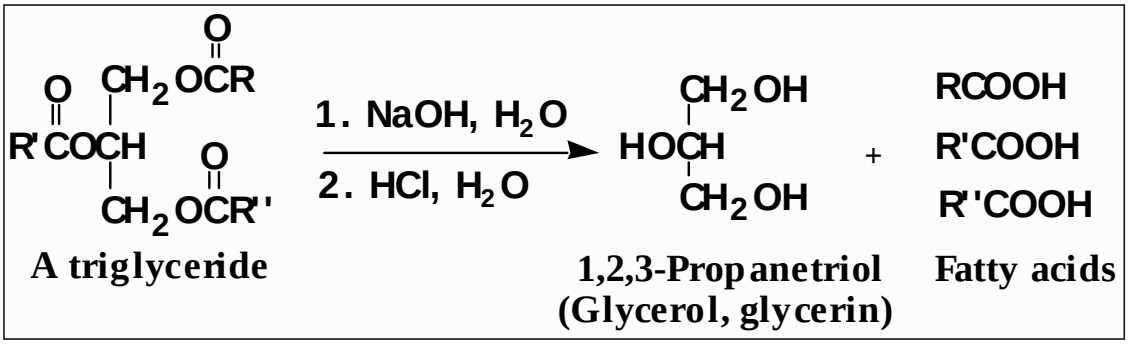
Lipids

- **Lipids:** a heterogeneous class of naturally occurring organic compounds classified together on the basis of common solubility properties
  - they are insoluble in water but soluble in aprotic organic solvents, including diethyl ether, methylene chloride, and acetone

- Lipids include
  - –triglycerides, phospholipids, prostaglandins, prostacyclins, and fat-soluble vitamins
  - –cholesterol, steroid hormones, and bile acids

Triglycerides

- **Triglyceride:** an ester of glycerol with three fatty acids

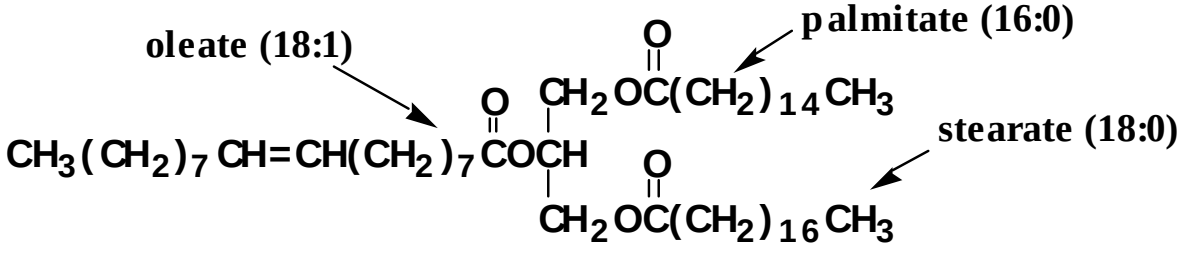


Fatty acid

- **Fatty acid:** a carboxylic acid derived from hydrolysis of animal fats, vegetable oils, or membrane phospholipids
  - nearly all have an even number of carbon atoms, most between 12 and 20, in an unbranched chain
  - the three most abundant are palmitic (16:0), stearic acid (18:0), and oleic acid (18:1)

Fatty acid

- the three most abundant are palmitic (16:0), stearic acid (18:0), and oleic acid (18:1)
- In this labeling system: (carbon #:alkene #)



Fatty acid

- in most unsaturated fatty acids, the *cis* isomer predominates; the *trans* isomer is rare
- unsaturated fatty acids have lower melting points than their saturated counterparts; the greater the degree of unsaturation, the lower the melting point

Triglycerides

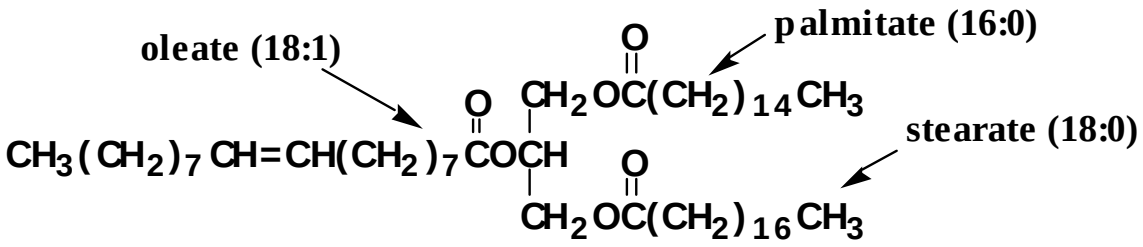
- Physical properties depend on the fatty acid components
  - melting point increases as the number of carbons in its hydrocarbon chains increases and as the number of double bonds decreases

Triglycerides

- –triglycerides rich in unsaturated fatty acids are generally liquid at room temperature and are called **oils**
- –triglycerides rich in **saturated fatty acids** are generally semisolids or solids at room temperature and are called **fats**

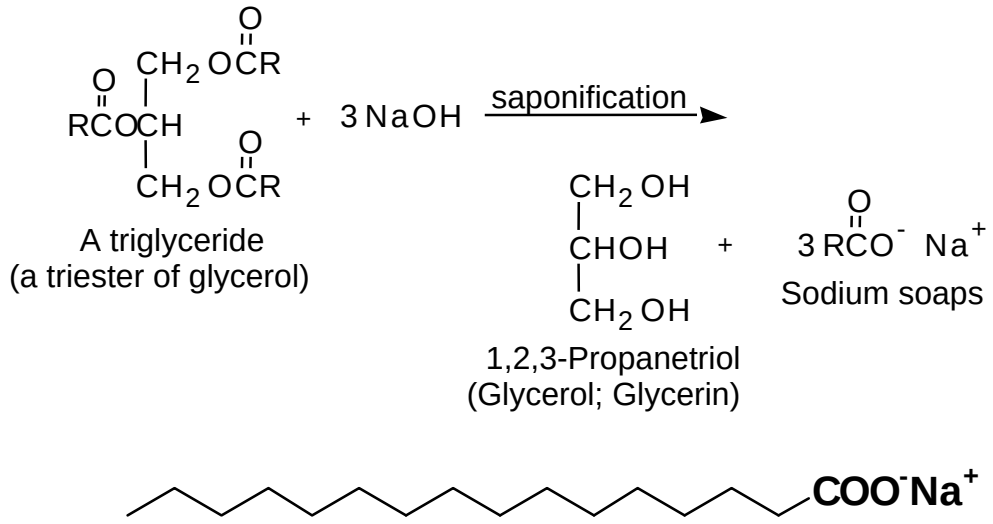
Triglycerides

– example: a triglyceride derived from one molecule each of palmitic acid, oleic acid, and stearic acid, the three most abundant fatty acids in the biological world



