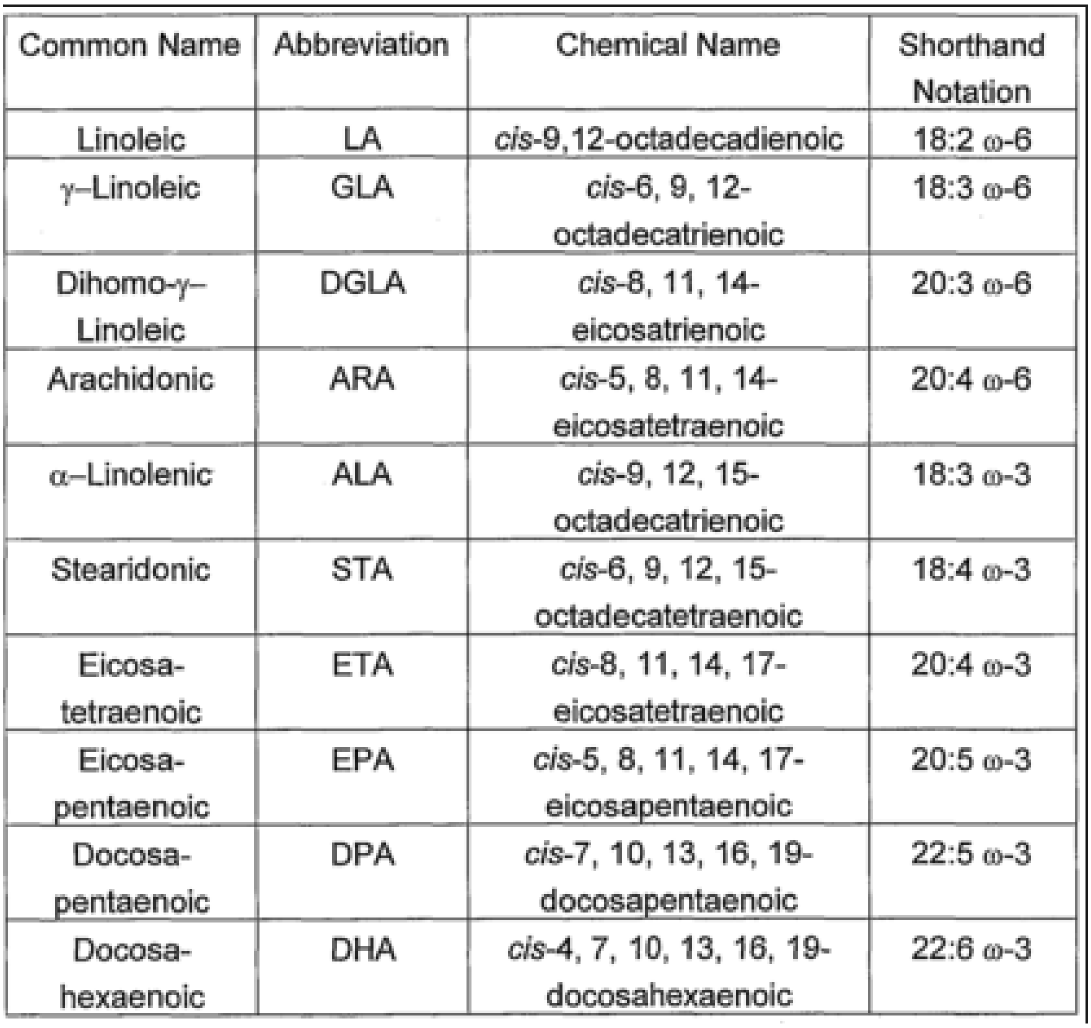
Learning goal: name biological macromolecules and their building blocks, know IUPAC or systematic and common names of a fatty acid, test samples for the presence of lipids.

THEORETICAL QUESTIONS

1. Definition of lipids, fatty acids.
2. Nomenclature of saturated fatty acids. IUPAC system. Common names.
3. Nomenclature of unsaturated fatty acids. Systematic names. Common names. Omega-numbering. Delta-numbering. Shortened form of nomenclature.
4. What are the essential fatty acids? Physical properties of fatty acids.
5. What are hydrophobic molecules (or hydrophobic molecular regions)? What are hydrophilic molecules? How can they be described in relation to their polarity?
6. What are Lipids? Classification of lipids.
7. Simple lipids (Fats, Oils, Waxes).

8. Complex lipids: Phospholipids, Glycolipids, Glycosphingolipids, Sulfolipids, Aminolipids, Lipolipids.
9. What are saponifiable lipids? Stereospecific numbering system of glycerol.
10. The general structure and properties of phospholipids. Phosphatidic acid, Phosphatidyl-ethanolamine (Cephaline), Phosphatidylcholine (Lecithin), Phosphatidylserine, Phosphatidylinositol, Phosphatidylglycerol.
11. Lysophospholipids, Plasmalogen, Sphingolipids, Ceremides.
12. Why do fats have thermal insulation properties?
13. Saponification number, acidic and iodine number.
14. Lipolysis.

The **fatty acids** are carboxylic acids with long carbon chains of 12–20 carbon atoms.



Common Name	Abbreviation	Chemical Name	Shorthand Notation
Linoleic	LA	*cis*-9,12-octadecadienoic	18:2 ω-6
γ–Linoleic	GLA	*cis*-6, 9, 12-octadecatrienoic	18:3 ω-6
Dihomo-γ–Linoleic	DGLA	*cis*-8, 11, 14-eicosatrienoic	20:3 ω-6
Arachidonic	ARA	*cis*-5, 8, 11, 14-eicosatetraenoic	20:4 ω-6
α–Linolenic	ALA	*cis*-9, 12, 15-octadecatrienoic	18:3 ω-3
Stearidonic	STA	*cis*-6, 9, 12, 15-octadecatetraenoic	18:4 ω-3
Eicosa-tetraenoic	ETA	*cis*-8, 11, 14, 17-eicosatetraenoic	20:4 ω-3
Eicosa-pentaenoic	EPA	*cis*-5, 8, 11, 14, 17-eicosapentaenoic	20:5 ω-3
Docosa-pentaenoic	DPA	*cis*-7, 10, 13, 16, 19-docosapentaenoic	22:5 ω-3
Docosa-hexaenoic	DHA	*cis*-4, 7, 10, 13, 16, 19-docosahexaenoic	22:6 ω-3

Fatty acids that have carbon–carbon double bonds are known as unsaturated. Fatty acids without double bonds are known as saturated. Fatty acid chains differ by length, often categorized as short to very long.

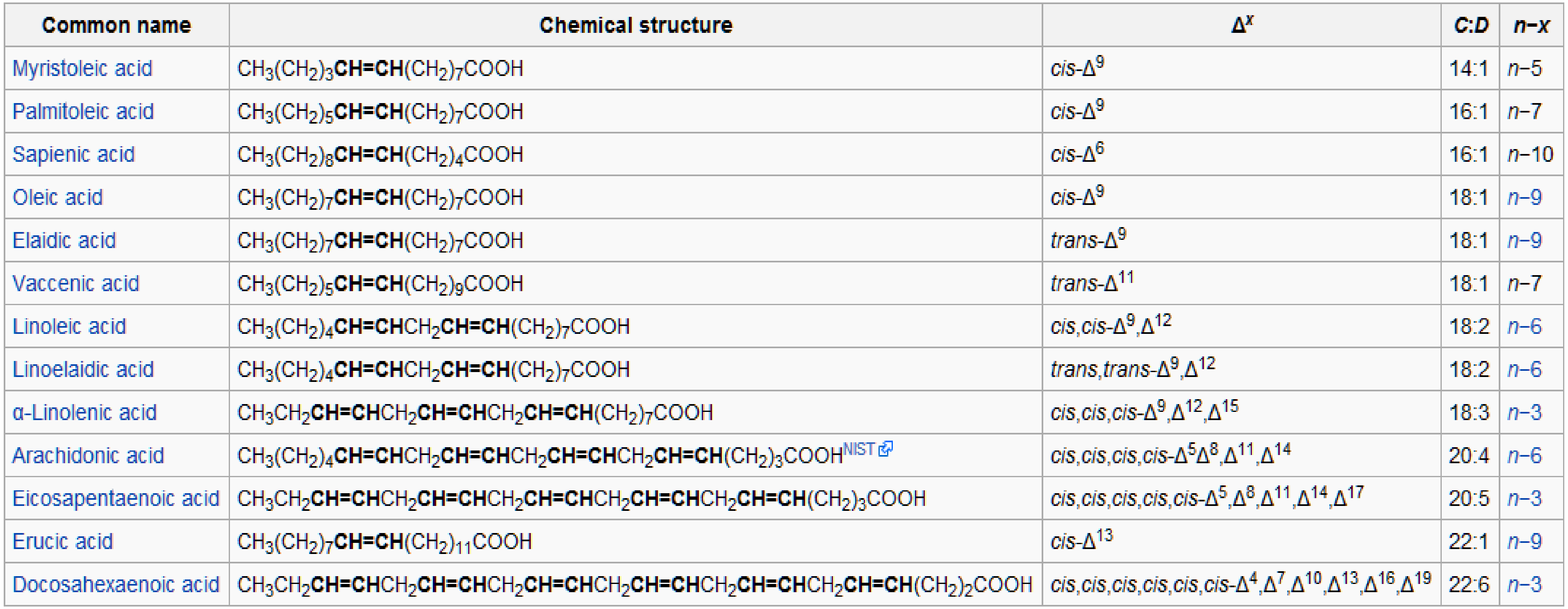
- Short-chain fatty acids (SCFA) are fatty acids with aliphatic tails of fewer than six carbons (e.g. butyric acid).
- Medium-chain fatty acids (MCFA) are fatty acids with aliphatic tails of 6–12 carbons, which can form medium-chain triglycerides.
- Long-chain fatty acids (LCFA) are fatty acids with aliphatic tails 13 to 21 carbons.
- Very long chain fatty acids (VLCFA) are fatty acids with aliphatic tails longer than 22 carbons.

Position of double bonds indicated by Δn, where n indicates lower numbered carbon of each pair. Shorthand notation example of arachidonic acid: $20{:}4\Delta 5,8,11,14$ (total # carbons : # double bonds, Δ double bond positions)

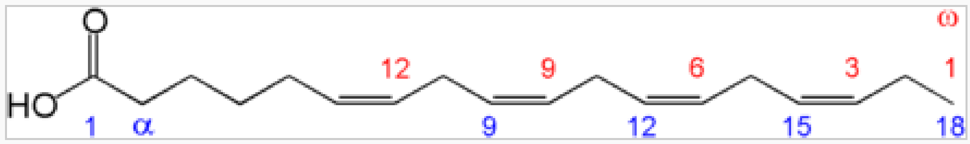
The nonpolar part of the molecule (comprised of C C and C H bonds) is not attracted to water, so it is said to be **hydrophobic** (water fearing). The polar part of the molecule is attracted to water, so it is said to be **hydrophilic** (water loving). In a lipid, the hydrophobic portion is always much larger than the hydrophilic portion. Naturally occurring fatty acids have an even number of carbon atoms. Saturated fatty acids have no double bonds in their long hydrocarbon chains.

Unsaturated fatty acids have one or more double bonds in their long hydrocarbon chains. Generally, double bonds in naturally occurring fatty acids are *cis*. The higher melting points of the saturated fatty acids reflect the uniform rod-like shape of their molecules. The *cis*-double bonds in the unsaturated fatty acids introduce a kink in their shape, which makes it more difficult to pack their molecules together in a stable repeating array or crystalline lattice. The *trans*-double bond isomer of oleic acid, known as elaidic acid, has a linear shape and a melting point of 45 ºC (32 ºC higher than its *cis* isomer).

The main fatty acids names.



Common name	Chemical structure	Δ^x	C:D	n−x
Myristoleic acid	$CH_3(CH_2)_3$**CH=CH**$(CH_2)_7COOH$	*cis*-Δ^9	14:1	*n*−5
Palmitoleic acid	$CH_3(CH_2)_5$**CH=CH**$(CH_2)_7COOH$	*cis*-Δ^9	16:1	*n*−7
Sapienic acid	$CH_3(CH_2)_8$**CH=CH**$(CH_2)_4COOH$	*cis*-Δ^6	16:1	*n*−10
Oleic acid	$CH_3(CH_2)_7$**CH=CH**$(CH_2)_7COOH$	*cis*-Δ^9	18:1	*n*−9
Elaidic acid	$CH_3(CH_2)_7$**CH=CH**$(CH_2)_7COOH$	*trans*-Δ^9	18:1	*n*−9
Vaccenic acid	$CH_3(CH_2)_5$**CH=CH**$(CH_2)_9COOH$	*trans*-Δ^{11}	18:1	*n*−7
Linoleic acid	$CH_3(CH_2)_4$**CH=CH**CH_2**CH=CH**$(CH_2)_7COOH$	*cis*,*cis*-Δ^9,Δ^{12}	18:2	*n*−6
Linoelaidic acid	$CH_3(CH_2)_4$**CH=CH**CH_2**CH=CH**$(CH_2)_7COOH$	*trans*,*trans*-Δ^9,Δ^{12}	18:2	*n*−6
α-Linolenic acid	CH_3CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_7COOH$	*cis*,*cis*,*cis*-Δ^9,Δ^{12},Δ^{15}	18:3	*n*−3
Arachidonic acid	$CH_3(CH_2)_4$**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_3COOH$NIST	*cis*,*cis*,*cis*,*cis*-$\Delta^5\Delta^8$,Δ^{11},Δ^{14}	20:4	*n*−6
Eicosapentaenoic acid	CH_3CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_3COOH$	*cis*,*cis*,*cis*,*cis*,*cis*-Δ^5,Δ^8,Δ^{11},Δ^{14},Δ^{17}	20:5	*n*−3
Erucic acid	$CH_3(CH_2)_7$**CH=CH**$(CH_2)_{11}COOH$	*cis*-Δ^{13}	22:1	*n*−9
Docosahexaenoic acid	CH_3CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_2COOH$	*cis*,*cis*,*cis*,*cis*,*cis*,*cis*-Δ^4,Δ^7,Δ^{10},Δ^{13},Δ^{16},Δ^{19}	22:6	*n*−3



Numbering of carbon atoms

Most fatty acids have an even number of carbons (synthesized from two-carbon units). IUPAC nomenclature: carboxyl carbon is C-1. Common nomenclature: α,β,γ,δ,ε etc. from C-1. Unsaturated fatty acids are sometimes classified as **omega-n acids**, where **n** is the carbon at which the first double bond occurs in the carbon chain, beginning at the end of the chain that contains the CH_3 group. Thus, linoleic acid is an omega-6 acid and linolenic acid is an omega-3 acid.

Two polyunsaturated fatty acids, linoleic and linolenic, are designated "**essential**" because their absence in the human diet has been associated with health problems, such as scaley skin, stunted growth and increased dehydration. These acids are also precursors to the prostaglandins, a family of physiologically potent lipids present in minute amounts in most body tissues.

Because of their enhanced acidity, carboxylic acids react with bases to form ionic salts, as shown in the following equations.

$$RCO_2H + NaHCO_3 \longrightarrow RCO_2^{(-)}\,Na^{(+)} + CO_2 + H_2O$$

$$RCO_2H + (CH_3)_3N: \longrightarrow RCO_2^{(-)}\,(CH_3)_3NH^{(+)}$$

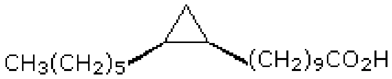
$$RCO_2H + AgOH \longrightarrow RCO_2^{\delta(-)}\,Ag^{\delta(+)} + H_2O$$

In the case of alkali metal hydroxides and simple amines (or ammonia) the resulting salts have pronounced ionic character and are usually soluble in water. Heavy metals such as silver, mercury and lead form salts having more covalent character (3rd example), and the water solubility is reduced, especially for acids composed of four or more carbon atoms.

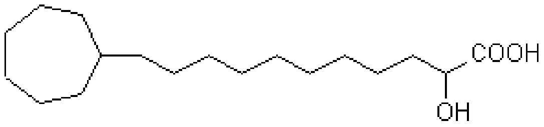
A wide array of unusual fatty acids is found in seed oils and microorganisms such as bacteria. Among these are fatty acids containing cis-cyclopropane fatty acids (e.g. lactobacillic acid), omega-cycloalkyl fatty acids (e.g. 2-hydroxy-11-cycloheptylundecanoic acid) and cyclopropene fatty acids (e.g. malvalic and sterculic acid).

A wide array of unusual fatty acids is found in seed oils and microorganisms such as bacteria. Among these are fatty acids containing cis-cyclopropane fatty acids (e.g. lactobacillic acid), omega-cycloalkyl fatty acids (e.g. 2-hydroxy-11-

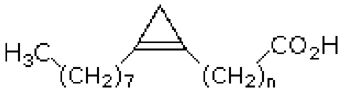
cycloheptylundecanoic acid) and cyclopropene fatty acids (e.g. malvalic and sterculic acid).



lactobacillic acid

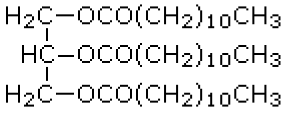


2-hydroxy-11-cycloheptylundecanoic acid



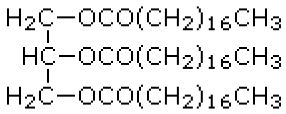
n = **6** Malvalic Acid
n = **7** Sterculic Acid

As might be expected from the properties of the fatty acids, fats have a predominance of saturated fatty acids, and oils are composed largely of unsaturated acids. Thus, the melting points of triglycerides reflect their composition, as shown by the following examples. Natural mixed triglycerides have somewhat lower melting points, the melting point of lard being near 30 ºC, whereas olive oil melts near -6 º C. Since fats are valued over oils and vegetable oils are extensively converted to solid triglycerides by partial hydrogenation of their unsaturated components. Some of the remaining double bonds are isomerized (to *trans*) in this operation. These saturated and trans-fatty acid glycerides in the diet have been linked to long-term health issues such as atherosclerosis. These unnatural **trans-fats** appear to be associated with increased heart disease, cancer, diabetes and obesity, as well as immune response and reproductive problems.



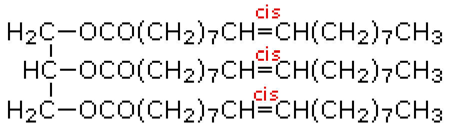
$$\begin{array}{l}H_2C-OCO(CH_2)_{10}CH_3\\ \;\;HC-OCO(CH_2)_{10}CH_3\\ H_2C-OCO(CH_2)_{10}CH_3\end{array}$$

trilaurin
mp 45° C



$$\begin{array}{l}H_2C-OCO(CH_2)_{16}CH_3\\ \;\;HC-OCO(CH_2)_{16}CH_3\\ H_2C-OCO(CH_2)_{16}CH_3\end{array}$$

tristearin
mp 71° C



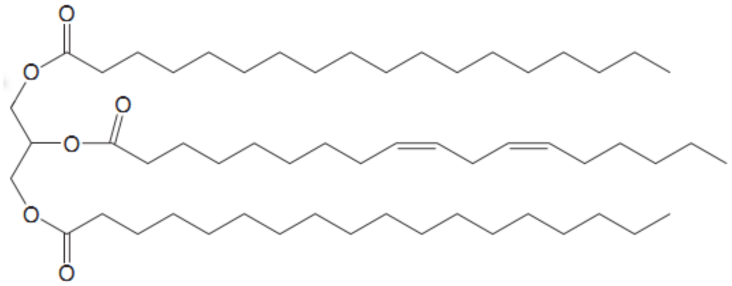
$$\begin{array}{l}H_2C-OCO(CH_2)_7CH\overset{cis}{=}CH(CH_2)_7CH_3\\ \;\;HC-OCO(CH_2)_7CH\overset{cis}{=}CH(CH_2)_7CH_3\\ H_2C-OCO(CH_2)_7CH\overset{cis}{=}CH(CH_2)_7CH_3\end{array}$$

triolein
mp -4° C

Fatty acids are important metabolic fuels (2-3 times the energy of proteins or carbohydrates).

• Fatty acids are stored as neutral lipids called **triaclyglycerols** (TGs). They are composed of 3 fatty acyl residues esterified to a glycerol (3-carbon sugar alcohol). TGs are very hydrophobic, and are stored in cells in an anhydrous form (e.g. in fat droplets).

Triacylglycerols contain three ester groups, each having a long carbon chain (abbreviated as R, R', and R") bonded to the carbonyl group.



Tg are hydrolyzed by Lipases show additive reactions including hydrogenation (hardening of vegetable oils), halogenation & oxidation (of double bonds) as in drying oils & paints.

Tg become rancid on standing in moist & warm temperature due to hydrolysis by lipases & oxidation of double bonds producing peroxides. Rancidity is prevented by antioxidants like vitamin E, Phenols, Tanins etc.

Triacylglycerols are **lipids.** The word lipid comes from the Greek word lipos for fat. **Lipids** are nonpolar or weakly polar molecules that are very soluble in organic solvents like hexane and carbon tetrachloride, and insoluble in a polar medium like water. The lipids are a heterogeneous group of compounds, including fats, oils, steroids, waxes, and related compounds,which are **related more by their physical than by their chemical properties.**

Lipids can be categorized as hydrolyzable or nonhydrolyzable.

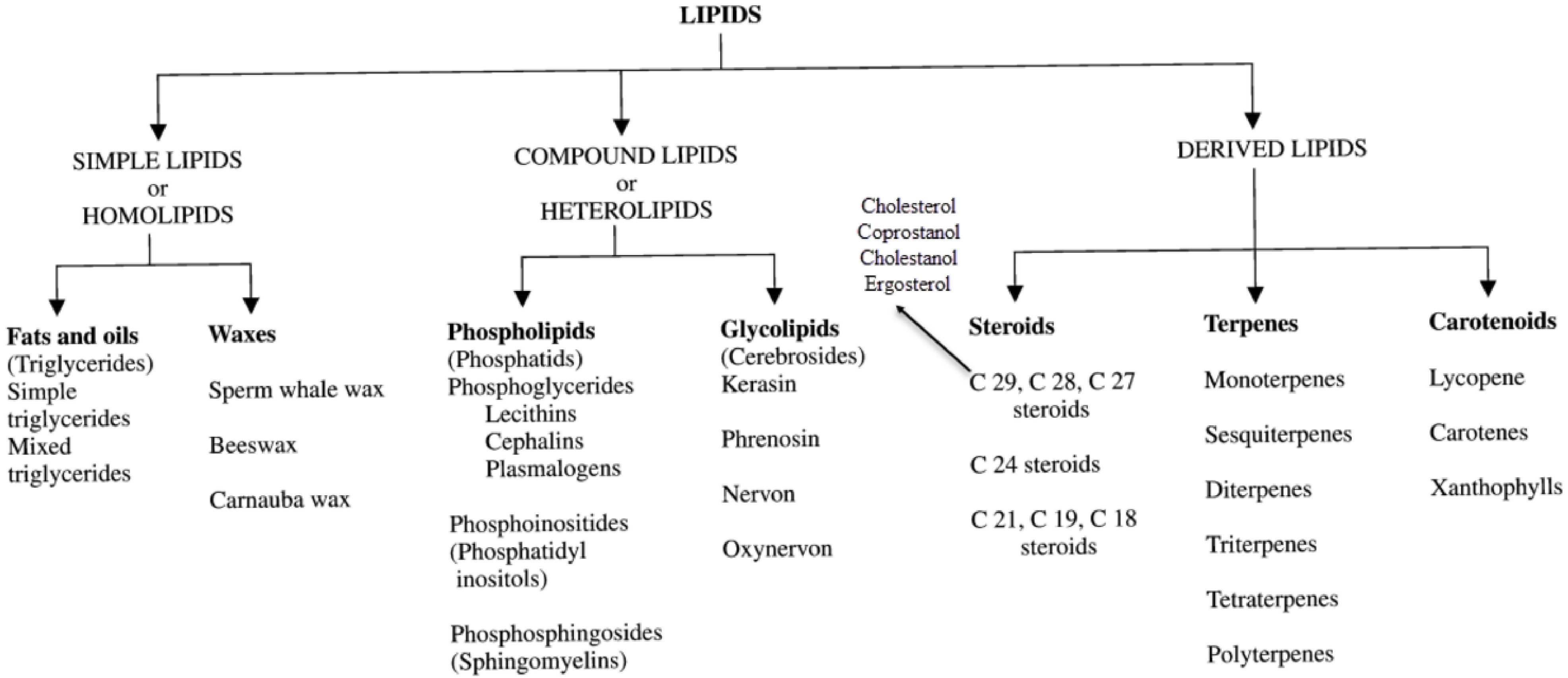
1. **Hydrolyzable lipids** can be converted into smaller molecules by hydrolysis with water: waxes, triacylglycerols, and phospholipids.

2. **Nonhydrolyzable lipids** cannot be cleaved into smaller units by aqueous hydrolysis. Non-hydrolyzable lipids tend to be more varied in structure: steroids, fat-soluble vitamins, and eicosanoids.

Saponifiable lipids can undergo saponification or base hydrolysis. **Non saponifiable** liquids can't.

Examples of saponifiable lipids (can be hydrolyzed) are the esters such as triglycerides, waxes, phospholipids and sphingolipids.

Lipids classification.

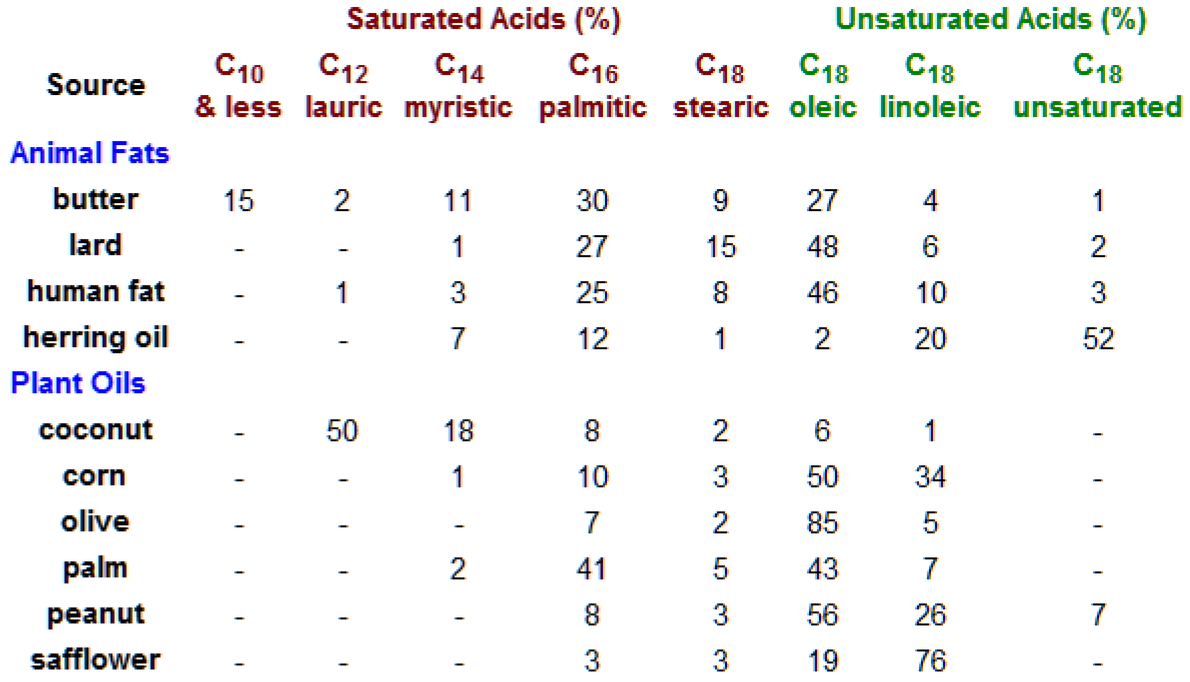


Examples of non saponifiable lipids (cannot be hydrolyzed) are compounds which are not esters such as steroids and prostaglandins.

Simple triacylglycerols are composed of three identical fatty acid side chains, whereas mixed triacylglycerols have two or three different fatty acids. The fatty acids may be saturated or unsaturated. Monounsaturated triacylglycerols have a single carbon–carbon double bond, while polyunsaturated triacylglycerols have more than one carbon–carbon double bond.

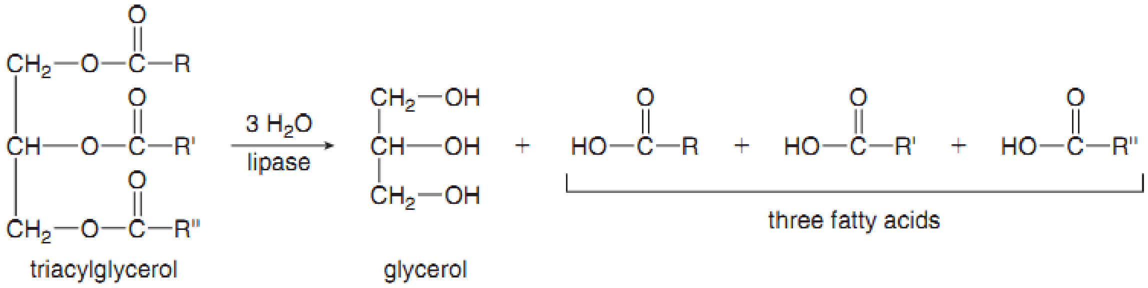
Fats have higher melting points - they are solids at room temperature; and derived from fatty acids having few double bonds. **Oils** have lower melting points - they are liquids at room temperature - derived from fatty acids having a larger number of double bonds. In the unsaturated lipid, a *cis* double bond places a kink in the side chain, making it more difficult to pack efficiently in the solid state, thus leading to a lower melting point.

