Lipids

lipids are a chemically diverse group of compounds, the common & defining feature of all is their insolubility in water.

Highly soluble in non-polar solvents chloroform, ether, benzene.

Their water-insolubility contributes to much of the complexity in their digestion, transport, and metabolism.

Essential to the overall energy economy of the cell.

Major Categories

a) Nonpolar : esters of fatty acids with alcohols e.g. glycerol and cholesterol.

Oil (i.e., olive oil) mainly contain triacyl-glycerols with unsaturated fatty acid.

Oils are liquids at room temperature.

Solid fats (i.e., butter) contain primarily saturated fatty acids

Thereby raising the melting temperature. They are more solid at room temp.

Melting point stearic acid C18= 69.9C

Melting point oleic acid C18(one double bond)= 13.4C

Melting point palmitic acid C16 = 6.5C

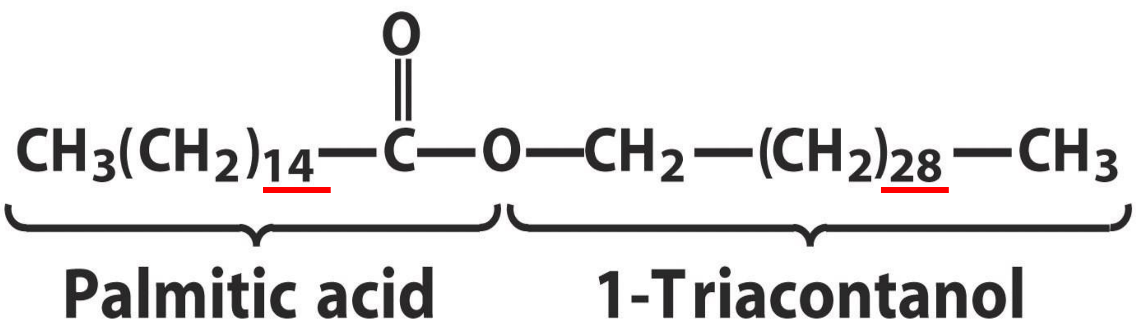
Short chain and unsaturation decrease ↓ melting point = enhance fluidity.

Biological Waxes :

Esters of long-chain fatty acids (C14-C36) with long chain alcohols (C16-C30).

function as energy stores, and act as water-impermeable coatings.

Plant leaves, ear wax, insects exoskeleton.



Triacontanylpalmitate is the major component of bees wax.

b) Polar Lipids:

contain a polar group such as phosphate, sulfate or a carbohydrate.

Consequently considered *amphipathic*.

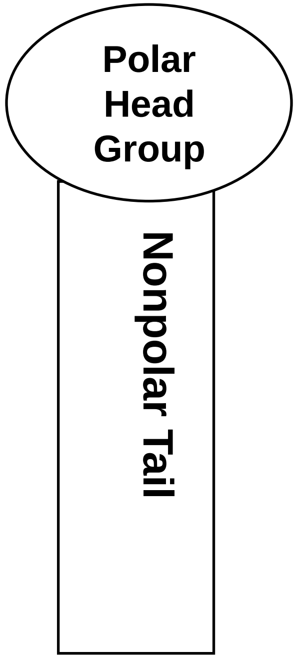
phospholipids – phosphate group

sulpholipid – sulphate group

glycolipid – sugar moiety

Important components of membranes.

General Polar Lipid Structure



Biological Roles

1. Energy Source:

9 Cal/g vs 4 Cal/g (CHO) for complete oxidation.

Highly nonpolar, stored in anhydrous form (unlike CHO).

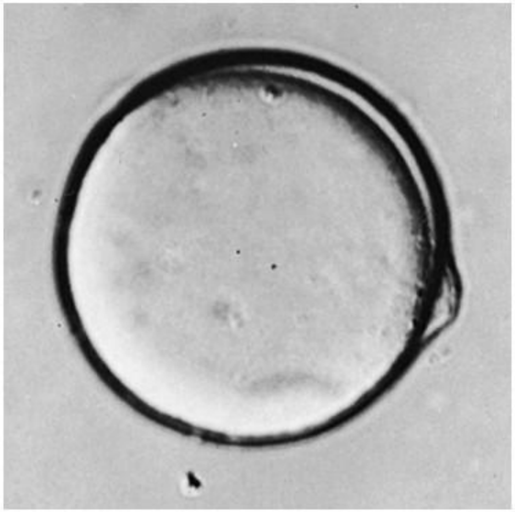
1 gram glycogen + 2 gram water.

Evolution selected TG over glycogen as energy reservoir

Glycogen short-term storage fuel molecule, TG long-term storage.

Fat Cells: Adipose tissue specialized for synthesis and storage of TG

- expand to accommodate increased lipid accumulation
- contain TG stored in cytoplasm
- TG droplets coalesce to form a large globule, occupy most cell vol.



2. Structure

major framework of membranes, phospholipids and glycolipids.

3. Communication

steroid hormones (derived from cholesterol); sex hormones; signal transduction - 2nd messenger

4. Enzyme Co-factors

Vitamin D,A,E, K are fat-soluble vitamins.

5. Digestion

Bile salts are derived from cholesterol; important in emulsification.

TA for insulation

- TA under skin→ low temperature
  
  
  
  - Seals, walruses, penguins etc (warm-blooded polar animals) →full of TA
  - Hibernating animals (bear) both energy and insulation

Fatty acids $CH_3(CH_2)_nCOOH$

classified either as:

- saturated or unsaturated
- according to chain length:
  - short chain FA: 2-4 carbon atoms
  - medium chain FA: 6 –10 carbon atoms
  - long chain FA: 12 – 26 carbon atoms
  - essential fatty acids vs nonessential.

  e.g. linoleic and linolenic are two examples of essential FA

table 11–1

Some Naturally Occurring Fatty Acids

Carbon skeleton	Structure*	Systematic name[†]	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent) Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus,* "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica,* nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma,* "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear,* "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis,* legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum,* "wood" + *cera,* "wax")	86.0		
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	−0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum,* "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon,* "flax")	−5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	−11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	−49.5		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

[†]The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

Two representations

of fully saturated acid

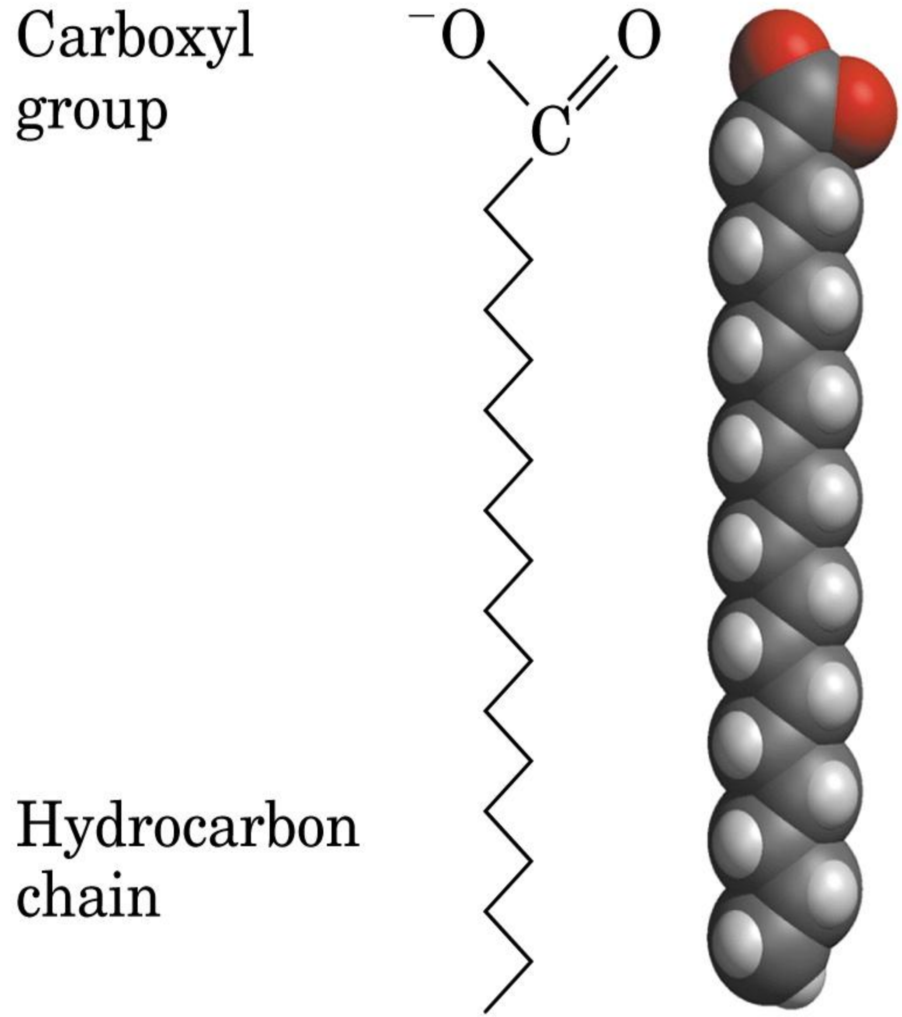
stearic acid (stearate at pH 7)

in its extended conformation.