Soaps and Detergents

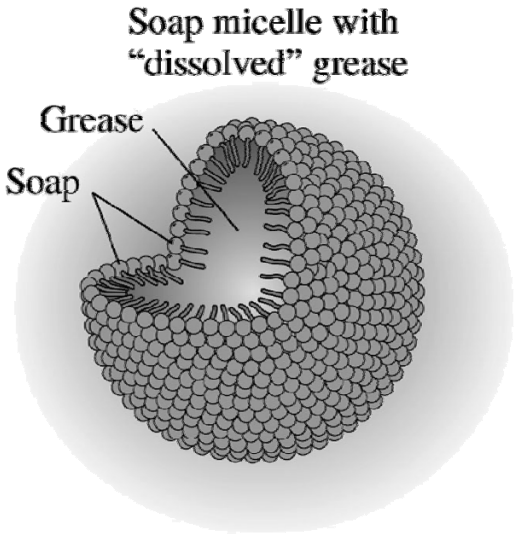
- Natural soaps are prepared by boiling lard or other animal fat with NaOH, in a reaction called ***saponification*** (Latin, *sapo*, soap)



Soaps and Detergents

- Soaps clean by acting as emulsifying agents
  - their long hydrophobic hydrocarbon chains are insoluble in water and tend to cluster in such a way as to minimize their contact with water
  - their polar hydrophilic carboxylate groups, on the other hand, tend to remain in contact with the surrounding water molecules
  - driven by these two forces, soap molecules spontaneously cluster into ***micelles***

– a soap micelle: nonpolar (hydrophobic) hydrocarbon chains cluster in the inside and polar (hydrophilic) carboxylate groups lie on the surface



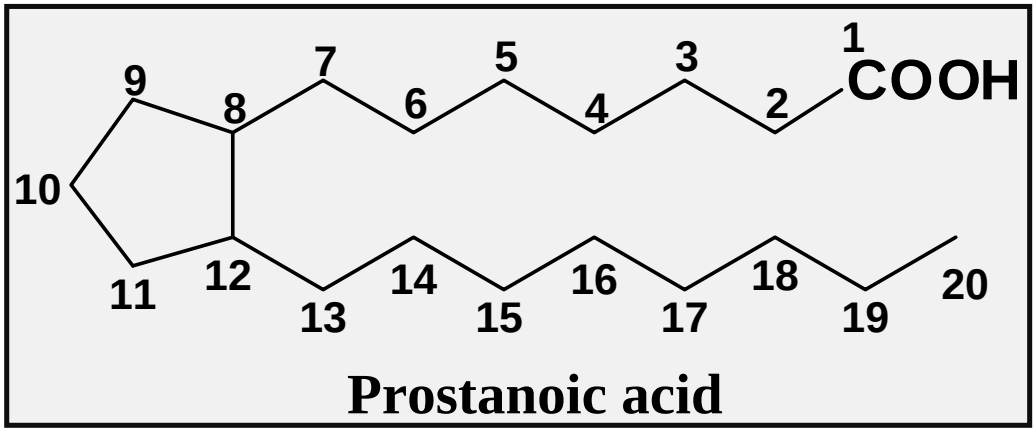
Soaps and Detergents

– **micelle**: a spherical arrangement of organic molecules in water clustered so that their hydrophobic parts are buried inside the sphere and their hydrophilic parts are on the surface of the sphere and in contact with water

– when soap is mixed with water-insoluble grease, oil, and fats, the nonpolar parts of the soap micelles "dissolve" these nonpolar dirt molecules and they are carried away in the polar wash water

Prostaglandins

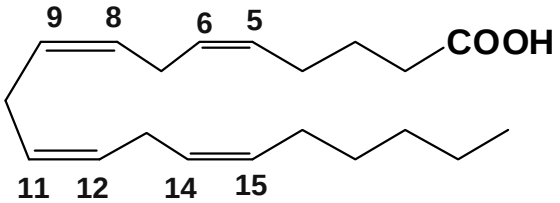
- **Prostaglandins**: a family of compounds that have the 20-carbon skeleton of prostanoic acid