Those triglycerides that are liquid are called oils and originate chiefly in plants, although triglycerides from fish are also largely oils. Some examples of the composition of triglycerides from various sources are given in the following table.



	Saturated Acids (%)					Unsaturated Acids (%)		
Source	C_{10} & less	C_{12} lauric	C_{14} myristic	C_{16} palmitic	C_{18} stearic	C_{18} oleic	C_{18} linoleic	C_{18} unsaturated
Animal Fats								
butter	15	2	11	30	9	27	4	1
lard	-	-	1	27	15	48	6	2
human fat	-	1	3	25	8	46	10	3
herring oil	-	-	7	12	1	2	20	52
Plant Oils								
coconut	-	50	18	8	2	6	1	-
corn	-	-	1	10	3	50	34	-
olive	-	-	-	7	2	85	5	-
palm	-	-	2	41	5	43	7	-
peanut	-	-	-	8	3	56	26	7
safflower	-	-	-	3	3	19	76	-

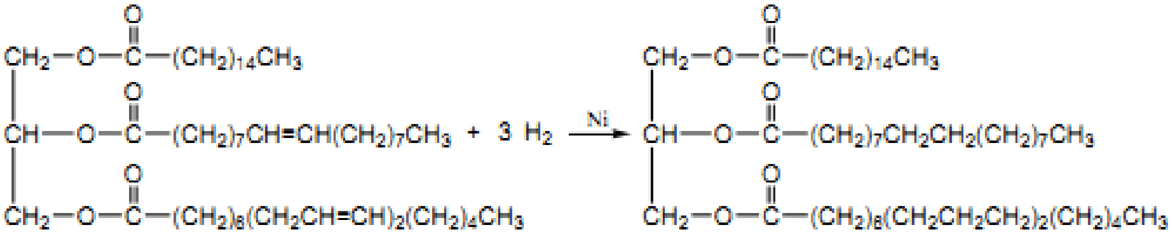
Like other esters, triacylglycerols are hydrolyzed with water in the presence of acid, base, or enzymes (in biological systems) to form glycerol and three molecules of fatty acids.



In saponification reactions, triglycerides react with strong bases (NaOH or KOH) to form the carboxylate salts of the fatty acids, called **soaps.**

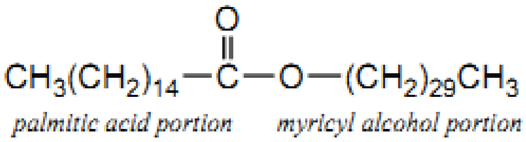
NaOH produces a “hard” soap, commonly found in bar soaps; KOH produces a “soft” soap, such as those in shaving creams and liquid soaps. These salts combine two solubility characteristics: – a long, nonpolar, water-insoluble (hydrophobic) hydrocarbon “tail” – a charged, water-soluble (hydrophilic) “head.” In water, the “tails” become tangled, leaving the charged heads sticking out into the solution, forming a structure called a micelle.

In hydrogenation reactions, alkenes are converted into alkanes with hydrogen gas (H_2) and a catalyst (Pt, Ni, or some other metal). This process is used to convert unsaturated vegetable oils, which are liquids at room temp., to saturated fats, which are solids at room temp. (shortening, etc.).



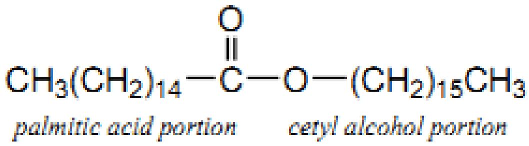
In partially hydrogenated vegetable oils, not all of the double bonds are saturated, allowing the texture of the product to be controlled. In the process, this twists some of the naturally-occurring *cis* double bonds into *trans* isomers (*trans* fats). Like saturated fats, trans fats also increase the amount of cholesterol in the bloodstream, thus increasing an individual’s risk of developing coronary artery disease.

Waxes are simple lipids contain a fatty acid joined to a long-chain (12-32 carbons) alcohol:



$$CH_3(CH_2)_{14}-\overset{\overset{O}{\|}}{C}-O-(CH_2)_{29}CH_3$$

myricyl palmitate — found in beeswax



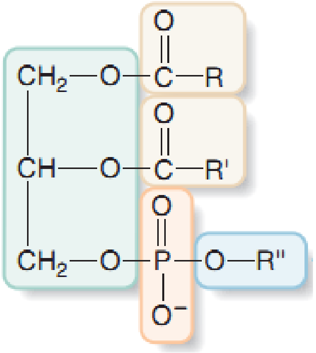
$$CH_3(CH_2)_{14}-\overset{\overset{O}{\|}}{C}-O-(CH_2)_{15}CH_3$$

cetyl palmitate — found in spermaceti oil

Waxes are insoluble in water and not as easily hydrolyzed as fats and oils. They often occur in nature as protective coatings on feathers, fur, skin, leaves, and fruits. Sebum, secreted by the sebaceous glands of the skin, contains waxes that help to keep skin soft and prevent dehydration. Waxes are used commercially to make cosmetics, candles, ointments, and protective polishes.

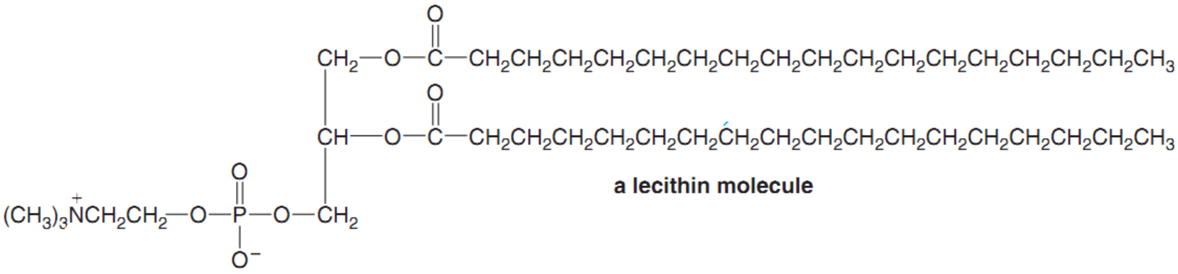
Phospholipids are lipids that contain a phosphorus atom. Two common types of phospholipids are phosphoacylglycerols and sphingomyelins. Both classes are found almost exclusively in the cell membranes of plants and animals.

Phosphoacylglycerols (or **phosphoglycerides**) are the second most abundant type of lipid. They form the principal lipid component of most cell membranes. Their structure resembles the triacylglycerols of the preceding section with one important difference. Only two of the hydroxyl groups of glycerol are esterified with fatty acids. The third OH group is part of a phosphodiester, which is also bonded to an alkyl group (R") derived from a low molecular weight alcohol.



The two fatty acid side chains form two nonpolar “tails” that lie parallel to each other, while the phosphodiester end of the molecule is a charged or polar “head.”

There are two prominent types of phosphoacylglycerols. They differ in the identity of the R" group in the phosphodiester. When R" $-CH_2CH_2NH_3^+$ (ethanolamine residue), the compound is called **a cephalin** or phosphatidylethanolamine. When R" $-CH_2CH_2N(CH_3)_3^+$ (choline residue), the compound is called **a lecithin** or phosphatidylcholine.

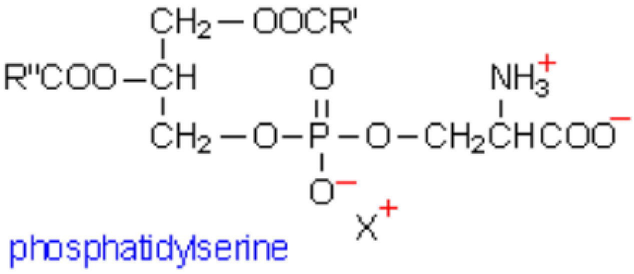


a lecithin molecule

Because lecithins contain negatively charged oxygen atoms in the phosphate group and positively charged nitrogen atoms in the quaternary ammonium salt group, that end of the molecule is highly hydrophilic, while the rest of the molecule is hydrophobic. This allows lecithin to act as an emulsifying agent: forms an important structural component of cell membranes; forms micelles which play a role in the transport of lipids in the blood stream. Commercially, lecithin extracted from soybeans is used as an emulsifying agent in margerine and candies to provide a smooth texture.

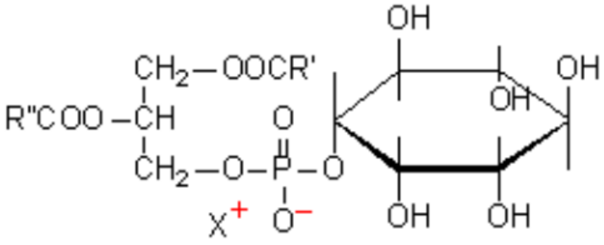
Cephalins are found in most cell membranes, and are particularly abundant in brain tissue. They are also found in blood platelets, and play a role in bloo**dclotting.**

Phosphatidylserine is a weakly acidic lipid that is present in most tissues of animals and plants and is also found in microorganisms. Phosphatidylserine is an essential in the blood coagulation process in platelets.



phosphatidylserine

Phosphatidylinositol, containing the optically inactive form of inositol, is a common constituent of animal, plant and microbial lipids.



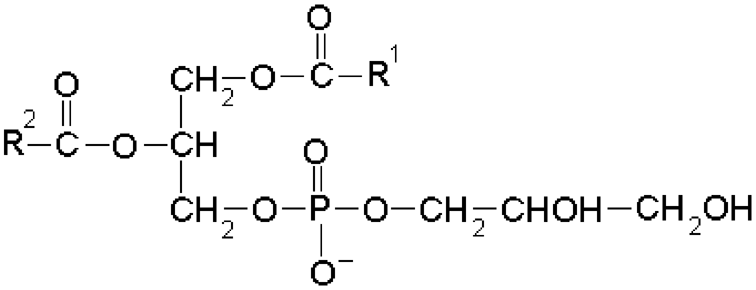
phosphatidylinositol

In such molecules the isomer of the inositol group is assumed to be the myo-conformer unless otherwise stated. Typically phosphatidylinositols form a minor component on the cytosolic side of eukaryotic cell membranes. The phosphate group gives the molecules a negative charge at physiological pH.

The form of phosphatidylinositol comprising the isomer muco-inositol acts as a sensory receptor in the taste function of the sensory system. In this context it is often referred to as PtdIns, but that does not imply any molecular difference from phosphatidylinositols comprising the myo- conformers of inositol.

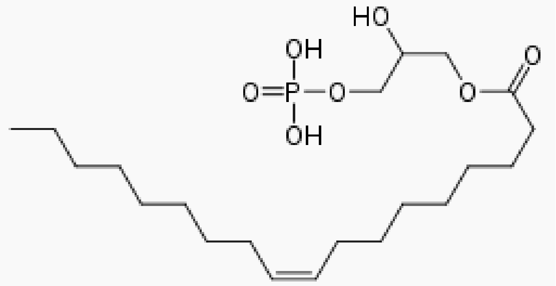
The phosphatidylinositol can be phosphorylated to form phosphatidylinositol phosphate (PI-4-P, referred to as PIP in close context or informally), phosphatidylinositol bisphosphate (PIP2) and phosphatidylinositol trisphosphate (PIP3). All lipids based on phosphatidylinositol are known as inositides, or sometimes phosphoinositides. The inositol ring can be phosphorylated by a variety of kinases on the three, four and five hydroxyl groups in seven different combinations. However, the two and six hydroxyl group is typically not phosphorylated due to steric hindrance.

Phosphatidylglycerol is a glycerophospholipid found in pulmonary surfactant. The general structure of phosphatidylglycerol consists of a L-glycerol 3-phosphate backbone ester-bonded to either saturated or unsaturated fatty acids on carbons 1 and 2. The head group substituent glycerol is bonded through a phosphomonoester. It is the precursor of surfactant and its presence (>0.3) in the amniotic fluid of the newborn indicates fetal lung maturity.



Approximately 98% of alveolar wall surface area is due to the presence of type I cells, with type II cells producing pulmonary surfactant covering around 2% of the alveolar walls. Once surfactant is secreted by the type II cells, it must be spread over the remaining type I cellular surface area. Phosphatidylglycerol is thought to be important in spreading of surfactant over the Type I cellular surface area. The major surfactant deficiency in premature infants relates to the lack of phosphatidylglycerol, even though it comprises less than 5% of pulmonary surfactant phospholipids. It is synthesized by head group exchange of a phosphatidylcholine enriched phospholipid using the enzyme phospholipase D.

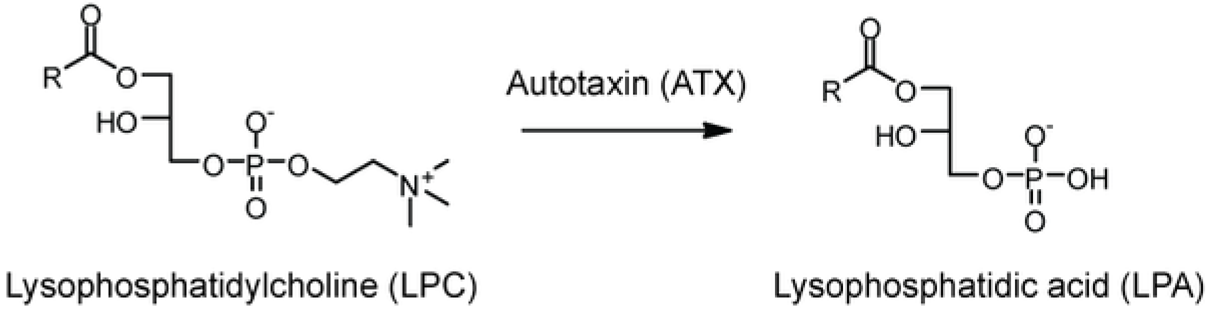
Lysophosphatidic acid (LPA) ((2-hydroxy-3-phosphonooxypropyl) (Z)-octadec-9-enoate) is a phospholipid derivative that can act as a signaling molecule.



Because of its ability to stimulate cell proliferation, aberrant LPA-signaling has been linked to cancer in numerous ways. Dysregulation of autotaxin or the LPA receptors can lead to hyperproliferation, which may contribute to oncogenesis and metastasis.

There are a number of potential routes to its biosynthesis, but the most well-characterized is by the action of a lysophospholipase D called autotaxin, which removes the choline group from lysophosphatidylcholine.

Lysophosphatidic acid is also an intermediate in the synthesis of phosphatidic acid.



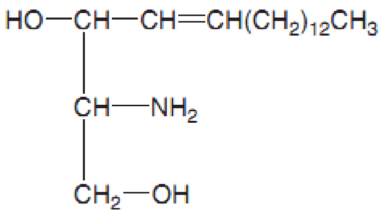
Why do fats have thermal insulation properties?

Triglycerides are poor heat conductors and, in addition, they form thick layers of fatty tissue when accumulated in an organism. That is why they are good thermal insulators. In animals that live in cold climates, such as polar bears, seals and whales, adipose tissue helps the maintenance of internal body temperature.

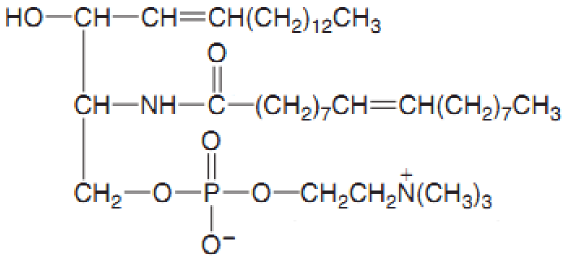
How are lipids used as an energy source by the body?

Carbohydrates are the main energy source for aerobic cell respiration. When such substances are absent or deficient, the body can use lipid stores since fats (like proteins) can be broken down into acetyl-CoA to feed the Krebs cycle (a stage of aerobic cellular respiration).

Sphingomyelins, the second major class of phospholipids, differ in two important ways from the triacylglycerols and the phosphoacylglycerols. Sphingomyelins do not contain a glycerol backbone. Instead, sphingomyelins are derived from sphingosine. Sphingomyelins do not contain an ester. Instead, their single fatty acid is bonded to the carbon backbone by an amide bond.



sphingosine

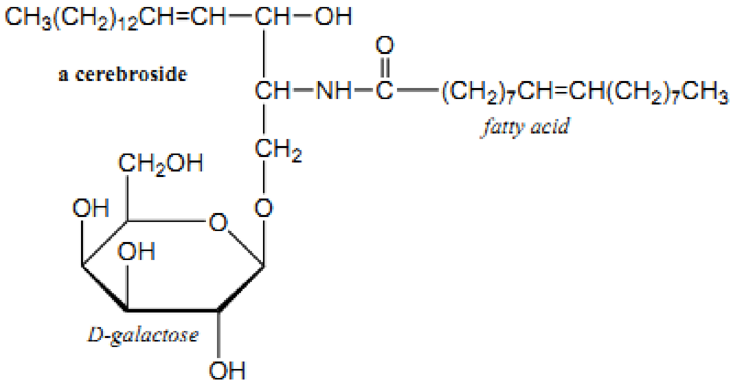


a sphingomyelin

The coating that surrounds and insulates nerve cells, the myelin sheath, is particularly rich in sphingomyelins, and is vital for proper nerve function. The sphingomyelins are also membrane lipids. Multiple Sclerosis is a devastating disease in which the myelin sheath is lost, causing eventual paralysis.

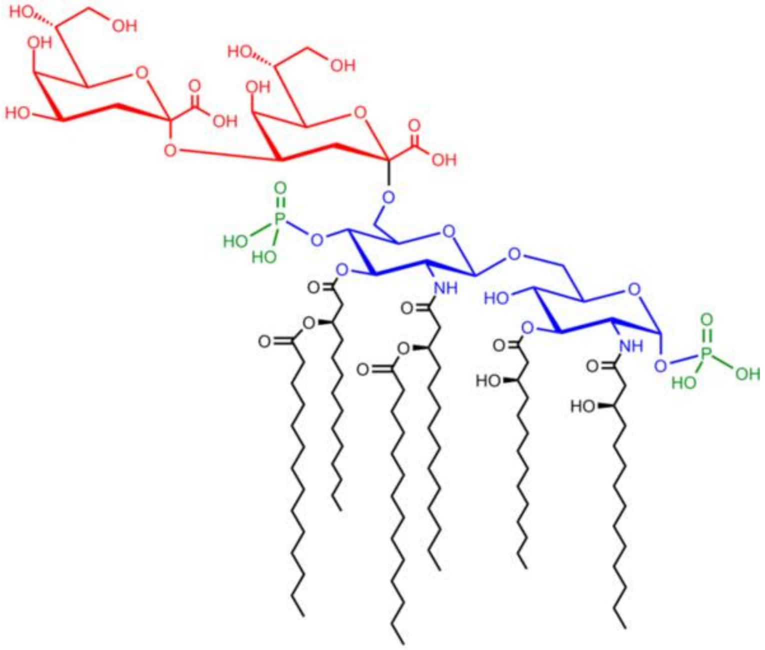
The other major class of sphingolipids are the **glycosphingolipids** , there are 4 major classes of glycosphingolipids:

- Cerebrosides: contain a single moiety, principally galactose.
- Sulfatides: sulfuric acid esters of galactocerebrosides.
- Globosides: contain 2 or more sugars.
- Gangliosides: similar to globosides except also contain sialic acid.



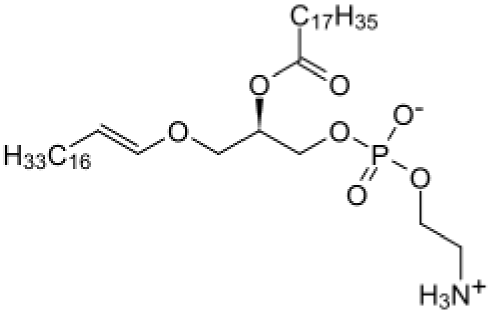
Glycolipids are sphingolipids that contain carbohydrates (usually monosaccharides). They are also referred to as **cerebrosides** (Kerasin, Cerebron, Nervon & Oxynervon) because of their abundance in brain tissue and **Gangliosides (GM1,GM2,GM3,GM4 etc)**.

Saccharolipids describe compounds in which fatty acids are linked directly to a sugar backbone, forming structures that are compatible with membrane bilayers. In the saccharolipids, a sugar substitutes for the glycerol backbone that is present in glycerolipids and glycerophospholipids. The most familiar saccharolipids are the acylated glucosamine precursors of the Lipid A component of the lipopolysaccharides in Gram-negative bacteria.



Structure of Kdo$_2$-Lipid A.

Plasmalogens. Plasmalogens are a special class of lipids especially abundant in the membranes of nerve and muscle cells and also characteristic of cancer cells. A plasmalogen is similar to a glycerophosphatide except that the fatty acid at the number 1 position of the glycerol is replaced by unsaturated ether. For example, phosphatidylethanolamine plasmalogen:



LIPOLYSIS: is the breakdown of fat stored in fat cells. During this process, free fatty acids are released into the bloodstream and circulate throughout the body. Ketones are produced, and are found in large quantities in **ketosis** (an adaptive metabolic state that occurs when insufficient carbohydrates are present in the diet). The following hormones induce lipolysis: epinephrine, norepinephrine, glucagon and adrenocorticotropic hormone. Triglycerides undergo lipolysis (hydrolysis by lipases) and are broken down into glycerol and fatty acids. Once released into the blood, the relatively hydrophobic free fatty acids bind to serum albumin for transport to tissues that require energy. The glycerol also enters the bloodstream and is absorbed by the liver or kidney where it is converted to glycerol 3-phosphate by the enzyme glycerol kinase. Hepatic glycerol 3-phosphate is mostly converted into dihydroxyacetone (DHAP) and then glyceraldehyde 3-phosphate (G3P) to rejoin the glycolysis and gluconeogenesis pathway.

Amphipathic lipids self-orient at oil : water interfaces.

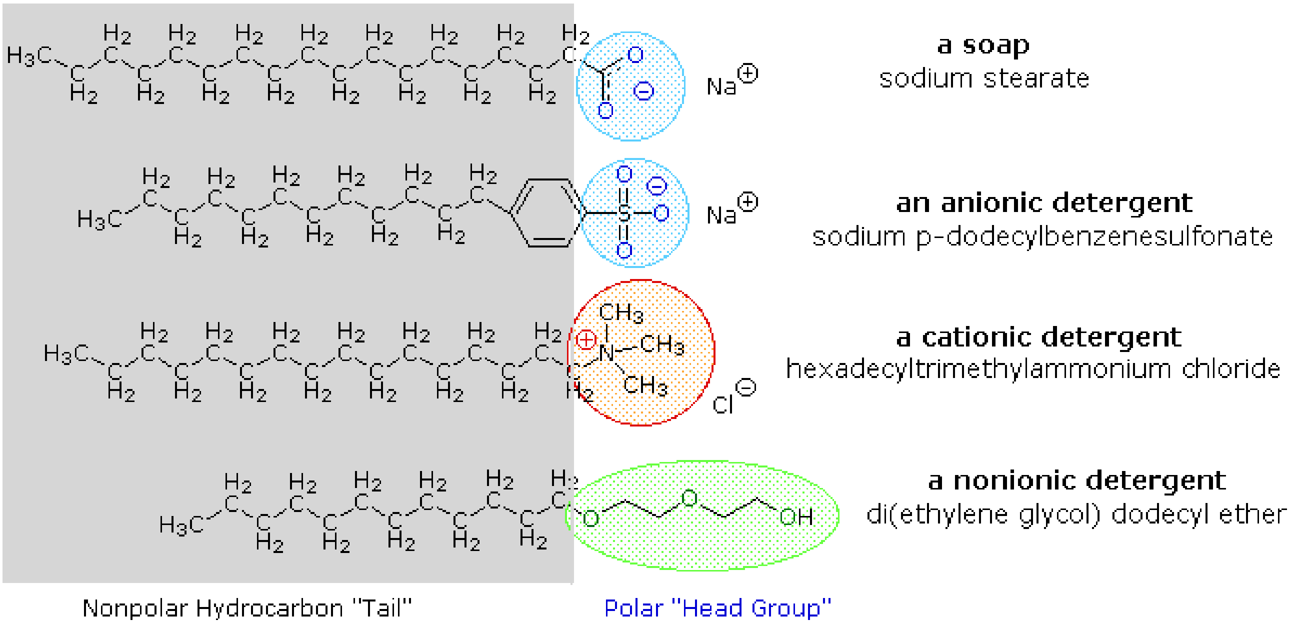
Hydrophobic molecules are molecules with little or no propensity to dissolve in water (hydro = water, phobia = fear). **Hydrophilic molecules** are those that have a large propensity to dissolve in water (philia = friendship).

Water is a polar substance. Remembering the rule that “equal dissolves equal”, it is easy to conclude that hydrophobic substances are non-polar molecules whereas hydrophilic molecules are polar molecules.

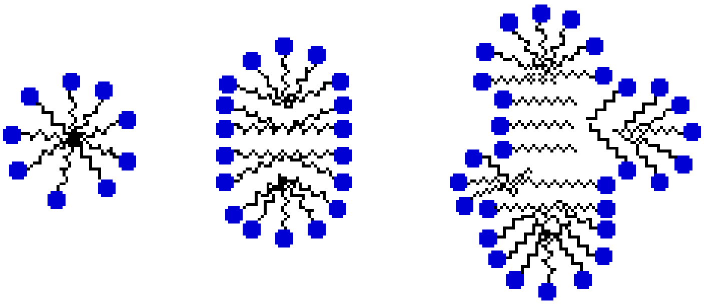
SOAPS AND DETERGENTS

Carboxylic acids and salts having alkyl chains longer than eight carbons exhibit unusual behavior in water due to the presence of both hydrophilic (CO_2) and hydrophobic (alkyl) regions in the same molecule. Such molecules are termed **amphiphilic** (Gk. amphi = both) or **amphipathic**. Fatty acids made up of ten or more carbon atoms are nearly insoluble in water, and because of their lower density, float on the surface when mixed with water. Unlike paraffin or other alkanes, which tend to puddle on the waters surface, these fatty acids spread evenly over an extended water surface, eventually forming a monomolecular layer in which the polar carboxyl groups are hydrogen bonded at the water interface, and the hydrocarbon chains are aligned together away from the water. This behavior is illustrated in the diagram on the right. Substances that accumulate at water surfaces and change the surface properties are called **surfactants**.

Alkali metal salts of fatty acids are more soluble in water than the acids themselves, and the amphiphilic character of these substances also make them strong surfactants. The most common examples of such compounds are soaps and detergents, four of which are shown below. Note that each of these molecules has a nonpolar hydrocarbon chain, the "tail", and a polar (often ionic) "head group". The use of such compounds as cleaning agents is facilitated by their surfactant character, which lowers the surface tension of water, allowing it to penetrate and wet a variety of materials.



Very small amounts of these surfactants dissolve in water to give a random dispersion of solute molecules. However, when the concentration is increased an interesting change occurs. The surfactant molecules reversibly assemble into polymolecular aggregates called **micelles**. By gathering the hydrophobic chains together in the center of the micelle, disruption of the hydrogen bonded structure of liquid water is minimized, and the polar head groups extend into the surrounding water where they participate in hydrogen bonding. These micelles are often spherical in shape, but may also assume cylindrical and branched forms. Here the polar head group is designated by circle, and the nonpolar tail is a zig-zag line.



micelle assemblies of amphiphiles

To summarize, the presence of a soap or a detergent in water facilitates the wetting of all parts of the object to be cleaned, and removes water-insoluble dirt by incorporation in micelles

The oldest amphiphilic cleaning agent known to humans is soap. Soap is manufactured by the base-catalyzed hydrolysis (saponification) of animal fat (see below). Before sodium hydroxide was commercially available, a boiling solution of potassium carbonate leached from wood ashes was used. Soft potassium soaps were then converted to the harder sodium soaps by washing with salt solution. The importance of soap to human civilization is documented by history, but some problems associated with its use have been recognized. One of these is caused by the weak acidity (pK_a ca. 4.9) of the fatty acids. Solutions of alkali metal soaps are slightly alkaline (pH 8 to 9) due to hydrolysis. If the pH of a soap solution is lowered by acidic contaminants, insoluble fatty acids precipitate and form a scum. A second problem is caused by the presence of calcium and magnesium salts in the water supply (hard water). These divalent cations cause aggregation of the micelles, which then deposit as a dirty scum.

These problems have been alleviated by the development of synthetic amphiphiles called detergents (or syndets). By using a much stronger acid for the polar head group, water solutions of the amphiphile are less sensitive to pH changes. Also the sulfonate functions used for virtually all anionic detergents confer greater solubility on micelles incorporating the alkaline earth cations found in hard water. Variations on the amphiphile theme have led to the development of other classes, such as the cationic and nonionic detergents shown above. Cationic detergents often exhibit germicidal properties, and their ability to change surface pH has made them useful as fabric softeners and hair conditioners. These versatile chemical "tools" have dramatically transformed the household and personal care cleaning product markets over the past fifty years.

