# 21: Lipids

- *Structures of Lipids*
- *Biosynthesis of Lipids*

## Preview

**Lipids** are biological molecules soluble in organic solvents such as alcohols and ethers. They include **fats**, **oils**, **waxes**, **terpenes**, **steroids**, **prostaglandins**, and molecular components of **membranes**. We begin this chapter with an exploration of their structures and properties and conclude it with a description of their biosynthetic origins. *Lipids* have different types of functional groups so they are not a discrete "class" of organic molecules such as those we have studied in previous chapters or will study in the final chapters of this text. However, they share the common feature that their biosynthetic origin is the fundamental biological building block **acetyl CoA**. [graphic 21.1]

## 21.1 Structures of Lipids

The functional groups of *fats*, *oils*, *waxes*, and *prostaglandins* are significantly different from those of *terpenes* and *steroids*.

***Fats, Oils, and Related Compounds*** (21.1A)

*Fats* and *oils* are **triacylglycerols** (**triglycerides**) with three ester (acyl) groups. [graphic 21.2] These groups $R_1C(=O)$, $R_2C(=O)$, and $R_3C(=O)$ have unbranched carbon chains (typically $C_{12}$ to $C_{24}$) that are saturated alkyl groups, or unsaturated groups with one or more C=C double bonds. [graphic 21.3] The three R groups can be the same (**simple triglycerides**) or different (**mixed triglycerides**). We refer to triglycerides that are solid at room temperature as *fats*, and those that are liquid as *oils*.

***Fatty Acids***. Hydrolysis of fats or oils converts their ester groups into free carboxylic acids and **glycerol**. [graphic 21.4] We call carboxylic acids from fats and oils **fatty acids** and common examples are given in Table 21.1 [next page]. We will see later in the chapter that *fatty acids* have an even number of C's

because they form from $CH_3C(=O)$ groups in acetyl-CoA. The C=C bonds of unsaturated fatty acids are *cis.* [Table 21.1]

**Table 21.1. Some Common Fatty Acids**

| $C_n$ | Structure | Common Name |
|---|---|---|
| Saturated | | |
| $C_{12}$ | $CH_3$-$(CH_2)_{10}$-$CO_2H$ | lauric acid |
| $C_{14}$ | $CH_3$-$(CH_2)_{12}$-$CO_2H$ | myristic acid |
| $C_{16}$ | $CH_3$-$(CH_2)_{14}$-$CO_2H$ | palmitic acid |
| $C_{18}$ | $CH_3$-$(CH_2)_{16}$-$CO_2H$ | stearic acid |
| Unsaturated* | | |
| $C_{18}$ | $CH_3$-$(CH_2)_7$-$(CH$=$CH$-$CH_2)_1$-$(CH_2)_6$-$CO_2H$ | oleic acid |
| $C_{18}$ | $CH_3$-$(CH_2)_4$-$(CH$=$CH$-$CH_2)_2$-$(CH_2)_6$-$CO_2H$ | linoleic acid |
| $C_{18}$ | $CH_3$-$(CH_2)_1$-$(CH$=$CH$-$CH_2)_3$-$(CH_2)_6$-$CO_2H$ | linolenic acid |
| $C_{20}$ | $CH_3$-$(CH_2)_4$-$(CH$=$CH$-$CH_2)_4$-$(CH_2)_2$-$CO_2H$ | arachidonic acid |

* Structural formulas are abbreviated for ease of comparison.

***A Comparison of Fats and Oils***. *Oils* have higher percentages of unsaturated fatty acid acyl groups, and lower percentages of saturated fatty acid acyl groups, than fats. You can see this in the acyl group compositions of **beef tallow** (a fat) and **peanut oil** in Table 21.2. [Table 21.2] The high percentage of unsaturated fatty acid acyl side chains in oils lowers their melting points compared to fats of the same molecular mass because *cis* C=C bonds decrease their solid-state packing efficiency.

**Table 21.2. Acyl Group Composition of Beef Tallow and Peanut Oil**

| Acyl Group | Beef Tallow %-Acyl Group* | Peanut Oil %-Acyl Group* |
|---|---|---|
| myristoyl ($C_{14}$) | 4 | 0 |
| palmitoyl ($C_{16}$) | 30 | 10 |
| stearoyl ($C_{18}$) | 20 | 4 |
| (total saturated) | (54) | (14) |
| oleoyl ($C_{18}$) | 40 | 45 |
| linoleoyl ($C_{18}$) | 2 | 30 |
| (total unsaturated) | (42) | (75) |

*Total percentages are <100% because there are other acyl groups not listed.