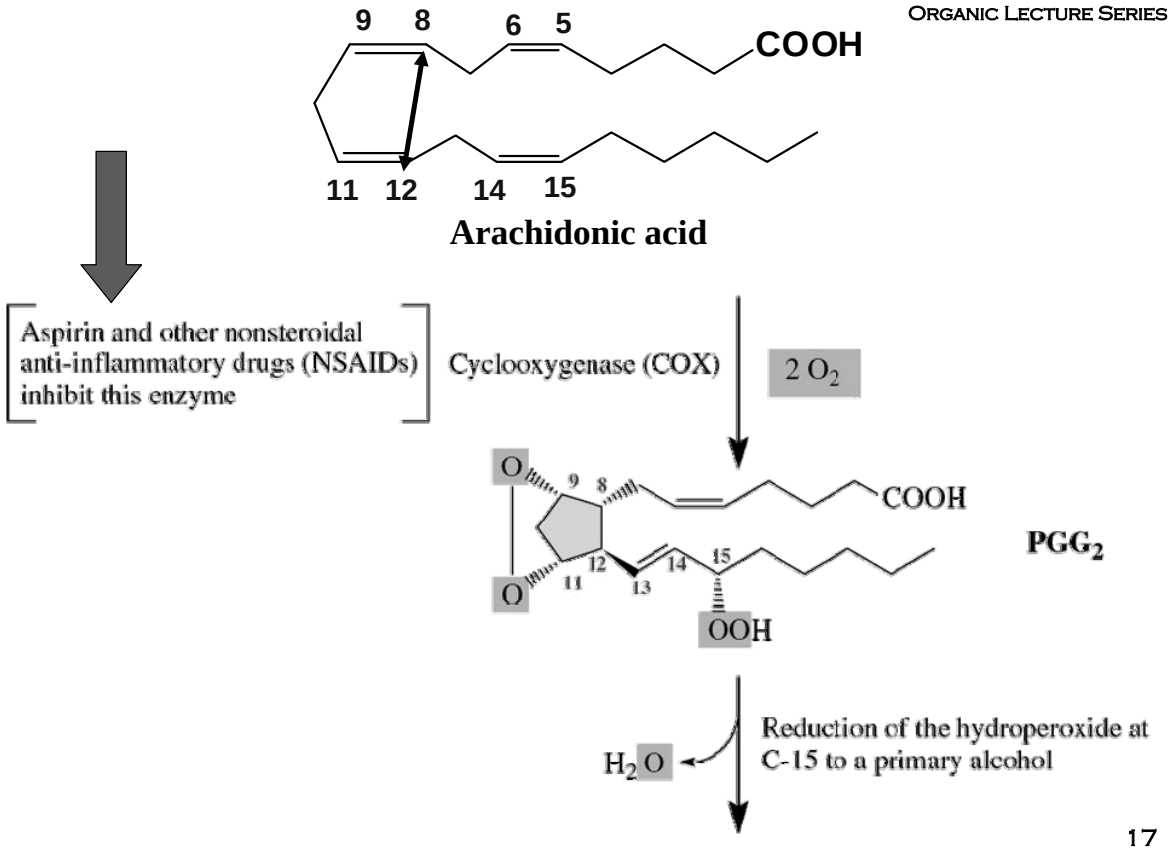
Prostanoic acid

Prostaglandins

- Prostaglandins are not stored in tissues as such, but are synthesized from membrane-bound 20-carbon polyunsaturated fatty acids in response to specific physiological triggers
  - one such polyunsaturated fatty acid is arachidonic acid (notice the all *cis* configurations)

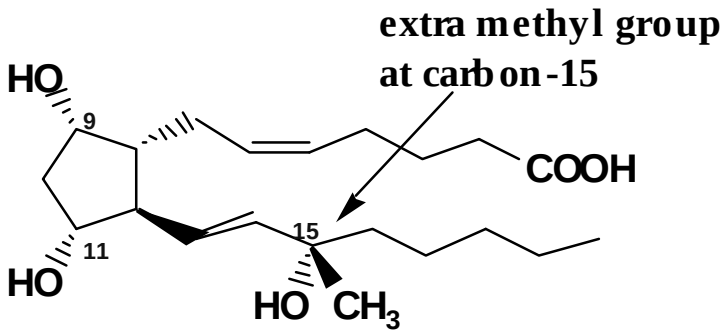


Arachidonic acid



Prostaglandins

- Research on the involvement of PGs in reproductive physiology has produced several clinically useful derivatives
  - (15*S*)-15-methyl-$PGF_{2\alpha}$ is used as a therapeutic abortifacient

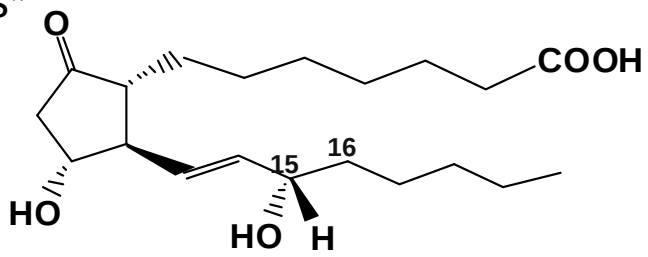


(15*S*)-15-Methyl-$PGF_{2\alpha}$

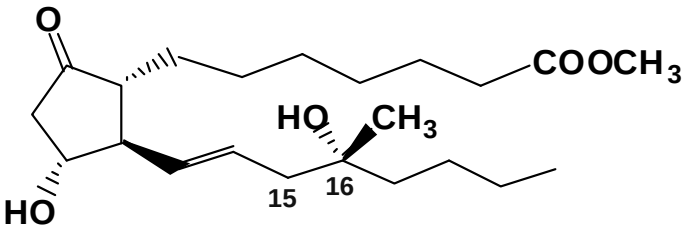
Prostaglandins

the PGE_1 analog, misoprostol, is used to prevent the ulceration associated with the use of aspirin-like NSAIDs*

PGE_1



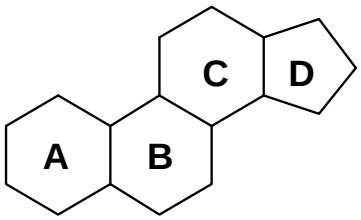
Misoprostol



*Non-Steroidal Anti-Inflamatory Drugs

Steroids

- **Steroids:** a group of plant and animal lipids that have this tetracyclic ring structure:

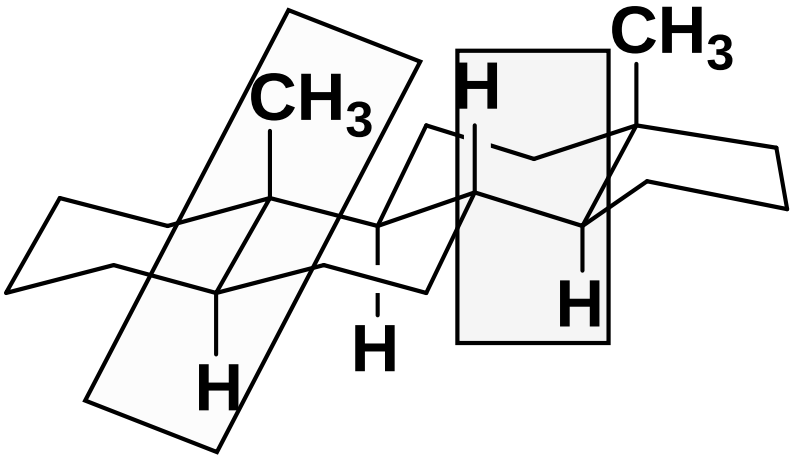


- The features common to the ring system of most naturally occurring steroids are:

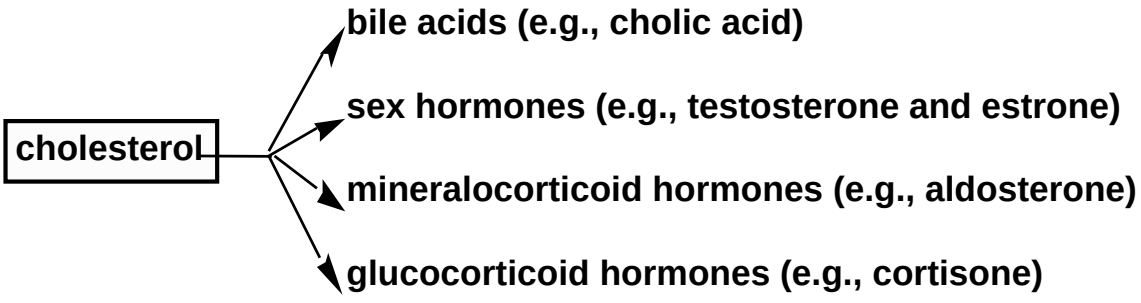
Steroids

– the fusion of rings is *trans* and each atom or group at a ring junction is axial

– the pattern of atoms or groups along the ring junctions is nearly always *trans*-anti-*trans*-anti-*trans*

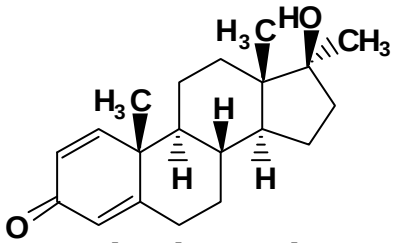


Cholesterol is the Precursor for Families of Steroids

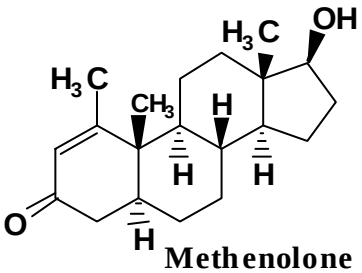


Synthetic Anabolic Steroids

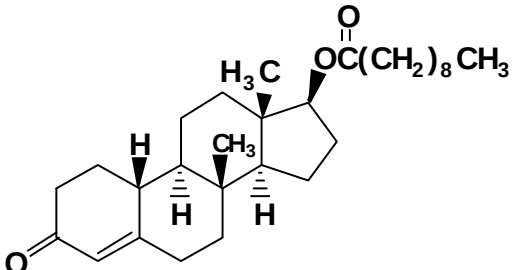
– a way to increase the testosterone concentration is to use a “prohormone”, which the body converts to testosterone; for example “andro”



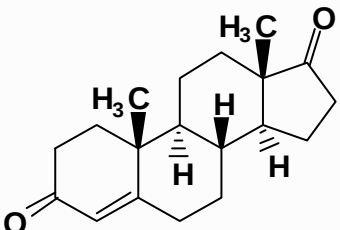
Methandrostenolone



Methenolone



Nandrolone decanoate

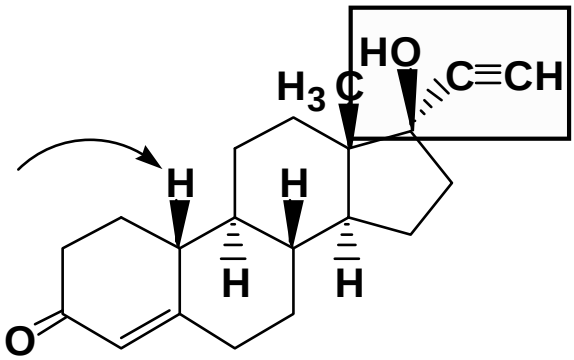


4-Androstene-3,17-dione
(andro)

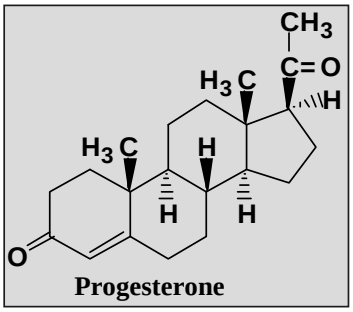
Synthetic Estrogens

- Progesterone-like analogs are used in oral contraceptives

"Nor" refers to the absence of a methyl group here. The methyl group is present in ethindrone

