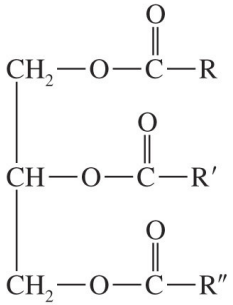
Chapter 23
Lipids

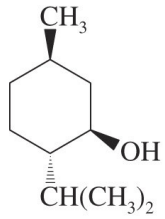
♦ Introduction

➔Lipids are compounds of biological origin that dissolve in nonpolar solvents such as chloroform and diethyl ether

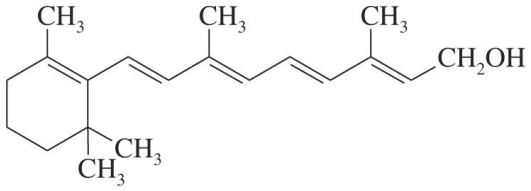
- **Lipids are defined by the physical operation used to isolate them**
- **Lipids include a variety of structural types, represented by the following examples:**



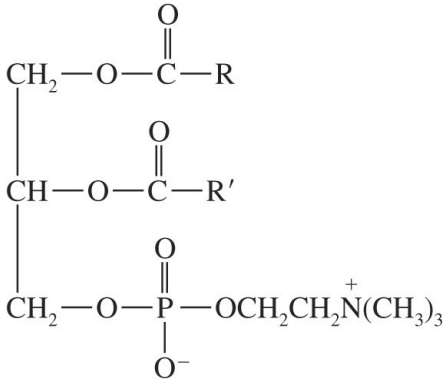
A fat or oil (a triacylglycerol)



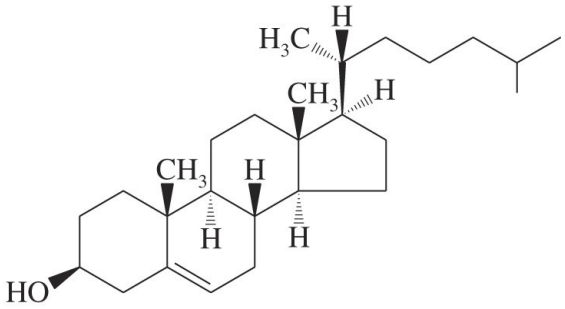
Menthol (a terpenoid)



Vitamin A (a terpenoid)



A lecithin (a phosphatide)



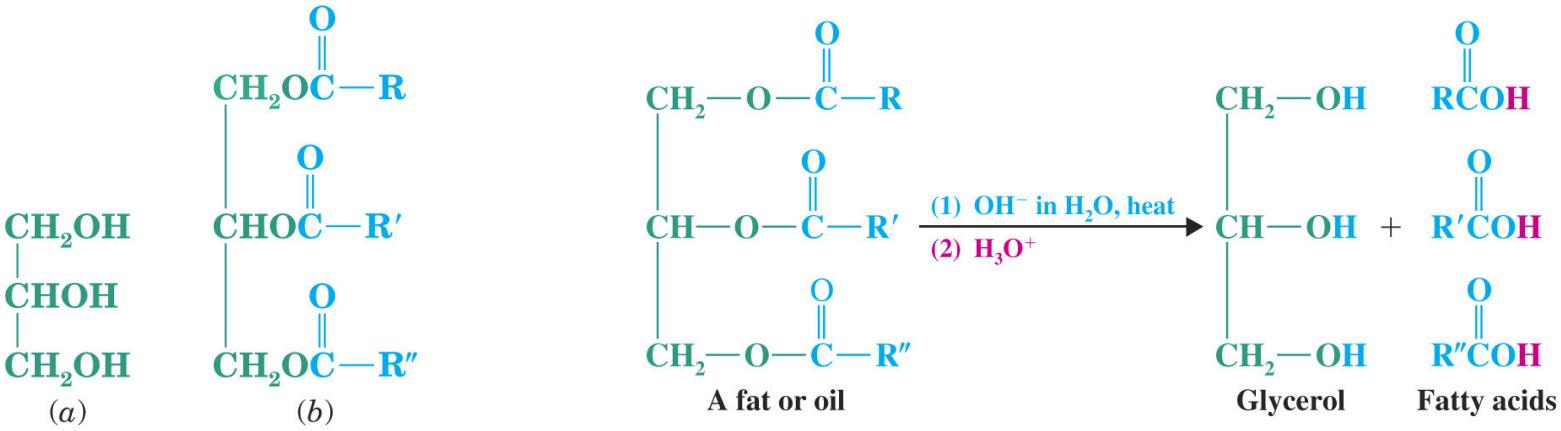
Cholesterol (a steroid)

♦ Fatty Acids and Triglycerides

➔ **Most long-chain carboxylic acids of biological origin are found as esters (b) of glycerol(a)**

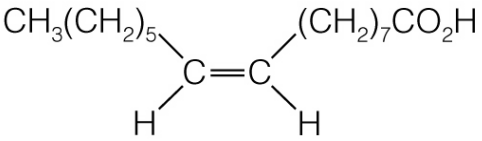
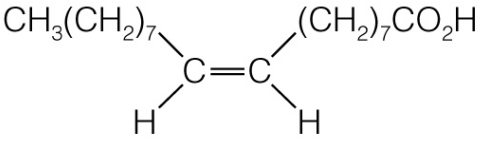
- Oils from plants and fats of animal origin are triacylglycerols
- Oils are generally liquids at room temperature, fats are solid

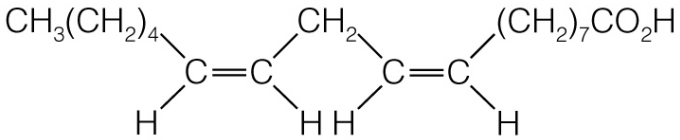
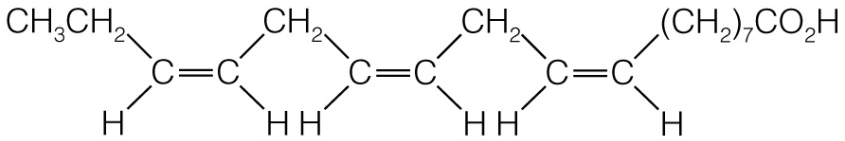
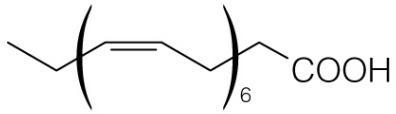
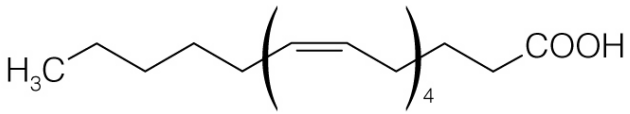
➔ **Hydrolysis of tracylglyerols yields fatty acids**



➔ **Most natural fatty acids have unbranched chains with an even number of carbon atoms**

- In natural unsaturated fatty acids the double bonds are all cis and are usually not conjugated

	mp (°C)
Saturated Carboxylic Acids	
$CH_3(CH_2)_{12}CO_2H$ **Myristic acid (tetradecanoic acid)**	54
$CH_3(CH_2)_{14}CO_2H$ **Palmitic acid (hexadecanoic acid)**	63
$CH_3(CH_2)_{16}CO_2H$ **Stearic acid (octadecanoic acid)**	70
Unsaturated Carboxylic Acids	
 **Palmitoleic acid (*cis*-9-hexadecenoic acid)**	32
 **Oleic acid (*cis*-9-octadecenoic acid)**	4