Each line segment of zigzag

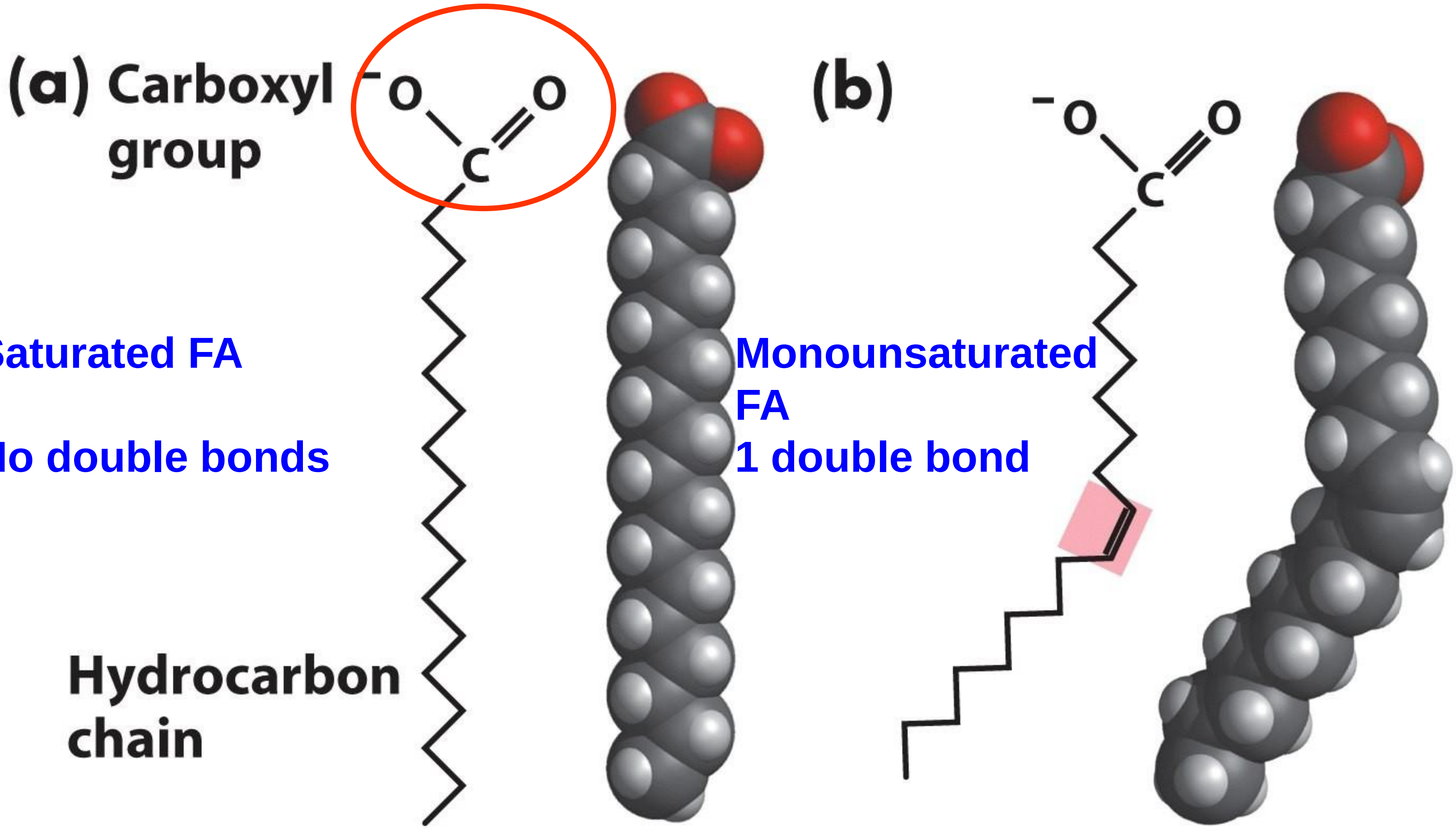
represents a single bond bw

adjacent carbons.



(a)

Saturated vs Unsaturated Fatty Acids



Saturated FA

No double bonds

Monounsaturated FA

1 double bond

Stearic Acid C-18

Oleic Acid C-18

- Cis double bonds causes FA to kink at that position;

- FA double bonds are always cis.

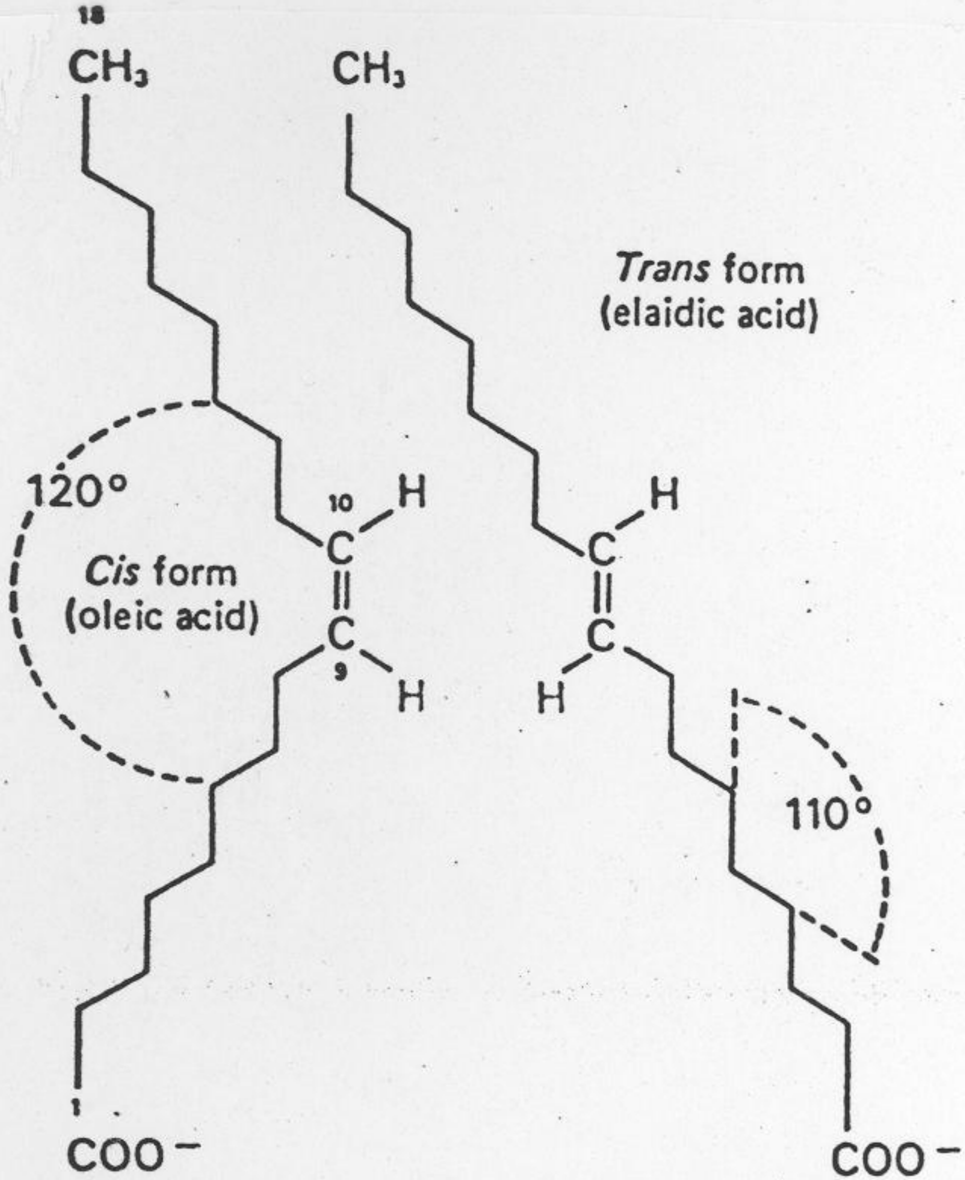
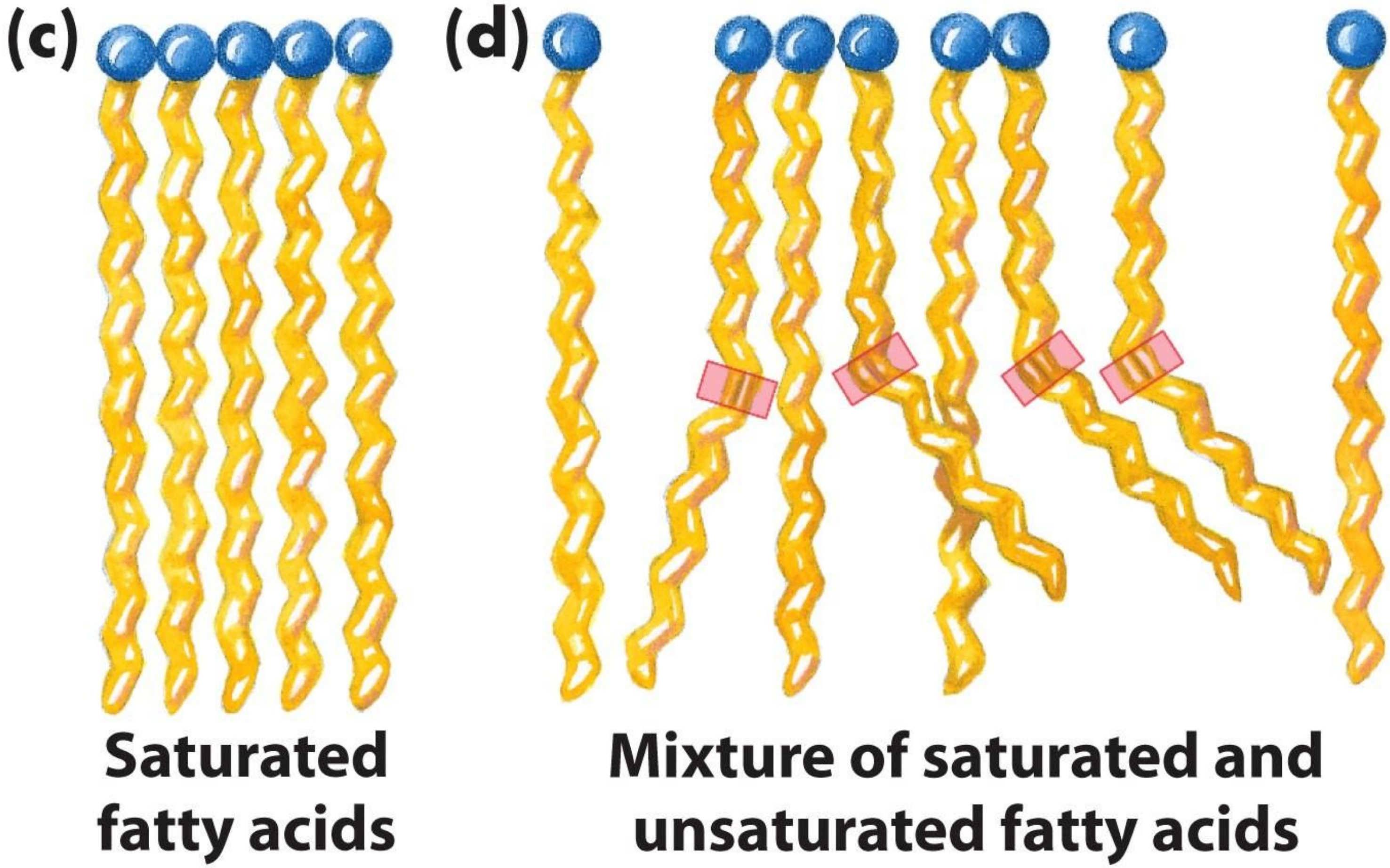


Figure 16–5. Geometric isomerism of Δ^9, 18:1 fatty acids (oleic and elaidic acids).

The packing of FA`s into stable aggregates.
extent of packing depends on the degree of saturation.

Fully saturated FA`s in the extended form.
stabilized by many hydrophobic interactions.



Double bonds introduce kinks in the tail and reduce its compaction.

Triacylglycerol:

3 FA in an ester linkage with 1 molecule of glycerol.

simple (contain the same FA at all 3 positions).

mixed (contain 2 or more different FA).

Excellent source of stored energy.