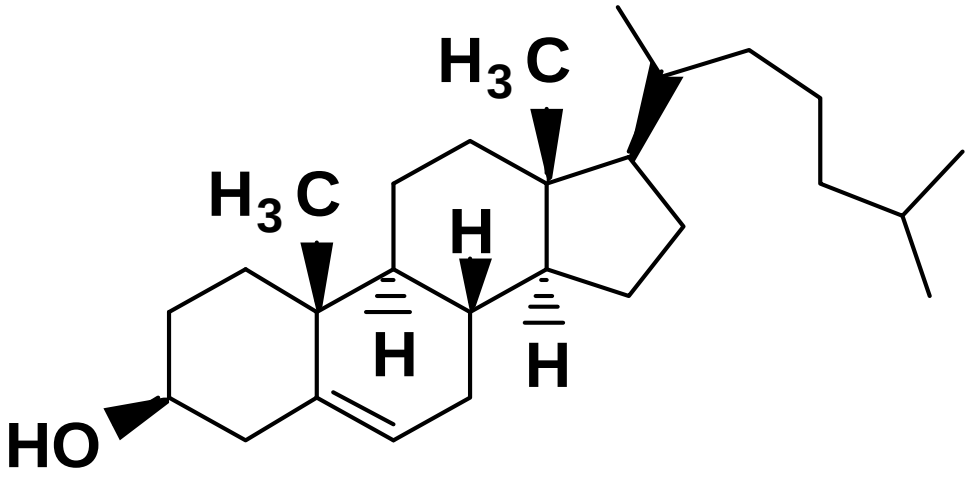


Norethindrone



Progesterone

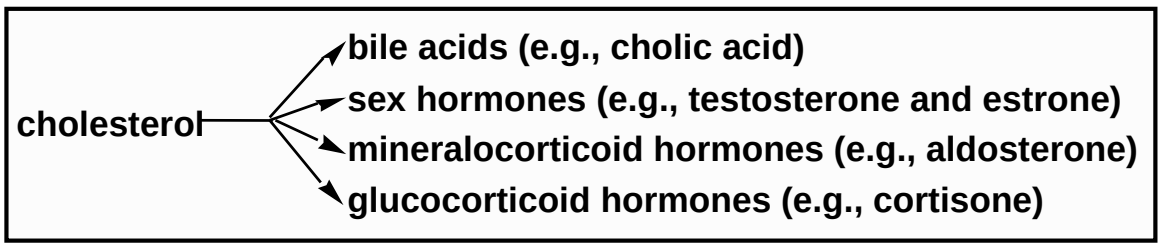
Cholesterol



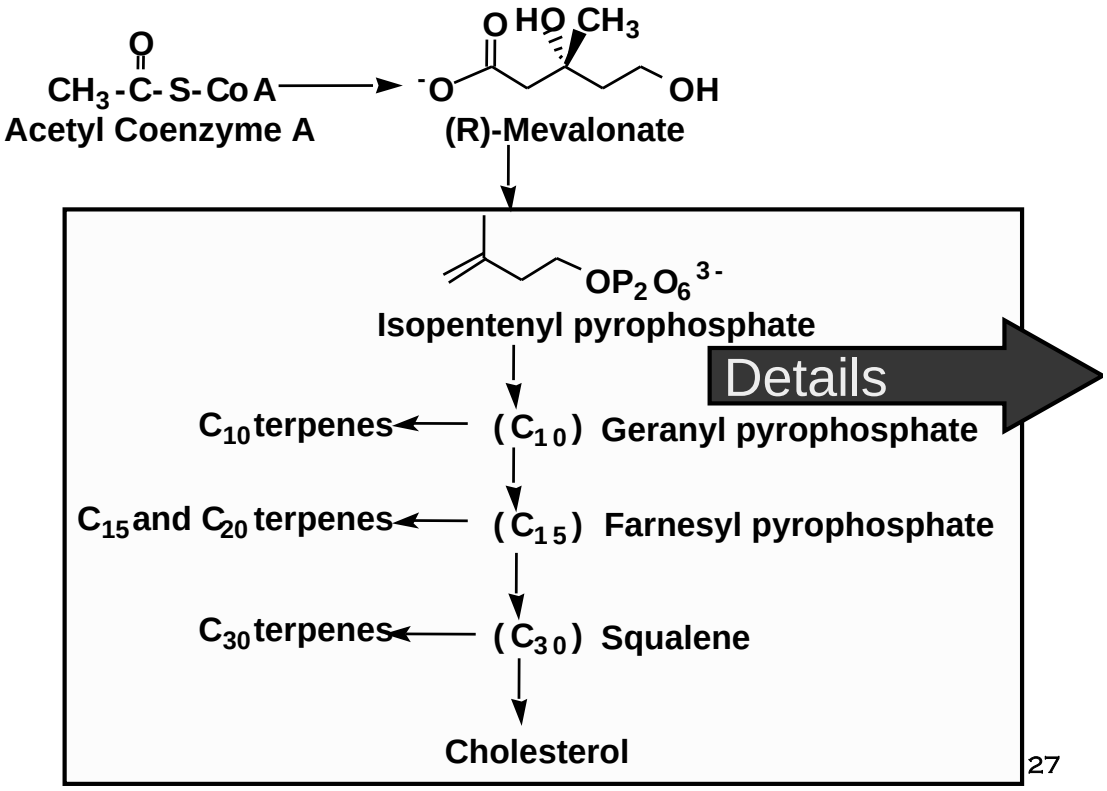
Biosynthesis of Steroids

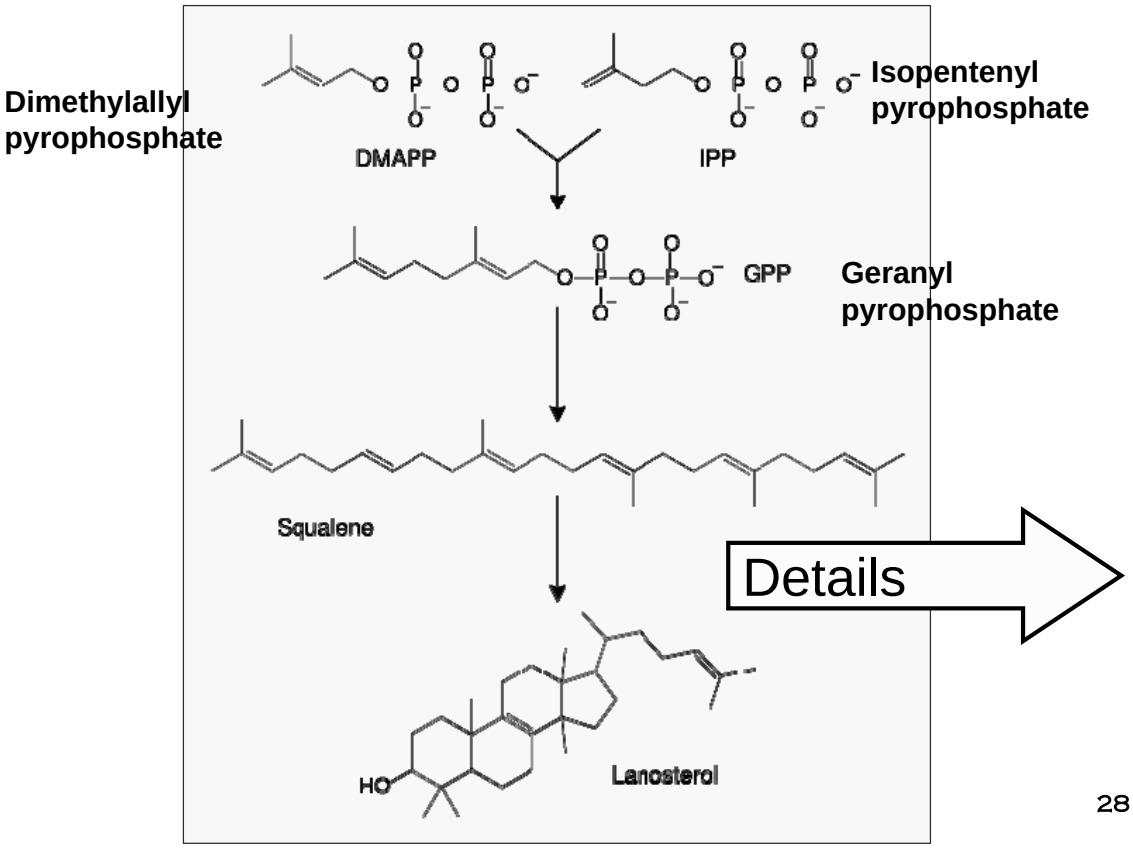
The building block from which all carbon atoms of steroids are derived is the two carbon acetyl group of acetyl-CoA-

- **Stage 1:** synthesis of isopentenyl pyrophosphate from three molecules of acetyl-CoA
- **Stage 2:** synthesis of cholesterol
- **Stage 3:** conversion of cholesterol to other steroids