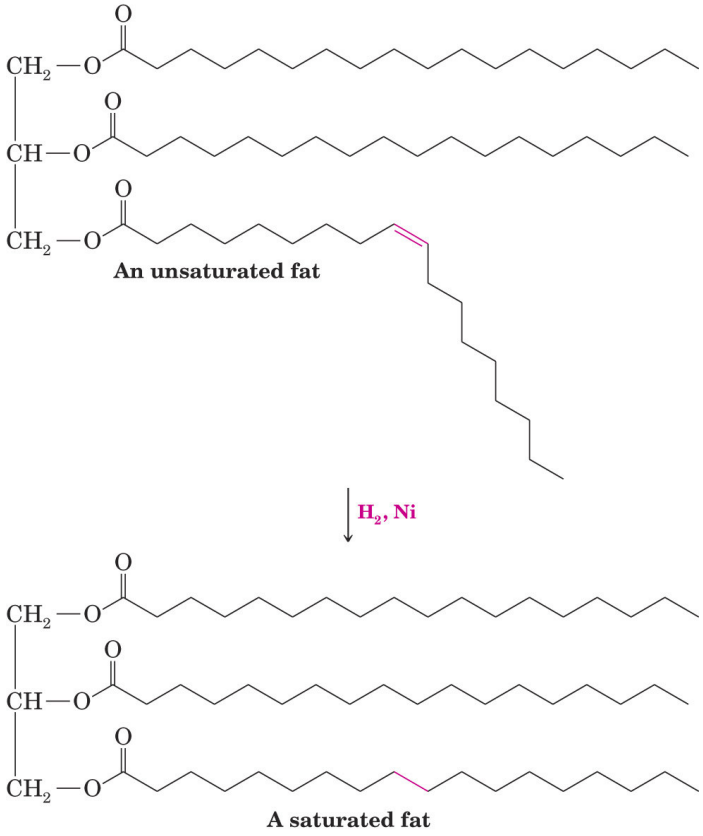
	mp (°C)
 **Linoleic acid** **(*cis*, *cis*-9,12-octadecadienoic acid)**	−5
 **Linolenic acid** **(*cis*, *cis*, *cis*-9,12,15-octadecatrienoic acid)**	−11
 **DHA, an omega-3 fatty acid** **[(4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-4,7,10,13,16,19-docosahexaenoic acid]**	−44
 **Arachidonic acid, an omega-6 fatty acid** **[(5*Z*,8*Z*,11*Z*,14*Z*)-5,8,11,14-eicosatetraenoic acid]**	−49

- **➔Saturated fatty acids have higher melting points than unsaturated fatty acids**
  - **Saturated fatty acids adopt a fully extended conformation, pack well, and have strong van der Waals attractions between molecules**
- **➔Cis double bonds in unsaturated fatty acids put bends in the chain**
  - **Unsaturated fatty acid chains pack poorly and have weaker van der Waals attractions between molecules than saturated fatty acids**
  - **Unsaturated fatty acids have lower melting points than saturated fatty acids with the same number of carbons**
- **➔Triacylglycerols with a higher content of saturated fatty acids have higher melting points**
  - **Triacylglycerols in animal fats contain mostly saturated fatty acids and are solids are room temperature**
  - **Triacylglycerols in oils have a large proportion of unsaturated and polyunsaturated fatty acids and are therefore liquids are room temperature**

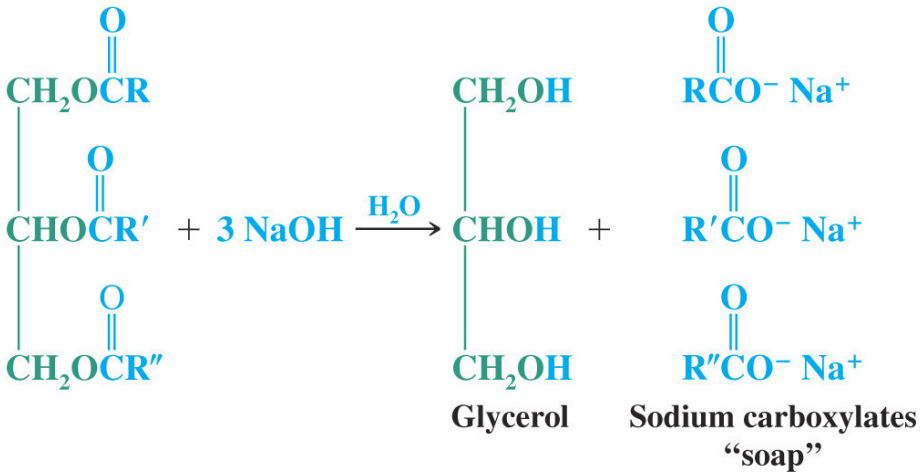
Fat or Oil	Average Composition of Fatty Acids (mol %)											
	Saturated								Unsaturated			
	C_4 Butyric Acid	C_6 Caproic Acid	C_8 Caprylic Acid	C_{10} Capric Acid	C_{12} Lauric Acid	C_{14} Myristic Acid	C_{16} Palmitic Acid	C_{18} Stearic Acid	C_{16} Palmitoleic Acid	C_{18} Oleic Acid	C_{18} Linoleic Acid	C_{18} Linolenic Acid
Animal Fats												
Butter	3–4	1–2	0–1	2–3	2–5	8–15	25–29	9–12	4–6	18–33	2–4	
Lard						1–2	25–30	12–18	4–6	48–60	6–12	0–1
Beef tallow						2–5	24–34	15–30		35–45	1–3	0–1
Vegetable Oils												
Olive						0–1	5–15	1–4		67–84	8–12	
Peanut							7–12	2–6		30–60	20–38	
Corn						1–2	7–11	3–4	1–2	25–35	50–60	
Cottonseed						1–2	18–25	1–2	1–3	17–38	45–55	
Soybean						1–2	6–10	2–4		20–30	50–58	5–10
Linseed							4–7	2–4		14–30	14–25	45–60
Coconut		0–1	5–7	7–9	40–50	15–20	9–12	2–4	0–1	6–9	0–1	
Marine Oils												
Cod liver						5–7	8–10	0–1	18–22	27–33	27–32	

[a]Data adapted from Holum, J. R. *Organic and Biological Chemistry;* Wiley: New York, 1978; p 220 and from Altman, P. L.; Ditmer, D. S., Eds. *Biology Data Book;* Federation of American Societies for Experimental Biology: Washington, DC; 1964.

- **Hydrogenation of Triacylglycerols**
  - ➔ **Liquid vegetable oils can be partially hydrogenated to yield solid cooking fats**
  - ➔ **Partial hydrogenation isomerizes some of the cis double bonds to trans double bonds**
    - **"Trans" fats have been associated with increased risk of cardiovascular disease**



- **Biological Functions of Triacylglycerols**
  - ➔ **Triacylglycerols are primarily used as an energy reserve in animals**
    - **When they are metabolized they yield more than twice the amount of energy per gram that carbohydrates do**
    - **Fats are a form of long-term energy storage, whereas carbohydrates are a source of rapid-release energy**
- **Saponification of Triacylglycerols**
  - ➔ **Basic hydrolysis of triacylglycerols yields salts of carboxylic acids and glycerol**