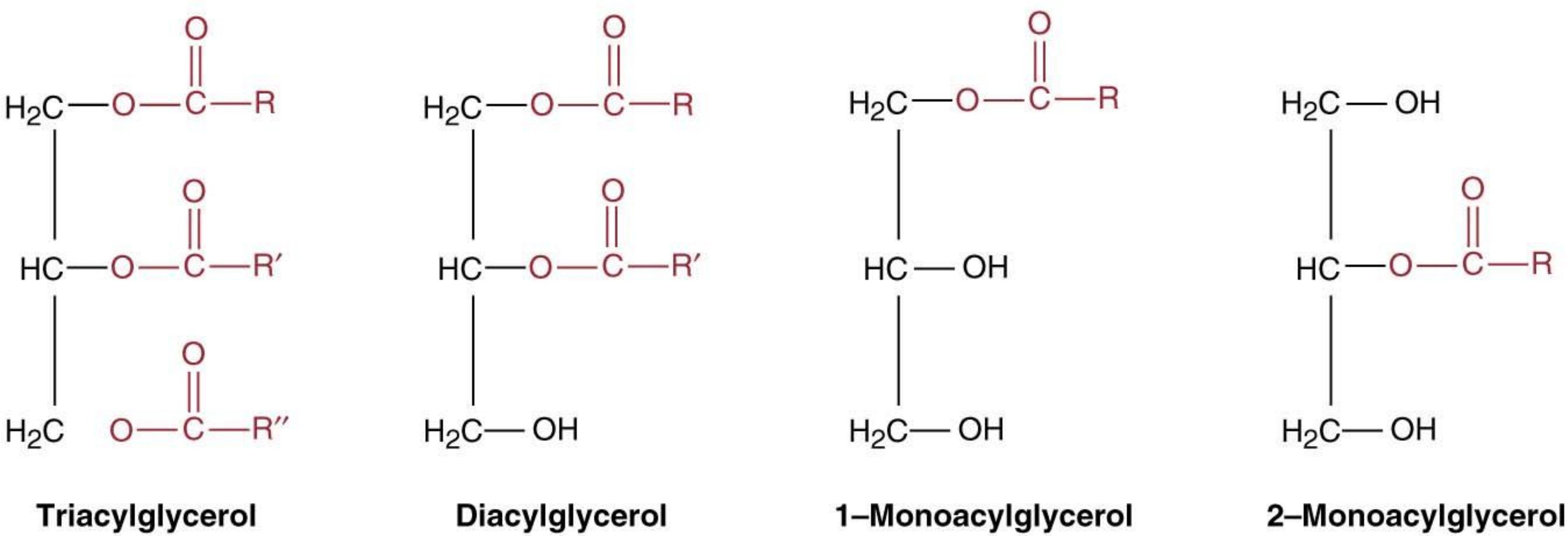
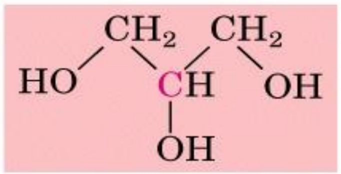


Figure 17.5. Acylglycerols.

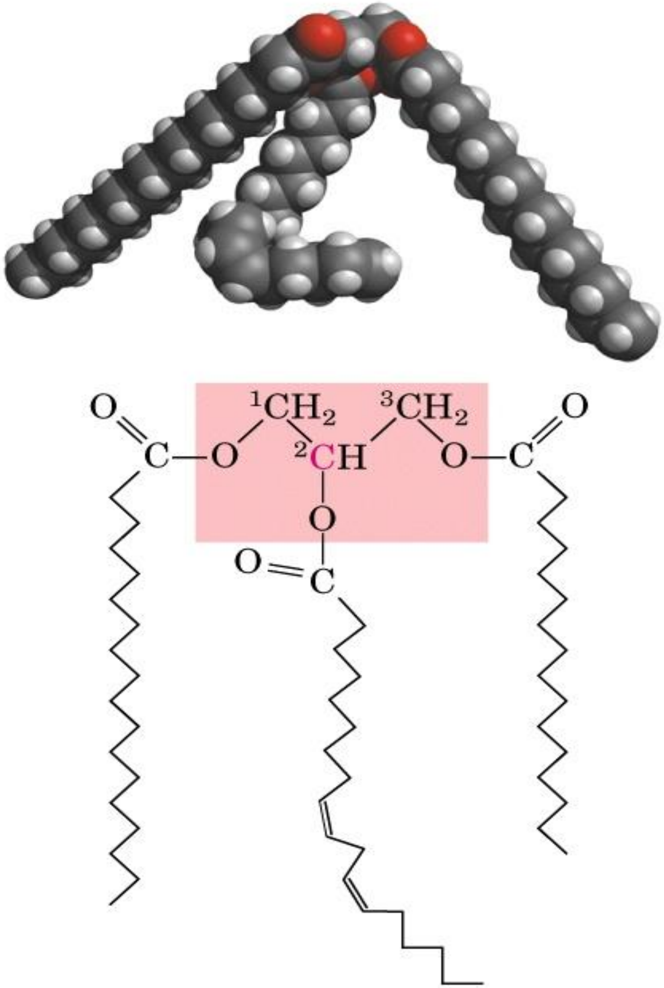
The mixed triacylglycerol

three different FA attached to the glycerol backbone.

If glycerol has 2 different FA at C-1 and C-3, the C-2 is a chiral center.

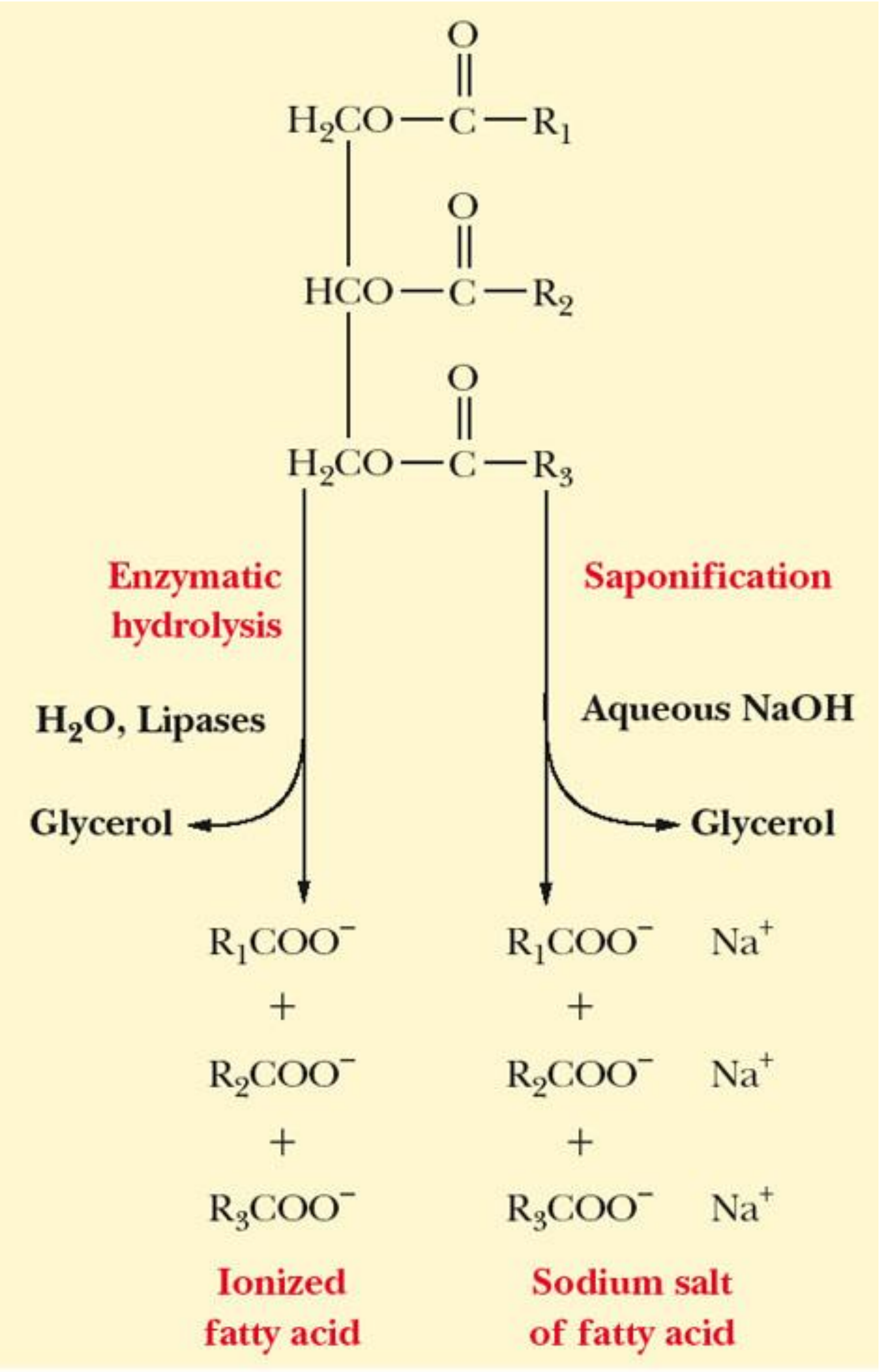


Glycerol



1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol, a mixed triacylglycerol

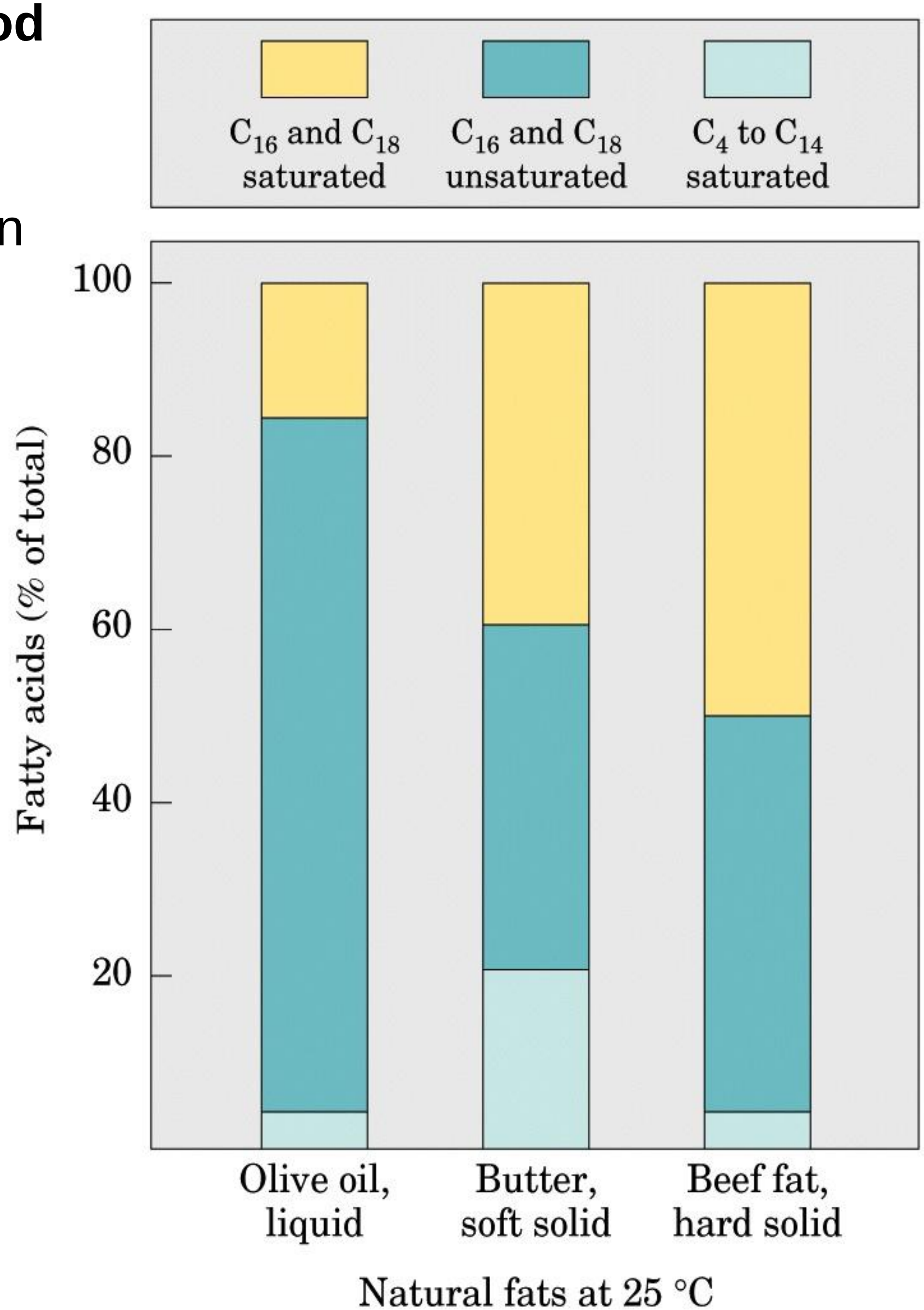
Hydrolysis of triacylglycerols. The term "saponification" refers to the reactions of glyceryl ester with sodium or potassium hydroxide to produce a soap, which is the corresponding salt of the long-chain fatty acid