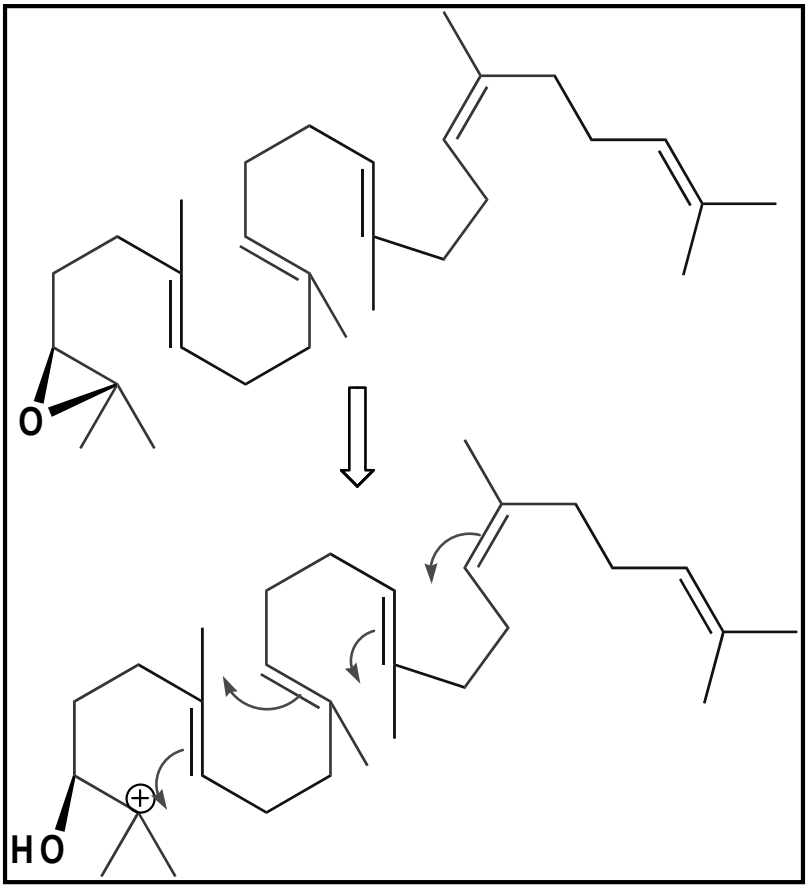


Biosynthesis of Cholesterol



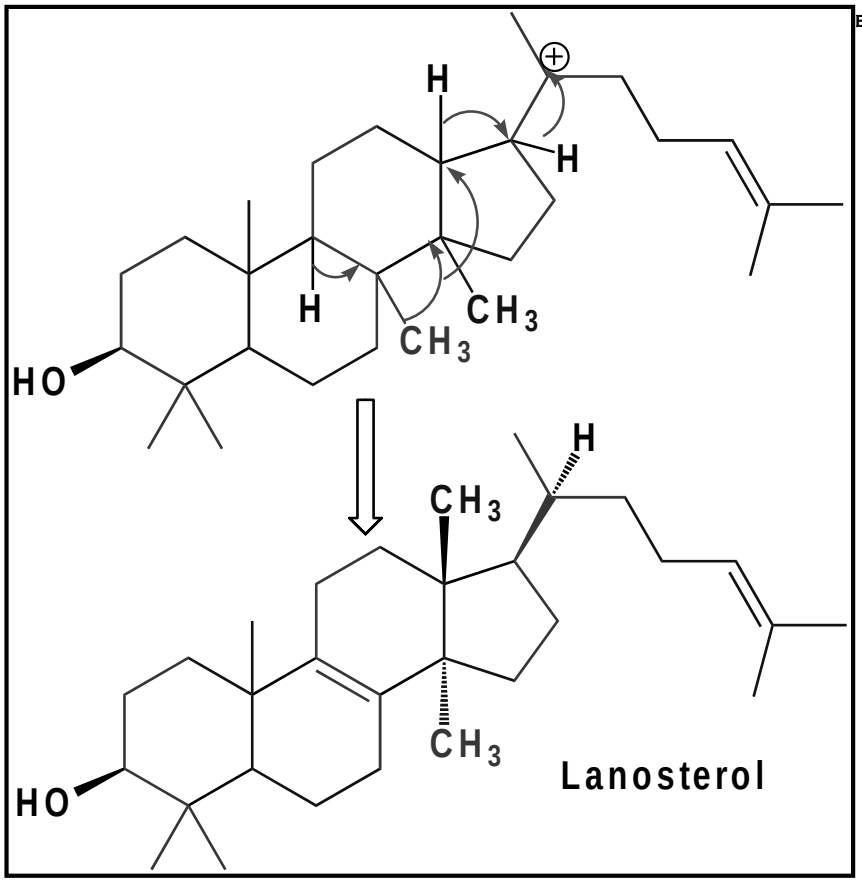


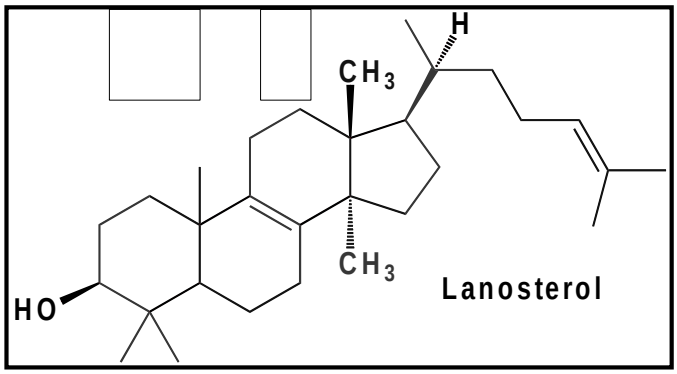
Squalene Oxide



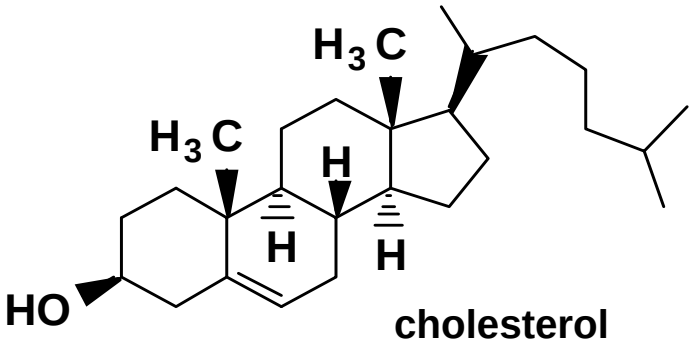
4-ring closures Form the ABCD ring system