As ionic amphiphiles, phospholipids aggregate or self-assemble when mixed with water, but in a different manner than the soaps and detergents. Because of the two pendant alkyl chains present in phospholipids and the unusual mixed charges in their head groups, micelle formation is unfavorable relative to a bilayer structure. If a phospholipid is smeared over a small hole in a thin piece of plastic immersed in water, a stable planar bilayer of phospholipid molecules is created at the hole. As shown in the following diagram, the polar head groups on the faces of the bilayer contact water, and the hydrophobic alkyl chains form a nonpolar interior. The phospholipid molecules can move about in their half the bilayer, but there is a significant energy barrier preventing migration to the other side of the bilayer.

This bilayer membrane structure is also found in aggregate structures called liposomes. Liposomes are microscopic vesicles consisting of an aqueous core enclosed in one or more phospholipid layers. They are formed when phospholipids are vigorously mixed with water. Unlike micelles, liposomes have both aqueous interiors and exteriors.

A cell may be considered a very complex liposome. The bilayer membrane that separates the interior of a cell from the surrounding fluids is largely composed of phospholipids, but it incorporates many other components, such as cholesterol, that contribute to its structural integrity. Protein channels that permit the transport of various kinds of chemical species in and out of the cell are also important components of cell membranes.

The interior of a cell contains a variety of structures (organelles) that conduct chemical operations vital to the cells existence. Molecules bonded to the surfaces of cells serve to identify specific cells and facilitate interaction with external chemical entities.

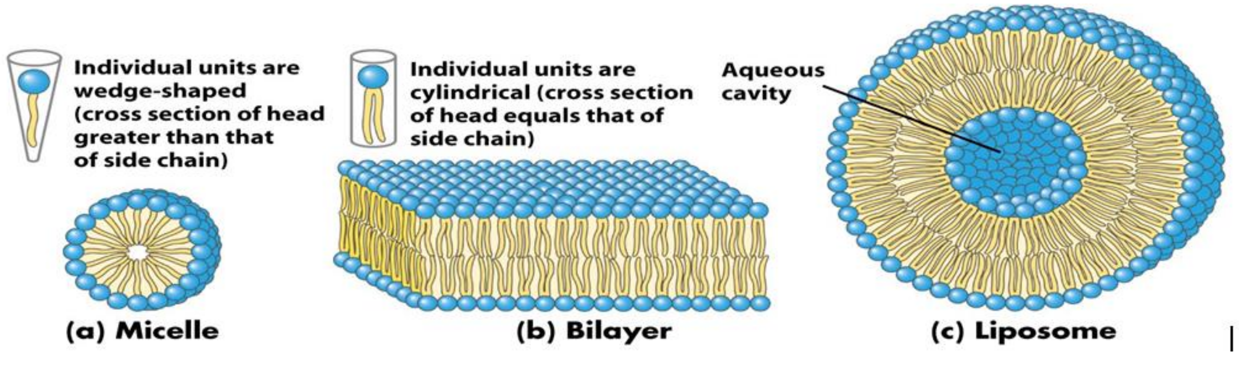
The sphingomyelins are also membrane lipids. They are the major component of the myelin sheath surrounding nerve fibers. Multiple Sclerosis is a devastating disease in which the myelin sheath is lost, causing eventual paralysis.

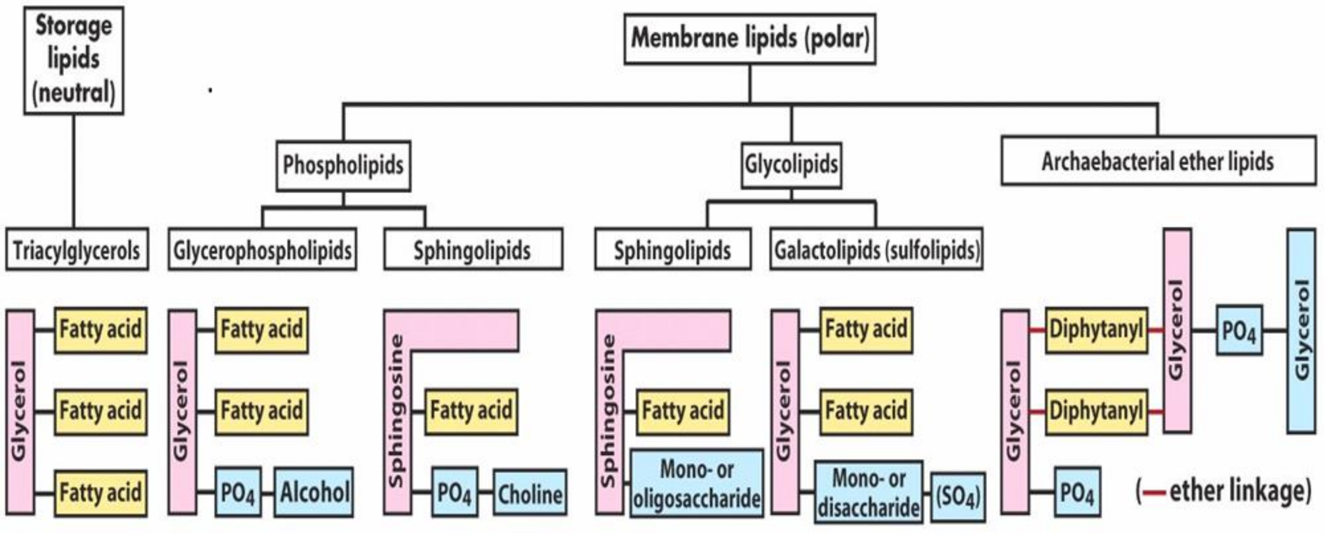
Aggregations of bile salts into micelles and **liposomes** and the formation of mixed micelles with the products of fat digestion are important in facilitating absorption of lipids

Liposomes may be formed by sonicating an amphipathic lipid in an aqueous medium.They consist of spheres of lipid bilayers that enclose part of the aqueous medium. They are of potential clinical use — particularly when combined with tissue specific antibodies — as carriers of drugs in the circulation, targeted to specific organs, eg, in cancer therapy.

In addition, they are being used for gene transfer into vascular cells and as carriers for topical and transdermal delivery of drugs and cosmetics.

Emulsions are much larger particles, formed usually by nonpolar lipids in an aqueous medium. These are stabilized by emulsifying agents such as amphipathic lipids (eg, lecithin), which form a surface layer separating the main bulk of the nonpolar material from the aqueous phase





LIPIDS TESTS

1. SOLUBILITY TEST

The test is based on the property of solubility of lipids in organic solvents and insolubility in water. The oil will float on water because of lesser specific gravity.

2. TRANSPARENCY TEST

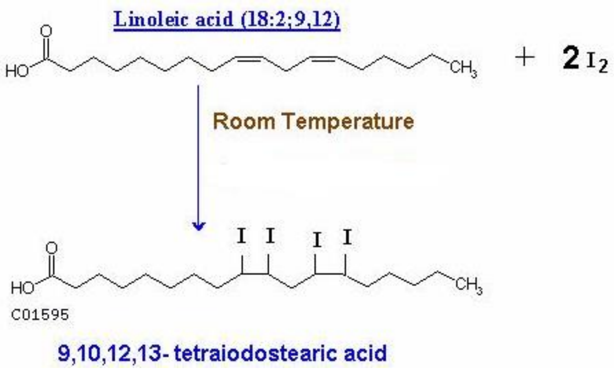
All the lipids are greasy in nature. Therefore the test may be taken as group test for lipids. The oil does not wet the paper. Take 3 ml of ether in a test tube and dissolve 5 drops of oil in tit. Put a drop of the solution on the filter paper and let it dry. A translucent spot on the filter paper was observed and this indicates the greasy character of the lipid.

3. EMULSIFICATION TEST

When oil and water, which are immiscible, are shaken together, the oil is broken up into very tiny droplets which are dispersed in water. This is known as oil in water emulsion. The water molecule due to the high surface tensions have tendency to come together and form a separate layer. This is why the oil and water emulsion is unstable in the presence of substances that lower the surface tension of water (sodium carbonate, soap, bile salts etc.) The tendency of the water molecule to coalesce is decreased and the emulsion becomes stable. Since bile salts cause the greatest decrease in surface tension they are best emulsifying agents.

4. TEST FOR UNSATURATION

The amount of iodine required to impart its color to the solution is a measure of the degree of the fatty acids. The unsaturated fatty acids react with iodine at the double bonds until all the double bonds are saturated with iodine.



5. COPPER ACETATE TEST

The copper acetate solution does not react with the oils, while saturated and unsaturated fatty acids react with copper acetate to form copper salt. The unsaturated fatty acids can only be extracted by petroleum ether.

In the case of olive oil notice that petroleum ether upper layer containing the dissolved oil and appears colorless, aqueous solution remains blue in the bottom.

In the case of oleic acid the upper layer of petroleum ether becomes green as a result of copper oleate. The lower layer becomes less in blue.

Lesson №10

Theme: NON-SAPONIFICATED LIPIDS: PROSTAGLANDINS, TERPENES, STEROIDS. STRUCTURE, NOMENCLATURE, CHEMICAL PROPERTIES.

Subject motivation: Investigated substances are among the most important biologically active ones. Prostaglandines functions are regulation of blood pressure and reproductive functions; induce inflammation, fever and pain; inhibit platelet aggregation. Most non-steroidal antiinflammatory drugs (NSAIDS) like aspirin and ibuprofen work by blocking the action of cyclooxygenase, thereby inhibiting prostaglandin production. Thromboxanes also produced from PGH2 but contain a 6-membered “oxane” ring with platelet aggregation, clotting, constriction of blood vessels functions. Leukotrienes are synthesized directly from arachidonic acid and are about mooth muscle contraction, allergic response, lung constriction and swelling. Terpenes are one of the largest and most varied group of plant chemicals. They have antibacterial properties and wound-healing properties. Squalene is precursor to steroids, etc. Cholesterol main functions are cell membrane structure and fluidity, precursor of steroid hormones and bile acids.

Learning goal: To strengthen knowledge of the structure and chemical properties of the main unsaponificated lipids, taking into account the influence of their characteristic functional groups as the basis of biochemical processes.

THEORETICAL QUESTIONS

1. What are lipids? How are lipids classified according to solubility?
2. What are saponifiable and non-saponifiable lipids? Precursor and derived lipids.

3. Structure and properties of the following compounds. Eicosanoids: Prostanoids (Prostaglandins (PGs), Prostacyclins (PGIs), Thromboxanes (TXs)), Leukotrienes (LTs), Lipoxins (LXs).
4. What are terpenes? Classification.
5. Isoprene rule. Biosynthesis of squalene.
6. Structure and physico-chemical properties and synthesis of limonene, myrcene, linalool, alpha bisabolol, delta-3 carene, borneol, alpha-pinene, beta-pinene, eucalyptol, terpineol, caryophyllene, cineole, camphora, etc.
7. What are steroids? Nomenclature. Their biological function?
8. Examples of cholestanes, cholanes, pregnanes, androstanes and estranes. Reactions of their identification.
9. Lipid peroxidation.

The lipids are a large and diverse group of naturally occurring organic compounds that are related by their solubility in nonpolar organic solvents (e.g. ether, chloroform, acetone & benzene) and general insolubility in water.

A saponifiable lipid is one with an ester functional group, that can be hydrolyzed under basic conditions. These include triglycerides, phospholipids, glycolipids, sphingolipids, and the waxes. These lipids are known as simple lipids.

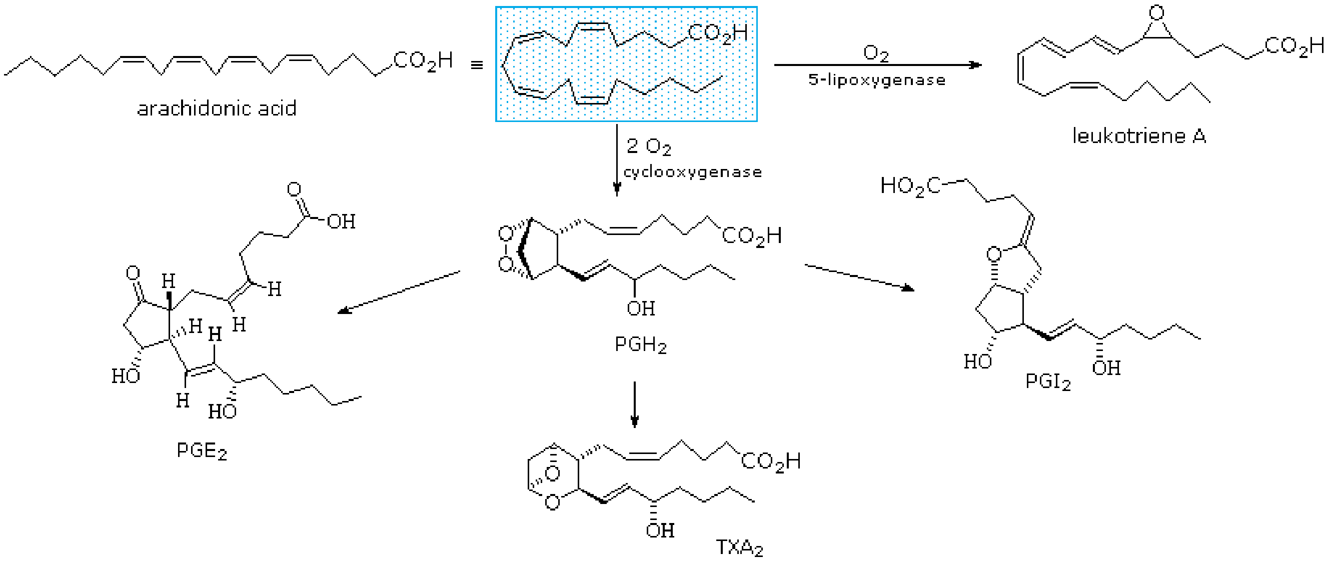
Non-saponifiable lipids cannot be hydrolyzed by sodium hydroxide because they have no ester bonds: steroids, prostaglandins, etc.

Precursor lipids are compounds produced when simple and complex lipids undergo hydrolysis. They include such substances as fatty acids, glycerol, sphingosine, and other alcohols.

Derived lipids are formed by metabolic transformation of fatty acids. They include ketone bodies, steroids, fatty aldehydes, prostaglandins, and lipid-soluble vitamins.

Prostaglandins. Thromboxanes & Leukotrienes.

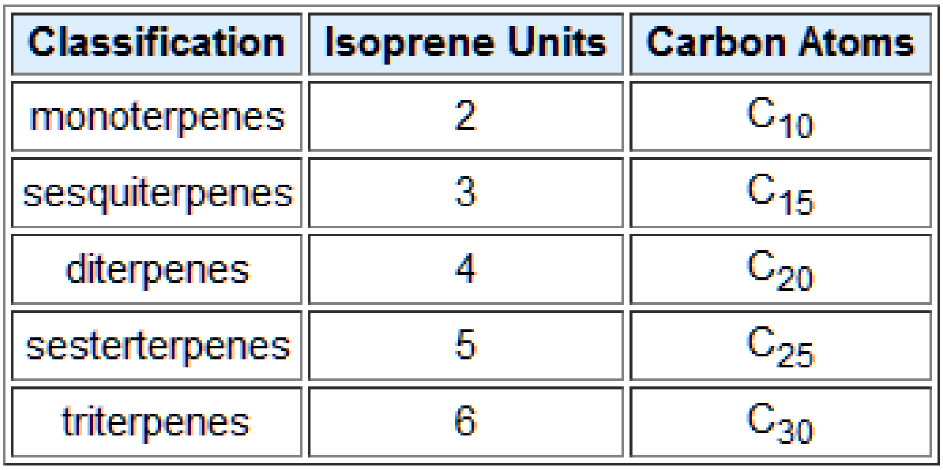
The members of this group of structurally related natural hormones have an extraordinary range of biological effects. They can lower gastric secretions, stimulate uterine contractions, lower blood pressure, influence blood clotting and induce asthma-like allergic responses. Because their genesis in body tissues is tied to the metabolism of the essential fatty acid arachadonic acid (5,8,11,14-eicosatetraenoic acid) they are classified as **eicosanoids**. Many properties of the common drug aspirin result from its effect on the cascade of reactions associated with these hormones. The metabolic pathways by which arachidonic acid is converted to the various eicosanoids are complex and will not be discussed here. A rough outline of some of the transformations that take place is provided below.



Leukotriene A is a precursor to other leukotriene derivatives by epoxide opening reactions. The prostaglandins are given systematic names that reflect their structure. The initially formed peroxide PGH2 is a common intermediate to other prostaglandins, as well as thromboxanes such as TXA2.

Terpenes

Compounds classified as terpenes constitute what is arguably the largest and most diverse class of natural products. A majority of these compounds are found only in plants, but some of the larger and more complex terpenes (e.g. squalene & lanosterol) occur in animals. Terpenes incorporating most of the common functional groups are known, so this does not provide a useful means of classification. Instead, the number and structural organization of carbons is a definitive characteristic. Terpenes may be considered to be made up of isoprene (more accurately isopentane) units, an empirical feature known as the isoprene rule. Because of this, terpenes usually have 5n carbon atoms (n is an integer), and are subdivided as follows:



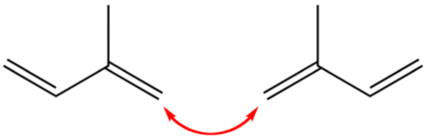
Classification	Isoprene Units	Carbon Atoms
monoterpenes	2	C_{10}
sesquiterpenes	3	C_{15}
diterpenes	4	C_{20}
sesterterpenes	5	C_{25}
triterpenes	6	C_{30}

Isoprene itself, a C_5H_8 gaseous hydrocarbon, is emitted by the leaves of various plants as a natural byproduct of plant metabolism. Next to methane it is the most common volatile organic compound found in the atmosphere.

Isoprene Rule

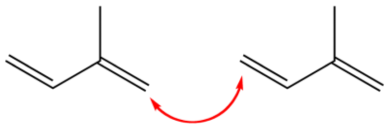
Formally, in biosynthesis of terpenes, two or more isoprene molecules are linked to one another. Linking between two isoprene molecules could occur in three ways, given that the head and the tail of the molecule are primarily involved in the linking:

1. The head of one isoprene molecule could link with the head of another isoprene molecule.



This link is called a **head-to-head** or 1-1 link.

2. The head of one isoprene molecule could link with the tail of another isoprene molecule.



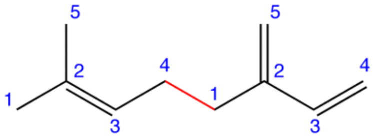
This link is called a **head-to-tail** or 1-4 link.

3. The tail of one isoprene molecule could link with the tail of another isoprene molecule.

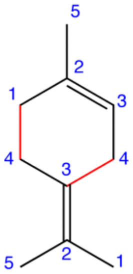
This link is called a **tail-to-tail** or 4-4 link.

Cyclic terpenes also contain links that are neither 1-1, 1-4, nor 4-4, which are called crosslinks.

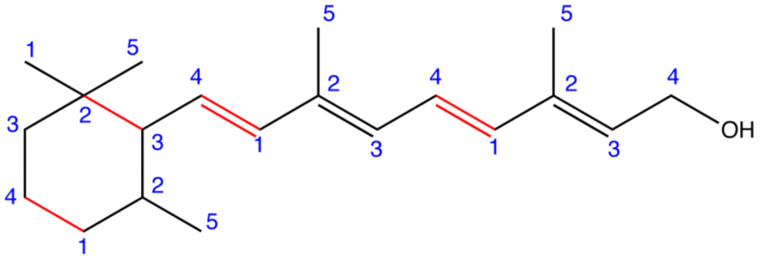
Isoprene rule states that, in most naturally occurring terpenes, there are no 1-1 or 4-4 links.



Myrcene

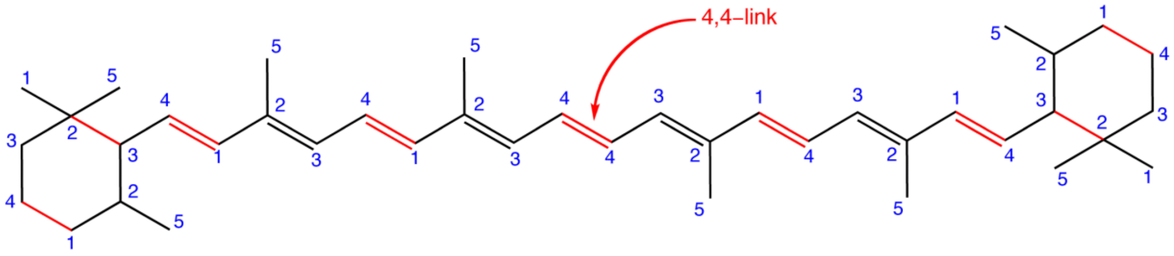


Limonene



Retinol

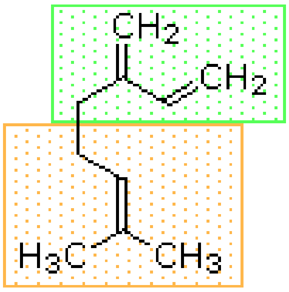
A terpene that does not obey the isoprene rule is called an **irregular terpene**:



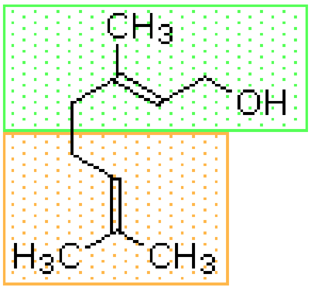
β-Carotene

Examples of C_{10} and higher terpenes, representing the four most common classes are shown in the following:

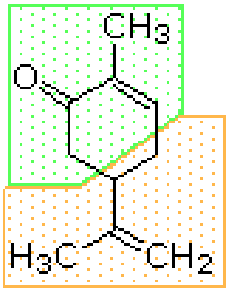
Monoterpenes



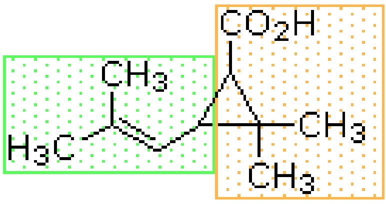
myrcene



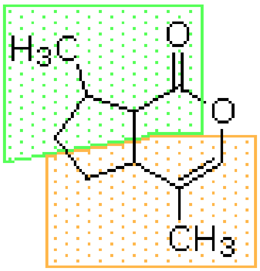
geraniol



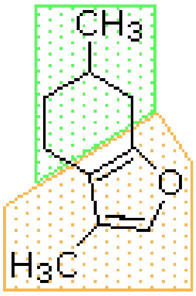
carvone



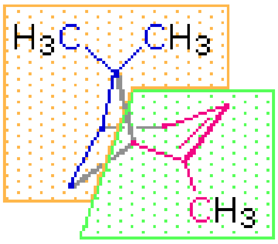
chrysanthemic acid



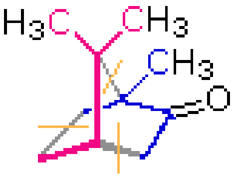
nepetalactone



menthofuran

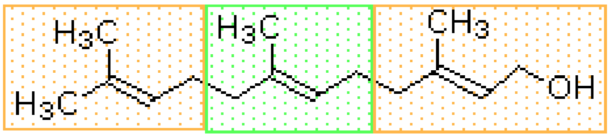


α-pinene

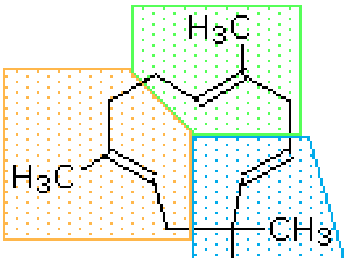


camphor

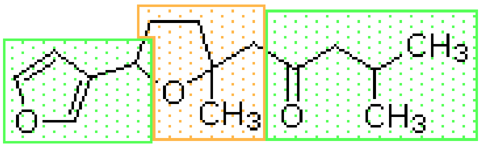
Sesquiterpenes



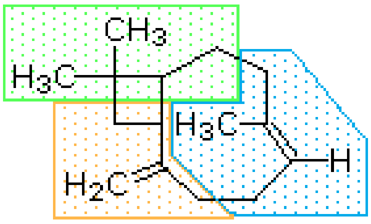
farnesol



humulene

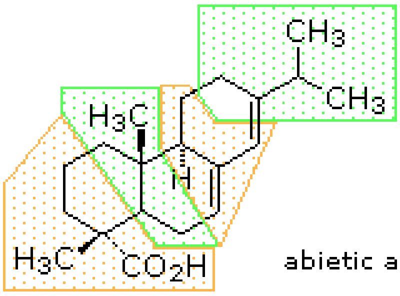


ngaione

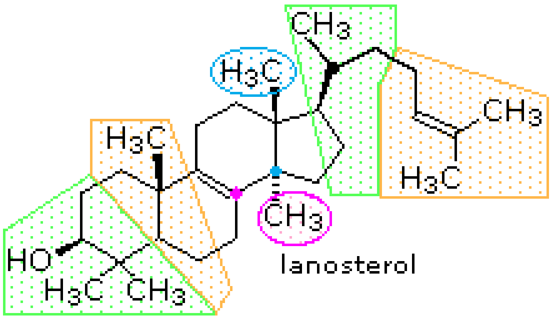


caryophyllene

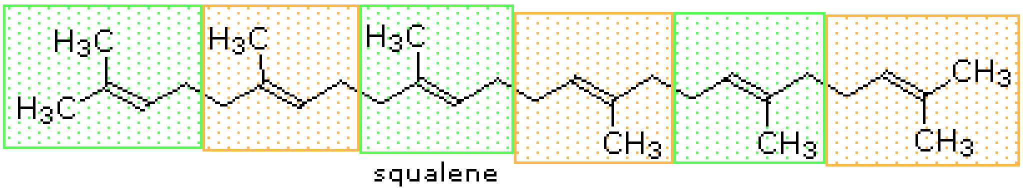
Di- and triterpenes



abietic acid

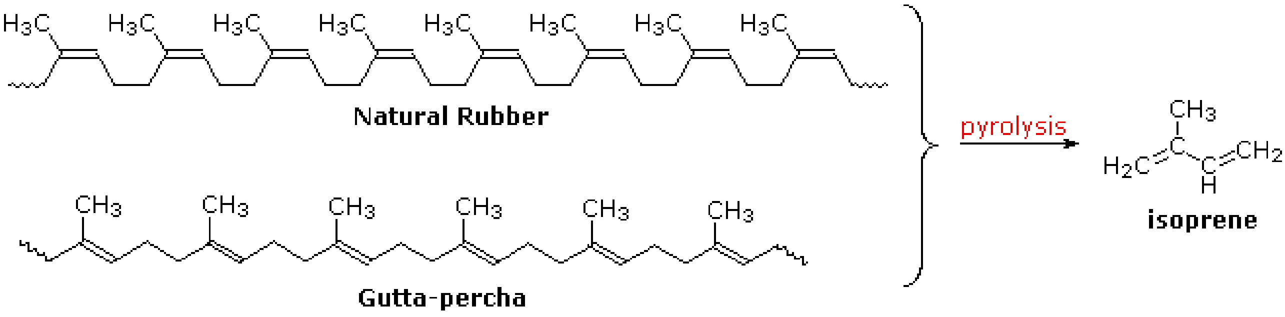


lanosterol



squalene

Polymeric isoprenoid hydrocarbons have also been identified. Rubber is undoubtedly the best known and most widely used compound of this kind. It occurs as a colloidal suspension called latex in a number of plants, ranging from the dandelion to the rubber tree (*Hevea brasiliensis*). Rubber is a polyene, and exhibits all the expected reactions of the C=C function. Bromine, hydrogen chloride and hydrogen all add with a stoichiometry of one molar equivalent per isoprene unit. Ozonolysis of rubber generates a mixture of levulinic acid ($CH_3COCH_2CH_2CO_2H$) and the corresponding aldehyde. Pyrolysis of rubber produces the diene isoprene along with other products.