Fatty acid composition of three food fats. Olive oil, butter, and beef fat :

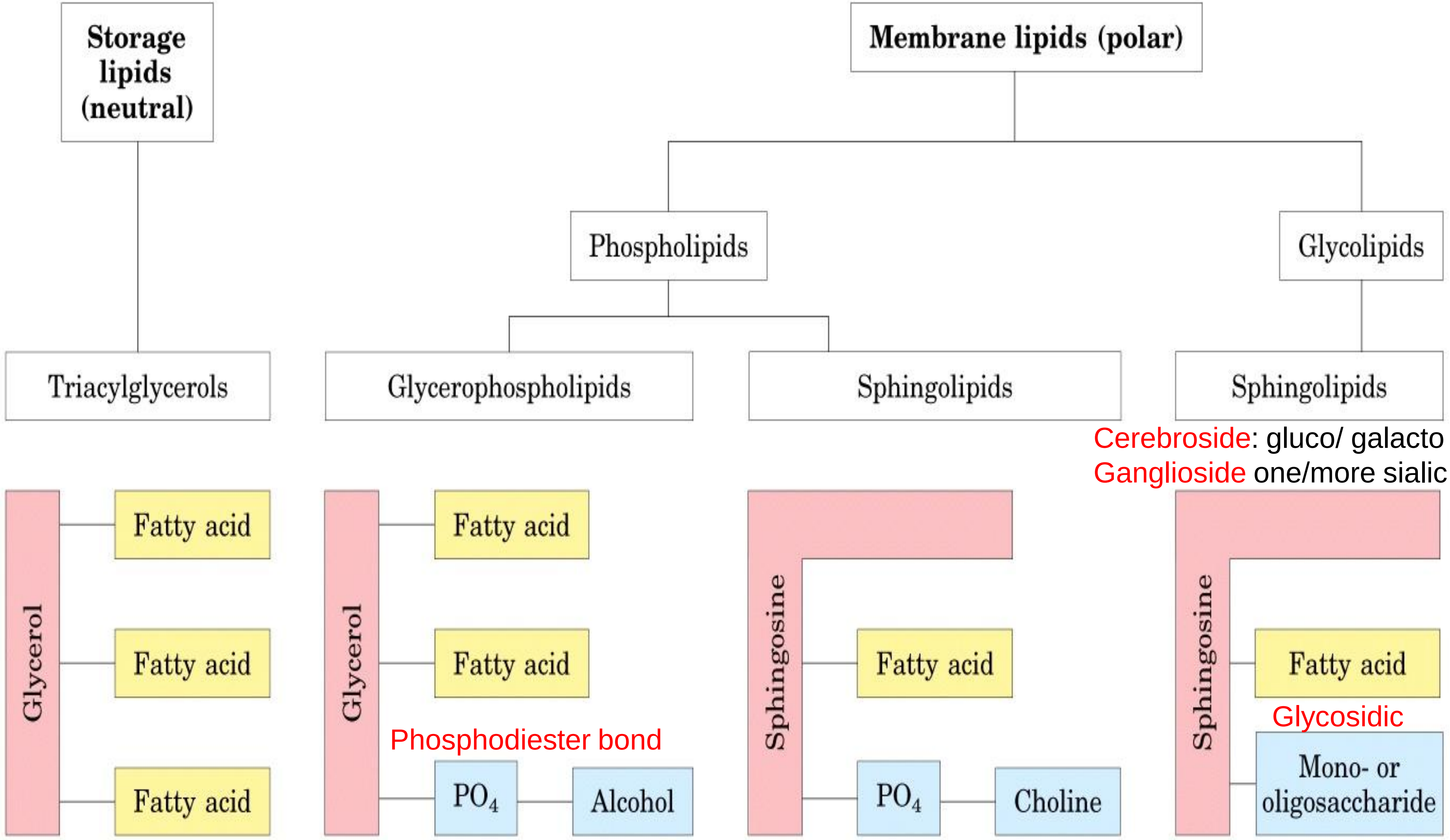
mixtures of triacylglycerols, differing in their FA composition. The melting points and physical state at room temperature (25 C)

Olive oil has a high proportion of long-chain (C16 and C18) unsaturated FA →accounts for its liquid state at 25 C.



Some common types of storage and membrane lipids.

the backbone is either glycerol / sphingosine to which attached one/ more long chain FA in ester bond and a polar head group.

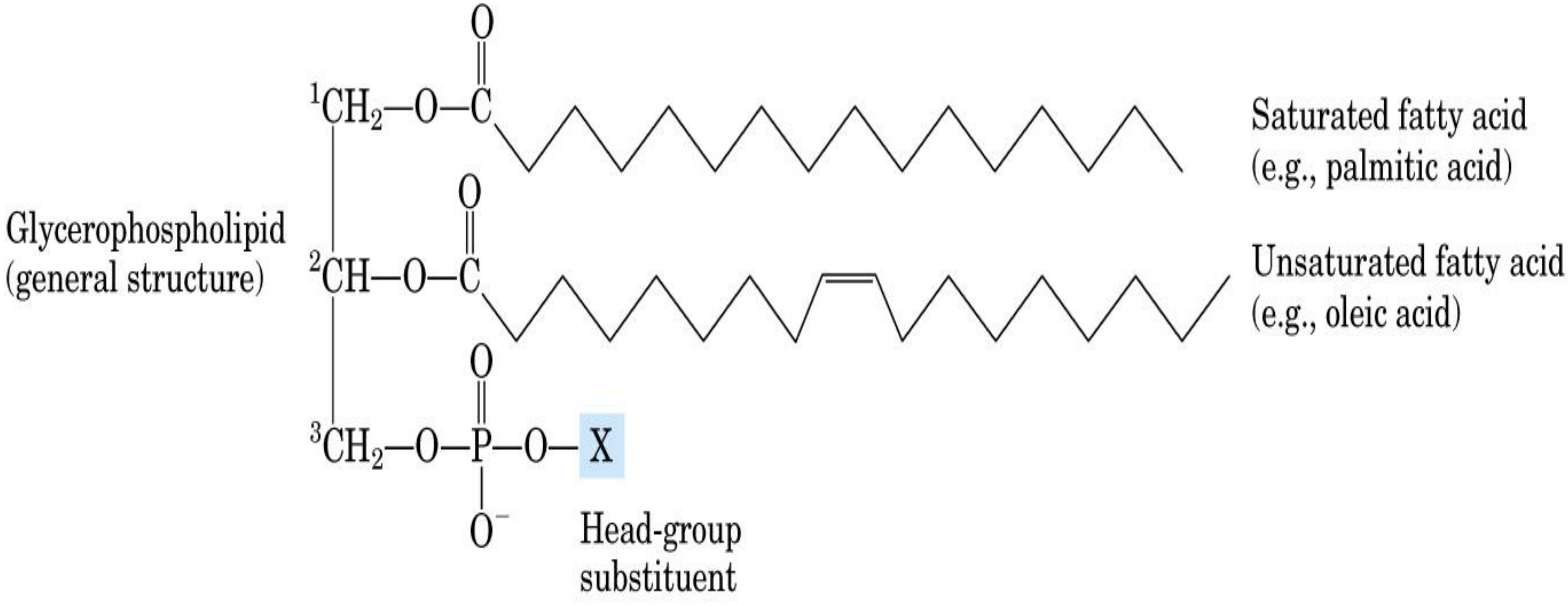


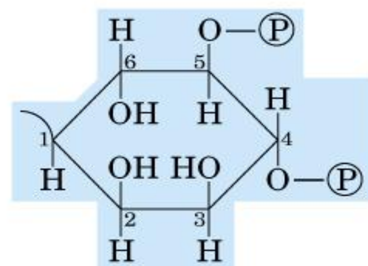
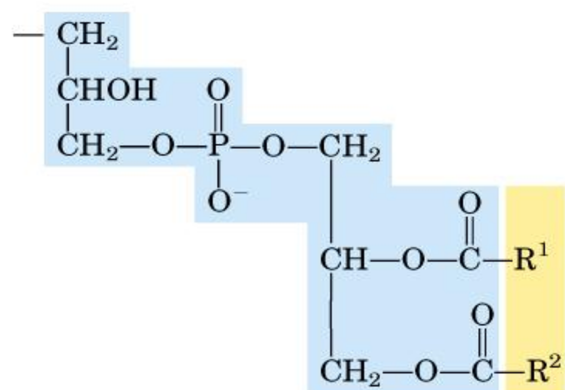
Glycerophospholipids.