Loss of proton; 2 hydride and 2 methyl group shifts gives Lanosterol

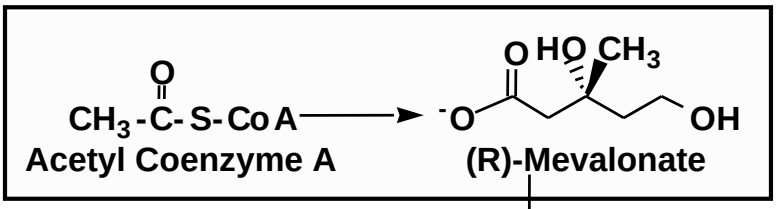




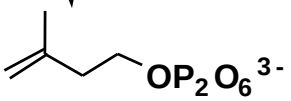
SEVERAL STEPS



cholesterol



Details



Isopentenyl pyrophosphate

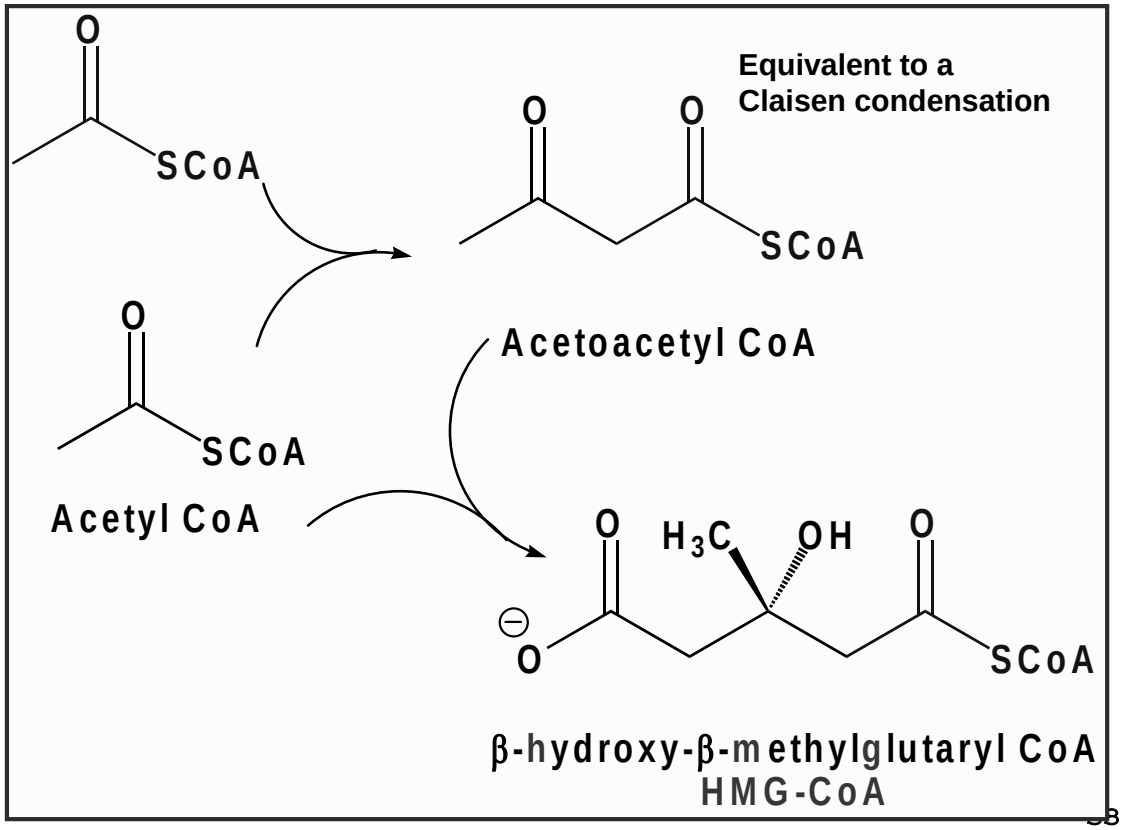
C_{10} terpenes ← (C_{10}) Geranyl pyrophosphate