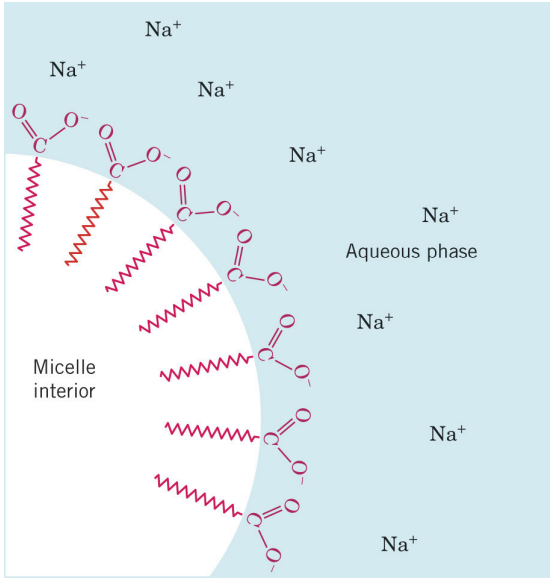


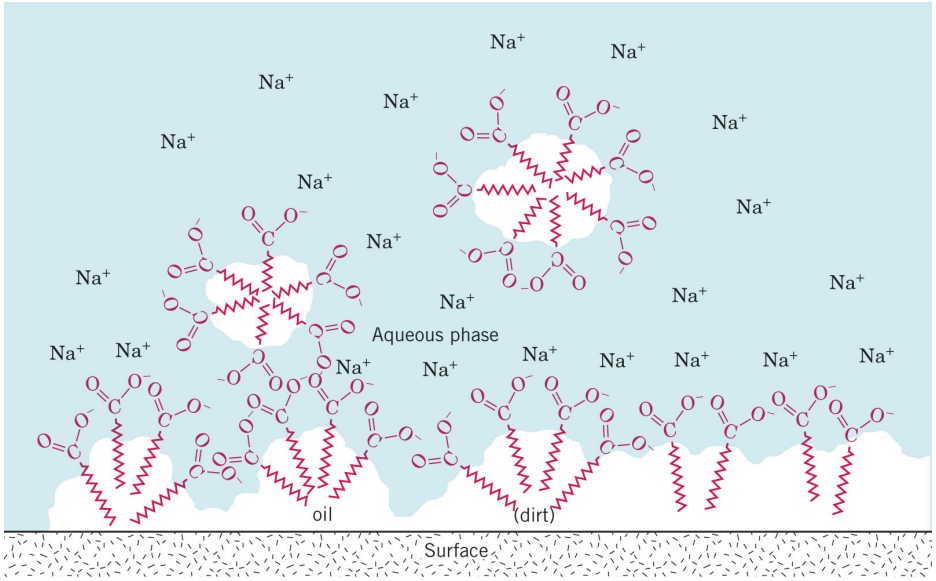
➔**Salts of long-chain carboxylic acids are called *soaps***

- **In water, soaps exist in soluble spherical clusters called *micelles***

➔**Micelles have the hydrophilic carboxylate group of the fatty acid salt on the outside exposed to water**

- **The nonpolar hydrophobic hydrocarbon chains of the fatty acids are oriented toward the interior of the micelle (away from water)**





➔**Soaps clean by incorporating greasy (hydrophobic) dirt molecules into the hydrophobic alkyl portion of micelles**

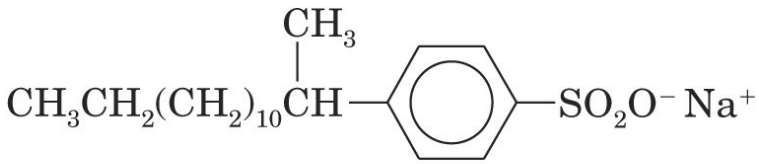
- **The polar carboxylate groups of the soap micelles serve to suspend the micelle in water so that it (with the enclosed dirt molecules) can be washed away**

➔ The polar groups of most synthetic detergents are sodium sulfonates or sodium sulfates

- Regular soaps tend to precipitate in hard water (water that contains the divalent and trivalent cations Ca^{2+} , Fe^{2+}, Fe^{3+} and Mg^{2+})
- The soap exchanges its sodium cations for these di- and trivalent metal cations and these salts tend not to be water insoluble
- In contrast, the di- and trivalent metal ion salts of synthetic detergents are more water soluble

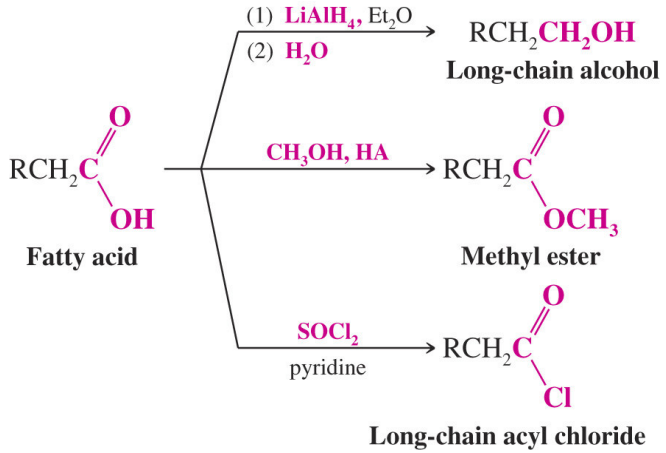
Sodium alkanesulfonates

Sodium alkyl sulfates

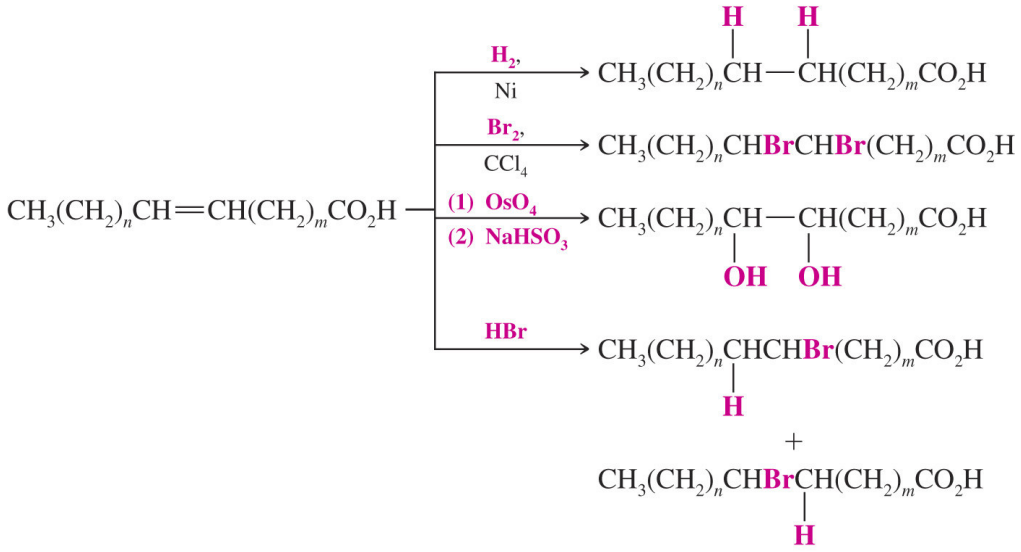


Sodium alkylbenzenesulfonates

- **Reactions of the Carboxyl Group of Fatty Acids**



- **Reactions of the Alkenyl Chain of Unsaturated Fatty Acids**



♦ Terpenes and Terpenoids

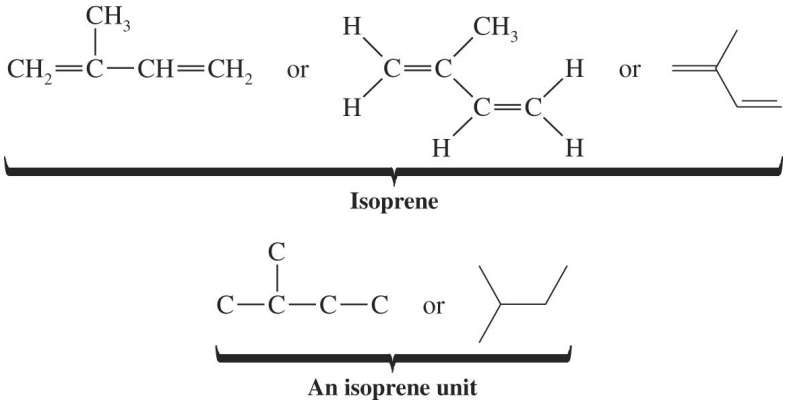
➔Terpenes and terpenoids are found in odoriferous essential oils of plants