***Hydrogenation of Fats and Oils***. Hydrogenation of fats or oils transforms *unsaturated* acyl side chains into *saturated* acyl side chains as shown here for conversion of liquid *trioleoylglycerol* (**triolein**, m.p. -5°) into solid *tristearoylglycerol* (**tristearin**, m.p. 55°). [graphic 21.5] Since oleoyl, linoleoyl, and linolenoyl groups are all $C_{18}$, complete hydrogenation transforms each of them into $C_{18}$ stearoyl groups. Industrial laboratories use hydrogenation to increase the melting points of fats and oils. You may have noticed that various "partially hydrogenated" oils are ingredients in many food products. The major difference between "soft margarines" sold in plastic tubs, and the harder margarine sold in wrapped "sticks" is the extent of hydrogenation of the vegetable oils that are their primary ingredients.

> **Partially Hydrogenated Vegetable Oils and Your Health**. Nutritional experts tell us that highly unsaturated triglycerides are better for our health than saturated triglycerides. Since hydrogenation reduces unsaturation, we can conclude that partially hydrogenated fats and oils are less nutritionally desirable than those that are not hydrogenated. During hydrogenation, *cis* C=C bonds isomerize to *trans* C=C bonds and recent studies suggest that fats and oils with *trans* C=C bonds have the same disadvantages with respect to our health as those with saturated side chains.

***Soaps.*** Base catalyzed hydrolysis of *fats* or *oils* (**saponification**) gives sodium or potassium salts of fatty acids that we call **soaps**. [graphic 21.6] *Soaps* are not lipids! We discuss them here because they come from lipids and are of significant historical and commercial importance.

> **Early Soap Making**. The art of making soap is thousands of years old. The Romans made soap by heating animal fat with ashes from wood fires and early immigrants and pioneers in this country made soap in the same way. Animal fat contains water, and ashes contain strong bases, so this soap-making process is akin to saponification carried out in a laboratory.

Soaps work as cleansing agents in water because they combine with grease to form **micelles**. [graphic 21.7] These *micelles* are water miscible aggregates with polar (**hydrophilic**) exteriors and nonpolar (**hydrophobic**) interiors. The long chain hydrocarbon "tails" of soap molecules dissolve in grease droplets in water forming a micelle with the $CO_2^-$ groups of the fatty acid carboxylates on its

surface. The negatively charged surface of the spherical micelle hydrogens bonds to water molecules. This solubilizes grease so that the rinsing process removes it along with the micelles.

***Detergents.*** While $Na^+$ and $K^+$ salts of fatty acid carboxylates (*soaps*) are soluble in water, this is not the case for their $Ca^{+2}$ and $Mg^{+2}$ salts. Since hard water contains high concentrations of $Ca^{+2}$ and $Mg^{+2}$ ions, the fatty acid carboxylate salts of these ions precipitate when we add soaps to hard water. Beside being unsightly, this insoluble soap "scum" ("bathtub ring") is not effective in solubilizing grease. In contrast, calcium and magnesium salts of organic sulfonates ($R\text{-}SO_3^-$) with long alkyl chains (R) are water soluble. [graphic 21.8] Since these long chain organic sulfonates (**synthetic detergents**) form grease dissolving micelles as effectively as soaps, they take the place of soaps in many cleaning products. While soaps come from base catalyzed hydrolysis of natural fats and oils, most synthetic detergents come from petroleum sources. Examples include $Na^+$, or $K^+$, or $NR_4^+$ alkylbenzenesulfonates ($R\text{-}Ph\text{-}SO_3^-$) prepared by alkylation followed by sulfonation of benzene. [graphic 21.9]

***Waxes***. Plants and animals synthesize high molecular mass esters called **waxes**. [graphic 21.10] The acyl components of *waxes* come from fatty acids that often have much higher molecular masses than those of fats and oils. Their alcohol components arise from reduction of these high mass fatty acids. Animal waxes include **spermaceti** from sperm whales, and **beeswax**. A representative plant wax is **Carnauba wax** found on the leaves of **Brazilian Wax Palms** (Table 21.3). [Table 21.3] Naturally occurring "waxes" can be mixtures of different esters (*waxes*) and they can also include small amounts of high molecular mass *alkanes* such as $CH_3(CH_2)_{19}CH_3$ and $CH_3(CH_2)_{27}CH_3$ found in beeswax.

**Table 21.3. Some Components of Animal and Plant Waxes.**

| Name | Formula |
|---|---|
| spermaceti | $CH_3\text{-}(CH_2)_{14}\text{-}C(=O)\text{-}O\text{-}CH_2(CH_2)_{14}\text{-}CH_3$ |
| beeswax | $CH_3\text{-}(CH_2)_{14}\text{-}C(=O)\text{-}O\text{-}CH_2(CH_2)_{28}\text{-}CH_3$<br>$CH_3\text{-}(CH_2)_{24}\text{-}C(=O)\text{-}O\text{-}CH_2(CH_2)_{24}\text{-}CH_3$ |
| Carnauba wax | $CH_3\text{-}(CH_2)_{30}\text{-}C(=O)\text{-}O\text{-}CH_2(CH_2)_{30}\text{-}CH_3$<br>$CH_3\text{-}(CH_2)_{32}\text{-}C(=O)\text{-}O\text{-}CH_2(CH_2)_{32}\text{-}CH_3$ |

***Glycerophospholipids***. Biological membranes contain a number of different types of molecular species including **glycerophospholipids** that we also call **phosphoglycerides** or simply **phospholipids**. [graphic 21.11] They are structurally similar to triglycerides except that they have an organophosphate group as shown for **phosphatidyl choline**.