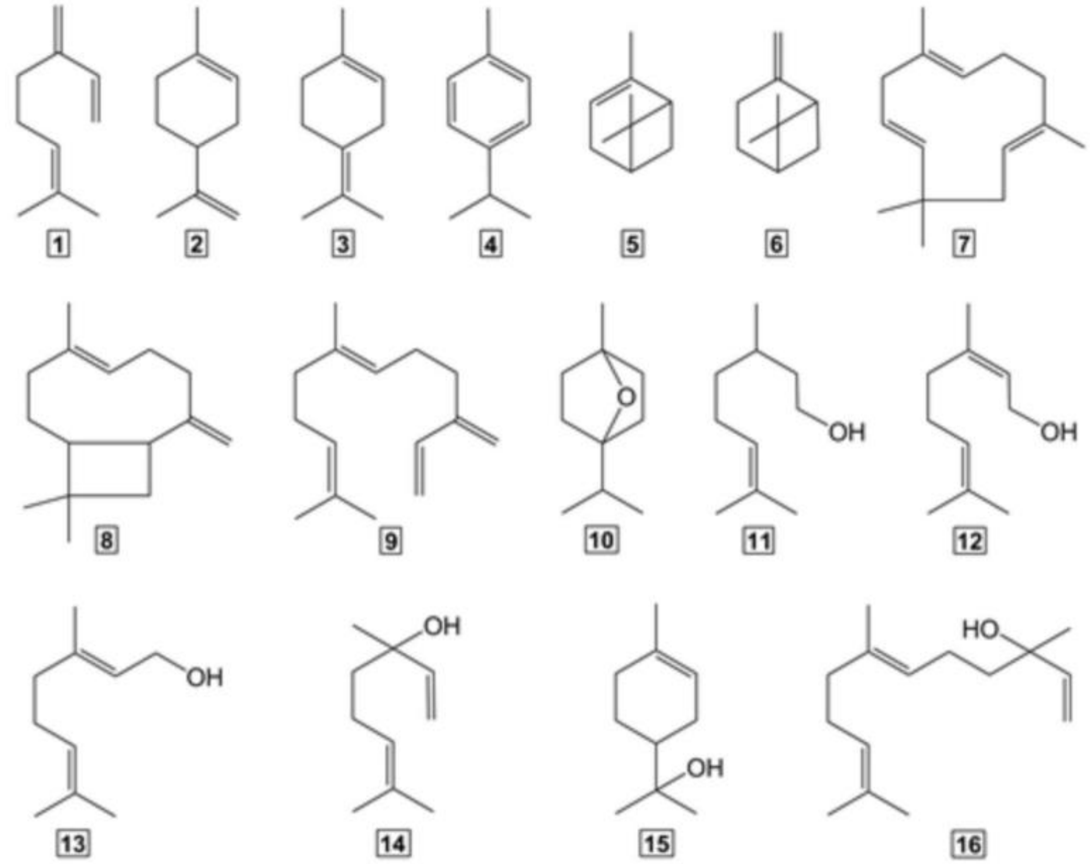


The double bonds in rubber all have a Z-configuration, which causes this macromolecule to adopt a kinked or coiled conformation. This is reflected in the physical properties of rubber. Despite its high molecular weight (about one million), crude latex rubber is a soft, sticky, elastic substance. Chemical modification of this material is normal for commercial applications. Gutta-percha (structure above) is a naturally occurring E-isomer of rubber. Here the hydrocarbon chains adopt a uniform zig-zag or rod like conformation, which produces a more rigid and tough substance. Uses of gutta-percha include electrical insulation and the covering of golf balls.

The words “terpenoid” and “terpene” are often used synonymously, but the two words actually have different meanings:

Terpenoids are terpenes that contain additional functional groups (functional groups are what make chemicals unique like alcohols, esters, carboxylic acid, etc). Terpenoids may refer to terpenes that have been chemically modified to produce a desired effect.

The chemical structure of the major brewing terpenes is illustrated in Figure, which includes typical terpene hydrocarbons (1-9), terpene epoxide (10) and terpene alcohols

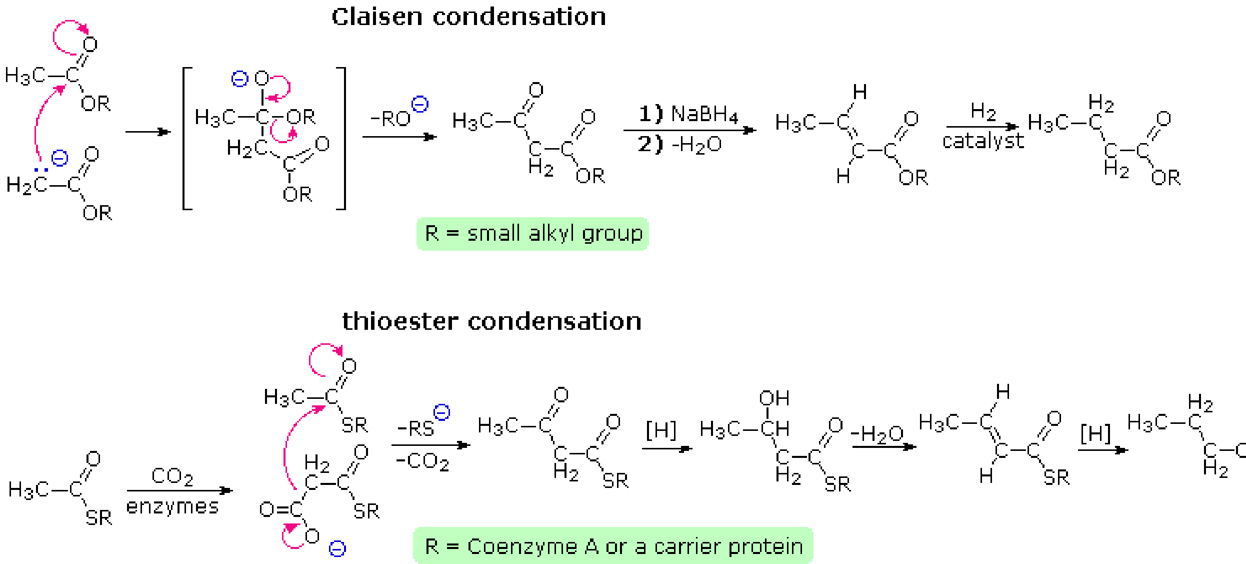


Chemical structures of *Humulus lupulus* L. derived terpenes: (1) β-myrcene; (2) limonene; (3) terpinolene; (4) *p*-cymene; (5) α-pinene; (6) β-pinene; (7) α-humulene; (8) β-caryophyllene; (9) *trans*-β-farnesene; (10) 1,4-cineole; (11) βcitronellol; (12) nerol; (13) geraniol; (14) linalool; (15) α-terpineol; and (16) nerolidol.

Biosynthesis

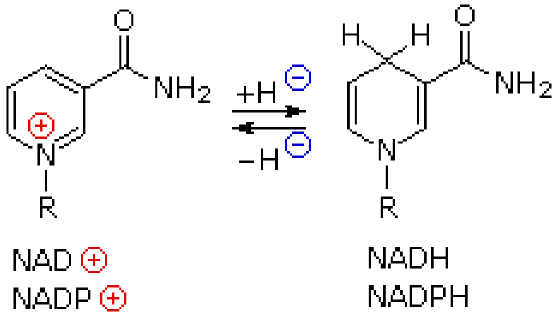
1. Condensations

Claisen condensation of ethyl acetate (or other acetate esters) forms an acetoacetate ester, as illustrated by the top equation in the following diagram. Reduction, dehydration and further reduction of this product would yield an ester of butyric acid, the overall effect being the elongation of the acetate starting material by two carbons. In principle, repetition of this sequence would lead to longer chain acids, made up of an even number of carbon atoms. Since most of the common natural fatty acids have even numbers of carbon atoms, this is an attractive hypothesis for their biosynthesis.



Nature's solution to carrying out a Claisen-like condensation in a living cell is shown in the bottom equation of the diagram. Thioesters are more reactive as acceptor reactants than are ordinary esters, and preliminary conversion of acetate to malonate increases the donor reactivity of this species. The thiol portion of the thioester is usually a protein of some kind, with efficient acetyl transport occurring by way of acetyl coenzyme A. Depending on the enzymes involved, the condensation product may be reduced and then further elongated so as to produce fatty acids (as shown), or elongated by further condensations to polyketone intermediates that are precursors to a variety of natural phenolic compounds. Click on the diagram to see examples of polyketone condensations.

The reduction steps (designated by [H] in the equations) and the intervening dehydrations needed for fatty acid synthesis require unique coenzymes and phosphorylating reagents. The pyridine ring of nicotinamide adenine dinucleotide (NAD) and its 2'-phosphate derivative (NADP) function as hydride acceptors, and the corresponding reduced species (NADH & NADPH) as a hydride donors. Partial structures for these important redox reagents are shown on the right.



The hydroxyl group is a poor anionic leaving group (hydroxide anion is a strong base). Phosphorylation converts a hydroxyl group into a phosphate (PO_4) or pyrophosphate (P_2O_7) ester, making it a much better leaving group (the pK_as at pH near 7 are 7.2 and 6.6 respectively). The chief biological phosphorylation reagents are phosphate derivatives of adenosine (a ribose compound). The strongest of these is the triphosphate ATP, with the diphosphate and monophosphate being less powerful.

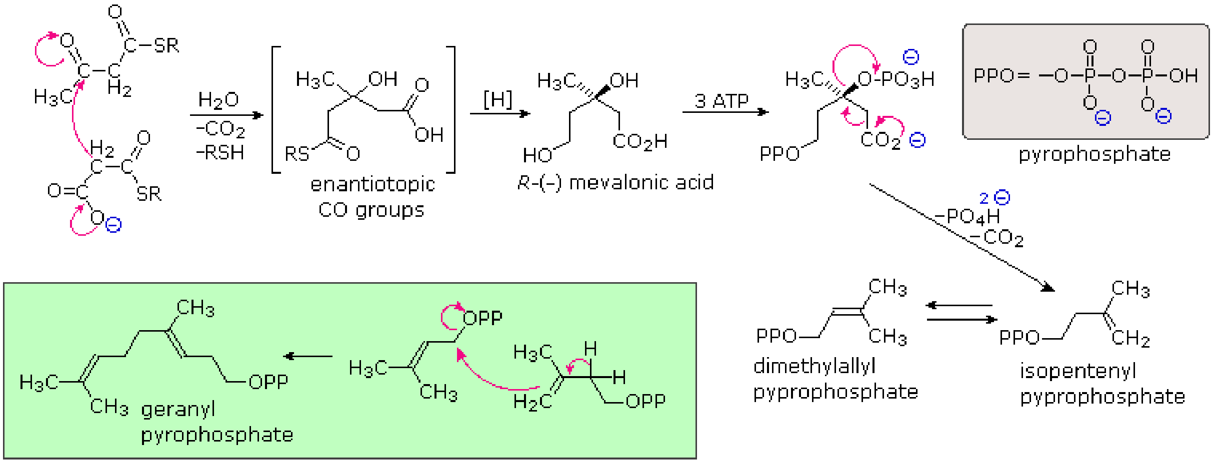
The overall process of fatty acid synthesis is summarized for palmitic acid, $CH_3(CH_2)_{14}CO_2H$, in the following equation:

$$8\ CH_3CO\text{-}CoA + 14\ NADPH + 14\ H^{(+)} + 7\ ATP + H_2O \longrightarrow CH_3(CH_2)_{14}CO_2H + 8\ CoA + 14\ NADP^{(+)} + 7\ ADP + 7\ H_2PO_4^{(-)}$$

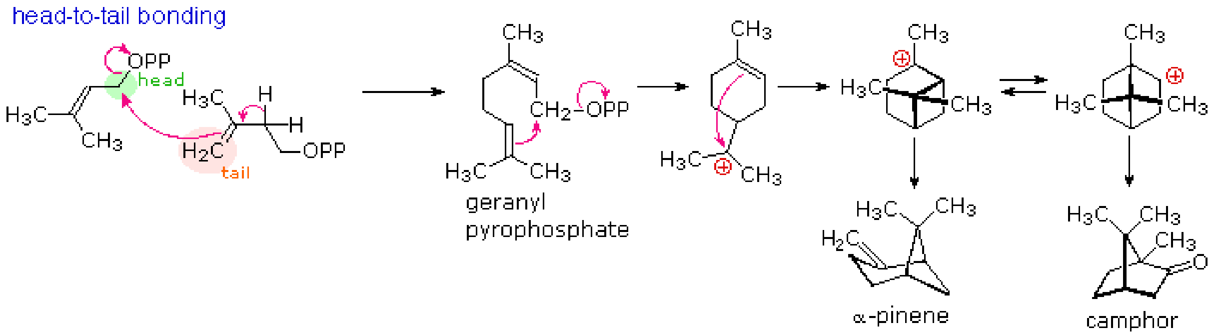
2. Alkylations

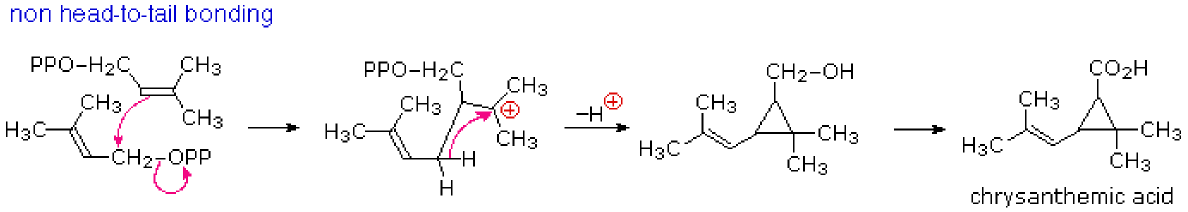
The branched chain and cyclic structures of the terpenes and steroids are constructed by sequential alkylation reactions of unsaturated isopentyl pyrophosphate units. As depicted in the following diagram, these 5-carbon reactants are made from three acetate units by way of an aldol-like addition of a malonate intermediate to acetoacetate. Selective hydrolysis and reduction gives a key intermediate called mevalonic acid. Phosphorylation and elimination of mevalonic acid then generate isopentenyl pyrophosphate, which is in equilibrium with its double bond isomer, dimethylallyl pyrophosphate. The allylic pyrophosphate group in the latter compound is reactive in enzymatically catalyzed alkylation reactions, such as the one drawn in the green box. This provides support for the empirical isoprene rule.

pyrophosphate intermediates in terpene synthesis



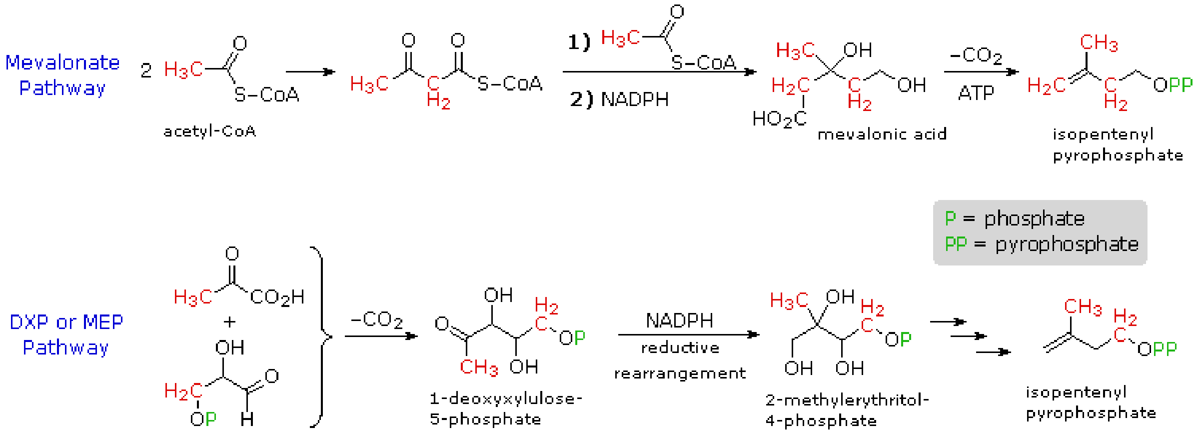
The simplest fashion in which isopentane units combine is termed "head-to-tail".





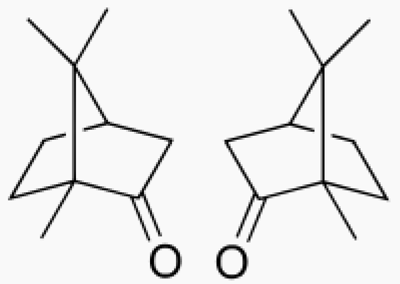
3. **An alternative isoprenoid synthesis**

For many years, the mevalonic acid route to isopentenyl pyrophosphate was considered an exclusive biosynthetic pathway. Recently, an alternative reaction sequence, starting from pyruvic acid and glyceraldehyde-3-phosphate, has been identified (bottom equations in the following diagram). By labeling selective carbon atoms (colored red) these distinct paths are easily distinguished. The new, DXP (1-deoxyxylulose-5-phosphate) path is widespread in microorganisms and chloroplast terpenes. The rearrangement to 2-methylerythritol-4-phosphate is an extraordinary transformation.



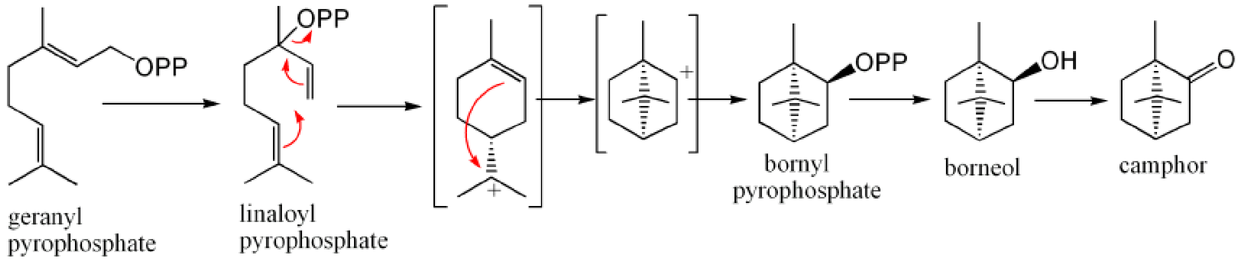
Camphor is a waxy, flammable, white or transparent solid with a strong aroma. It is a terpenoid with found in the wood of the camphor laurel (*Cinnamomum camphora*), a large evergreen tree found in Asia (particularly in Sumatra, Indonesia and Borneo) and also of the unrelated kapur tree, a tall timber tree from the same region. It also occurs in some other related trees in the laurel family, notably *Ocotea usambarensis*. The oil in rosemary leaves (*Rosmarinus officinalis*), in the mint family, contains 10 to 20% camphor, while camphorweed (*Heterotheca*) only contains some 5%. Camphor can also be synthetically produced from oil of turpentine. It is used for its scent, as an ingredient in cooking (mainly in India), as an embalming fluid, for medicinal purposes, and in religious ceremonies. A major source of camphor in Asia is camphor basil (the parent of African blue basil).

The molecule has two possible enantiomers as shown in the structural diagrams. The structure on the left is the naturally occurring (R)-form, while its mirror image shown on the right is the (S)-form.



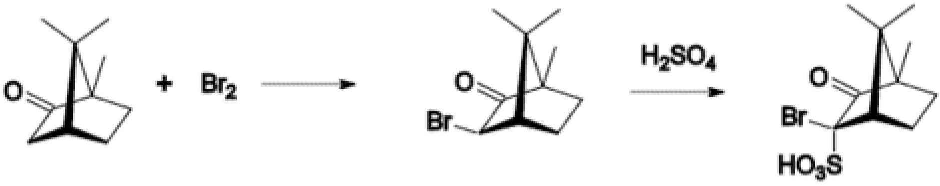
Norcamphor is a camphor derivative with the three methyl groups replaced by hydrogen.

In biosynthesis, camphor is produced from geranyl pyrophosphate, via cyclisation of linaloyl pyrophosphate to bornyl pyrophosphate, followed by hydrolysis to borneol and oxidation to camphor.

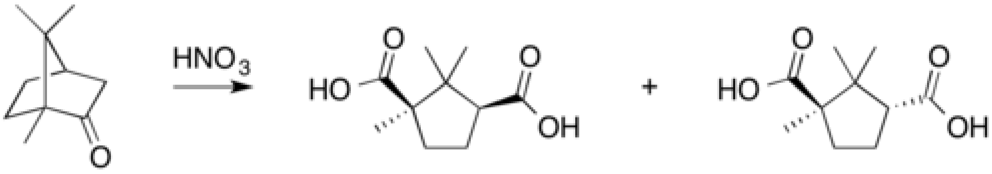


Typical camphor reactions are:

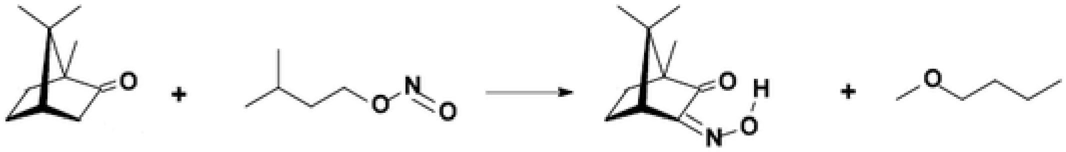
- bromination,



- oxidation with nitric acid,

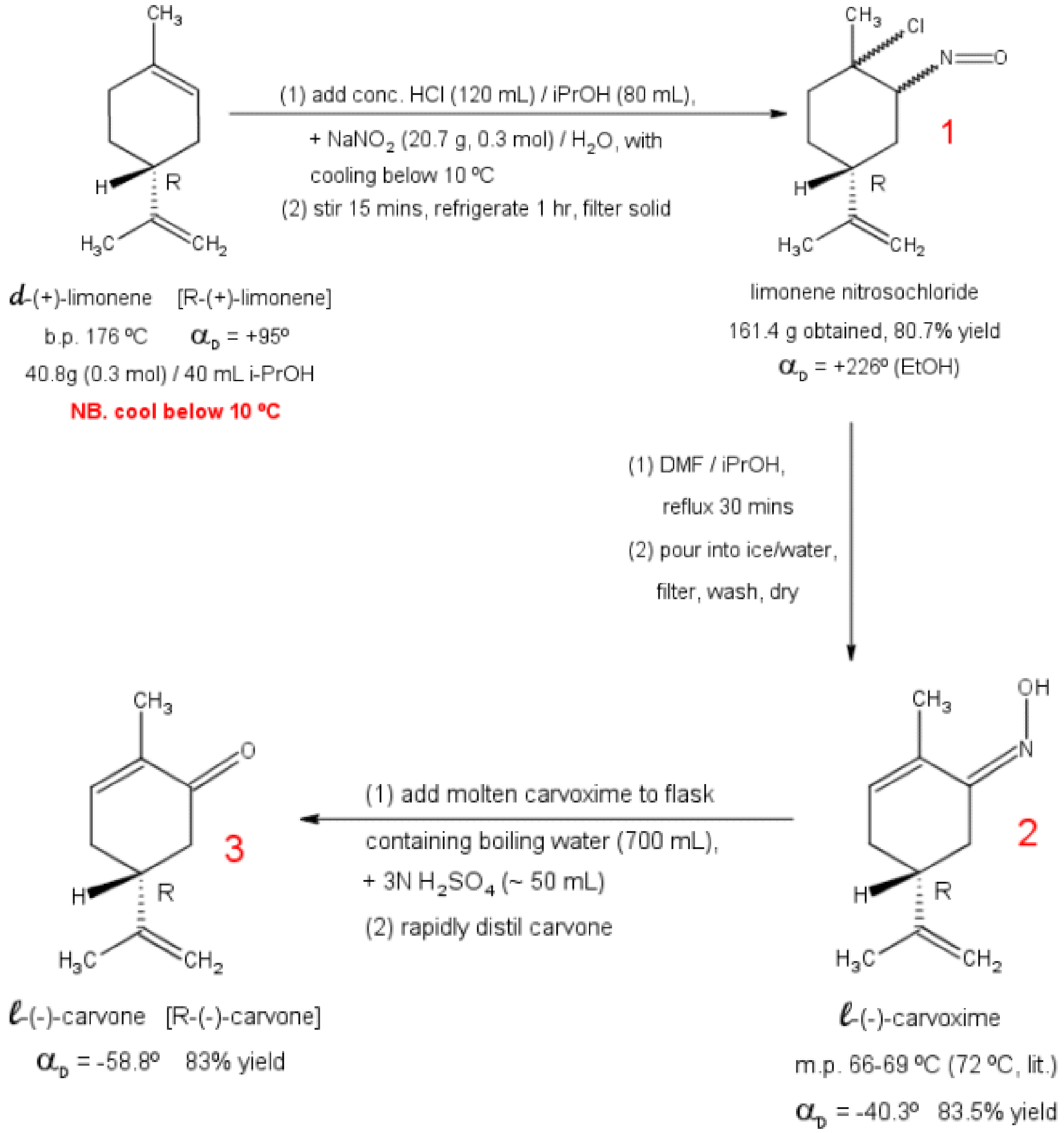


- conversion to isonitrosocamphor.



Camphor can also be reduced to isoborneol using sodium borohydride.

Other terpene - Carvone can be isolated by the careful fractional distillation of spearmint oil , which is produced in large quantities in the United States , with additional supplies from China and South America . Total world production of spearmint oil was about 1500 tones per annum back in 2006 .



(1) add conc. HCl (120 mL) / iPrOH (80 mL),
+ $NaNO_2$ (20.7 g, 0.3 mol) / H_2O, with cooling below 10 ºC
(2) stir 15 mins, refrigerate 1 hr, filter solid

d-(+)-limonene [R-(+)-limonene]
b.p. 176 ºC α_D = +95º
40.8g (0.3 mol) / 40 mL i-PrOH
NB. cool below 10 ºC

1

limonene nitrosochloride
161.4 g obtained, 80.7% yield
α_D = +226º (EtOH)

(1) DMF / iPrOH,
reflux 30 mins
(2) pour into ice/water,
filter, wash, dry

2

l-(-)-carvoxime
m.p. 66-69 ºC (72 ºC, lit.)
α_D = -40.3º 83.5% yield

(1) add molten carvoxime to flask containing boiling water (700 mL),
+ 3N H_2SO_4 (~ 50 mL)
(2) rapidly distil carvone

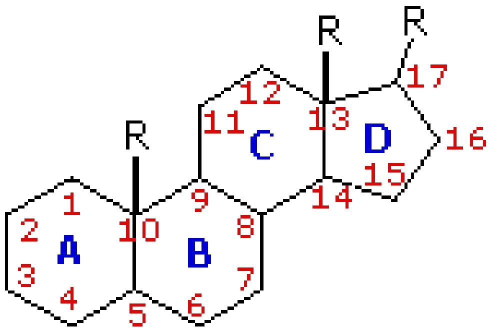
3

l-(-)-carvone [R-(-)-carvone]
α_D = -58.8º 83% yield

Another agricultural sector, the citrus industry (again , mostly in the United States) produces large quantities of waste (eg. orange peels) from the processing of fruit into juices. This waste can be extracted with a hydrocarbon solvent such as naphtha to obtain substantial amounts of the monoterpene d-(+)-limonene , which can be converted into l-(–)-carvone *via* its nitrosochloride addition compound . Several of these "nitrosochloride routes" to carvone have been developed; the most efficient one is probably that of Reitsema (1958) :
R.H. Reitsema , "Nitrosochloride Syntheses and Preparation of Carvone", J. Org. Chem. 23 (12) , pp. 2038-2039 (1958) .

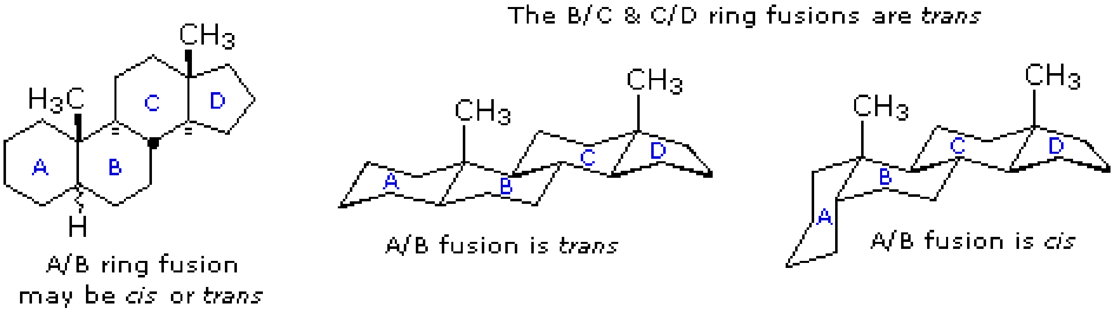
STEROIDS

The important class of lipids called **steroids** are actually metabolic derivatives of terpenes, but they are customarily treated as a separate group. Steroids may be recognized by their tetracyclic skeleton, consisting of three fused six-membered and one five-membered ring, as shown in the diagram to the right.

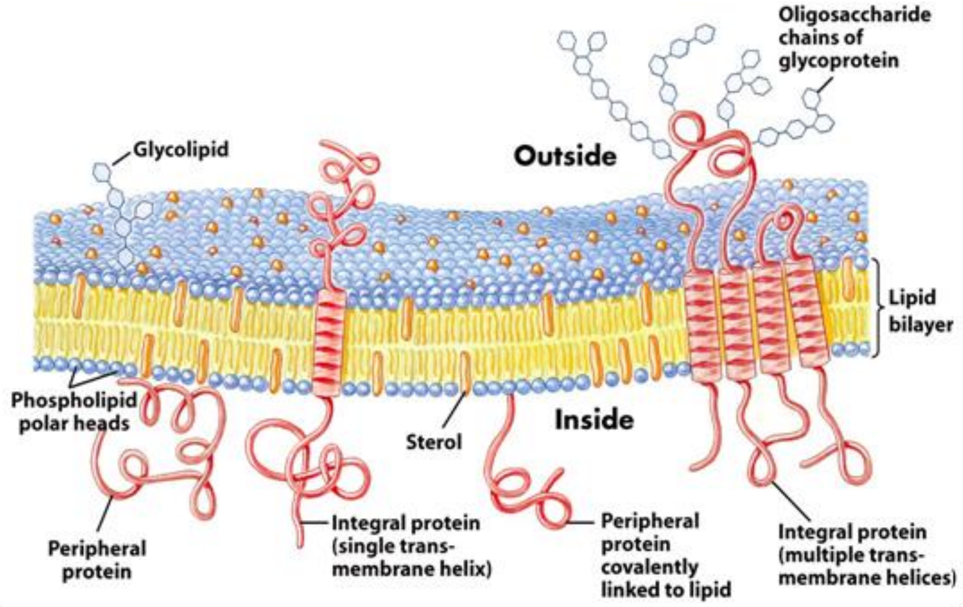


The four rings are designated A, B, C & D as noted, and the peculiar numbering of the ring carbon atoms (shown in red) is the result of an earlier misassignment of the structure. The substituents designated by R are often alkyl groups, but may also have functionality. The R group at the A:B ring fusion is most commonly methyl or hydrogen, that at the C:D fusion is usually methyl. The substituent at C-17 varies considerably, and is usually larger than methyl if it is not a functional group. The most common locations of functional groups are C-3, C-4, C-7, C-11, C-12 & C-17. Ring A is sometimes aromatic. Since a number of tetracyclic triterpenes also have this tetracyclic structure, it cannot be considered a unique identifier.