- They are lipids that generally contain carbon skeletons of 10, 15, 20 or 30 carbons
- Terpenoids are terpenes that contain oxygen

Number of Carbon Atoms	Class
10	Monoterpenes
15	Sesquiterpenes
20	Diterpenes
30	Triterpenes

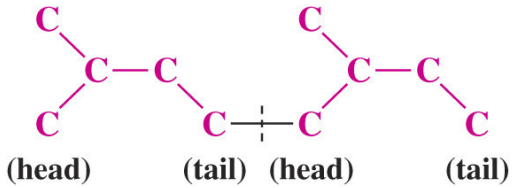
➔Terpenes are formally viewed as coming from C_5 units called isoprene units

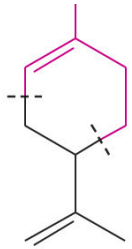
- Isoprene itself is not involved in the biosynthesis of terpenes, however (See Special Topic D)



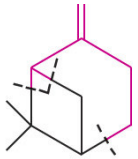
➔Isoprene units in terpenes are usually linked head to tail

- Dashed lines can be used to delineate the isoprene units comprising a terpene

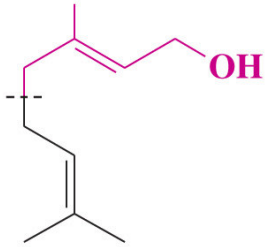




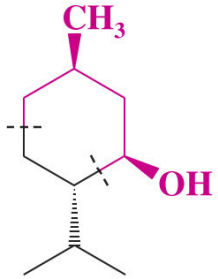
Limonene
(from oil of lemon or orange)



β-Pinene
(from oil of turpentine)



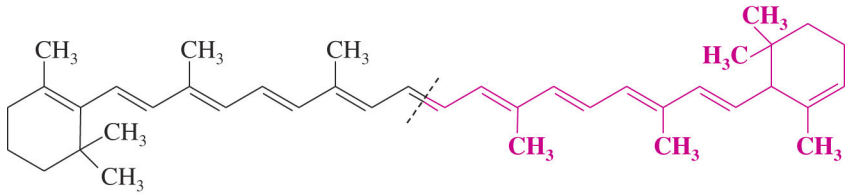
Geraniol
(from roses and other flowers)



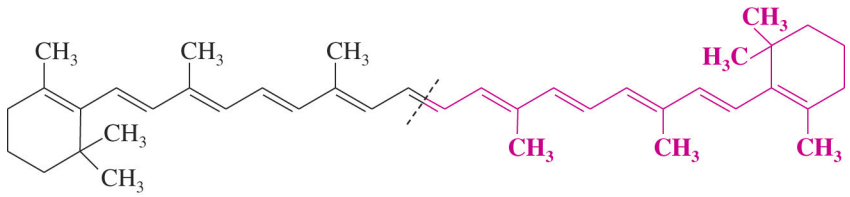
Menthol
(from peppermint)

➔ Carotenes are tetraterpenes (C_{40} terpenes)

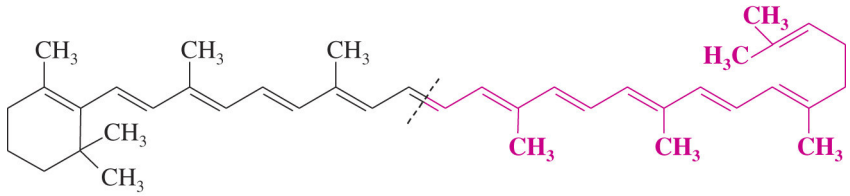
- Tetraterpenes can be viewed as two diterpenes (C_{20} terpenes) that are joined in a tail-to-tail fashion in the middle



α-Carotene



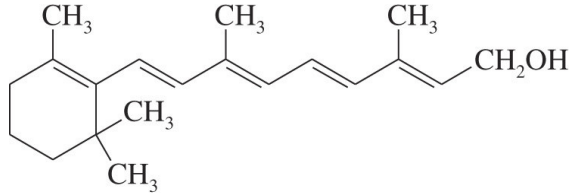
β-Carotene



γ-Carotene

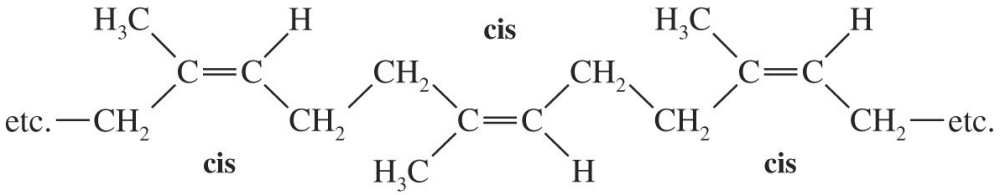
➔ The carotenes are biosynthetic precursors to Vitamin A

- Carotenes are converted to vitamin A by enzymes in the liver



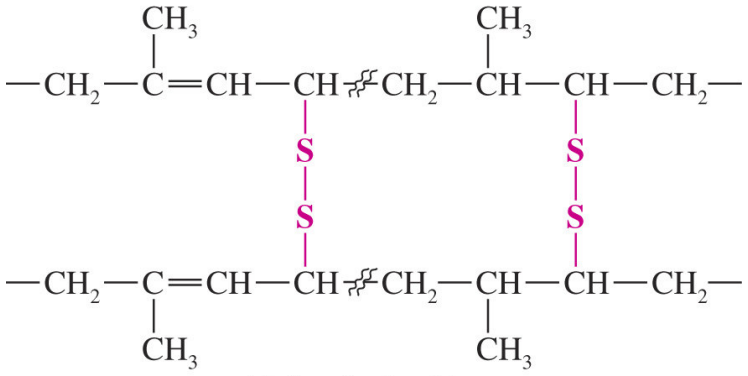
Vitamin A

- **Natural Rubber**
  - **➔Natural rubber can be viewed as a 1,4-addition polymer of isoprene**
    - **Isoprene units in natural rubber are linked head-to-tail and all of the double bonds are cis**



Natural rubber
(*cis*-1,4-polyisoprene)

  - **➔Pure natural rubber is tacky and must be *vulcanized* to be useful**
    - **Vulcanization involves heating natural rubber with sulfur to form cross-links; this makes the rubber much harder**



Vulcanized rubber

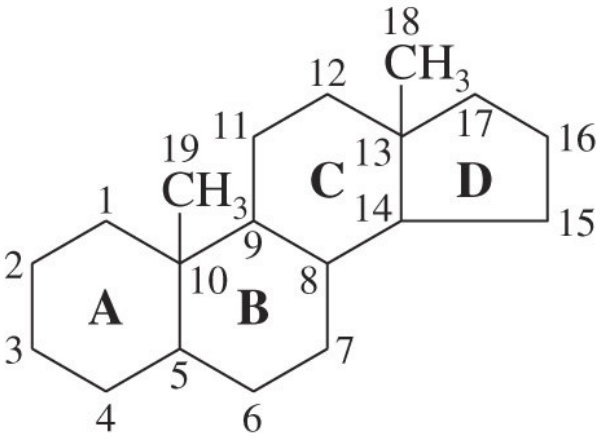
♦ Steroids

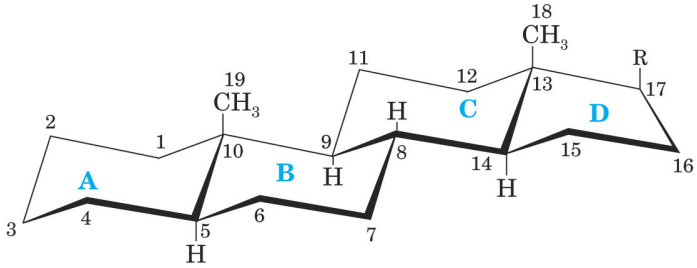
➔ Steroids are important "biological regulators"