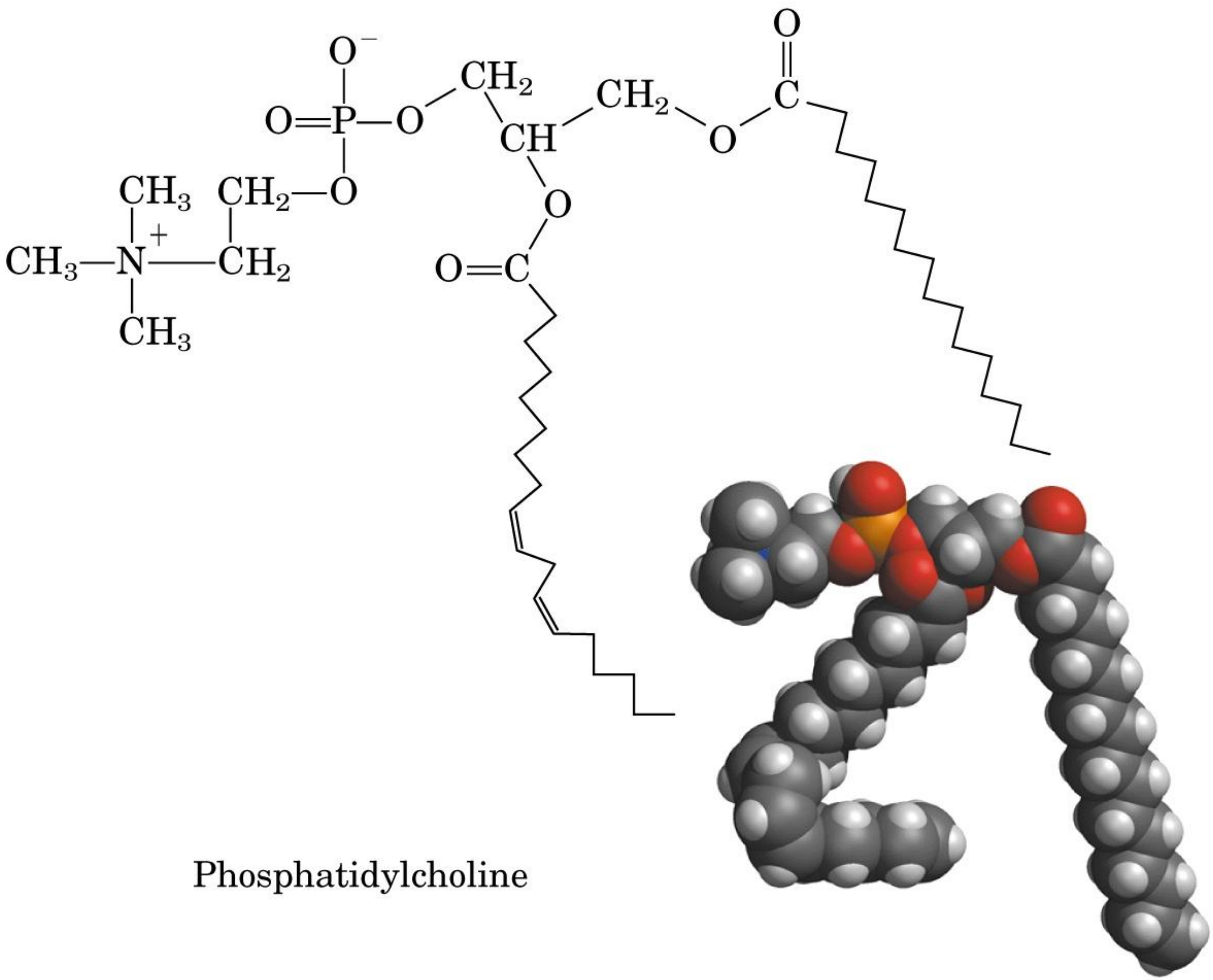
diacylglycerols linked to head-group alcohols through a phosphodiester bond.

Phosphatidic acid, a phosphomonoester, the parent compound.

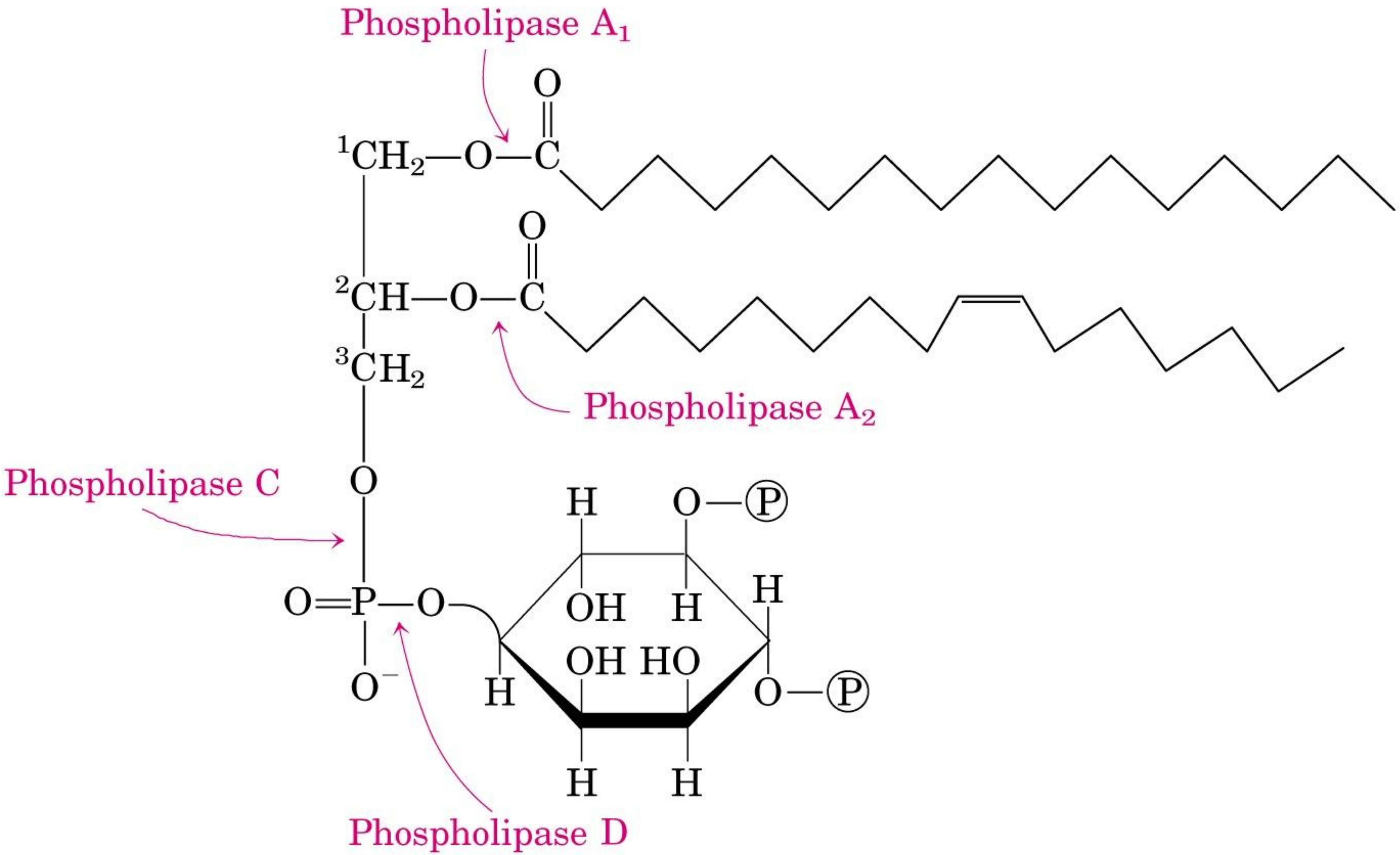
Derivatives named for the head-group alcohol X with the prefix "phosphatidyl-"



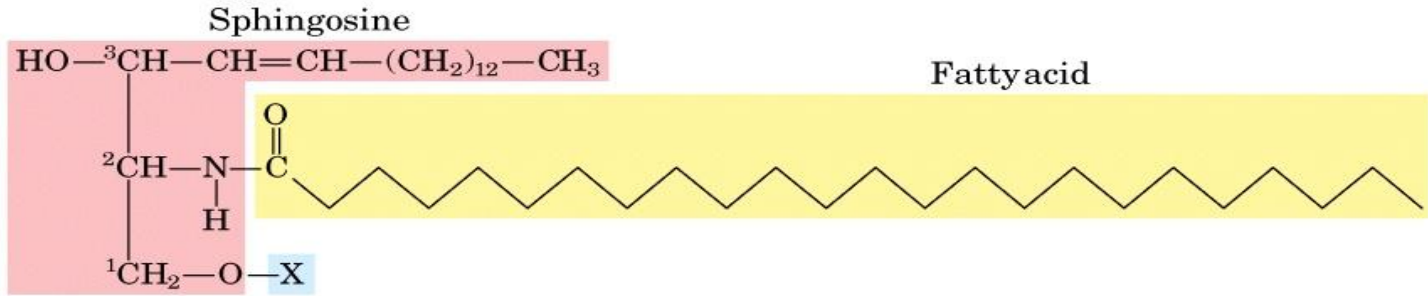
Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	$-H$	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-CH(COO^-)-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-CH(OH)-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2



Phosphatidylcholine


Phospholipase A1
Phospholipase A2
Phospholipase C
Phospholipase D

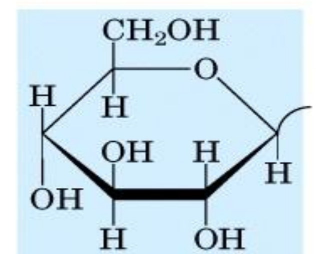
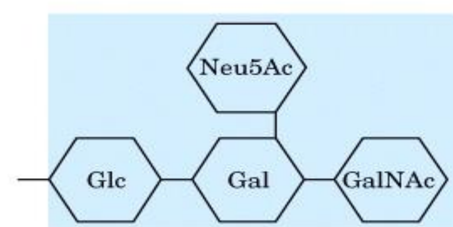
Sphingolipid (general structure)



Sphingolipids:

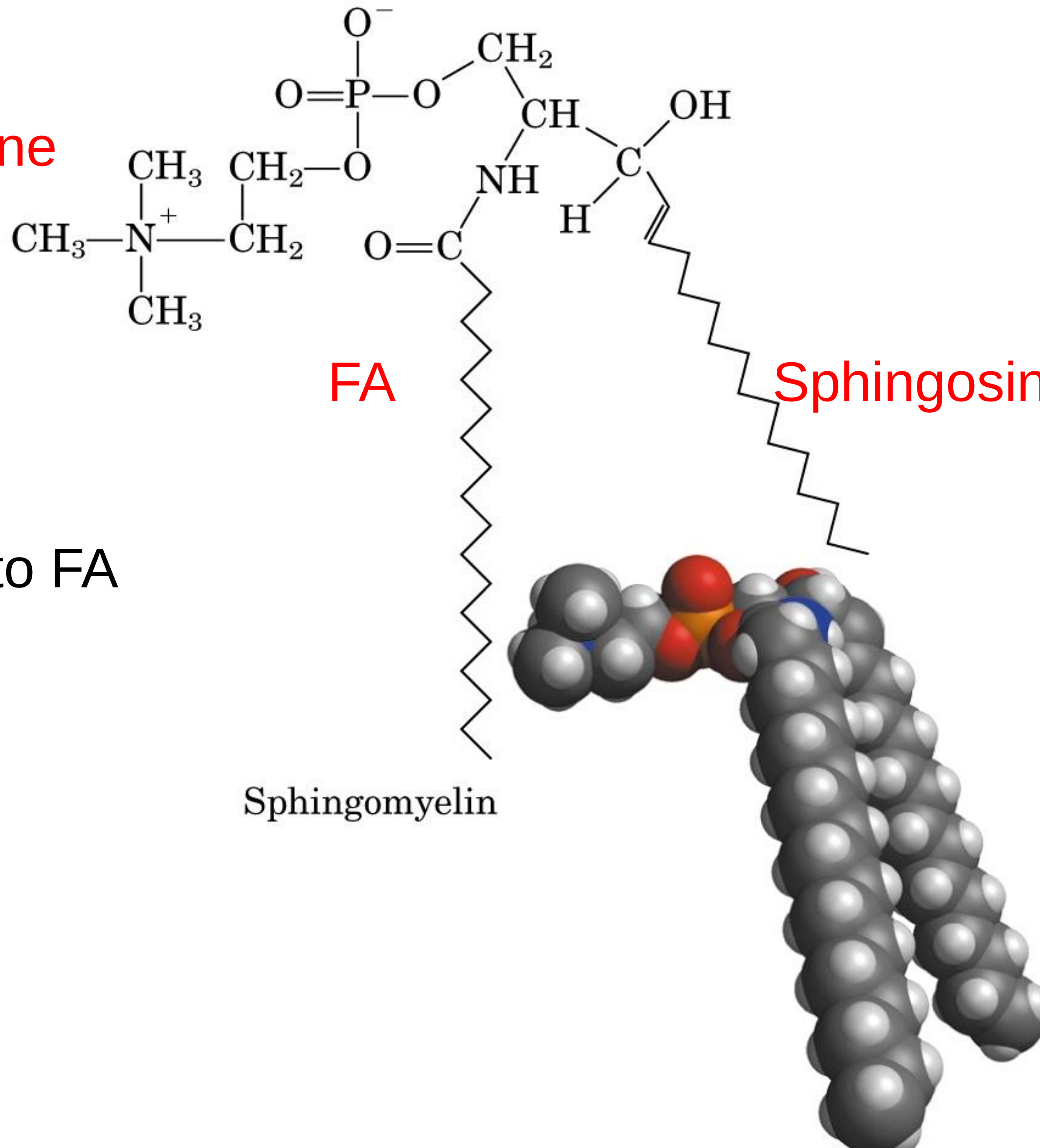
complex lipids

contain a FA + sphingosine backbone + polar head group.

Name of sphingolipid	Name of X	Formula of X
Ceramide	—	— H
Sphingomyelin	Phosphocholine	$-P(=O)(O^-)-O-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
Neutral glycolipids Glucosylcerebroside Cerebroside: Glucocerebroside Galactocerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Sphingomyelin:

Phosphocholine

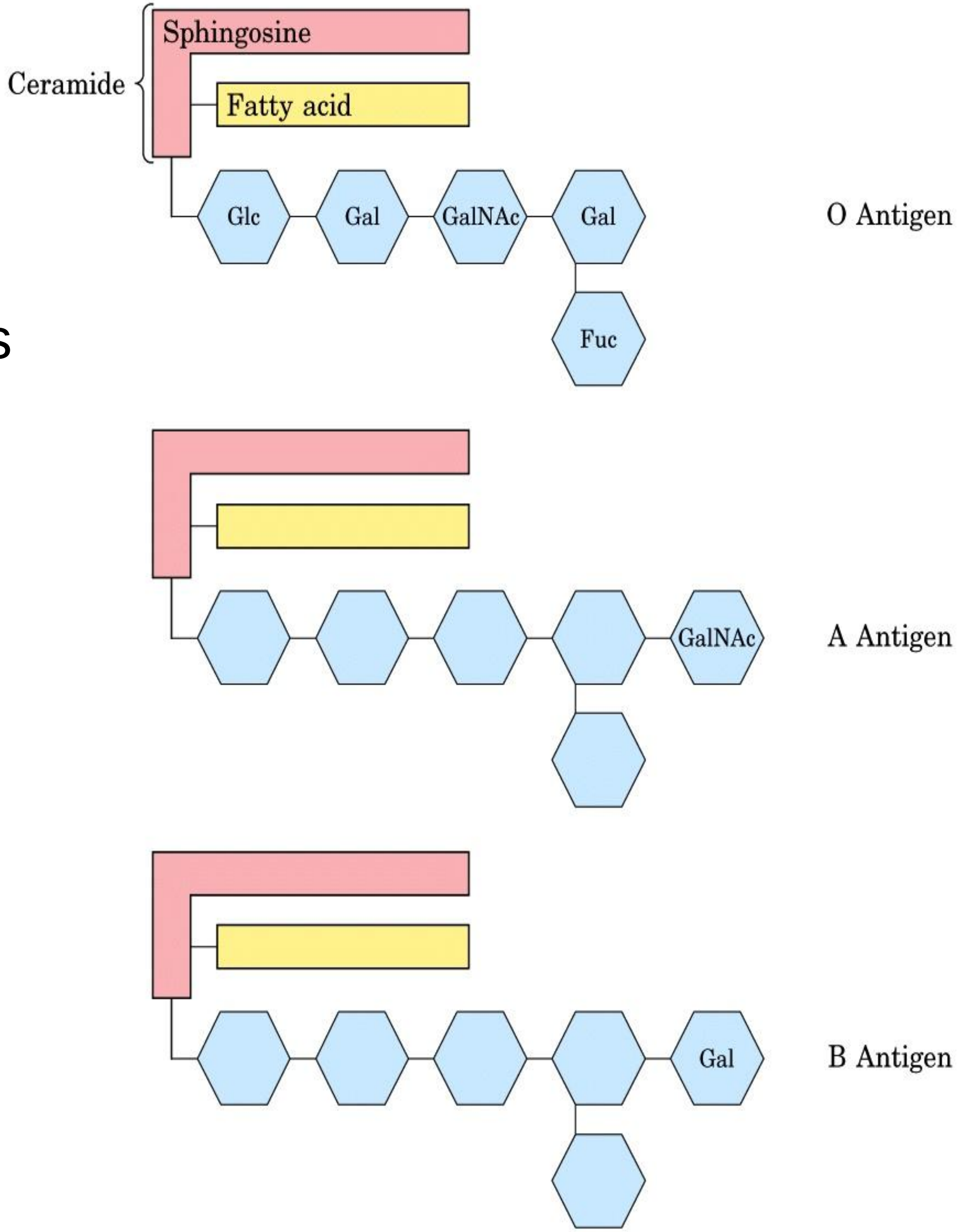


Note:

Sphingosine =
a long alcohol similar to FA

Glycosphingolipids as determinants of blood groups.

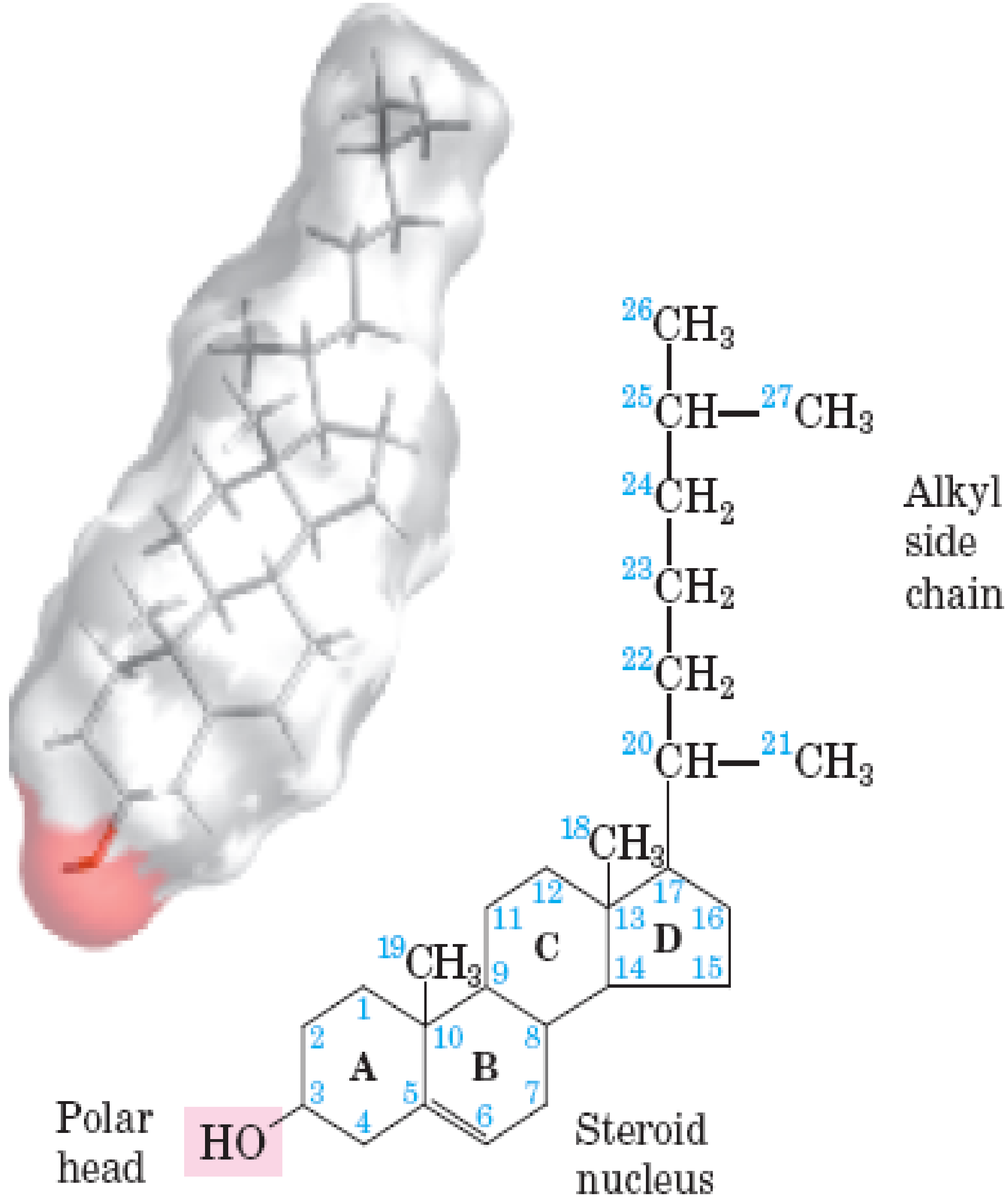
oligosaccharide head groups (blue) of these glycosphingolipids.



Sterols:
four fused rings & a hydroxyl group.

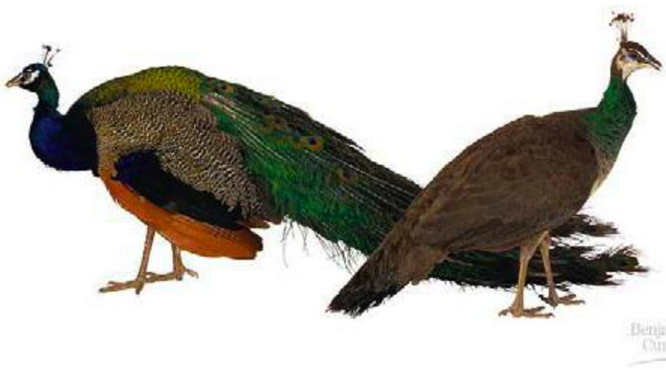
Cholesterol : major sterol in animals.