***The Biological Origin of Fatty Acids***. We have mentioned that fatty acids found as acyl groups in fats, oils, and waxes, have an even number of C atoms because they form from $C_2$ acyl groups of acetyl-CoA ($CH_3$-C(=O)-SCoA). [graphic 21.12] We will explore the reactions and intermediates of these biosynthetic pathways later in this chapter.

### ***Prostaglandins*** (21.1B)

*Prostaglandins* are $C_{20}$ carboxylic acids containing a $C_5$ ring substituted with a $C_8$ chain, and an adjacent $C_7$ chain with a terminal $CO_2H$ group. [graphic 21.13] Their common biosynthetic precursor is the $C_{20}$ unsaturated fatty acid *arachidonic acid* (four C=C bonds) that comes from *linoleic acid* (two C=C bonds) (Table 21.1). [graphic 21.14] Neither humans nor animals biosynthesize linoleic acid, so it is an essential nutrient that we and they must obtain from sources such as plant fats and oils. Prostaglandins such as those shown here have dramatic influences on biological processes including inflammation, blood clotting, blood pressure, pain, fever, and reproduction. [graphic 21.15] We will outline their biosynthesis later in this chapter.

### ***Terpenes and Steroids*** (21.1C)

Lipids that we have described so far all have ester or carboxylic acid functional groups and even numbers of C atoms. None of these features characterize *terpenes* or *steroids*.

***Terpenes***. We find *terpenes* or derivatives of terpenes in both plants and animals. [graphic 21.16] They are branched polyenes with isolated C=C bonds, that often have no other functional groups. We can dissect the carbon skeletons of terpenes into $C_5$ fragments called **isoprene units**. [graphic 21.17] You can think of an *isoprene unit* as a $C_2$ "ethyl" fragment bonded to the central C of a $C_3$ "isopropyl" fragment. This "ethyl-isopropyl" skeleton is called an *isoprene unit*

because **isoprene** (2-methyl-1,3-butadiene) has the same $C_5$ σ-skeleton. We have highlighted isoprene units in some terpenes using structures that show just their carbon σ-skeletons. [graphic 21.18] When you set out to identify isoprene units in a terpene, do not look for the conjugated C=C bonds of *isoprene*. Most isoprene units in terpenes have only one C=C bond and its position varies.

A consistent pattern for most terpenes is the "head" to "tail" attachment of isoprene units. [graphic 21.19] One of the terminal C's of the $C_3$ fragment is its "head" (C1), while the terminal C of its $C_2$ fragment is the end of its "tail" (C5). You can see in the structures above that C5 (the tail C) of one isoprene unit bonds to C1 (the head C) of another with the exception of the central C5-C5 (tail to tail) bond in squalene. While terpenes are structurally different from fats, oils, waxes, and prostaglandins, they are lipids because of their solubility in organic solvents and their biosynthetic origin from acetyl-CoA described below.

***Steroids***. *Steroids* are lipids that arise from the terpene squalene. [graphic 21.20] *Squalene* cyclizes in three steps to give **lanosterol** that then gives rise to **cholesterol** *via* a sequence of 19 reactions. *Cholesterol* is the biosynthetic precursor of all steroid hormones. [graphic 21.21] While biochemists group steroids into five major categories as shown along with these examples, they all have a number of common features. Each steroid has four fused rings (three 6-membered rings and one 5-membered ring) labeled A, B, C, and D. They also have an OH or keto group at C3, a methyl (or carbonyl) group at C10 and/or C13, and a side-chain or OH group on C17. When you consider the contrasting biological effects of *testosterone* and *estradiol*, it seems amazing that there are such small differences in their chemical structures!

## 21.2 Biosynthesis of Lipids

We can include all lipids in a general biosynthetic scheme that begins with *acetyl-CoA*. [graphic 21.22]

***Acetyl-CoA*** (21.2A)

*Acetyl-CoA* is the product of reaction sequences in which *carbohydrates* (Chapter 20), *proteins* (Chapter 22), and even *fats* and *oils*, break down *via* **catabolic pathways**. [graphic 21.23] *Acetyl-CoA* contains a $C_2$ acetyl group ($CH_3$-C(C=O)) bonded to a coenzyme called **Coenzyme A** (**CoA**) and we show it at different

levels of molecular detail in Figure (graphic 21.24). [graphic 21.24] *CoA* includes a **nucleotide** (**adenosine-3'-phosphate**) (Chapter 24), a *pyrophosphate group*, and a large organic group ("**R**") containing two amide linkages and a terminal SH group. In *acetyl-CoA*, the acetyl group replaces the H on the SH group of CoA as shown in Figure (graphic 21.24).