● Structure and Systematic Nomenclature of Steroids

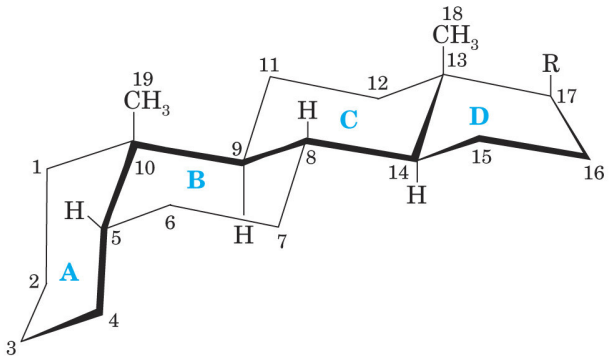
➔ Steroids have a characteristic tetracyclic ring structure

- The rings are given letter designations A-D
- Steroid carbons are numbered as shown





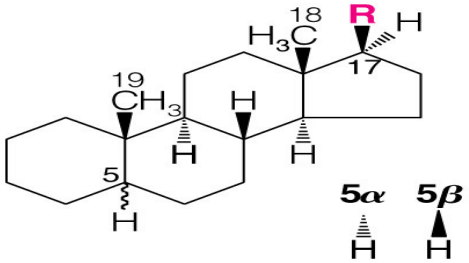
5α Series of steroids
(all ring junctions are trans.)



5β Series of steroids
(A,B ring junction is cis.)

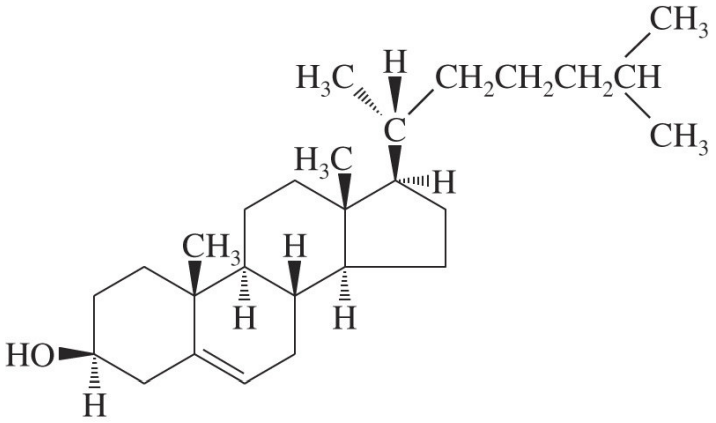
- **Methyl groups at C18 and C19 ring junctions are called *angular methyl groups***
  - **Angular methyl groups occur above the plane of the steroid as written**
  - **Other groups on the same side of the steroid plane as the angular methyl groups are said to be β substitutents**
  - **Groups below the plane of the steroid ring system are said to be α substituents**
- **Steroids of the 5α series have their C5 hydrogen *below* the plane of the ring system and all ring junctions are trans**
  - **Steroids of the 5β series have their C5 hydrogen *above* the plane of the ring system and the A,B ring junction is cis**
  - **The B-C and C-D ring junctions are usually trans**

➔ **The substituent at C17 usually determines the base name of an individual steroid**



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

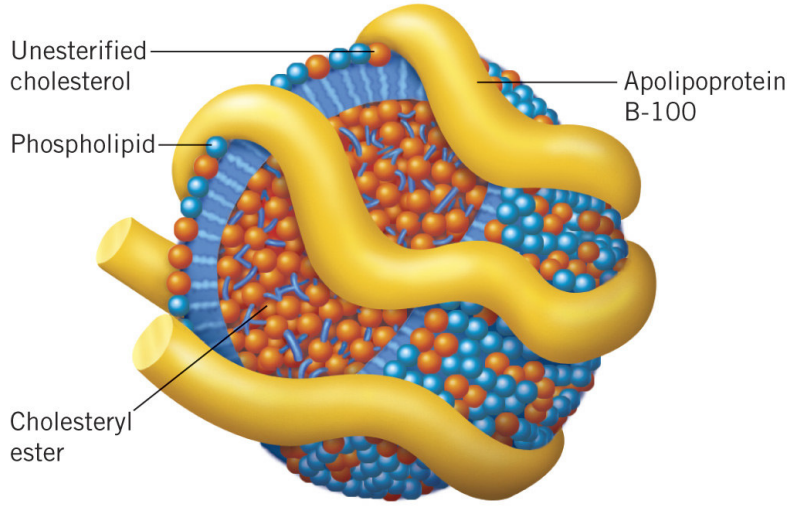
- **Cholesterol**
  - ➔ **Cholesterol is the most widely occurring steroid and the biosynthetic precursor of all other steroids**



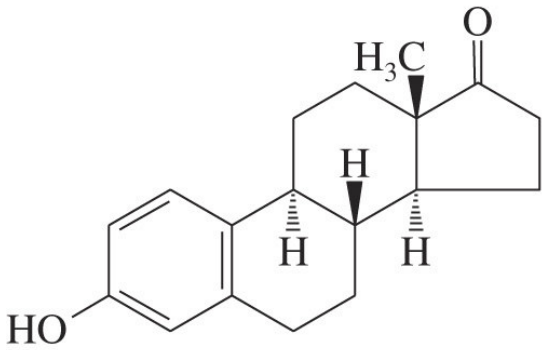
5-Cholesten-3β-ol
(absolute configuration of cholesterol)

  - ➔ **The human body makes sufficient cholesterol for its needs**
    - **Dietary cholesterol usually causes the body to make less of its own**
    - **High levels of blood cholesterol have been implicated in development of arterioschlerosis (hardening of the arteries) and in heart attacks**

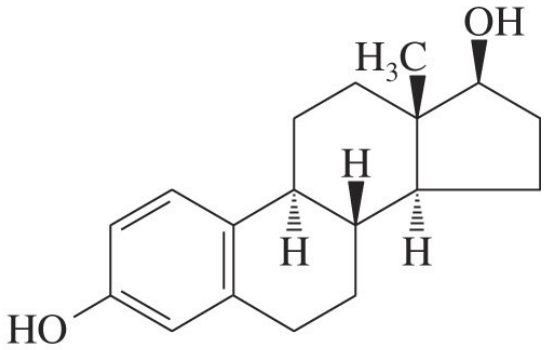
- **Cholesterol is found in the body often as an aggregate with other lipids and proteins**
  - **These aggregates are called chylomicrons, high-density lipoproteins (HDLs) and low-density lipoproteins (LDLs) and are generally in micelle form**
  - **These aggregates serve to transport water-insoluble cholesterol and other lipids in the body**
- **HDLs ("good cholesterol") carry lipids from the tissues to the liver for degradation and excretion**
- **LDLs ("bad cholesterol") carry biosynthesized cholesterol from the liver to tissues**
- **Chylomicrons carry dietary lipids from the intestines to the tissues**



- **Sex Hormones**
  - **➔There are 3 major classes of sex hormones**
    - **Estrogens (female sex hormones)**
    - **Androgens (male sex hormones)**
    - **Progestins (pregnancy hormones)**
  - **➔Estradiol is the major female sex hormone; estrone is a metabolized form of estradiol that is excreted**
    - **Estradiol is secreted by the ovaries and promotes the development of secondary female characteristics**
    - **Estrogens also stimulate the mammary glands during pregnancy**