Steroids are widely distributed in animals, where they are associated with a number of physiological processes. A common strategy in pharmaceutical chemistry is to take a natural compound, having certain desired biological properties together with undesired side effects, and to modify its structure to enhance the desired characteristics and diminish the undesired. This is sometimes accomplished by trial and error. The generic steroid structure drawn above has seven chiral stereocenters (carbons 5, 8, 9, 10, 13, 14 & 17), which means that it may have as many as 128 stereoisomers. With the exception of C-5, natural steroids generally have a single common configuration. The below are the preferred conformations of the rings.

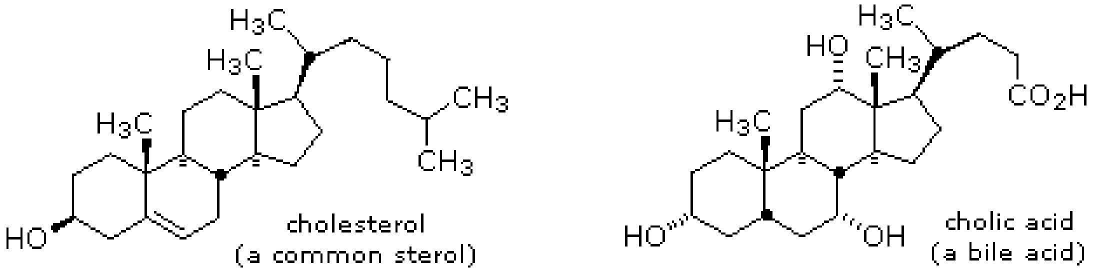


Common Steroid Conformations



FLUID MOSAIC MODEL OF PLASMA MEMBRANE

Cholesterol is widely distributed in all cells of the body but particularly in nervous tissue. It is a major constituent of the plasma membrane and of plasma lipoproteins. It is often found as cholesteryl ester, where the hydroxyl group on position 3 is esterified with a long-chain fatty acid. *It occurs in animals but, not in plants.*

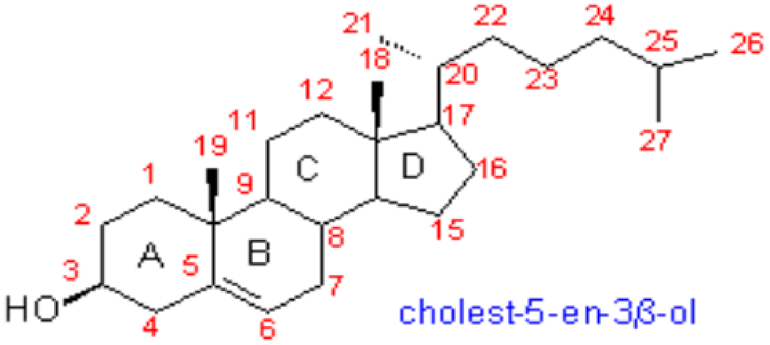


cholesterol (a common sterol)

cholic acid (a bile acid)

Typical Animal Steroids

Cholesterol: is by far the most common member of a group of steroids in animal tissues; it has a tetracyclic ring system with a double bond in one of the rings and one free hydroxyl group. It is found both in the free state, where it has an essential role in maintaining membrane fluidity, and in esterified form, i.e. as cholesterol esters. It consists of a tetracyclic cyclopentaphenanthrene structure.



cholest-5-en-3β-ol

Biosynthesis of cholesterol

Slightly less than half of the cholesterol in the body derives from biosynthesis. Biosynthesis in the liver accounts for approximately 10%, and in the intestines approximately 15%, of the amount produced each day. Cholesterol synthesis occurs in the cytoplasm and in the microsomes from the two-carbon acetate group of acetyl-CoA.

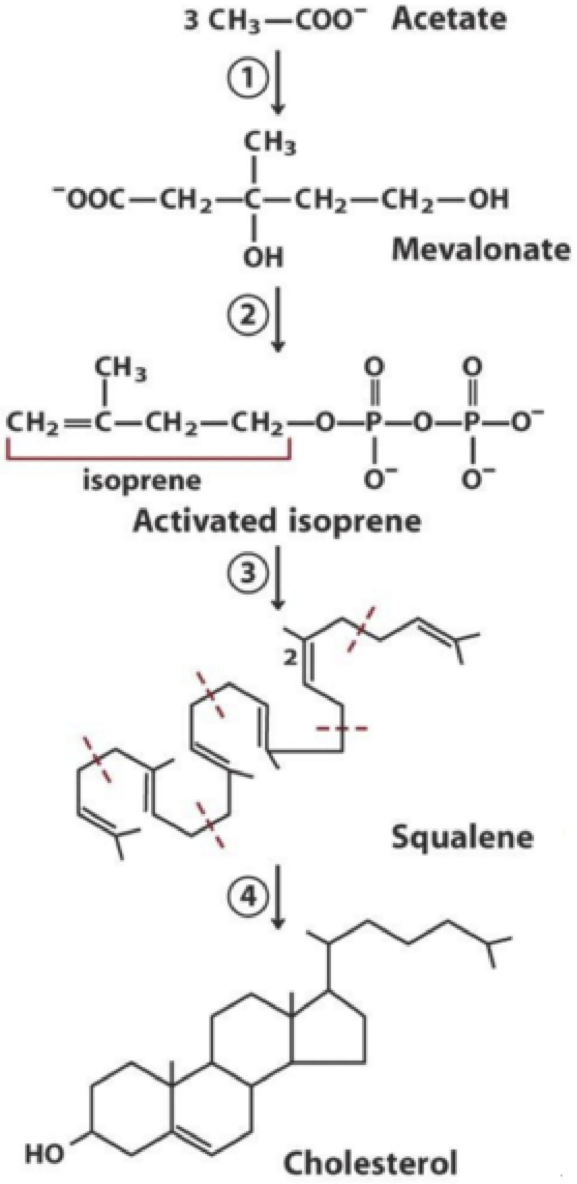
The process has five major steps:

1 - Acetyl-CoAs are converted to 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA).

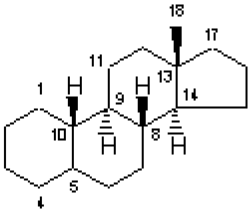
2 - HMG-CoA is converted to mevalonate. 3- Mevalonate is converted to the isoprene based molecule, isopentenyl pyrophosphate (IPP), with the concomitant loss of CO_2.

4 - IPP is converted to squalene.

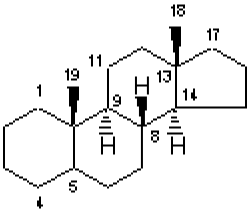
5 - Squalene is converted to cholesterol.



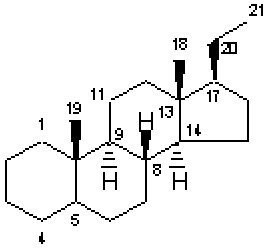
Steroids are compounds consistuted of four fused rings, for example, the most common and best known steroid in humans, cholesterol. In animals, steroids are biosynthesized from lanosterol and are widely distributed. The distinctive feature in steroids is lack of methyl group at C-4 position as compared to terpenes. In this section, we have classified steroids into five basic categories based upon their chemical composition.



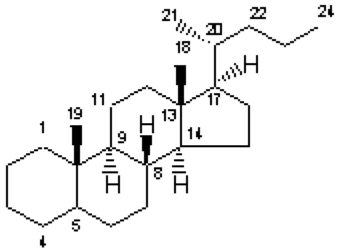
Estrane



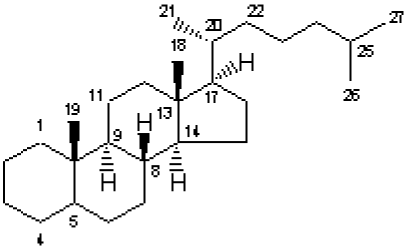
Androstane



Pregnane



Cholane



Cholestane

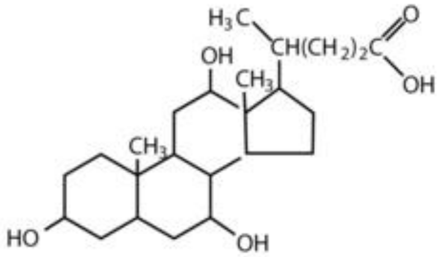
Hormones are chemical messengers that are released in one tissue and transported through the circulatory system to one or more other tissues. One group of hormones is known as steroid hormones because these hormones are synthesized from cholesterol, which is also a steroid. There are two main groups of steroid hormones: adrenocortical hormones and sex hormones.

The adrenocortical hormones, such as aldosterone and cortisol, are produced by the adrenal gland, which is located adjacent to each kidney. Aldosterone acts on most cells in the body, but it is particularly effective at enhancing the rate of reabsorption of sodium ions in the kidney tubules and increasing the secretion of potassium ions and/or hydrogen ions by the tubules. Because the concentration of sodium ions is the major factor influencing water retention in tissues, aldosterone promotes water retention and reduces urine output. Cortisol regulates several key metabolic reactions (for example, increasing glucose production and mobilizing fatty acids and amino acids). It also inhibits the inflammatory response of tissue to injury or stress. Cortisol and its analogs are therefore used pharmacologically as immunosuppressants after transplant operations and in the treatment of severe skin allergies and autoimmune diseases, such as rheumatoid arthritis.

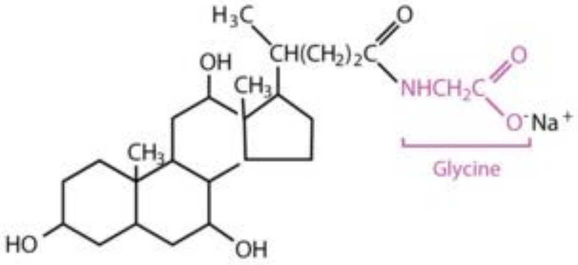
The sex hormones are a class of steroid hormones secreted by the gonads (ovaries or testes), the placenta, and the adrenal glands. Testosterone and androstenedione are the primary male sex hormones, or androgens, controlling the primary sexual characteristics of males, or the development of the male genital organs and the continuous production of sperm. Androgens are also responsible for the development of secondary male characteristics, such as facial hair, deep voice, and muscle strength. Two kinds of sex hormones are of particular importance in females: progesterone, which prepares the uterus for pregnancy and prevents the further release of eggs from the ovaries during pregnancy, and the estrogens, which are mainly responsible for the development of female secondary sexual characteristics, such as breast development and increased deposition of fat tissue in the breasts, the buttocks, and the thighs. Both males and females produce androgens and estrogens, differing in the amounts of secreted hormones rather than in the presence or absence of one or the other.

Sex hormones, both natural and synthetic, are sometimes used therapeutically. For example, a woman who has had her ovaries removed may be given female hormones to compensate. Some of the earliest chemical compounds employed in cancer chemotherapy were sex hormones. For example, estrogens are one treatment option for prostate cancer because they block the release and activity of testosterone. Testosterone enhances prostate cancer growth. Sex hormones are also administered in preparation for sex-change operations, to promote the development of the proper secondary sexual characteristics. Oral contraceptives are synthetic derivatives of the female sex hormones; they work by preventing ovulation.

Bile is a yellowish green liquid (pH 7.8–8.6) produced in the liver. The most important constituents of bile are bile salts, which are sodium salts of amidelike combinations of bile acids, such as cholic acid and an amine such as the amino acid glycine . They are synthesized from cholesterol in the liver, stored in the gallbladder, and then secreted in bile into the small intestine. In the gallbladder, the composition of bile gradually changes as water is absorbed and the other components become more concentrated.



(a) Cholic acid (a bile acid)



(b) Sodium glycocholate (a bile salt)

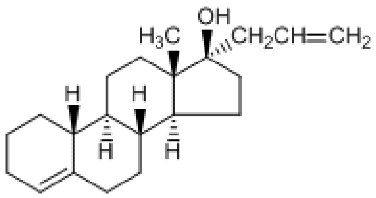
Because they contain both hydrophobic and hydrophilic groups, bile salts are highly effective detergents and emulsifying agents; they break down large fat globules into smaller ones and keep those smaller globules suspended in the aqueous digestive environment. Enzymes can then hydrolyze fat molecules more efficiently. Thus, the major function of bile salts is to aid in the digestion of dietary lipids.

Steroid Hormones: Estranes, Androstanes, Pregnanes

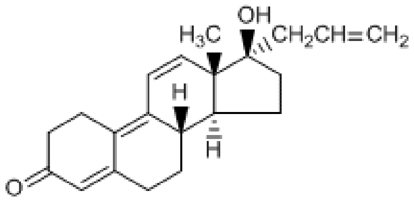
Certain kinds of steroids like estrogenes, androstanes and pregnanes can act as hormones, their activities being closely related to their structures (Table 1). Pregnane-type steroids can be classified into glucocorticoids and progestogens based on their bioactivities.

Estrogens: Estrogens function as the primary female sex hormone and in combination with synthetic progestogens can be used as oral contraceptives to suppress ovulation. Recently, it is also reported that they are effective for the prevention of osteoporosis, heart attacks and Alzheimer's disease in women.

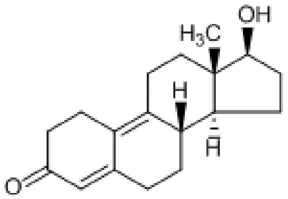
ESTRANES



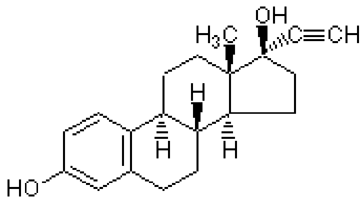
Allylestrenol



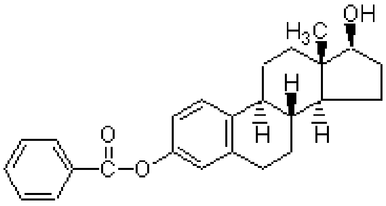
Altrenogest



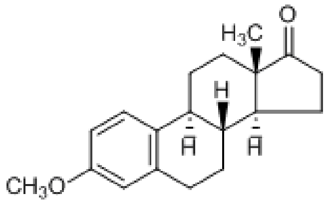
9(10)-Dehydronandrolone



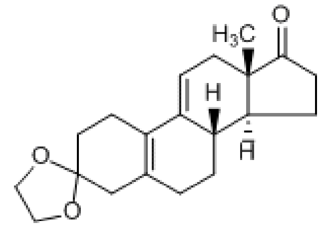
Ethynylestradiol



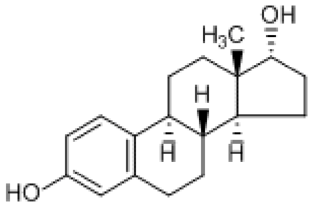
Estradiol Benzoate



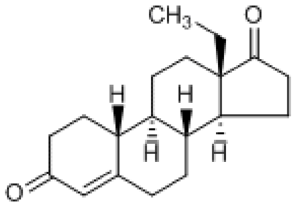
Estrone 3-Methyl Ether



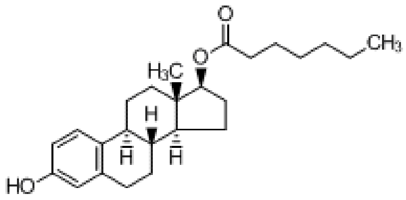
Estra-5(10),9(11)-diene-3,17-dione 3-Ethylene Ketal



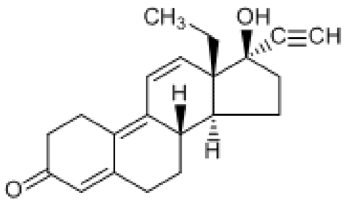
α-Estradiol



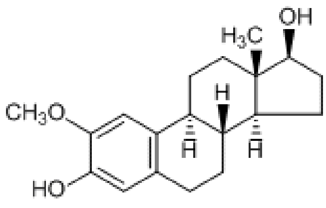
Ethylgonendione



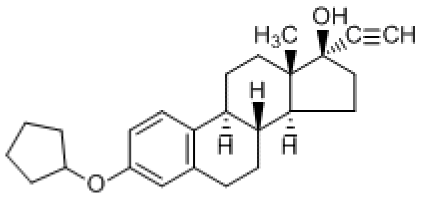
β-Estradiol 17-Heptanoate

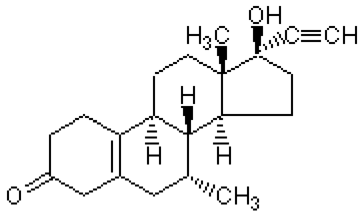


Gestrinone



2-Methoxy-β-estradiol

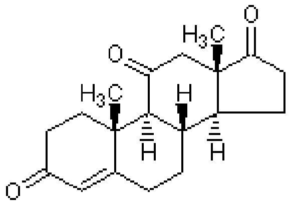


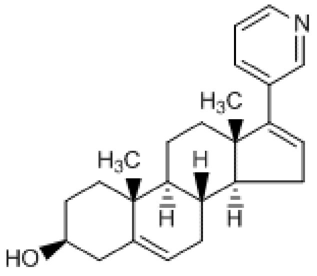


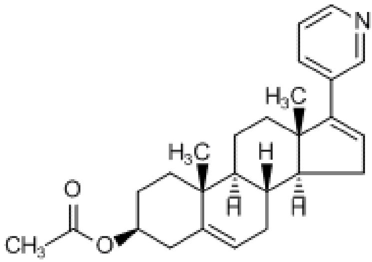
Quinestrol **Tibolone**

Androgens: Testosterone is not only the principal and most well known male sex hormone but is also known to exert anabolic effects. This is also the main reason why some of them have been banned from use as bone density enhancers and muscle-building drugs by several sports organizations. They are also the intermediates of estrogene biosynthetic pathway or rather the precursors of all estrogens.

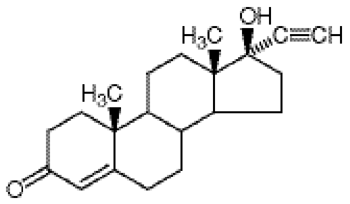
ANDROSTANES

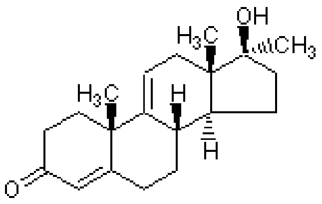


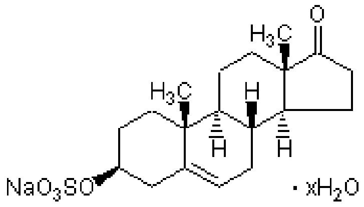




Adrenosterone **Abiraterone** **Abiraterone Acetate**





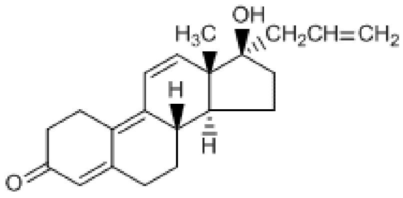
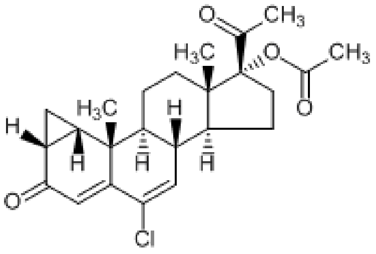
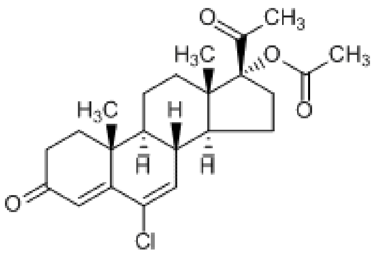


Ethisterone **Δ9(11)-Methyltestosterone**

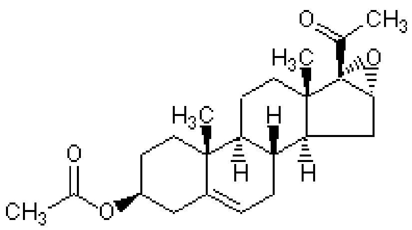
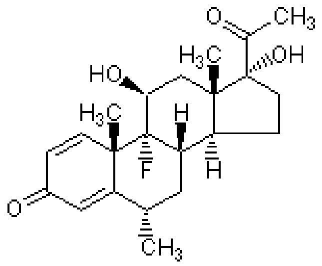
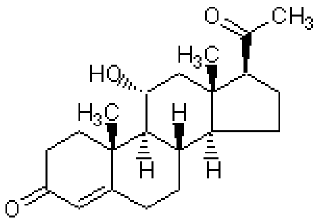
Dehydroepiandrosterone-
3-sulfate Sodium Salt
Hydrate

Progestogens: The only naturally occuring progestogen, i.e., progesterone, exhibits antiovulatory action. Based on its structure, derivatives of 19-nortestosterone were synthesized and can be used as oral contraceptives.

PREGNANES (PROGESTOGEN)

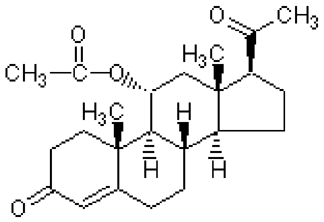
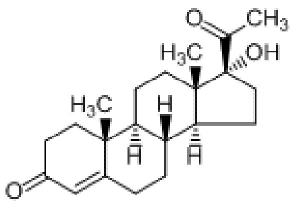
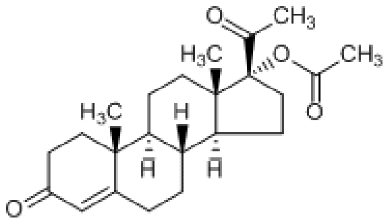




Altrenogest **Cyproterone Acetate** **Chlormadinone Acetate**

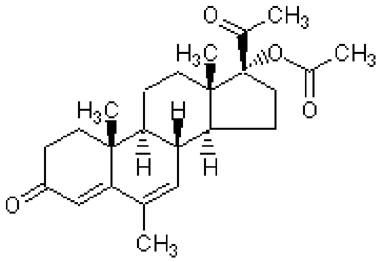
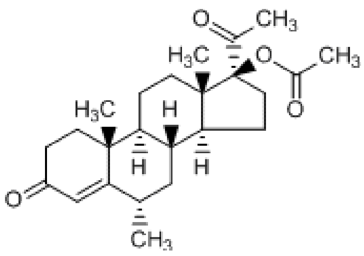
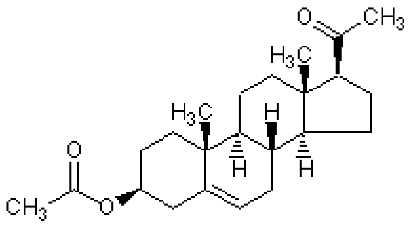
16,17-Epoxypregnenolone Acetate **Fluorometholone**

11α-Hydroxyprogesterone

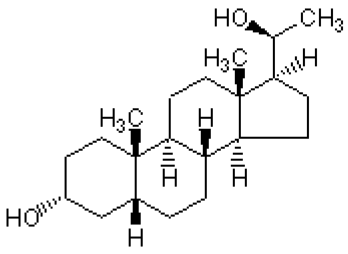




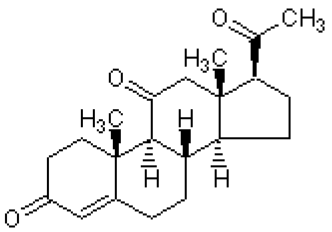
11α-Hydroxyprogesterone **11α-Hydroxyprogesterone Acetate**

17α- Hydroxyprogesterone Acetate

Megestrol Acetate **Medroxyprogesterone Acetate** **Pregnenolone Acetate**

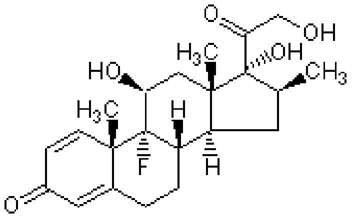


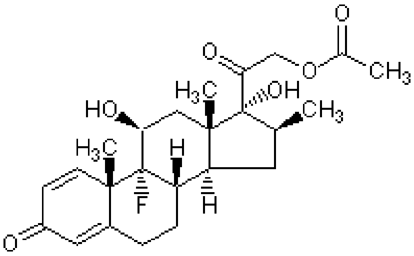


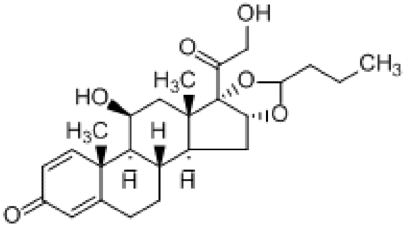
5β-Pregnane-3α,20α-diol **4-Pregnene-3,11,20-trione**

Glucocorticoids: Synthetic glucocorticoids such as dexamethasone and prednisolone find clinical use as anti-inflammatory agents. They are synthetically developed based on the structure of cortisone, a natural glucocorticoid.