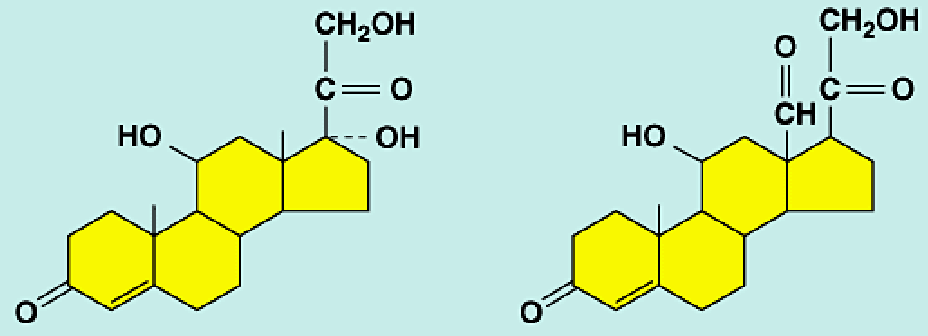
Function:
1) structural component of membranes
2) precursor to a wide variety of steroids



Site for FA esterification

From Cholesterol → Sex Hormones

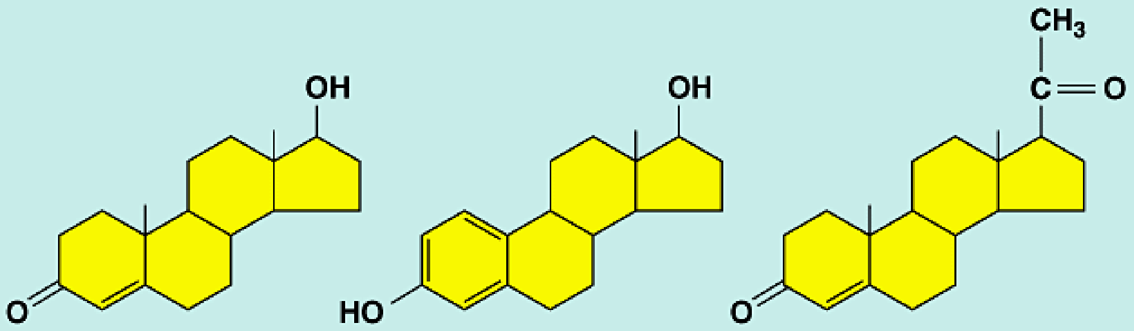




Cortisol
(a glucocorticoid)

Aldosterone
(a mineralocorticoid)

(a) Steroid hormones made in adrenal cortex



Testosterone
(an androgen)

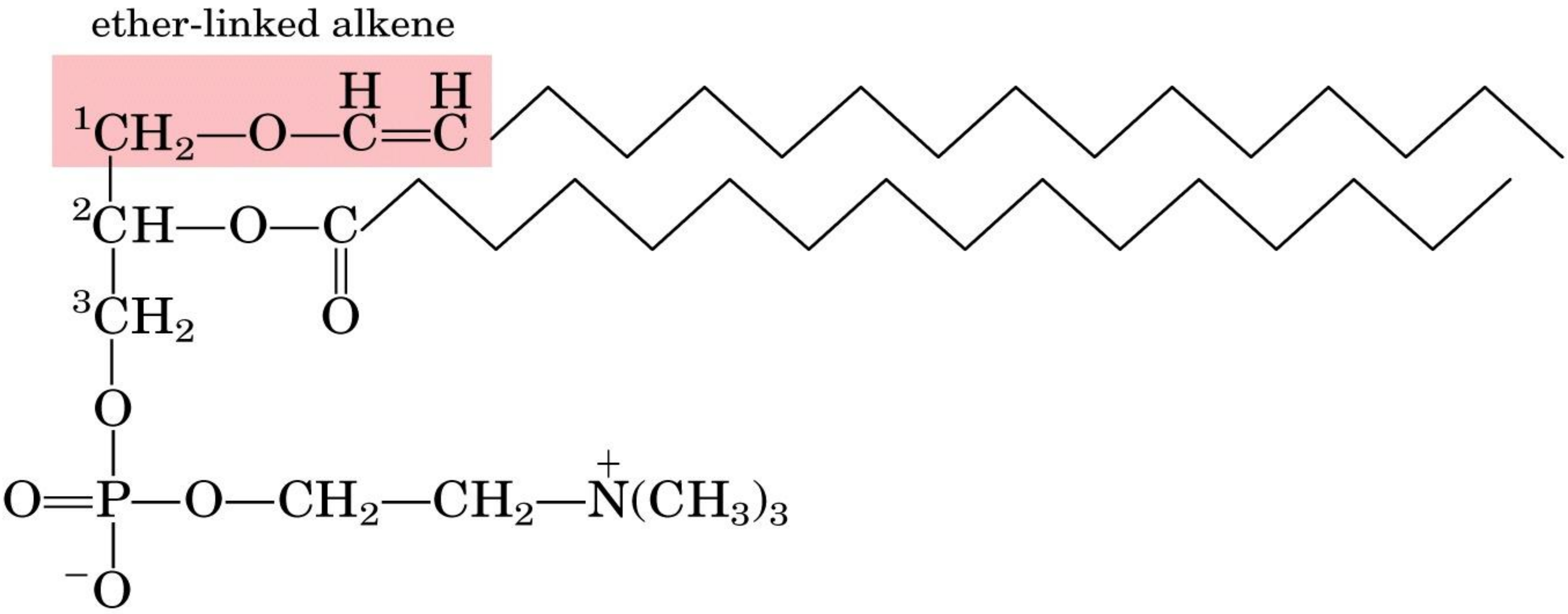
Estradiol
(an estrogen)

Progesterone
(a progestin)

(b) Steroid hormones made primarily in gonads

Ether lipids. Plasmalogens

The head-group alcohol is choline in plasmalogens and in platelet-activating factor.



Plasmalogen

All eicosanoids are derived from arachidonic acid (20:4($\Delta^{5,8,11,14}$)) **(Fig. 10–18)**, the 20-carbon polyunsaturated fatty acid from which they take their general name (Greek *eikosi*, "twenty"). There are three classes of eicosanoids: prostaglandins, thromboxanes, and leukotrienes.

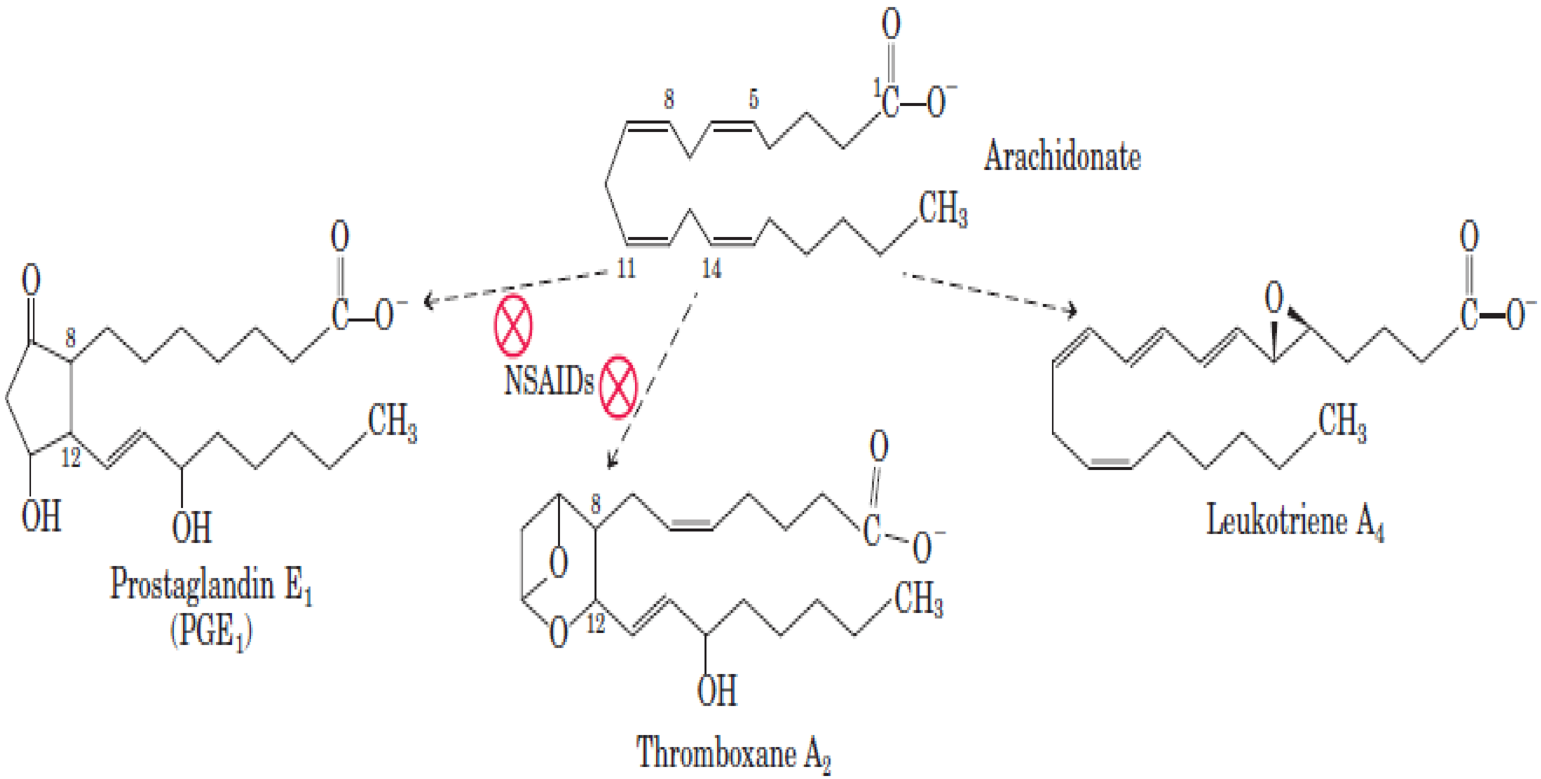


FIGURE 10–18 Arachidonic acid and some eicosanoid derivatives. Arachidonic acid (arachidonate at pH 7) is the precursor of eicosanoids, including the prostaglandins, thromboxanes, and leukotrienes. In prostaglandin E_1, C-8 and C-12 of arachidonate are joined to form the characteristic five-membered ring. In thromboxane A_2, the C-8 and C-12 are joined and an oxygen atom is added to form the six-membered ring. Leukotriene A_4 has a series of three conjugated double bonds. Nonsteroidal antiinflammatory drugs (NSAIDs) such as aspirin and ibuprofen block the formation of prostaglandins and thromboxanes from arachidonate by inhibiting the enzyme cyclooxygenase (prostaglandin H_2 synthase).