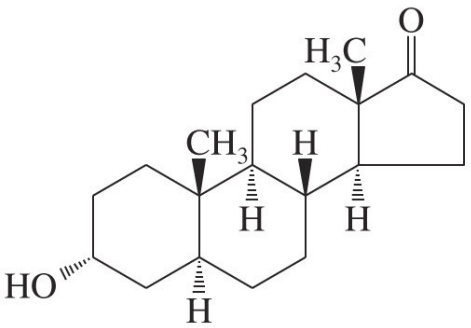


Estrone
[3-hydroxy-1,3,5(10)-estratrien-17-one]

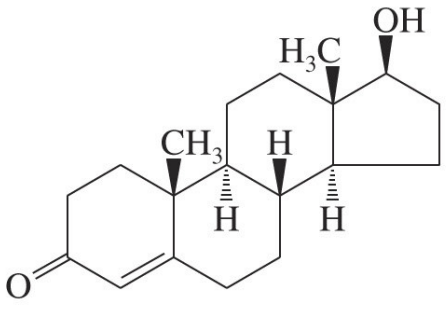


Estradiol
[1,3,5(10)-estra-triene-3,17β-diol]

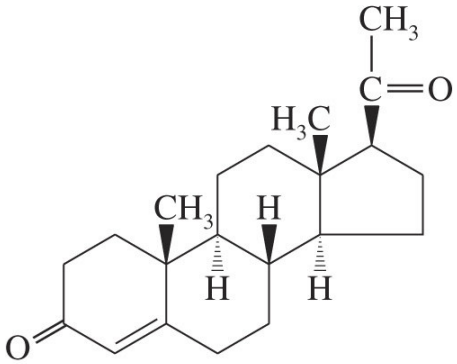
- **Testosterone is the primary male sex hormone; androsterone is a metabolized form of testosterone that is excreted**
  - **Testosterone is secreted by the testes and promotes the development of secondary male characteristics**
- **Progesterone is the most important *progestin* (pregnancy hormone**
  - **After ovulation, the ruptured ovarian follicle begins to secrete progesterone to prepare the lining of the uterus for implantation of the fertilized ovum**
  - **Progesterone is also secreted by the placenta and is necessary for pregnancy to continue**



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



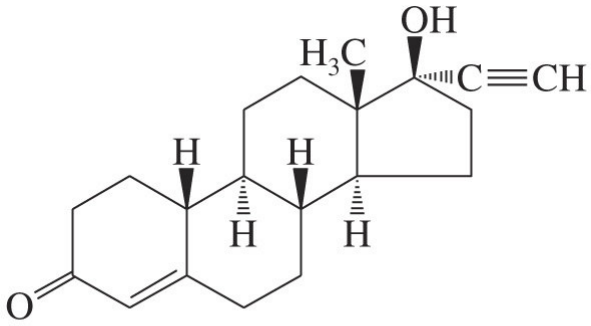
Testosterone
(17β-hydroxy-4-androsten-3-one)



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

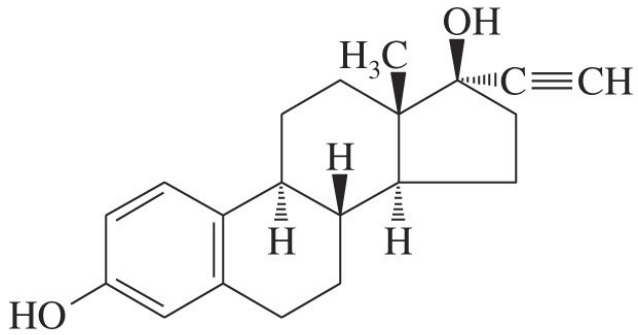
➔ **Progesterone suppresses ovulation; this is the basis for its use in oral contraceptives**

- **Progesterone is degraded in the intestinal tract, however, and therefore more robust synthetic progestins such as norethindrone are used**



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

➔ **Synthetic estrogens such as ethynylestradiol are also used in oral contraceptives**



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

♦ Adrenocortical Hormones

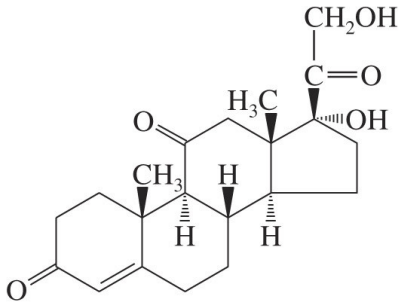
➔ **The adrenal glands (located on the top of the kidneys) produce many steroid hormones**

- **Adrenocortical hormones are very important in the regulation of carbohydrate, protein and lipid metabolism**
- **They are also important in water and electrolyte balance and the inflammatory response**
- **Cortisol is the primary adrenocortical hormone**

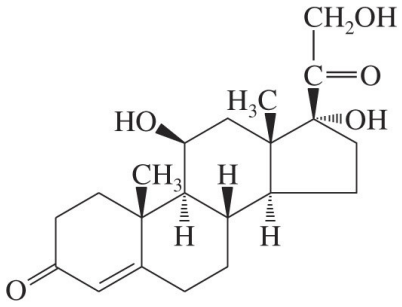
♦ D Vitamins

➔ **Vitamin D_2 is important for bone growth**

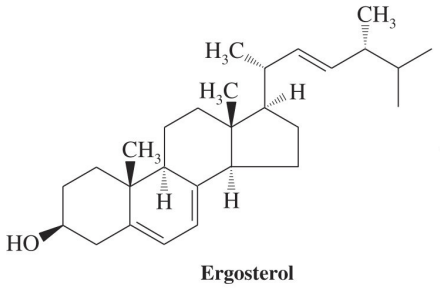
➔ **Ergosterol is converted to Vitamin D_2 by a photochemical-ring opening reaction**



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

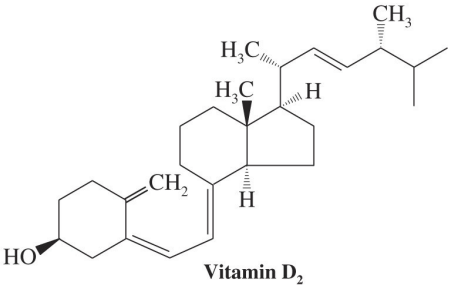


Cortisol
(11β,17α,21-trihydroxy-4-pregnene-3,20-dione)



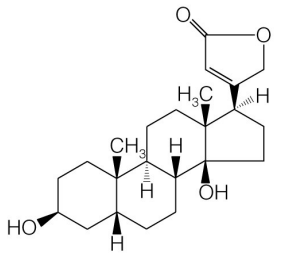
Ergosterol

UV light, room temperature



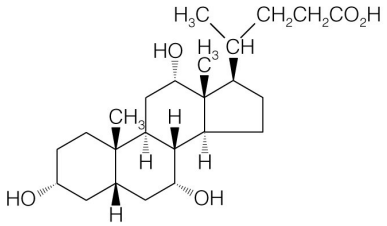
Vitamin D_2

♦ Other Steroids



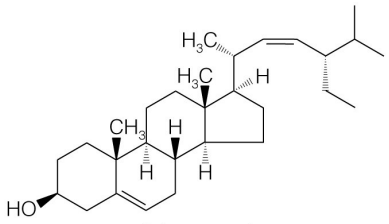
Digitoxigenin

Digitoxigenin is a cardiac aglycone that can be isolated by hydrolysis of digitalis, a pharmaceutical that has been used in treating heart disease since 1785. In digitalis, sugar molecules are joined in acetal linkages to the 3-OH group of the steroid. In small doses digitalis strengthens the heart muscle; in larger doses it is a powerful heart poison. The aglycone has only about one-fortieth the activity of digitalis.