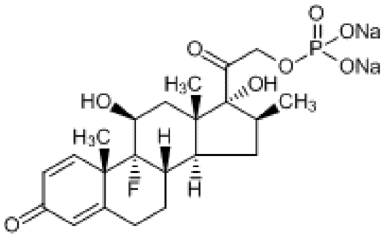
PREGNANES (GLUCOCORTICOIDS)

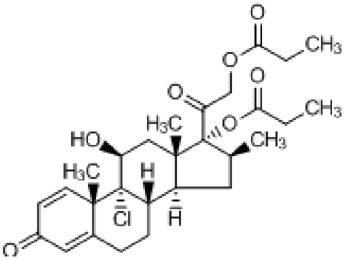


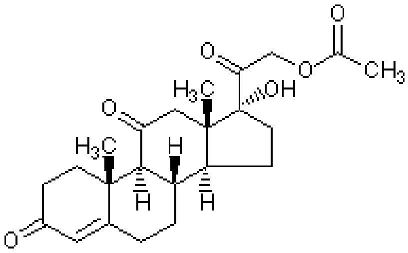




Betamethasone **Betamethasone 21-Acetate** **Budesonide**

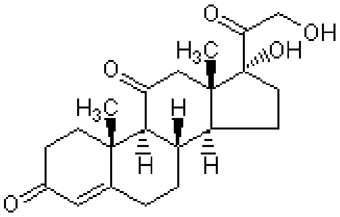


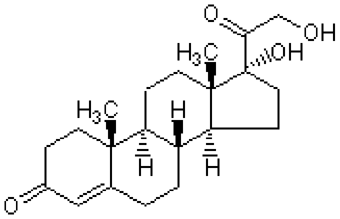


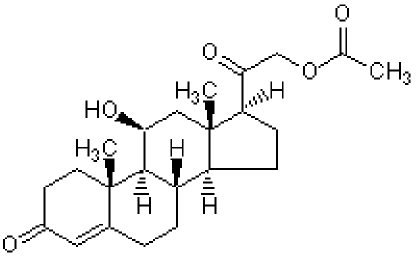


Betamethasone 21-Phosphate Disodium Salt

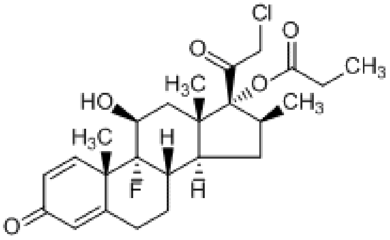
Beclometasone Dipropionate **Cortisone Acetate**

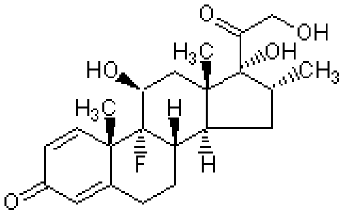


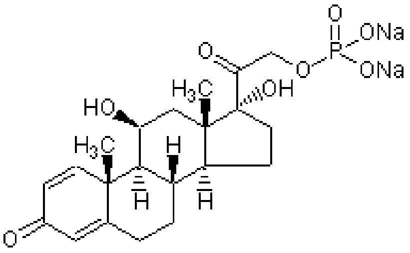




Cortisone **Cortexolone** **Corticosterone 21-Acetate**

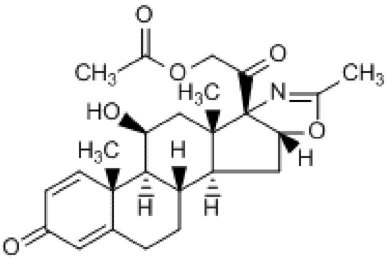


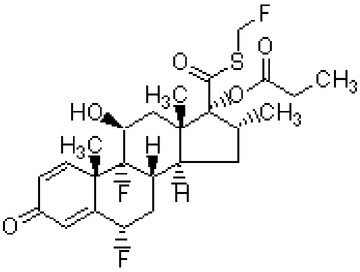


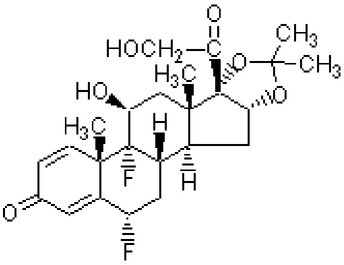


Clobetasol 17-Propionate **Dexamethasone**

Prednisolone 21-Phosphate Disodium Salt

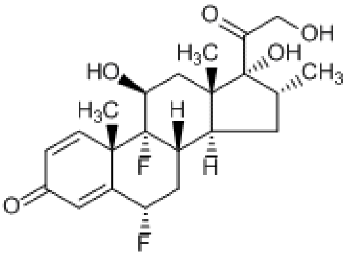


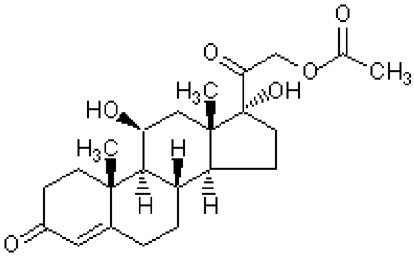


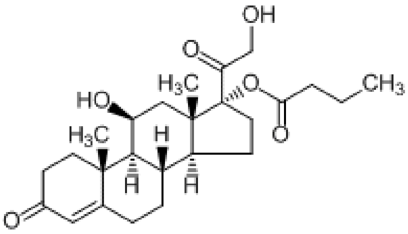


Deflazacort **Fluticasone Propionate** **Fluocinolone**

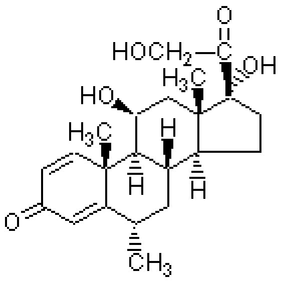
Acetonide



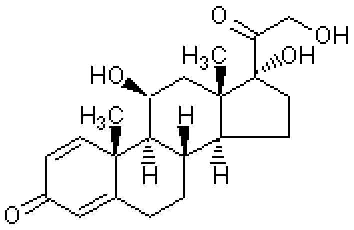




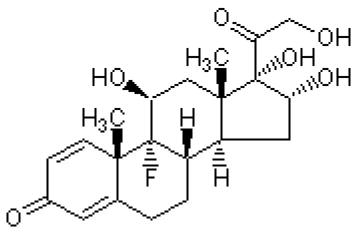
Flumetasone **Hydrocortisone Acetate** **Hydrocortisone 17-Butyrate**



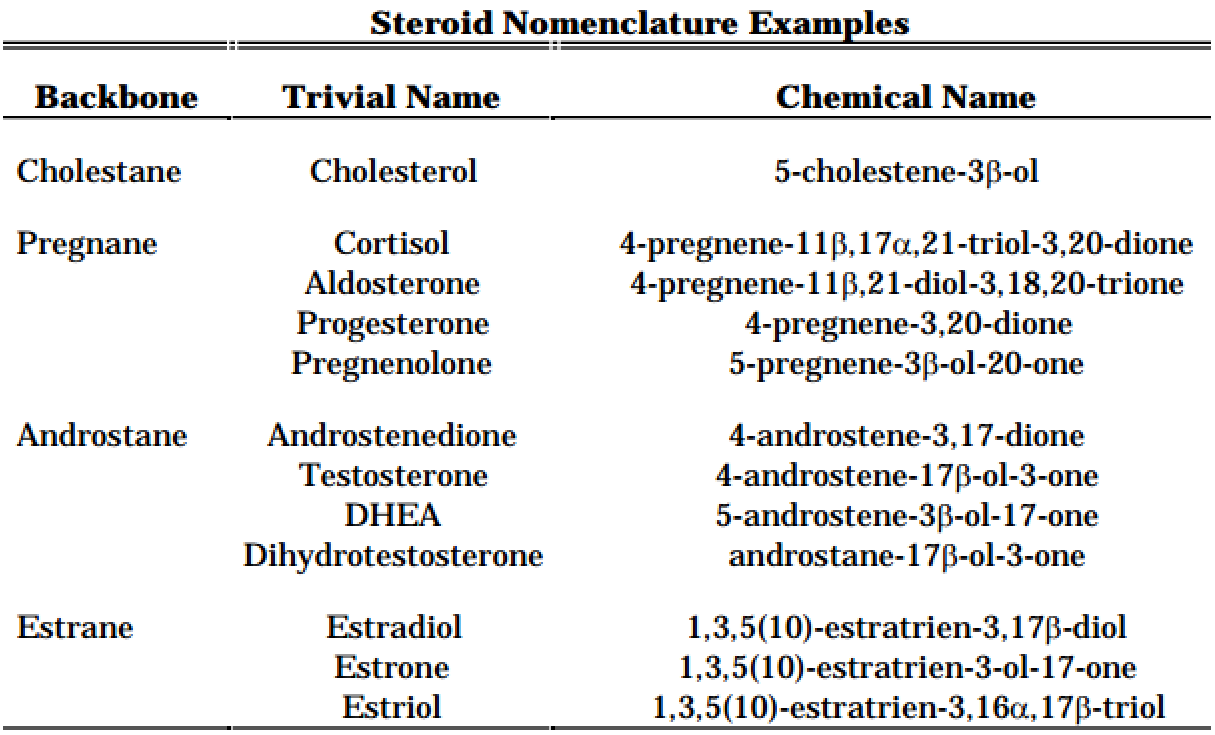
6α-Methylprednisolone



Prednisolone



Triamcinolone

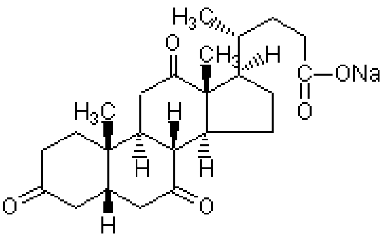


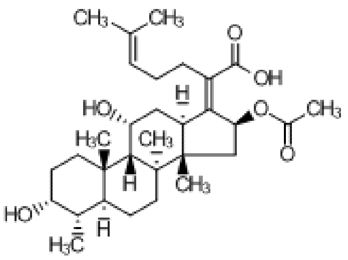
Steroid Nomenclature Examples

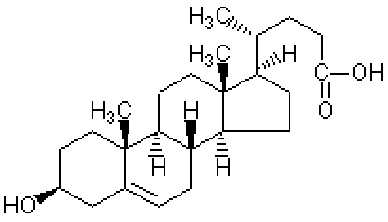
Backbone	Trivial Name	Chemical Name
Cholestane	Cholesterol	5-cholestene-3β-ol
Pregnane	Cortisol	4-pregnene-11β,17α,21-triol-3,20-dione
	Aldosterone	4-pregnene-11β,21-diol-3,18,20-trione
	Progesterone	4-pregnene-3,20-dione
	Pregnenolone	5-pregnene-3β-ol-20-one
Androstane	Androstenedione	4-androstene-3,17-dione
	Testosterone	4-androstene-17β-ol-3-one
	DHEA	5-androstene-3β-ol-17-one
	Dihydrotestosterone	androstane-17β-ol-3-one
Estrane	Estradiol	1,3,5(10)-estratrien-3,17β-diol
	Estrone	1,3,5(10)-estratrien-3-ol-17-one
	Estriol	1,3,5(10)-estratrien-3,16α,17β-triol

BILE ACIDS: CHOLANES

Cholane type steroids are predominantly found in the bile. Cholic acid and its derivatives exist in bile as the major component as conjugates of glycine and taurine. Since conjugated cholates are amphiphilic, they assist in the digestion and absorption of lipids in small intestine. This characteristic is also exploited also in its use as a surfactant.

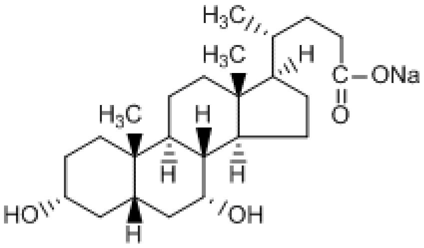


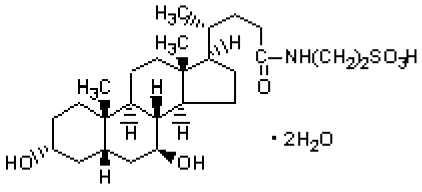




Sodium Dehydrocholate **Fusidic Acid**

3β-Hydroxy-Δ5-cholenic Acid

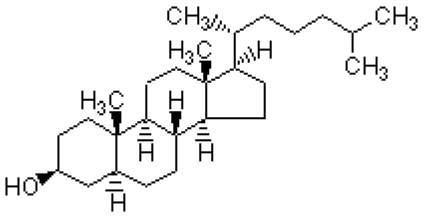


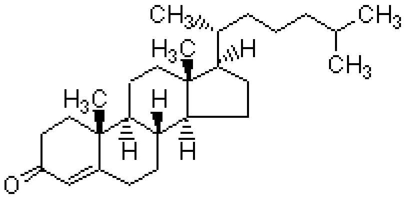


Sodium Chenodeoxycholate **Tauroursodeoxycholic Acid Dihydrate**

Cholesterol: Cholestanes

Cholesterol possesses a cholestane-type skeleton and in conjugation with fatty acids, it forms the main component of cell membranes in animals and microorganisms. These cholesterol conjugates establish and maintain proper membrane permeability. In addition, it is a precursor of steroids as mentioned above and also exists in its liberated form in organisms.



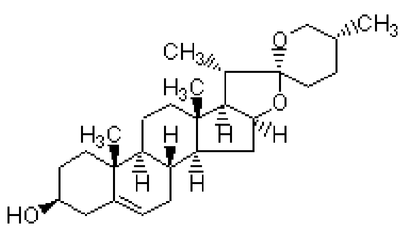


β-Cholestanol **(+)-4-Cholesten-3-one**

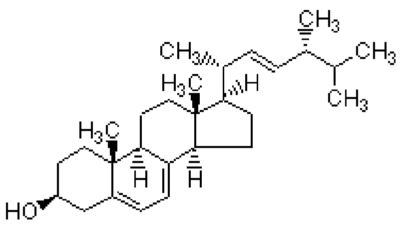
Phytosteroids, Steroid Glycosides, Miscellaneous Steroids

Steroids of plant origin have different biosynthetic pathways: they are synthesized from cycloartenol. They possess structural features distinct from animal steroids, for instance, a characteristic alkyl side-chain at C-24.

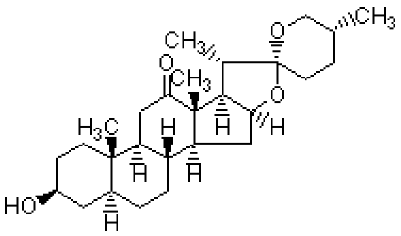
PHYTOSTEROIDS



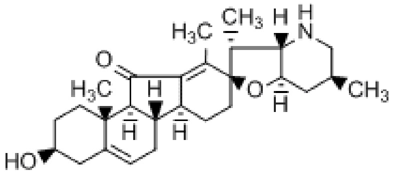
Diosgenin



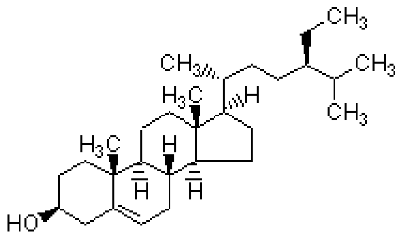
Ergosterol



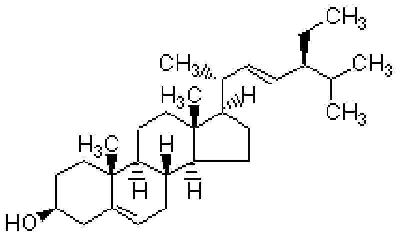
Hecogenin



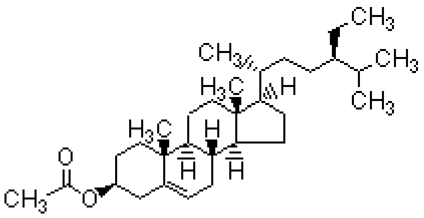
Jervine



β-Sitosterol

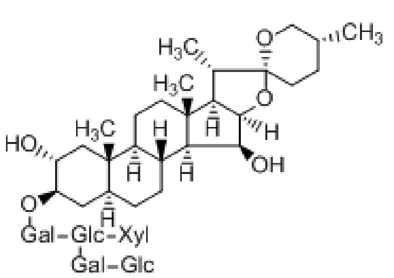


Stigmasterol

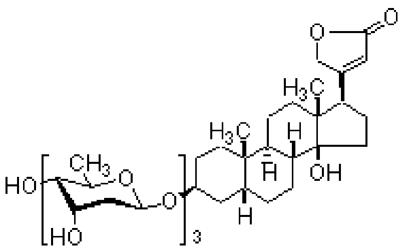


β-Sitosterol Acetate

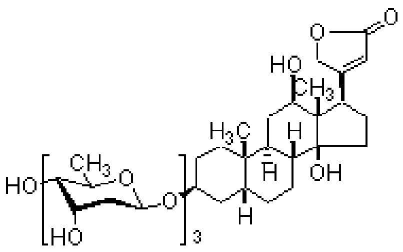
STEROID GLYCOSIDES



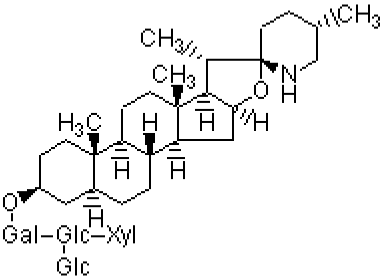
Digitonin



Digitoxin

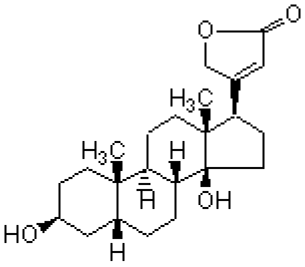


Digoxin

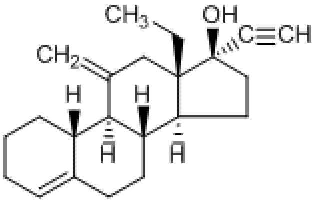


Tomatine

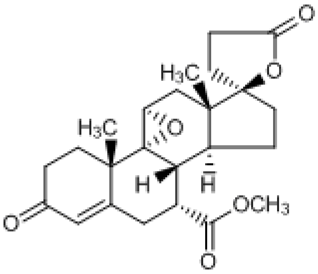
OTHER STEROIDS



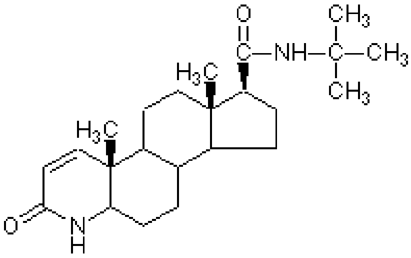
Digitoxigenin



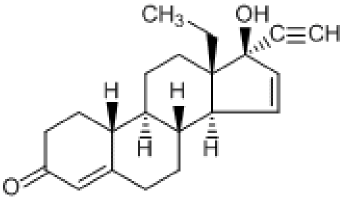
Desogestrel



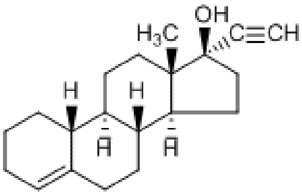
Eplerenone



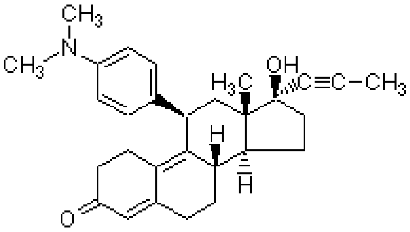
Finasteride



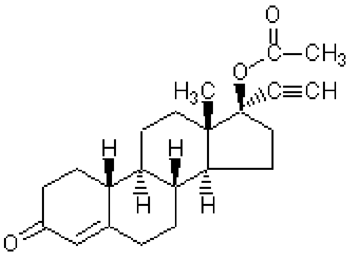
Gestodene



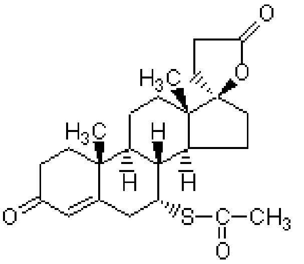
Lynestrenol



Mifepristone

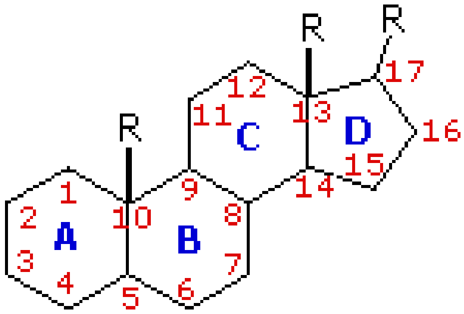


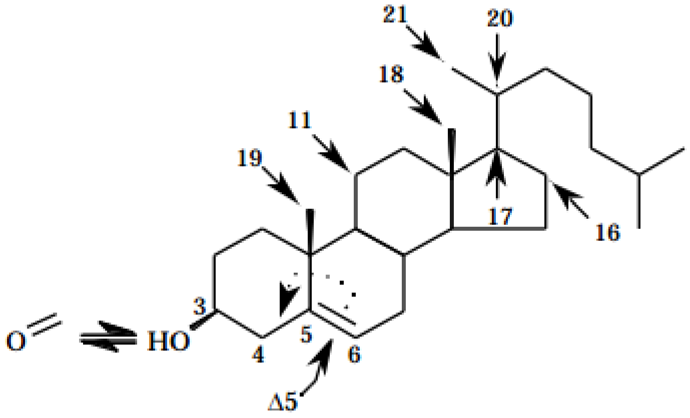
Norethisterone Acetate



Spironolactone

REACTIONS OF IDENTIFICATION

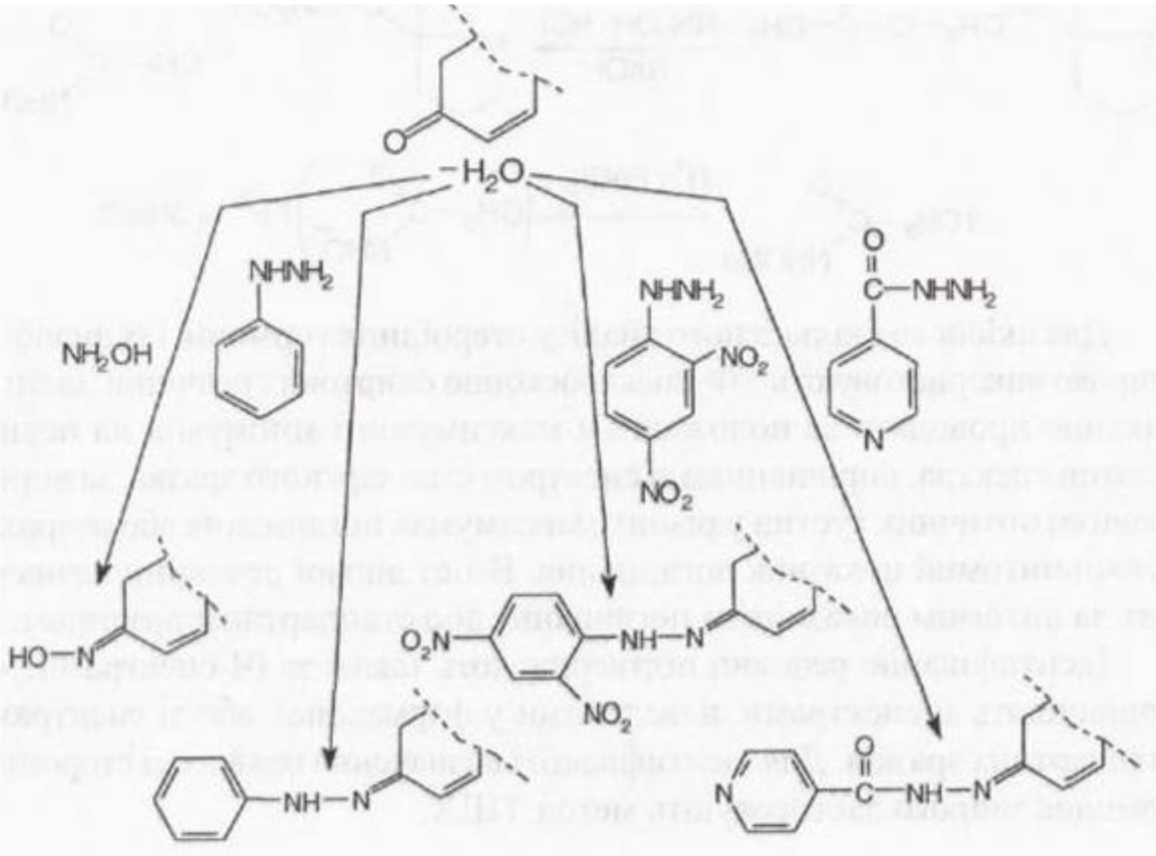




Methyl groups attached to the steroid cycle in the 10-th and 13-th position, are named *angularly*. Radical R and the hydrogen atoms (in 8, 9, 14 positions) are oriented to the space in a cis-or trans-position relative to the angularly groups. Conventionally assumed that the angularly methyl groups are located above the plane of the drawing (the bond is indicated by solid (full) line). If the other substituents are in cis-position, in the same plane as the angularly groups (β-configuration), then their relationship are denoted by the solid line, and if the trans-position (α-configuration) - dotted line.

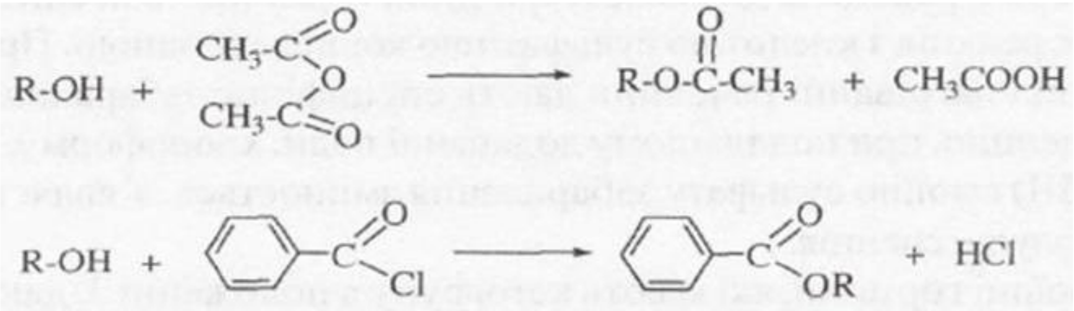
Because the structure of the steroid hormones have much in common, a lot of their analysis method are common. Steroid hormones - crystalline substances, so for them to determine the melting point it is one of the method to measure the purity and identity. Steroid hormones and their analogues are an optically-active substances, most of them are dexter isomers (methylandrostendiol - levogyrate). AND for the identification and confirmation of purity recommends to determine the angle of rotation of the plane of polarized light by the solution of the compounds in organic solvents and to calculate the specific rotation.

General reaction for all steroid hormones and their synthetic analogues is the reaction with concentrated H_2SO_4. When to dissolve in it and to heat the substances give appearance a specific color, sometimes fluorescence, with a further addition of water, chloroform, the color changes, there is a specific fluorescence. Steroid hormones possessi keto group in 3-d position, they give the addition reaction Steroid hormones possessing keto group in position 3, given the addition reaction with elimination of water with hydroxylamine, phenylhydrazine, 2,4-dinitrophenylhydrazine, isoniazid and elimination of water – observing the precipitation with a characteristic melting point, or there is a characteristic color (yellow, orange) : with hydroxylamine, phenylhydrazine, 2,4-dinitrophenylhydrazine, isoniazid - observing precipitation with a characteristic melting point, or there is a characteristic color (yellow, orange):

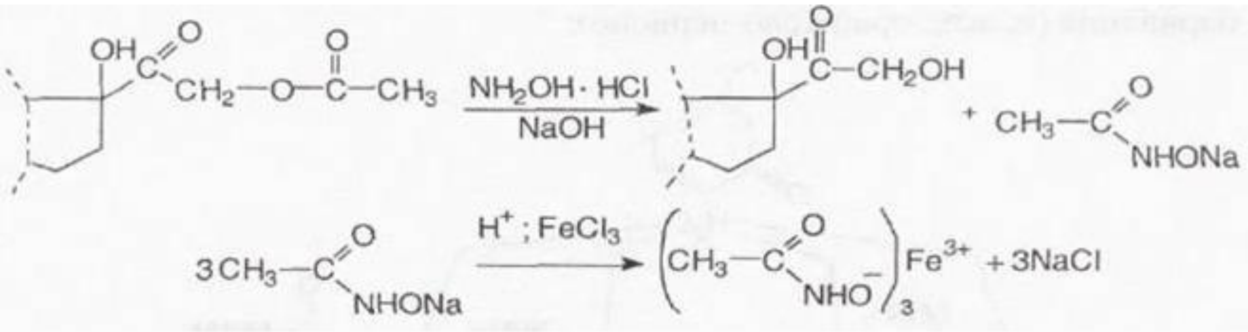


These reactions can be used for the quantity determination of the steroid hormones and their analogues by the gravimetry method ((mass of sediment formed) or photometric (optical density of colored solutions).

For the hormone’s identification which have hydroxyl groups in 3 or 17 position, often there is using the reaction of the esters forming (acetate, benzoate), with a characteristic melting point:



For the hormone’s identification and their synthetic analogues that are used as esters (acetate, propanoate), apply the hydroxamic reaction:



For the identification and quantitative analysis of steroid hormones and their analogues are widely used UV spectroscopy of alcohol solutions. The identification is carried out according to the location of the maximus and minimum on a particular part of the spectrum, comparing with the spectrum of standard sample, according to the relative between the optical densities in the various absorption maximus and calculate the spesific absorbtion valur. The content of the active substance is determined by the specific absorption rate or standard solution.

The substance’s indentification is confirmed by the IR-spectropy, which is compared with the pharmacopeial or standard samples.

For the identifying and determining the presence of impurities there is widely used method of TLC.

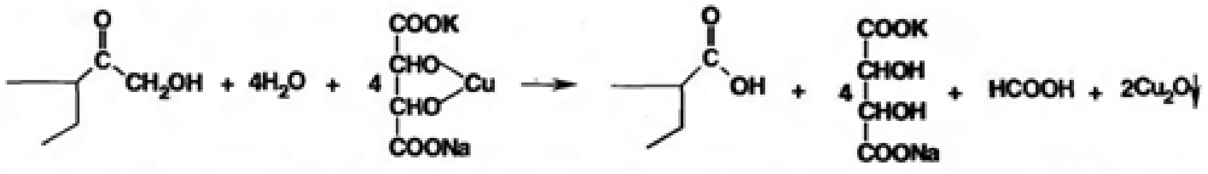
Corticosteroids’ structure is confirmed by:

a) Boscot reaction: corticosteroids are dissolved in the mixture of 88% H_3PO_4 and concentrated CH_3COOH, the solution heated 2 minutes at 100ºC and leave for 1 hour at room temperature, and then it is diluted by CH_3COOH. Under the UV lamp (Bah lamp) fluorescence occurs.

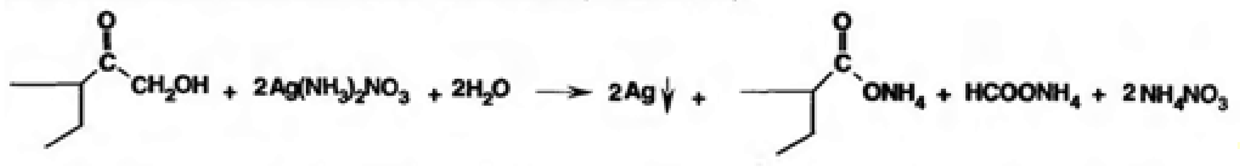
b) reaction with concentrated sulfuric acid.

α-Ketonic group – reducing properties (oxidizing to carboxilic group.

a) Felling reaction (copper-tartrate reagent). At the heating of the mixture of the alcohol substance's solution and Felling reagent on the waterbathe Cu2O is settled down.

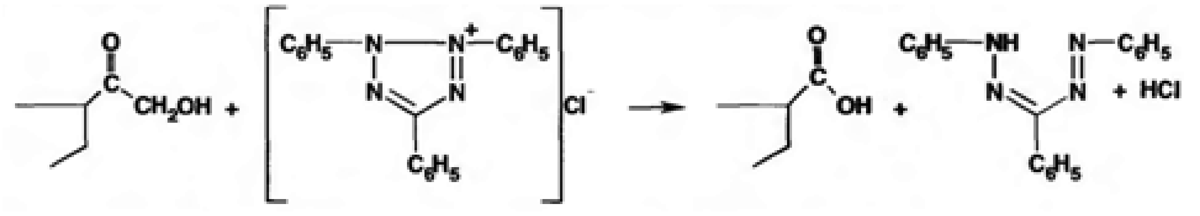


b) Except Felling reagent as a oxidizing agent Tollens reagent can be used (ammonia solution of silver nitrate) – reaction of "silver mirror", Zonnenshten reagent - H_3P0_4 • $12Mo0_3$•$2H_20$), Iron (III) salt.



c) Gorega reaction. At the oxidation of corticosteroids with ethanolic solution of triphenyltetrazolium chloride in the presence of a solution of tetrametylamine hydroxide, as a reducing product there is formed red color of formazans

The reaction is used for the identification and quantification by a spectrophotometry.



d) At the oxidation of potassium periodate there is released 17-carboxylic acid, formaldehyde, which can be associated by chromotropic acid (aurine dye).