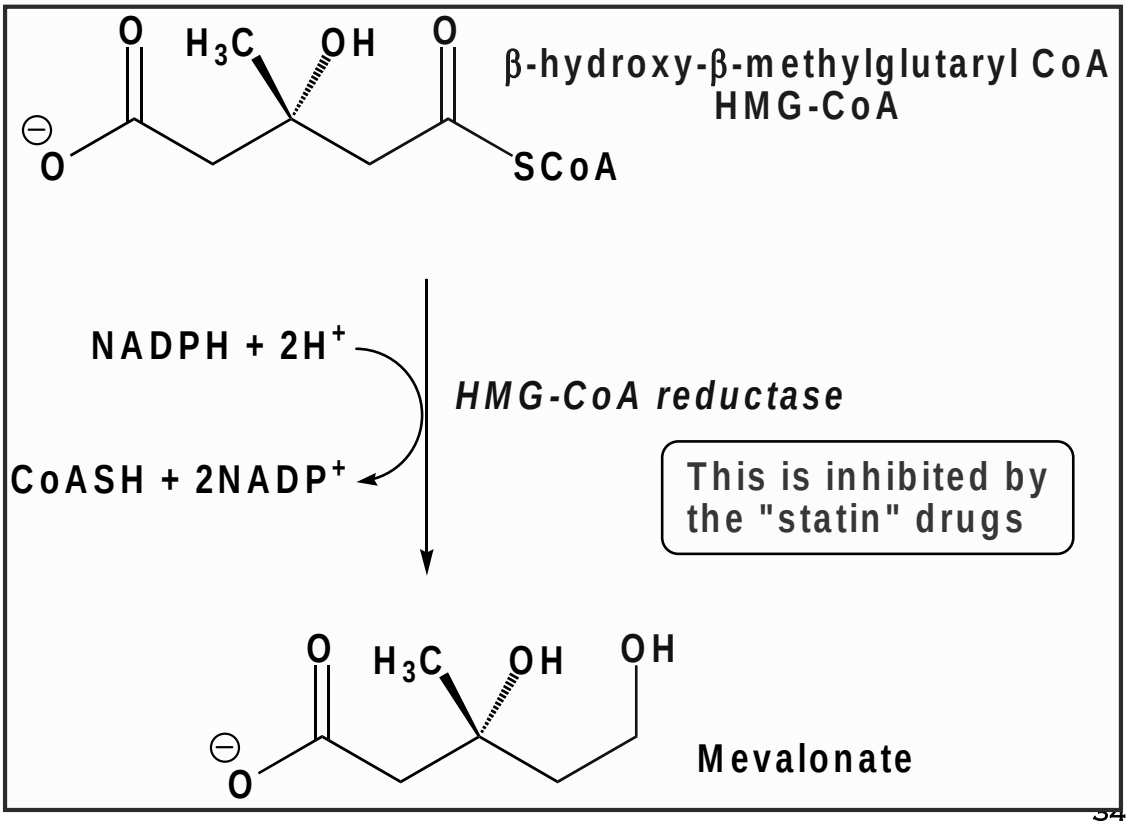
C_{15} and C_{20} terpenes ← (C_{15}) Farnesyl pyrophosphate

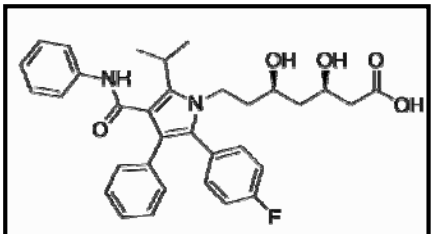
C_{30} terpenes ← (C_{30}) Squalene

Lanosterol

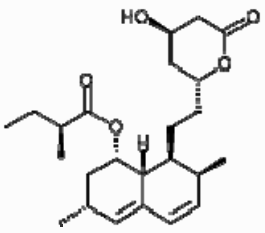
Cholesterol


Equivalent to a
Claisen condensation
SCoA
SCoA
Acetoacetyl CoA
SCoA
Acetyl CoA
H3C
OH
SCoA
β-hydroxy-β-methylglutaryl CoA
HMG-CoA

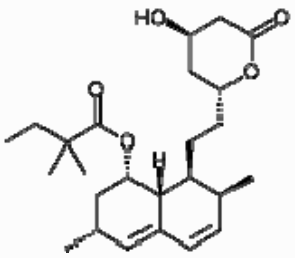

H3C
OH
SCoA
β-hydroxy-β-methylglutaryl CoA
HMG-CoA
NADPH + 2H+
CoASH + 2NADP+
HMG-CoA reductase
This is inhibited by
the "statin" drugs
H3C
OH
OH
Mevalonate



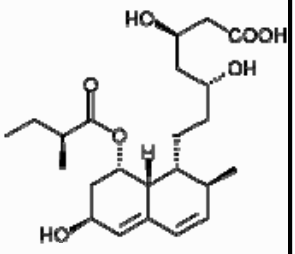
Atorvastatin
Lipitor



Lovastatin
Mevacor



Simvastatin
Zocor



Pravastatin
Pravacol