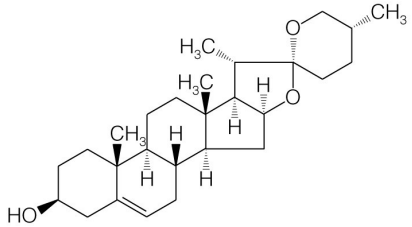
Cholic acid

Cholic acid is the most abundant acid obtained from the hydrolysis of human or ox bile. Bile is produced by the liver and stored in the gallbladder. When secreted into the small intestine, bile emulsifies lipids by acting as a soap. This action aids in the digestive process.



Stigmasterol

Stigmasterol is a widely occurring plant steroid that is obtained commercially from soybean oil. β-Sitostanol (a phytostanol, esters of which inhibit dietary cholesterol absorption) has the same formula except that it is saturated (C5 hydrogen is α).



Diosgenin

Diosgenin is obtained from a Mexican vine, *cabeza de negro,* genus *Dioscorea.* It is used as the starting material for a commercial synthesis of cortisone and sex hormones.

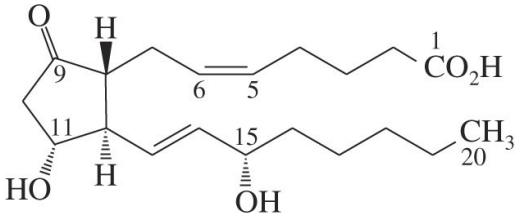
♦ Prostaglandins

➔ **Prostaglandins have a five-membered ring and two hydrocarbon tails, one of which ends in a carboxylic acid group**

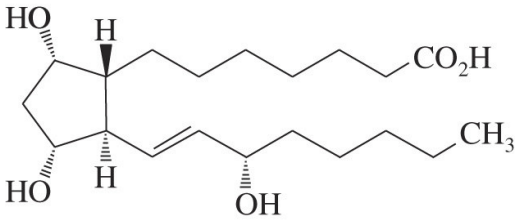
- **They mediate inflammation, heart rate, blood pressure, blood clotting, conception, fertility, and allergic responses**

➔ **Prostaglandins are biosynthesized from arachidonic acid, a C_{20} unsaturated fatty acid**

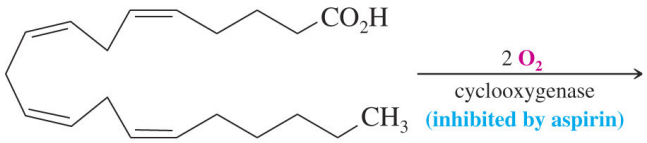
- **Aspirin inhibits the biosynthesis of prostaglandins**



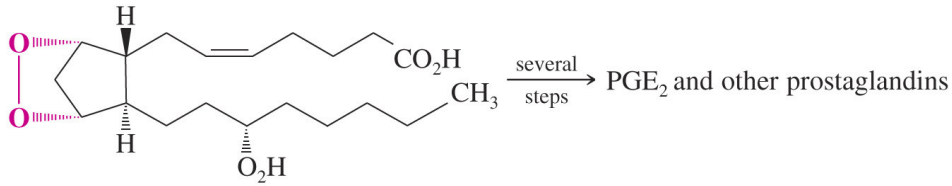
Prostaglandin E_2 (PGE_2)



Prostaglandin $F_{1\alpha}$ ($PGF_{1\alpha}$)



Arachidonic acid



PGG_2
(a cyclic endoperoxide)

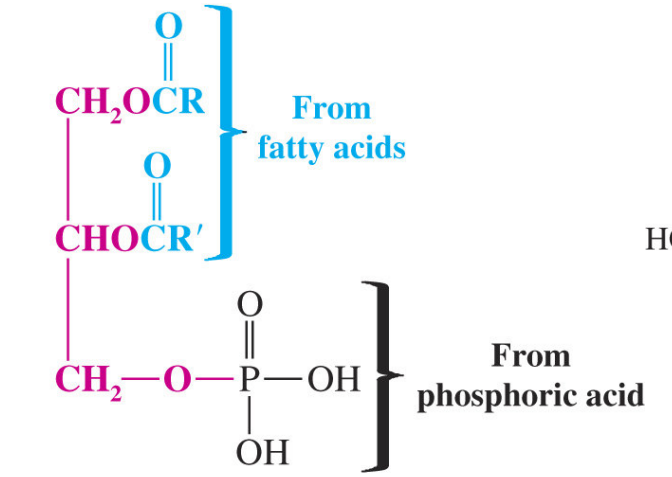
♦ Phospholipids and Cell Membranes

➔ **Most phospholipids are derived from phosphatidic acid**

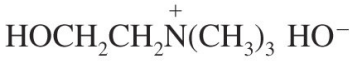
- **A phosphatidic acid is a glycerol molecule esterified at one terminal hydroxyl group with phosphoric acid and the other hydroxyl groups esterified with fatty acids (it is a diacylphosphoglycerate)**

● Phosphatides

➔ **When the phosphate group of a phosphatidic acid is bound to one of the following nitrogen-containing groups, a phosphatide is the result**

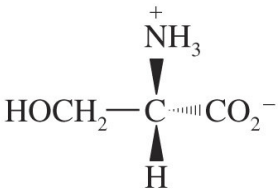


A phosphatidic acid (a diacylglyceryl phosphate)



Choline

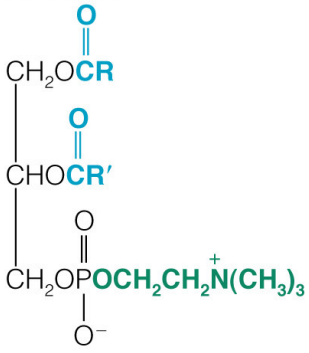
2-Aminoethanol (ethanolamine)



L-Serine

➔ Phosphatides include lecithins, cephalins, phosphatidylserines, and plasmalogens

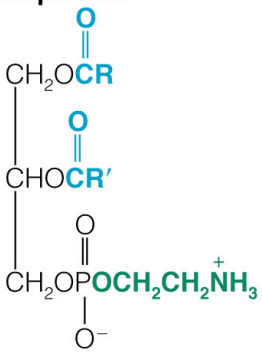
Lecithins



(from choline)

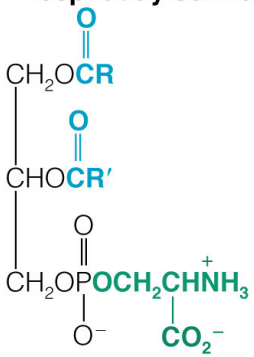
R is saturated and R′ is unsaturated.

Cephalins



(from 2-aminoethanol)

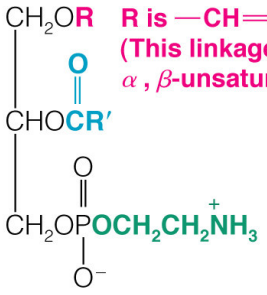
Phosphatidylserines



(from L-serine)

R is saturated and R′ is unsaturated.

Plasmalogens



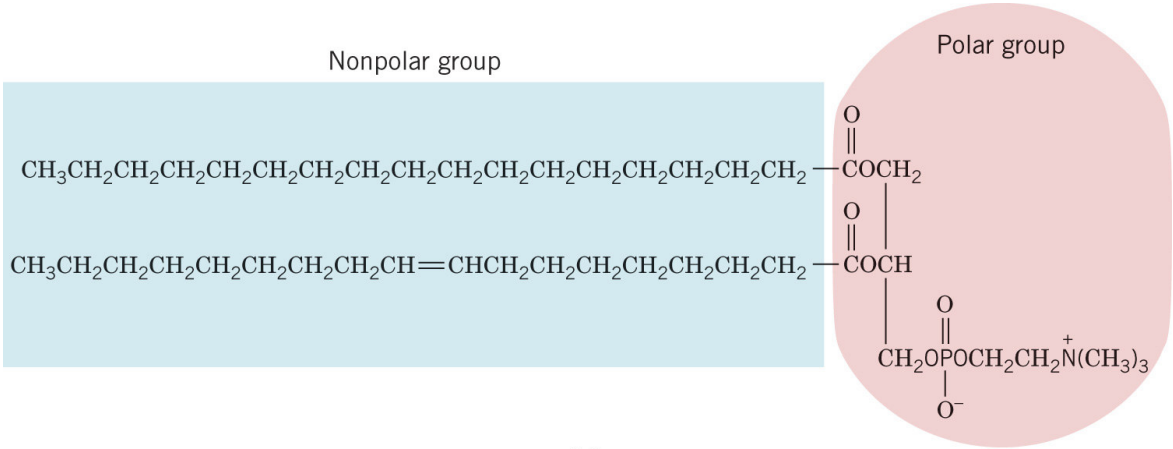
R is $-CH=CH(CH_2)_nCH_3$ (This linkage is that of an α,β-unsaturated ether.)