Carbonyl (keto) group in the 3-d position: the reaction of association with the elimination of water with hydroxylamine, phenylhydrazine, 2,4-

dinitrophenylhydrazine, isoniazid - observed precipitation with a characteristic melting point, or there is a characteristic color.

Esteric group:

a) hydroxamic test

b) alkaline hydrolysis with subsequent identification of the hydrolysis products.

Identification of the covalently bounded fluorite. In fluorine continuing corticosteroids the present of fluorine is identified after the mineralization (to burn with oxygen in flask) with zirconium-alizarine complex.

Identification of Desoxycorticosterone acetate:

1. On the steroid system – Boscot reaction. A violet color wiyh a fluorescence.

2. With concentrated H_2SO_4 – cherry color with greenish-brown fluorescence. After adding chloroform and shaking, the lower layer is painted in yellow top - green (a steroid cycle).

3. On the oxyacetylic group, which is acetylated:

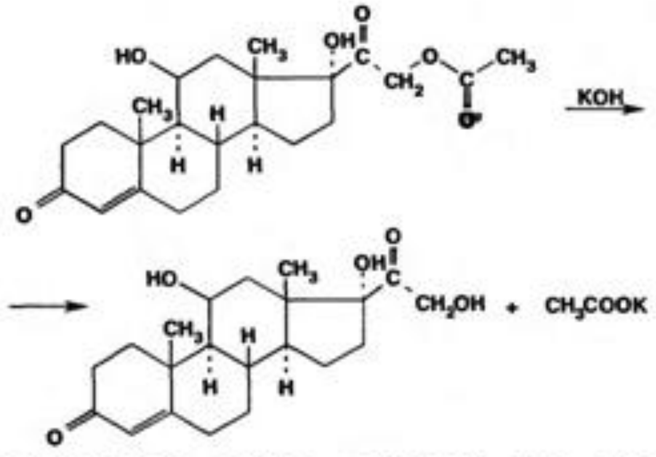
a) with Felling reagent – forming the red sediment Cu_2O

b) With Tollens reagent – metallic silver settled down

4. On the ester group – hydroxamic reaction (red-brown color)

5. On the keto-group in 3-th position – the oxym formation, phenylhydrazine, 2,4-dinitrophenylhydrazone.

6. Acetylic group after hydrolysis KOH is identified according to the formation ethylacetate (specific smell):



$$2CH_3COOK + H_2SO_4 + 2C_2H_5OH \longrightarrow 2CH_3COOC_2H_5 + K_2SO_4 + 2H_2O$$

Identification of Cortisone acetate:

1. Boscot reaction. A violet fluorescence.

2. Basic hydrolysis (heating with KOH solution). At the addition of the concentrated H2SO4 appearance the fruit smell of ethyl acetate.

3. On the oxyacetylic group, which is acetylated:

a) With Felling reagent – formation red sediment Cu_2O

b) With Tollens reagent – metallic silver settled down

5. On ester group – hydroxamic reaction (dark red color)

4. On keto group in 3-th position – formation of phenylhydrazone (bright-yellow color), 2,4-dinitrophenylhydrazone (melting temperature 240ºC).

5. The drug solution in the concentrated H_2SO_4 in UV-light gives intensive yellow fluorescence.

Identification of Hydrocortisone acetate

1. Using physical-chemical constant: IR-spectroscopy, TLC.

2. Remedy solution in ethanol with H2SO4 gives an intense brownish-red color with a green fluorescence. The resulting solution is added to water and stirred, the solution decolorized, and the fluorescence disappears (a steroid cycle).

3. Substance gives a characteristic response to acetyl.

4. Not pharmacopeial reaction:

a) Boscot reaction. Violet fluorescence.

b) On the oxyacetylic group which is acetylated, the reaction:

with triphenyltetrazolium chloride in alkaline medium - red color (formazan formation); with Felling and Tollens reagents.

c) On the ester group - hydroxamic reaction (dark cherry color)

d) On the keto group in the 3-d position:

- the formation of phenylhydrazone (yellow color);
- with isoniazid in the presence of HCl - yellow in color (this reaction prednisolone and dexamethasone don’t give).

Identification of Dexamethasone

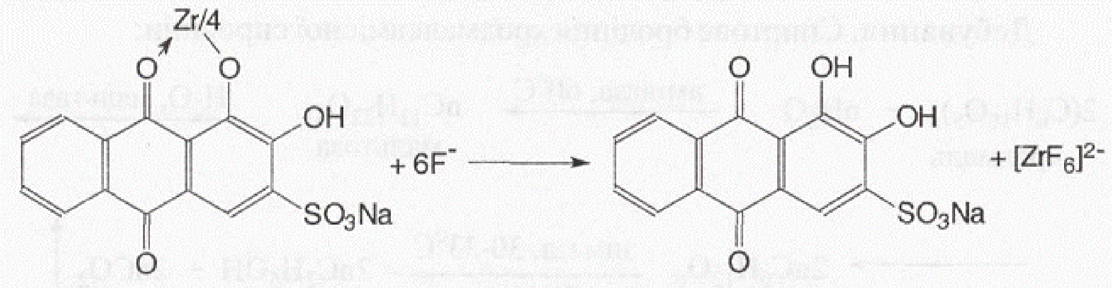
1. IR-, UV-spectroscopy, TLC.

2. Remedy solution in the concentrated H_2SO_4 stays coloeless and at the action of UV lights the fluorescence is not observed.

3. On the oxyacetylic group, the reaction: with triphenyltetrazolium chloride and KOH solution - red color (formazan formation); with Felling and Tollens reagents.

4. On the keto group in the 3-d position: at the heating of the remedy in the alcohol solution with phenylhydrazine hydrochloride and sulfuric acid solution during 5 minutes there is apparent yellow color; with isoniazid in the presence of HCl – solution is staying colorless.

5. Organically connected Fluorine is converted into fluoride ions by the mineralization, fluoride ions have the ability decolorize the alizarin red lacquer (alizarinate zirconium). Alizarin red lacquer is a complex compound of zirconium with alizarin. At interacting with the F- ions Alizarin red is decolorized to a pale yellow color, due to formation of a stable colorlessing complex $Na_2 [ZrF_6]$.



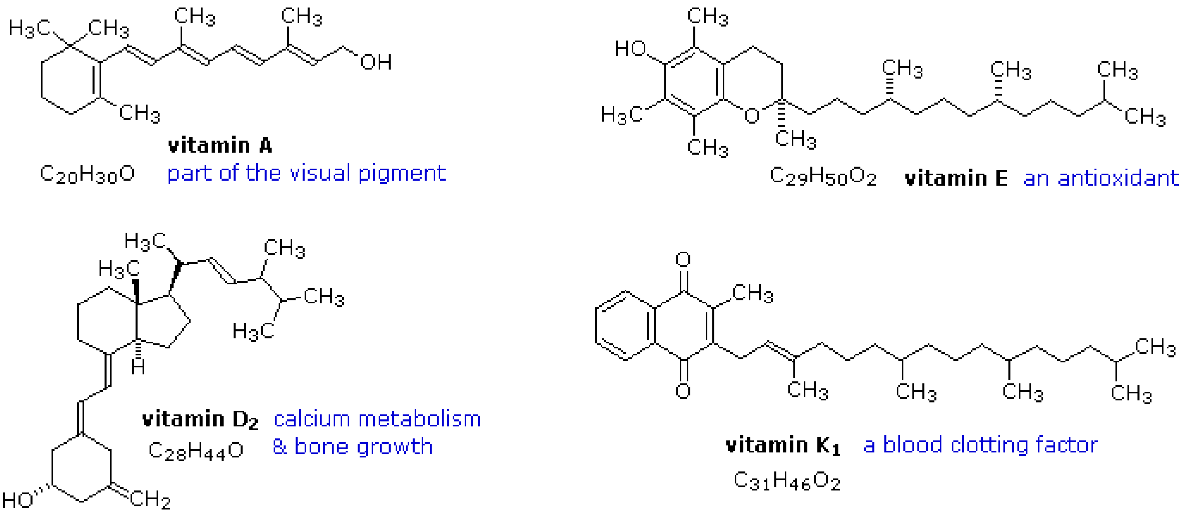
Lipid Soluble Vitamins

The essential dietary substances called **vitamins** are commonly classified as "water soluble" or "fat soluble". Water soluble vitamins, such as vitamin C, are rapidly eliminated from the body and their dietary levels need to be relatively high. The recommended daily allotment (RDA) of vitamin C is 100 mg, and amounts as large as 2 to 3 g are taken by many people without adverse effects. The lipid soluble vitamins, shown in the diagram below, are not as easily eliminated and may accumulate to toxic levels if consumed in large quantity. The RDA for these vitamins are:

Vitamin A   800 µg (upper limit ca. 3000 µg)
Vitamin D   5 to 10 µg (upper limit ca. 2000 µg)
Vitamin E   15 mg (upper limit ca. 1 g)
Vitamin K   110 µg (upper limit not specified)

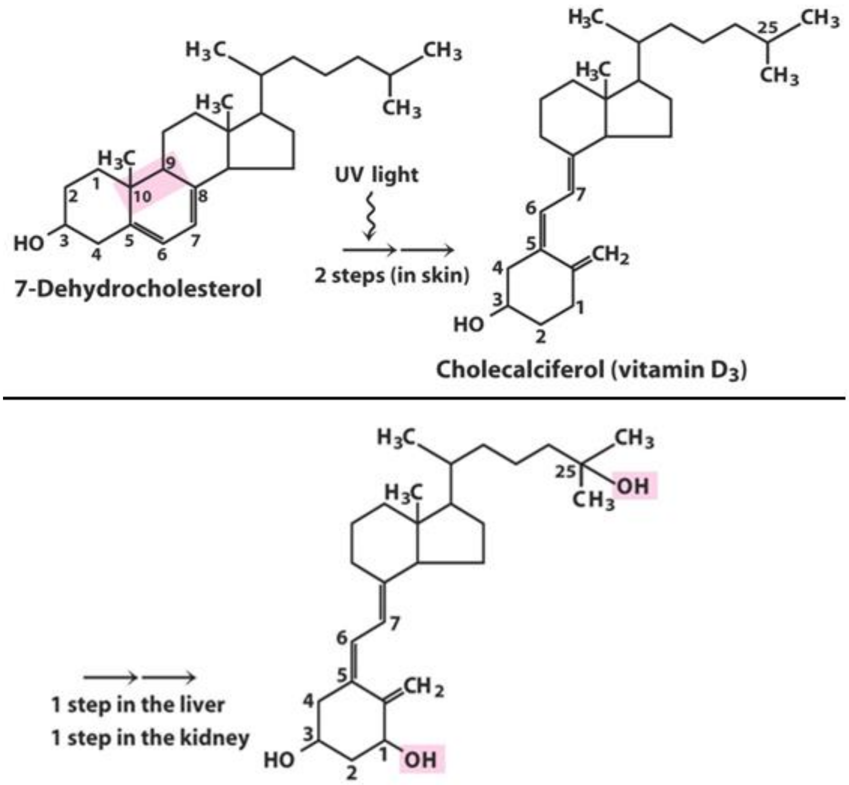
From this data it is clear that vitamins A and D, while essential to good health in proper amounts, can be very toxic. Vitamin D, for example, is used as a rat poison, and in equal weight is more than 100 times as poisonous as sodium cyanide.

Lipid Soluble Vitamins

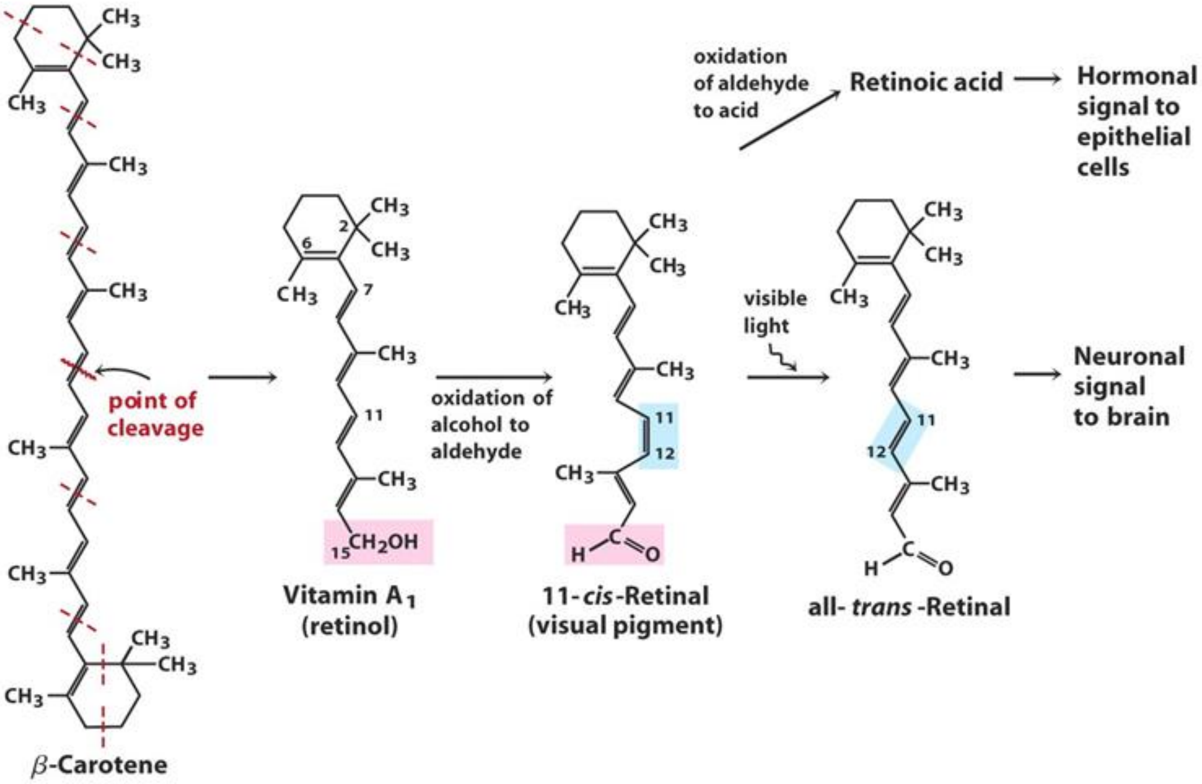


From the structures shown here, it should be clear that these compounds have more than a solubility connection with lipids. Vitamins A is a terpene, and vitamins E and K have long terpene chains attached to an aromatic moiety. The structure of vitamin D can be described as a steroid in which ring B is cut open and the remaining three rings remain unchanged. The precursors of vitamins A and D have been identified as the tetraterpene beta-carotene and the steroid ergosterol, respectively.

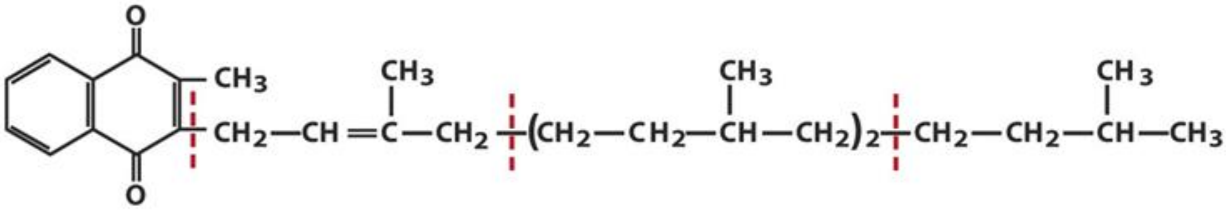
Vitamin D3 biological roles



Vitamin A metabolism



Vitamin K_1: blood-clotting cofactor (phylloquinone).



LIPID PEROXIDATION is a source of free radicals.

Peroxidation **(auto-oxidation)** of lipids exposed to oxygen is responsible not only for deterioration of foods **(rancidity)** but also for damage to tissues in vivo, where it may be a cause of **cancer, inflammatory diseases, atherosclerosis, and aging**.

The deleterious effects are considered to be caused by free radicals (ROO•,RO•, OH•) produced during peroxide formation from fatty acids containing methylene-interrupted double bonds, ie, those found in the naturally occurring polyunsaturated fatty acids

Lipid peroxidation is a chain reaction providing a continuous supply of free radicals that initiate further peroxidation.

Since the molecular precursor for the initiation process is generally the hydroperoxide product ROOH, lipid peroxidation is a chain reaction with potentially devastating effects. To control and reduce lipid peroxidation, both humans in their activities and nature invokethe use of **antioxidants.**

Propyl gallate, butylated hydroxyanisole (BHA), and butylated hydroxytoluene (BHT) are antioxidants used as food additives. Naturally occurring antioxidants include **vitamin E** (tocopherol), which is lipid-soluble, and **urate** and **vitamin C**, which are water-soluble. **Beta-carotene** is an antioxidant at low PO2.Others are **ceruloplasmin, glutathione** etc.

Antioxidants fall into two classes:

- **Preventive antioxidants**, which reduce the rate of chain initiation;
- **Chain-breaking antioxidants,** which interfere with chain propagation.

Preventive antioxidants include **catalase and other peroxidases** that react with ROOH and **chelators of metal ions** such as EDTA(ethylenediaminetetraacetate) and DTPA (diethylenetriaminepentaacetate).

In vivo, the principal ***chain breaking antioxidants*** are **superoxide dismutase**, which acts in the aqueous phase to trap superoxide free radicals(O2−•); perhaps **urate**; and **vitamin E**, which acts in the lipid phase to trap ROO• radicals

Peroxidation is also catalyzed *in vivo* by heme compounds and by **lipoxygenases** found in platelets and leukocytes. Other products of auto-oxidation or enzymic oxidation of physiologic significance include **oxysterols** (formed from cholesterol) and **isoprostane** (prostanoids).

FUNCTIONS OF LIPIDS.

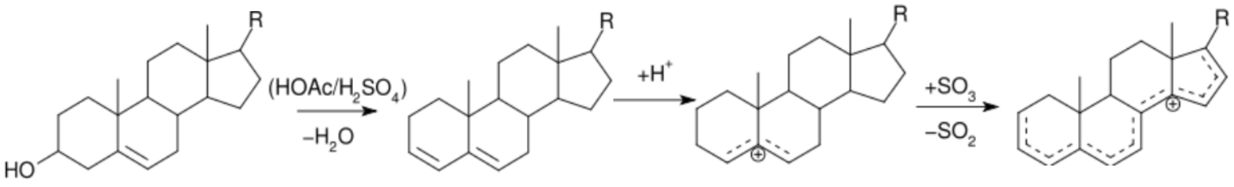
- **They are stored in adipose tissue** (triglycerides) and are one of the major energy source. Lipids are the best energy source for humans since at a parity of weight they provide the major part of calories: if carbohydrates, on average, gives 4 kcal/g, as proteins, lipids provide, on average, 9 kcal/g. Moreover, they can be present in foods without there are also fiber or water (for polysaccharides 2 g water/g) allowing to contain a great quantity of energy in a little weight.
Mostly of Nutrition Organizations recommend that lipids must contribute up to 30% (with saturated fatty acids only less than 10%) of the total daily energy intake.
- Some lipids are **essential nutrients** like fat-soluble vitamins A, (necessary for vision) and D (necessary for calcium metabolism), present in some fats and oils of animal origin, vitamin E (prevention of autoxidation of unsaturated lipids), present in vegetable oils, and vitamin K (normal clotting of blood) present in green leaves, essential fatty acids, in particular linoleic and α-linolenic acids, founders of the family of omega-6 and omega-3 fatty acids respectively.
- During growth they are utilized as “bricks” for construction of**biological membranes** (phospholipids, cholesterol and glycolipids together with proteins), so contributing to construction of that barrier that separates intracellular environment from extracellular one and, inside cell, circumscribes organelles like mitochondria, Golgi apparatus or nucleus, and whose integrity is the basis of life itself; moreover they are also important for maintenance, physiochemical properties and repairing of cell membranes themselves.
- **Many hormones are lipids**: steroid hormones, like estrogens, androgens and cortisol, are formed from cholesterol (essential also during embryogenesis), prostaglandins, prostacyclin, leukotrienes, thromboxanes, and other compounds (all eicosanids) from omega-3 and omega-6 polyunsaturated fatty acids with 20 carbon atoms.

- On plasmatic cell membranes they can act as **receptors, antigens and membrane anchors** for proteins and can modify the structure, and therefore the functionality, of membrane enzymes.
- Many lipids, like diacylglycerol, ceramides, sphingosine and platelet-activating factor act as regulators of intracellular processes.
- There are fat deposits not accessed during a fast, classified as**structural fat**, the function of which is to hold organs and nerves in the right position protecting them against traumatic injuries and shock; fat pads on the palms and buttocks protect the bones from mechanical pressure.
- A subcutaneous layer of fat is present in humans: it insulates the body **reducing the loss of body heat** and contributing to maintain body temperature.
- On epidermis they are involved in maintaining water barrier.
- They are **electrical insulator of axon of neurons** that are covered over and over again by plasmatic membranes of Swann cells, in peripheral nervous system, and of oligodendrocytes in central nervous system; these plasmatic membranes have a lipid content greater than that of the other cells. This lipoprotein coating is called myelin sheath.
- On digestive tract they f**acilitate the digestive process** depressing gastric secretion, slowing gastric emptying and stimulating biliary and pancreatic flow.
- Bile salts (by-products of cholesterol) are natural detergents synthesized in the liver and secreted into bile. They solubilize phospholipids and cholesterol in the bile, permitting the secretion of cholesterol into the intestine (the excretion of both cholesterol and bile acids is the major way by which cholesterol is removed from the body). Bile salts also aid in the digestion and absorption of fat and soluble-fat vitamins in gut.
- In many animals, some lipids are secreted into external environment and act as **pheromones** that attract or repel other organisms.
- They affect the **texture and flavor of food** and so its palatability.

Food manufacturers use fat for its textural properties, e.g. in baked goods fat increase the tenderness of the product. Chefs know that fat addiction add to the palatability of meal and increase satiety after a meal.

LIEBERMANN - BURCHARD TEST

The cholesterol reacts as a typical alcohol with a strong concentrated acids and forms colored products. Acetic anhydrides are used as solvent and dehydrating agents, and the sulfuric acid is used as dehydrating and oxidizing agent. A positive result is observed when the solution becomes red-blue, and finally bluish - green color.



ADDITIONAL PROBLEMS

1. Fats are abundantly found in:

*a) Reproductive tissue

b) Vegetative tissue

c) Both a and b

d) None of these

2. Natural lipids are readily soluble in:

a) Oil

b) Mercury

c) Water

*d) None of these

3. Which of the following is/are unsaturated fatty acids?

a) Linoleic acid

b) Oleic acid

c) Palmitoleic acid

*d) All of these

4. Fats can be stored in the cell without disturbing their:

a) Hygroxyl bond

b)Aleurone layer

*c) Osmotic relations

d) None of these

5. Liquid form of triglycerides at ordinary room temperature are called:

*a) Oils

b)Solid

c) Fats

d) None of these

6. The synthesis of glucose from fat is called:

a) Glycolysis

b)Krebs cycle

c) Saponification

*d) Gluconeogenesis

7. Hydrolysis of fats by alkalies into fatty acids and glycerol is called:

a) Coagulation

*b) Saponification

c) Suspension

d) Colloidal

8. The fats and oils are respectively rich in:

a) Unsaturated fatty acids

b) Saturated fatty acids

*c) Saturated and unsaturated fatty acids:

d) None of these

9. β-oxidation takes place in:

*a) Mitochondria

b) cytoplasm

c) Chloroplasts

d) nucleus

10. Which is a phospholipid:

*a) Lecithin

b) Cholesterol

c) Sterol

d) Steroid

11. The number of double bonds in Arachido:

a) 1

b) 2

c) 3

*d) 4

12. Essential fatty acids are:

a) Linoleic acid

b) Arachidonic acid

c) Linolenic acid

*d) All of these

13. The following is not a phospholipid:

a) Sphingomyelin

b) Lecithin

c) Cephalin

*d) Cerebroside

14. Examples of monounsaturated fatty acids are:

*a) Oleic acid

b) Arachidonic acid

c) Palmitic acid

d) Linolenic acid

15. High content of Triglycerides are seen in:

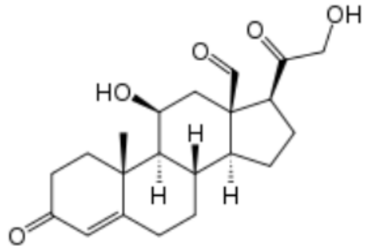
a) LDL

b) HDL

c) VLDL

*d) Chylomicrons

16. The C 21 steroid hormones include



a) Vitamin D3

b) Estradiol

c) Testosterone

*d) Aldosterone

17. A lipid is formed by the condensation reactions between:
    a) Carbon and hydrogen
    b) *Fatty acids and alcohol
    c) Fatty acids and amino acids
    d) Fatty acids and amines

18. Which of the following statement is wrong regarding lipids:
    a) Lipids are insoluble in water
    b) *Lipids are insoluble in ethanol
    c) Lipids are soluble in benzene
    d) Lipids are insoluble in chloroform
    e)

19. Lipids are important constituents of :
    a) nucleus
    b) ribosome
    c) both a and b
    d) *biological membranes

20. Which of the following is a derived lipid:
    a) Fats
    b) Oils

c) *Steroids
d) waxes

21. Fats consists of :

a) alcohol linked by ester bonds to 3 fatty acids
b) *glycerol molecule linked by ester bonds to 3 fatty acids
c) glycerol molecule linked by ester bonds to a fatty acid
d) glycerol molecule linked by ester bonds to 4 fatty acids

22. Compounds with carbohydrates along with fatty acids are called:

a) Simple lipids
b) waxes
c) *Glycolipids
d) phospholipids

23. Cardiolipin is a :

a) Glycolipids
b) *phopholipids
c) Simple lipids
d) none of these

24. Cerebrosides are glycolipids that are important constituent of :

a) biological membrane
b) lung
c) *brain
d) bones

25. Phytosterol include:

a) ergosterol

b) stigmasterol
c) *both a and b
d) cholesterol

26. Which of the following is not a derivative of cholesterol:
a) Steroid hormones
b) *Vitamin E
c) Bile salts
d) Vitamin D

Lesson №11

FINAL SUBMODULE CONTROL II:
«HETEROFUNCTIONAL ORGANIC COMPOUNDS - METABOLITES AND BASIS OF THE MOST IMPORTANT GROUPS OF DRUGS. CARBONYL COMPOUNDS. CARBOXYLIC ACIDS AND THEIR FUNCTIONAL DERIVATIVES".

Subject motivation: The heterofunctional organic compounds are involved in different kinds of tissue, cytosolic and genetic processes, providing a pronounced effect on the vital functions of organism. A lot of them s are potent bioregulators of physiological processes and essential medicines. Lipids are essential structural components of cell membranes.

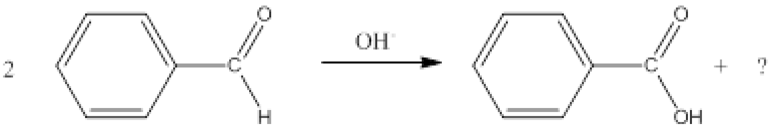
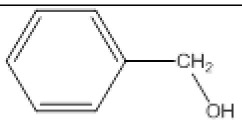
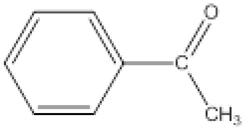
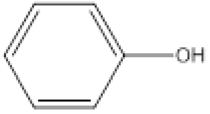
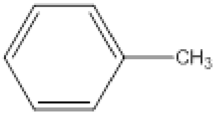
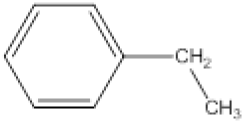
Learning goal: To strengthen knowledge of the structure and chemical properties of the main heterofunctional organic compounds taking into account the mutual influence of their characteristic functional groups as the basis of biochemical processes.

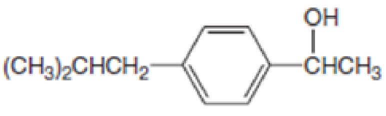
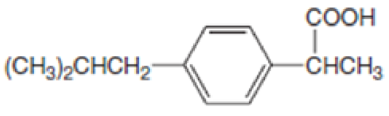
THEORETICAL QUESTIONS

1. Carbonyl compounds. Chemical properties and biomedical significance of aldehydes and ketones.
2. Carboxylic acids. Structure and chemical properties of functional derivatives of carboxylic acids (anhydrides, amides, esters). The reactions of decarboxylation.
3. Structure and properties of dicarboxylic acids: oxalic, malonic, succinic, glutaric, fumaric acid.
4. Structure and properties of carboxylic acid and its derivatives. Urethane, ureido acids, urea.
5. Carboxylic acids esters: nomenclature, preparation, properties.