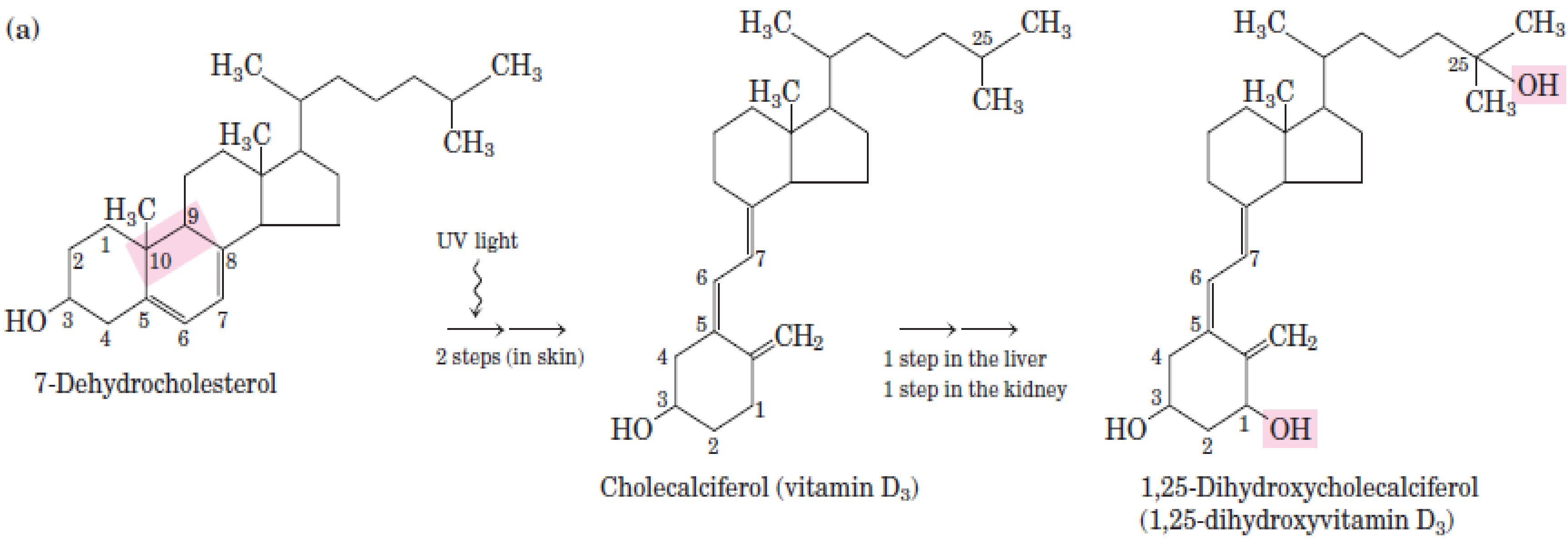
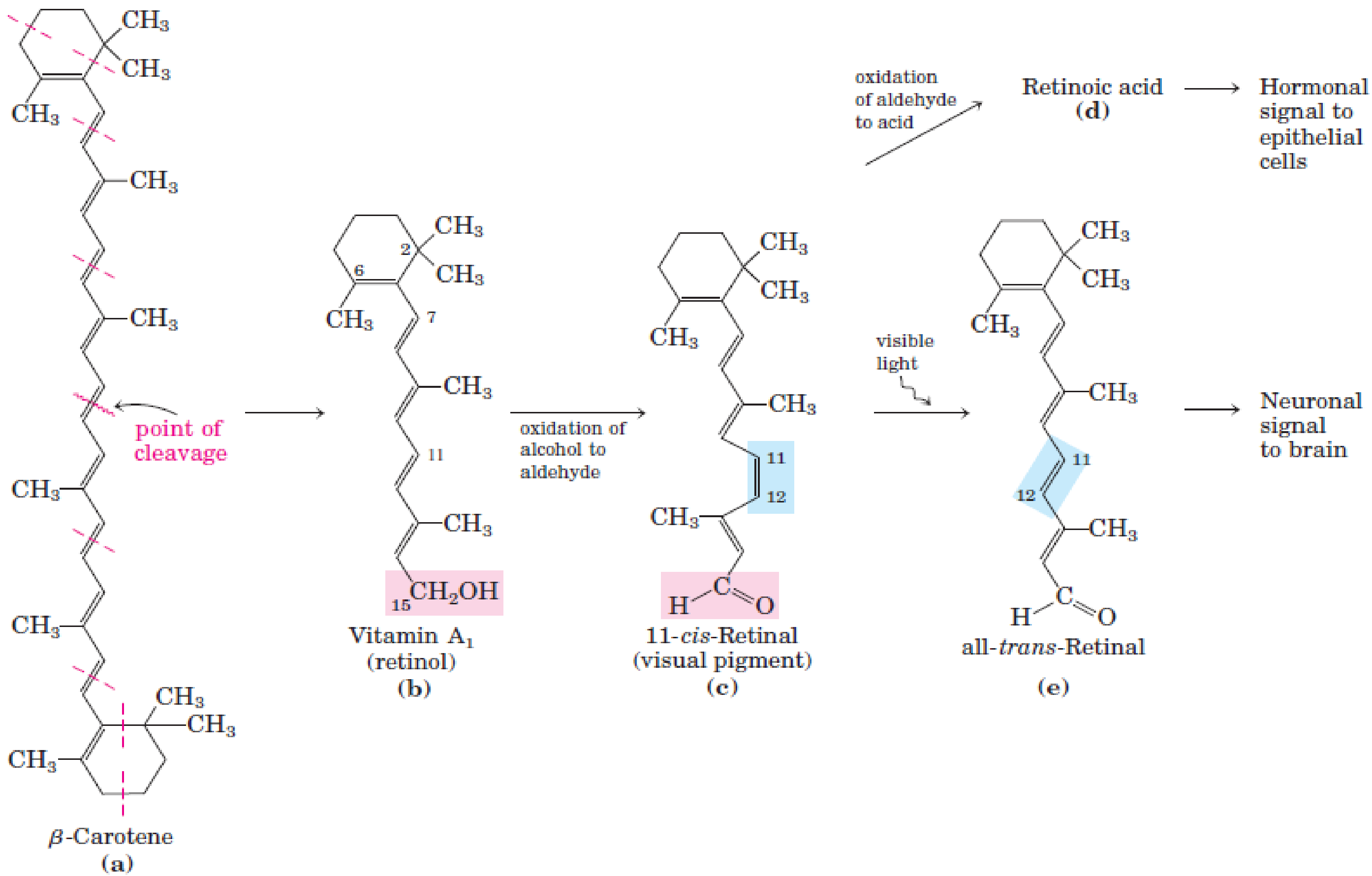


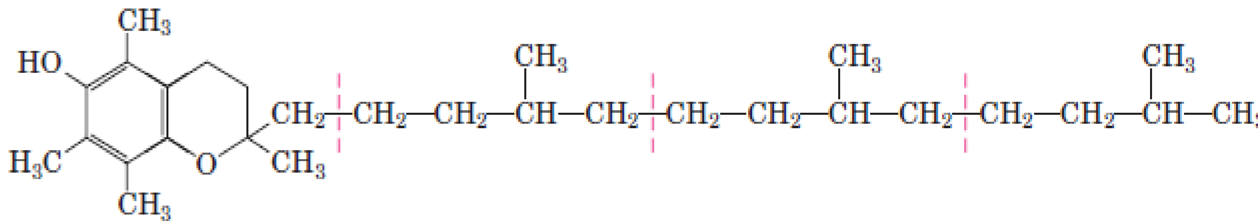
FIGURE 10–20 Vitamin D_3 production and metabolism. **(a)** Cholecalciferol (vitamin D_3) is produced in the skin by UV irradiation of 7-dehydrocholesterol, which breaks the bond shaded pink. In the liver, a hydroxyl group is added at C-25; in the kidney, a second hydroxylation at C-1 produces the active hormone, 1,25-dihydroxycholecalciferol. This hormone regulates the metabolism of Ca^{2+} in kidney, intestine, and bone. **(b)** Dietary vitamin D prevents rickets, a disease once common in cold climates where heavy clothing blocks the UV component of sunlight necessary for the production of vitamin D_3 in skin. In this detail from a large mural by John Steuart Curry,



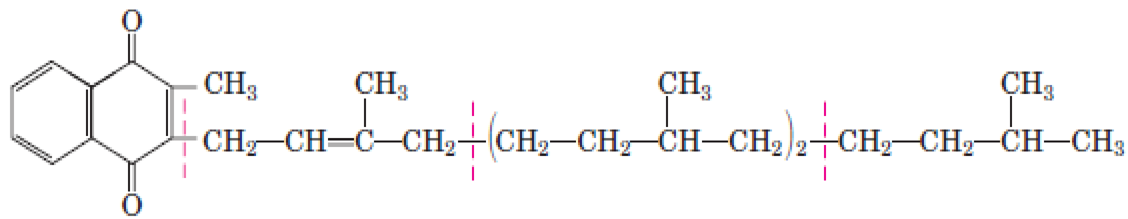
(a)

FIGURE 10–21 Vitamin A_1 and its precursor and derivatives. (**a**) β-Carotene is the precursor of vitamin A_1. Isoprene structural units are set off by dashed red lines (see p. 359). Cleavage of β-carotene yields two molecules of vitamin A_1 (retinol) (**b**). Oxidation at C-15 converts retinol to the aldehyde, retinal (**c**), and further oxidation produces retinoic acid (**d**), a hormone that regulates gene expression. Retinal combines with the protein opsin to form rhodopsin (not shown), a visual pigment widespread in nature. In the dark, retinal of rhodopsin is in the 11-*cis* form (**c**). When a rhodopsin molecule is excited by visible light, the 11-*cis*-retinal undergoes a series of photochemical reactions that convert it to all-*trans*-retinal (**e**), forcing a change in the shape of the entire rhodopsin molecule. This transformation in the rod cell of the vertebrate retina sends an electrical signal to the brain that is the basis of visual transduction, a topic we address in more detail in Chapter 12.

(a)
Vitamin E: an antioxidant



(b)
Vitamin K_1: a blood-clotting cofactor (phylloquinone)



(c)
Warfarin: a blood anticoagulant

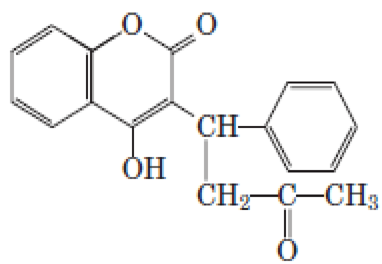


FIGURE 10–22 Some other biologically active isoprenoid compounds or derivatives. Units derived from isoprene are set off by dashed red lines. In most mammalian tissues, ubiquinone (also called coenzyme Q) has 10 isoprene units. Dolichols of animals have 17 to 21 isoprene units (85 to 105 carbon atoms), bacterial dolichols have 11, and those of plants and fungi have 14 to 24.