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

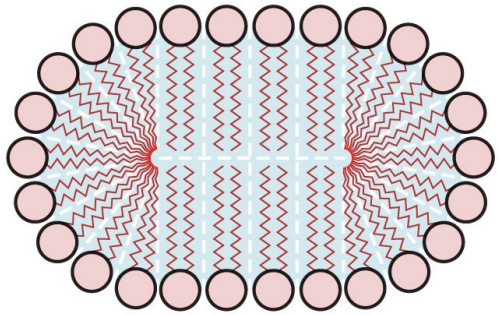
R is that of an unsaturated fatty acid.

➔Phophatides form lipid bilayers in biological systems

- **See the central portion of diagram (b) below**



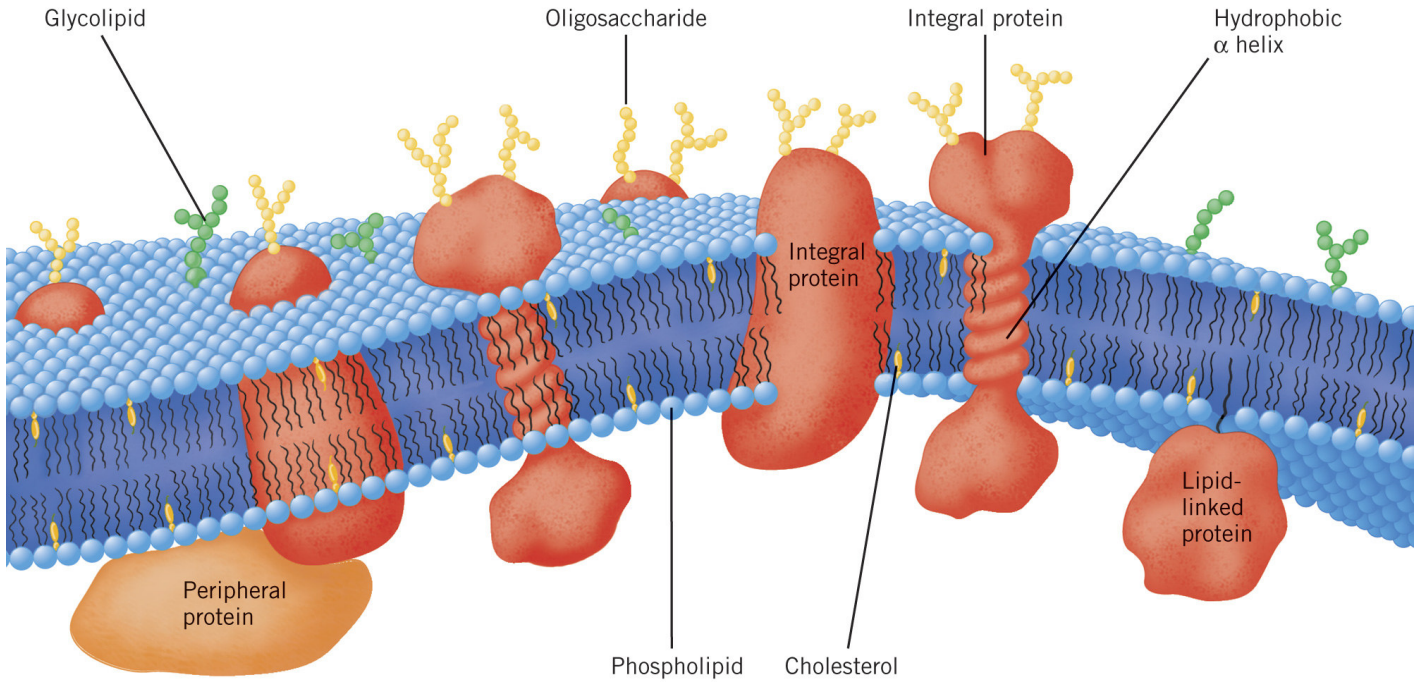
(*a*)



(*b*)

➔ **Plasma membranes are primarily lipid bilayers with associated proteins and glycolipids**

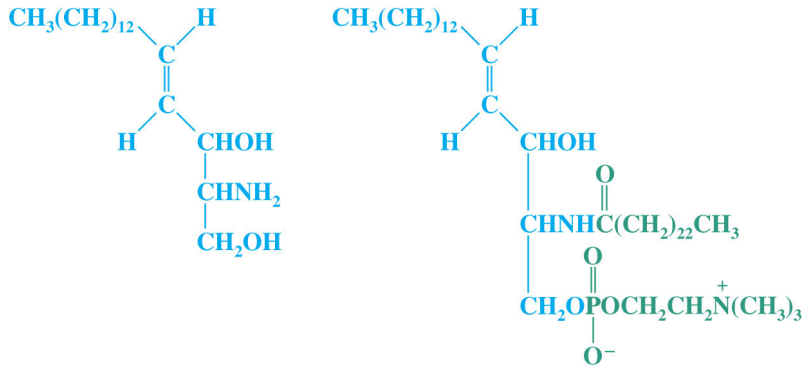
- **Cholesterol is also a major component of plasma membranes**



♦ Sphingolipids

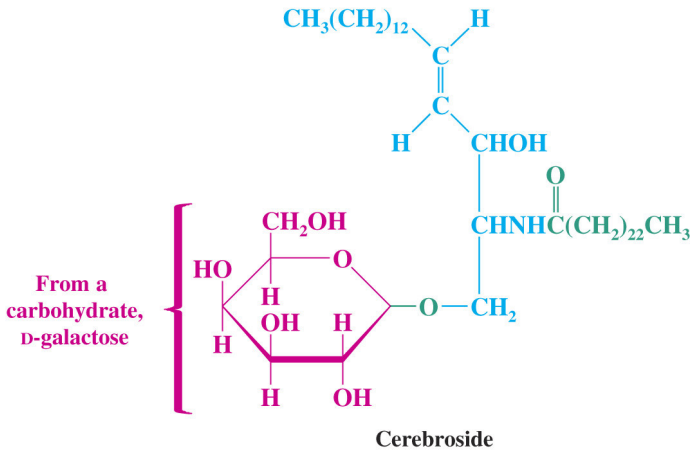
➔ Sphingolipids are derived from sphingosine

➔ Sphingolipids are components of myelin, the protective coating of axon nerve fibers



Sphingosine

Sphingomyelin (a sphingolipid)



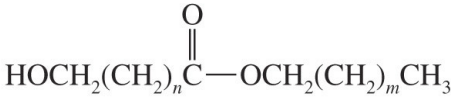
Cerebroside

♦ Waxes

➔ Waxes are esters of long-chain fatty acids

Cetyl palmitate
(from spermaceti)

***n* = 24 or 26; *m* = 28 or 30**
(from beeswax)



***n* = 16–28; *m* = 30 or 32**
(from carnauba wax)