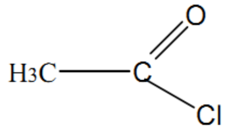
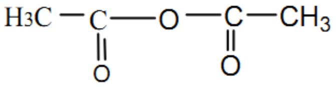
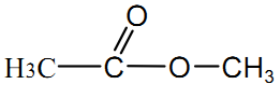
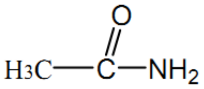
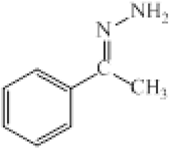
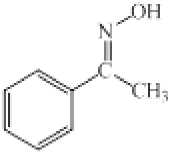
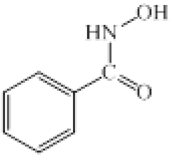
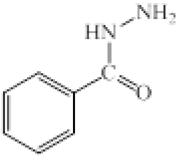
6. Aromatic amines: structure, properties. Aniline as a precursor in the synthesis of pharmaceuticals - sulfanilamide, phenacetin, anaesthesin, novocaine.
7. Hydroxy acids. Structure and properties of monocarboxylic, dicarboxylic and tricarboxylic hydroxy acids.
8. Structure and properties of the most common oxo acids: pyruvic, acetoacetic, oxaloacetic, α-ketoglutaric. The concept of ketone bodies.
9. Phenolic acids. Salicylic acid and its anti-inflammatory derivatives (acetylsalicylic acid, methyl salicylate, sodium salicylate) and antimicrobial (phenyl salicylate) compounds.
10. Lipids: definition, classification. Fatty acids: palmitic, stearic, oleic, linoleic, linolenic, arachidonic. Lipids. Triacylglycerols (neutral fats): structure, physiologic significance, the hydrolysis.
11. Complex lipids. Phospholipids: phosphatidic acid, phosphatidyl-ethanolamine, phosphatidylcholine, phosphatidylserine. Sphingolipids. Glycolipids. The role of complex lipids in the structure of biological membranes.
12. Steroids as derivatives of sterane. The structure of biologically important representatives of steroids: cholesterol, vitamin D, bile acids, corticosteroids, sex hormones.

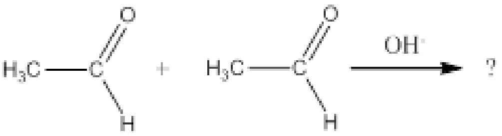
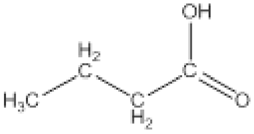
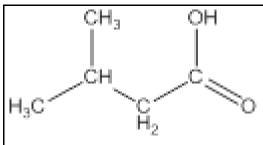
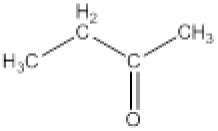
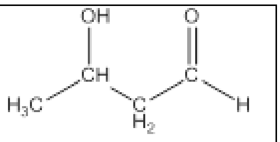
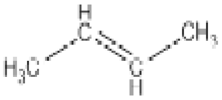
ADDITIONAL PROBLEMS

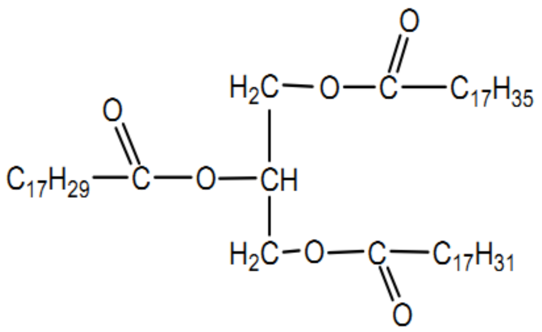
#	Question	Answer
1	Complete the reaction 	 ***
		
		
		
		
2	Select products of oxidation of methylethylketone	formic acid acid and acetic acid
		acetic acid and propanoic acid
		butanoic acid
		propionic acid
		*** formic acid, acetic acid and propanoic acid
3	The cyanide ion −CN reacts with a ketone to give	an acid
		*** a cyanohydrin
		an aldehyde

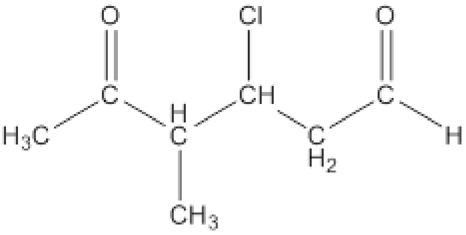
#	Question	Answer
		an amine
4	The oxidation of 1-propanol with chromic acid yields	an alcohol
		an aldehyde
		a ketone
		*** an acid
5	. Which functional group is in the carboxylic acids?	Carbonyl group
		*** Carboxyl group
		Nitro group
		Phenyl group
		Sulfo group
6	A polyester is a condensation polymer in which the reacting monomers are a dicarboxylic acid and which of the following?	*** Carboxylic acid anhydride
		Carboxylic acid salt
		Monoalcohol
		Dialcohol
7	Acetone is the common name for	1-butanone
		1-propanone
		*** 2-propanone
		2-butanone
8	Alcohol can be converted to the anti-inflammatory agent ibuprofen by:  A  ibuprofen	*** oxidation
		reduction
		methylation
		acylation
		amination

#	Question	Answer
9	Amino acid as precursor of histamine synthesis is:	glutamic acid
		*** histidin
		glutamine
		aspartic acid
		methionine
10	Amino acids as precursors of the catecholamines production are:	glutamic acid
		*** phenylalanine
		histidin
		aspartic acid
11	Amino acids as precursors of the catecholamines production is:	glutamic acid
		histidin
		aspartic acid
		*** tyrosine
12	Ammonia reacts with an aldehyde to give an	alcohol
		amide
		*** imine
		amine
13	An ester is a carboxylic acid derivative in which the —OH portion of the carboxyl group has been replaced with which of the following?	*** —OR group
		—OCl group
		—Cl atom
		—ONa group
14	Arrange in a number on decrease of reactivity in S_N reactions of the following compounds:	*** 1>3>2>4
		3>1>2>4
		2>3>4>1

#	Question	Answer
	1)  3)  2)  4) 	4>3>1>2
15	Choose more strong acid in following line:	ethanoic acid methanoic acid benzoic acid propanoic acid *** succinic acid
16	Choose the compound, from which we can synthesize benzene in one step:	acetone methanol *** acetylene acetaldehyde ethanol
17	Complete the reacton.. 	 ***   

#	Question	Answer
18	Complete the reacton.. 	
		
		
		 ***
		
19	Component of phospholipids is the following amino acid:	methionine
		cysteine
		*** serine
		tyrosine
		?-alanine
20	Decarboxylation reaction of 2-amino-3-hydroxypropanoic acid leads to the formation:	*** 2-aminoethanol
		3-hydroxypropanoic acid
		2-aminopropanol
		2-aminoethanal
21	Enamines may be formed as result of:	oxidation of aldehydes
		interaction between

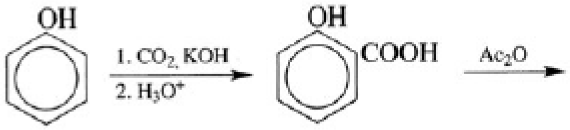
#	Question	Answer
		aldehydes or ketones with secondary amines
		*** interaction between aldehydes or ketones with primary amines
		interaction between aldehydes or ketones with tertiary amines
		oxidation of ketones
22	In which of the following pairs of carboxylic acids does the first member of the pair have more carbon atoms than the second member of the pair?	Malonic acid and succinic acid
		*** Glutaric acid and succinic acid
		Oxalic acid and malonic acid
		Oxalic acid and glutaric acid
23	Indicate the correct fat name having the following structure 	1-stearoyl-2-palmitoyl-3-linolenoylglycerol
		1-linolenoyl-2-palmitoyl-3-linoleoylglycerol
		1-oleoyl-2-stearoyl-3-arahydoyl glycerol

#	Question	Answer
		*** 1-stearoyl-2-linolenoyl-3-linoleoylglycerol
24	Interaction of unknown aldehyde with propylmagnesium bromide yielded butanol-1. Define unknown aldehyde.	*** acetaldehyde
		propanal
		methanal
		butanal
		described reaction is impossible
25	Linoleic acid (C17H31COOH) is contained in plants oils. How many moles of bromine can be added to one mole of linoleic acid?	1
		*** 2
		3
		4
		5
26	Name the following compound according to IUPAC rules. 	*** 3-chloro-4-methyl-5-oxohexanal
		4-cloro-3-methyl-5-formylpentanon-2
		2-oxo-3-methyl-4-chloro-5-formylpentane
		5-acetyl-3-chloro-4-methylbutanal
		3-chloro-4-methyl-5-oxohexanoic acid
2	Oligosaccharide of galactose presents in the following	sulpholipids

#	Question	Answer
7	lipids:	cerebrosides
		*** gangliosides
		sphingomielins
		plasmalogenes
28	Reduction of acetic acid with complex hydride yields	an acid
		*** an aldehyde
		an alcohol
		a ketone
29	Select the strongest electrophile among listed compounds.	propanon-2
		*** propanal
		ethanol
		methanol
		butanon-2
30	Silver ion, Ag+, reacts with aldehydes to form	a red precipitate
		*** a silver “mirror”
		a blue solution
		there is no reaction
31	Specify the senior functional group in the molecule:	–I
		–OH
		–NH2
		*** –COOH
		aromatic ring
32	Sulfanylamides action mechanism for enzymes:	*** They are competitive inhibitors

#	Question	Answer
		They are reversible competitive inhibitors for bacteria enzymes
		They change the primary structure of the enzyme
		They are noncompetitive inhibitors
		They act as allosteric inhibitors
33	The acid-catalyzed addition of 2 mol of alcohol to 1 mol of aldehyde yields	a ketal
		a hemiacetal
		*** an acetal
		a hydrate
34	The acid-catalyzed addition of water to formaldehyde gives	a ketal
		a hemiacetal
		an acetal
		*** a hydrate
35	The acid-catalyzed hydration of cyclodecyne yields	*** cyclodecanone
		cyclodecadiene
		cyclodecanediol
		cyclodecanedial
36	The formal name for aldehydes ends in	-one
		-ide

#	Question	Answer
		*** -al.
		–ane
37	The formal name for ketones ends in	-ane
		-ide
		-al
		*** -one
38	The oxidation of 2-propanol with chromic acid yields	an alcohol
		an aldehyde
		*** a ketone
		an acid
39	The reaction of acetyl chloride with excess Grignard reagent followed by acidification yields	a ketone
		an ester
		*** a secondary alcohol
		a tertiary alcohol
40	The reaction of ketone with hydroxylamine yields	semicarbazone.
		hydrazone.
		*** oxime.
		phenylhydrazone.
		Schiff base.
41	What compounds NOT belong to saponified lipids:	*** cholesterol
		glycolipids
		phospholipids
		waxes

#	Question	Answer
42	What is a ceramide?	triacylglycerol
		phospholipids
		plasmalogen
		sterid
		*** sphingomyelin
43	What is the mechanism of the paracetamol interaction with C2H5OH to form phenacetin:	AN;
		*** SN_2
		SN_1;
		E
44	What is the product of the iodoform reaction (acetone identifying reaction), that is yellowish-white precipitate with a characteristic odor?	CH_3I
		*** CHI_3
		$CHCl_3$
		$CHBr_3$
		CH_2Cl_2
45	What is the product of this reactions? 	*** aspirin
		methyl salicylate
		benzal chloride
		phenoxyacetic acid
		phenoxyanisole
46	What product is formed when carbonyl compound is treated with K2Cr2O7?	alcohol
		*** carboxylic acid
		ketone
		amine
		amide

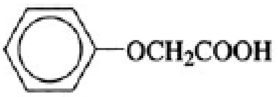
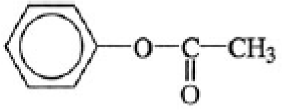
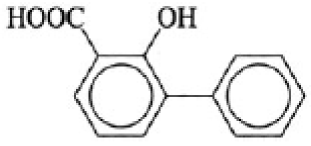
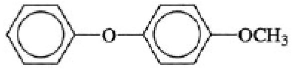
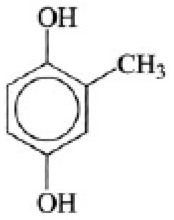
#	Question	Answer
47	What product is made in the reaction interaction the carboxylic acids with the alcohol?	Amide Anhydride Ketal Ether *** Ester
48	What reactant is used to detect oxalic acid and its salts	barium chloride *** calcium chloride zinc chloride sodium chloride
49	Which is the mechanism of fat hydrolysis in the acidic medium:	AE; AN; AR; *** SN
50	Which lipid is ceramide?	triacylglycerol phosphatidylcholine *** sphingomielin ganglioside plasmalogen
51	Which material is most reactive toward nucleophilic addition?	*** acetaldehyde dimethyl ketone diisopropyl ketone di-tert-butyl ketone
52	Which of the following aldehydes forms stable hydrate?	methanol ethanol

#	Question	Answer
		propanal
		4-chlorobutanal
		*** 2,2,2-trichloroacetaldehyde
53	Which of the following compounds does not yielded iodoform under action of alkaline solution of iodine?	ditertbutylketone
		*** formaldehyde
		dimethylketone
		benzaldehyde
		diphenylketone
54	Which of the following esters, upon hydrolysis, produces a two-carbon alcohol as one of the products?	Methyl methanoate
		Propyl ethanoate
		Methyl propanoate
		*** Ethyl methanoate
55	Which of the following hydroxyacids at oxidation in vivo with coenzyme NAD+ participation turns to an oxalacetic acid:	lactic acid
		citric acid
		*** malic acid
		pyruvic acid
56	Which of the following is a monohydroxy carboxylic acid?	Tartaric acid
		*** Lactic acid
		Citric acid
		Pyruvic acid
57	Which of the following is neither a reactant nor a product in an ester saponification reaction?	*** A strong base
		An alcohol
		A carboxylic acid

#	Question	Answer
		A carboxylic acid salt
58	Which of the following oxoacids participate in a cycle of tricarboxylic acids:	pyruvic acid
		acetoacetic acid
		*** oxalacetic acid
		β-ketoglutaric acid
59	Which of the following reaction yielded primary alcohols?	Oxidation of ketones
		Oxidation of aldehydes
		*** Reduction of aldehydes
		Interaction between gringard reagent and aldehydes
		Interaction between gringard reagent and ketones
60	Which of the following reaction yielded secomdary alcohols?	Oxidation of ketones
		Oxidation of aldehydes
		Reduction of aldehydes
		*** Interaction between gringard reagent and aldehydes
		Interaction between gringard reagent and

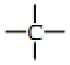
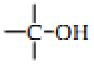
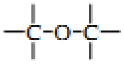
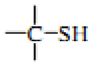
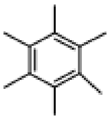
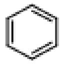
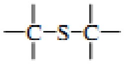
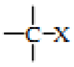
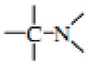
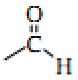
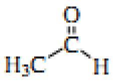
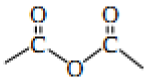
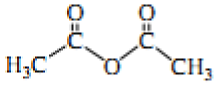
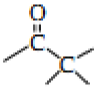
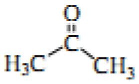
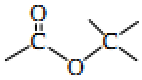
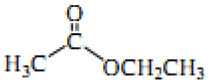
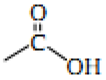
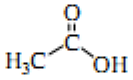
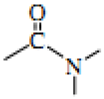
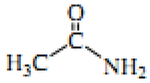
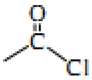
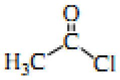
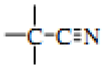
#	Question	Answer
		ketones
61	Which of the following reaction yielded tertiary alcohols?	Oxidation of ketones
		Oxidation of aldehydes
		Reduction of aldehydes
		Interaction between gringard reagent and aldehydes
		*** Interaction between gringard reagent and ketones
62	Which of the following reactions can not be used for preparation of aldehydes?	reducing of acylhalides
		*** oxidation of secondary alcohols
		Vilsmeier–Haack reaction
		oxidation of primary alcohols
63	Which of the following statements are not correct for unsaturated fatty acids:	have a nonbranched structure
		contain one or a few ?-bonds
		*** always have trans-configuration

#	Question	Answer
		contain the even number of the carbon atoms
64	Which of the following statements concerning the carboxylic acid functional group is not correct?	*** It is called a carboxylate group It can be denoted using the notation —COOH An oxygen–oxygen single bond is present A carbon–hydrogen single bond is present
65	Which products are formed at interaction of salicylic acid with acetic anhydride:	acetic acid aspirin *** acetylsalycilic acid CO_2
66	Which reagents is used to detect several hydroxyl groups in tartaric acid:	*** Fehling’s reagent Tollens Lugol Vagner
67	Which statement is true for the carboxyl carbon atom in the IUPAC nomenclature system for monocarboxylic acids?	*** It is always assigned the number one It is always assigned the highest number

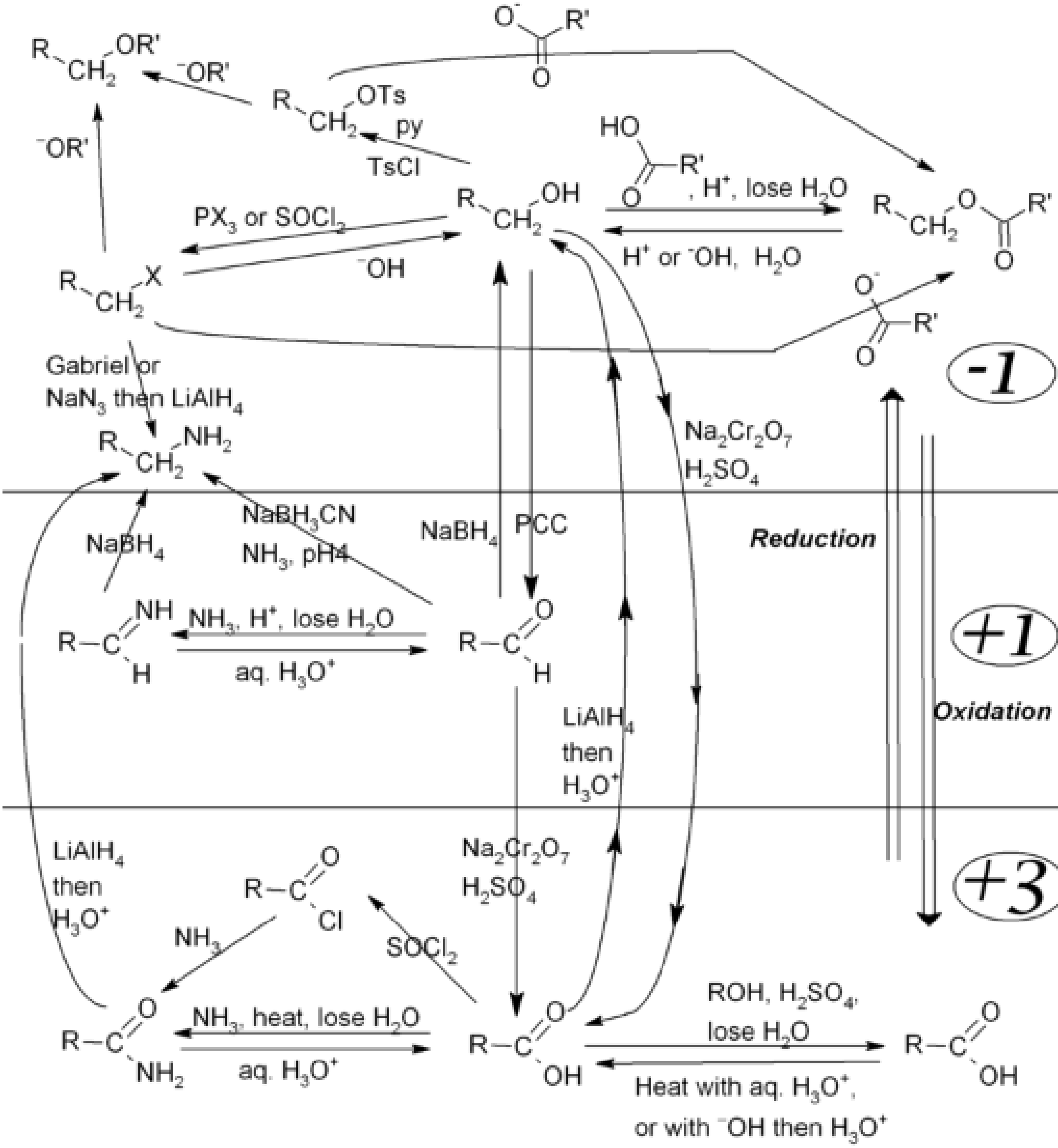
#	Question	Answer
		possible.
		It is always known as the alpha carbon atom.
		It is always known as the beta carbon atom.
68	Write the structure for phenoxyacetic acid:	*** 
		
		
		
		

APPENDIX

Organic compounds are generally classified based on the reactive parts of their structures, known as **FUNCTIONAL GROUPS**. The remainder of the molecule is usually based upon alkyl chains, which are relatively unreactive. Each functional group has its own characteristic reactions, and it tends to determine many of the chemical and physical properties of the overall compound.

Functional Group – General Structure	Example	Functional Group – General Structure	Example
 **Alkane**	CH_3CH_3 **Ethane**	 **Alcohol**	CH_3CH_2OH **Ethanol**
 **Alkene**	$CH_2{=}CH_2$ **Ethylene**	 **Ether**	$CH_3OCH_2CH_3$ **Ethyl methyl ether**
$-C\equiv C-$ **Alkyne**	$H-C\equiv C-H$ **Acetylene**	 **Thiol**	CH_3CH_2SH **Ethanethiol**
 **Aromatic Ring (Arene)**	 **Benzene**	 **Sulfide**	CH_3SCH_3 **Dimethyl sulfide**
 (X = F, Cl, Br, I) **Alkyl Halide**	CH_3CH_2Br **Ethyl bromide**	 **Amine**	$CH_3CH_2NH_2$ **Ethylamine**
 **Aldehyde**	 **Acetaldehyde**	 **Acid anhydride**	 **Acetic anhydride**
 **Ketone**	 **Acetone**	 **Ester**	 **Ethyl acetate**
 **Carboxylic acid**	 **Acetic acid**	 **Amide**	 **Acetamide**
 **Acid chloride**	 **Acetyl chloride**	 **Nitrile**	$H_3C-C\equiv N$ **Acetonitrile**

The **REACTION MAP** shown below shows most of the common functional groups, and how to convert between them. The large numbers on the right hand side indicate the oxidation state for the carbon attached to the functional group.[1]



James B. Hendrickson, *J. Chem. Educ.*, **1978**, *55* (4), 216. DOI: 10.1021/ed055p216.

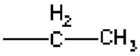
The IUPAC prefixes of the first 20 alkanes names

Prefix	number of carbon atoms	prefix	number of carbon atoms
meth-	1	undec-	11
eth-	2	dodec-	12
prop-	3	tridec-	13
but-	4	tetradec-	14
pent-	5	pentadec-	15
hex-	6	hexadec-	16
hept-	7	heptadec-	17
oct-	8	octadec-	18
non-	9	nonadec-	19
dec-	10	icos-	20

$-CH_3$

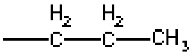
methyl

—Me


$-\overset{H_2}{C}-CH_3$

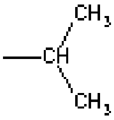
ethyl

—Et


$-\overset{H_2}{C}-\overset{H_2}{C}-CH_3$

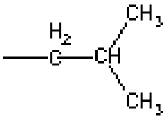
propyl

—Pr



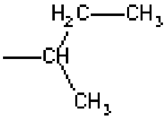
isopropyl

—iPr



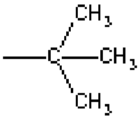
isobutyl

—iBu



sec-butyl

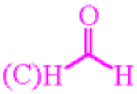
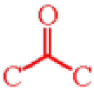
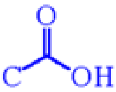
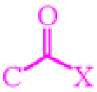
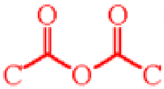
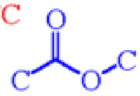
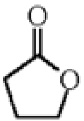
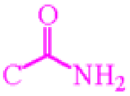
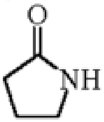
—sBu

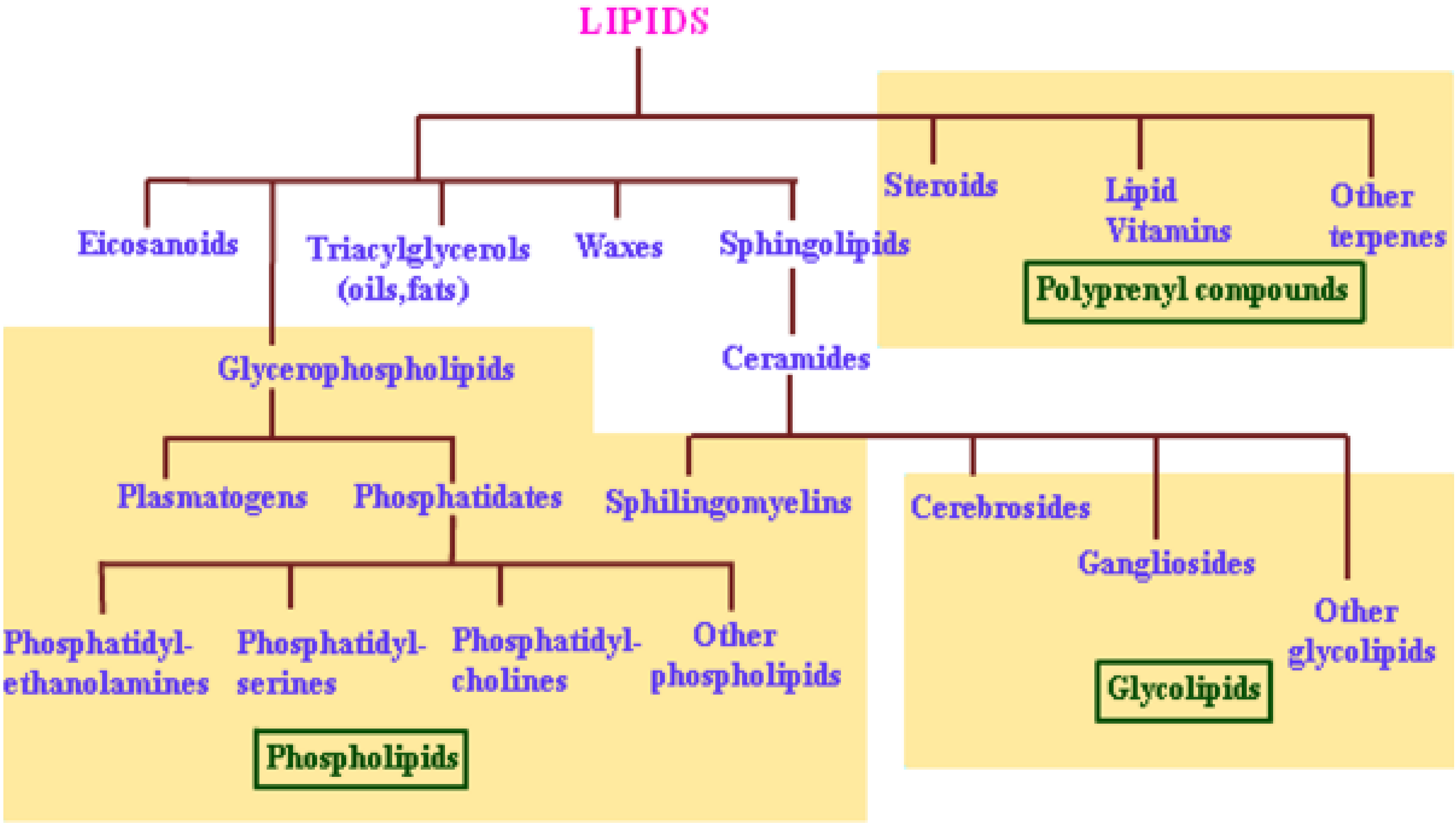


tert-butyl

—tBu

Types of Carbonyl Compounds

Type	General Formula	Name Ending
Aldehyde		-al
Ketone		-one
Carboxylic Acid		-oic acid
Acid Halide		-yl or -oyl halide
Acid Anhydride		-oic anhydride
Ester		-oate
Lactone	 Cyclic Ester	lactone of
Amide		-amide
Lactam	 Cyclic Amide	lactam of


LIPIDS
Eicosanoids
Triacylglycerols (oils,fats)
Waxes
Sphingolipids
Steroids
Lipid Vitamins
Other terpenes
Polyprenyl compounds
Glycerophospholipids
Ceramides
Plasmatogens
Phosphatidates
Sphilingomyelins
Cerebrosides
Gangliosides
Other glycolipids
Glycolipids
Phosphatidyl-ethanolamines
Phosphatidyl-serines
Phosphatidyl-cholines
Other phospholipids
Phospholipids

References

1. https://www2.chemistry.msu.edu/faculty/reusch/virttxtjml/lipids.htm#phoslpd

2. https://en.wikipedia.org/wiki/Plasmalogen

3. http://www.mcqbiology.com/

4. https://www.wikipedia.org/

5. P. M. Dewick, in Medicinal Natural Products, 3rd ed., John Wiley & Sons,Chichester, 2009, pp. 247-298.