We can represent *acetyl-CoA* as $CH_3$-C(=O)-Y because its chemical reactivity is analogous to that of *carboxylic acid derivatives* (R-C(=O)-Y) (Chapters 15 and 16). Nucleophiles can add to the C=O group followed by loss of "Y-" or "YH" (overall nucleophilic substitution), and bases can remove protons from $CH_3$-C(=O) to give species that behave as enolate ions ($^-CH_2$-C(=O)-Y). [graphic 21.25] We will see such reactions in the following biosynthetic pathways and will point out the analogies between them and those that we have studied in previous chapters.

> **Complete Details of the Biosynthetic Pathways**. We will show only the most general features of biosynthetic pathways in this chapter. We will not describe the structures of enzymes, or other "biological reagents", that participate in these reactions. In some cases, we will depict transformations as single steps when multiple steps actually occur. You will find many of these missing details in modern biochemistry textbooks such as "Biochemistry", 2nd Edition, by D. Voet and J. G. Voet, John Wiley & Sons, Inc., New York, N. Y., 1995.

## ***Fatty Acids*** (21.2B)

Fatty acid biosynthesis occurs by several different pathways.

***Palmitic Acid***. One of these pathways combines eight $C_2$ fragments from acetyl-CoA ($CH_3$-C(=O)-S-CoA) in a stepwise manner to give the $C_{16}$ fatty acid *palmitic acid*. [graphic 21.26] It first transforms a $C_2$ *acetyl* group ($CH_3C(=O)$) into a $C_4$ *butryl* group ($CH_3(CH_2)_2C(=O)$), then into a $C_6$ *hexanoyl* group ($CH_3(CH_2)_4C(=O)$), and so on in $C_2$ increments until it reaches the $C_{16}$ *palmitoyl* group ($CH_3(CH_2)_{14}C(=O)$). In each of the 7 cycles of the pathway, the molecule that provides the $C_2$ fragment to the growing chain of the acyl group is <u>not</u> *acetyl-CoA*, but is one derived from its carboxylated derivative **malonyl-CoA**. [graphic 21.27] Before it provides the $C_2$ fragment to the growing acyl chain, the protein containing group **ACP** (**acyl-carrier protein**) replaces the CoA group of *malonyl-*

*CoA*. The resultant *malonyl-ACP* transfers the $C_2$ fragment to the growing acyl chain increasing its length from $C_n$ to $C_{n+2}$.

> **ACP**. If we represent the general structure of *CoA* as *[nucleotide]-[pyrophosphate]-["R"]*, then we can represent the general structure of *ACP* as *[protein]-[phosphate]-["R"]*. In CoA and ACP, the large organic sequence *["R"]* is the same and it binds to acyl groups *via* a terminal S atom (see Figure (graphic 21.24)).

The growing acyl chain that receives the $C_2$ fragment from *malonyl-ACP* in Step (3) is in bold font in the general structure **$CH_3$-$(CH_2)_n$-C(=O)**-S-ACP (an "acyl"-ACP) (Figure (graphic 21.27)). In the first reaction cycle, the "acyl"-ACP that reacts with malonyl-ACP in Step (3) is *acetyl-ACP* ($CH_3$-C(=O)-S-ACP). It corresponds to the general "acyl"-ACP structure when n = 0, and it forms directly from *acetyl-CoA* by a nucleophilic substitution of ACP for CoA.

In subsequent reaction cycles (Steps (3) through (6)), the "acyl"-ACP ($CH_3$-$(CH_2)_n$-C(=O)-S-ACP) that participates in Step (3) is the product of Step (6) of the preceding cycle. In the final cycle, the "acyl"-ACP from Step (6) is *palmitoyl-ACP* ($CH_3$-$(CH_2)_{14}$-C(=O)-S-ACP) and it releases *palmitic acid.*

> **A Comment about these Formulas**. The sulfur atom S attached to C=O is shown in structures such as *$CH_3$-C(=O)-S-CoA* or *$CH_3$-$(CH_2)_n$-C(=O)-S-ACP* to emphasize that *RC(=O)-Y* is a thioester (*RC(=O)-S-R'*). However, that S is actually part of *CoA* or *ACP* (see Figure (graphic 21.24)). Although we may not show S in general formulas such as *acetyl-CoA* that have no chemical symbols, it is still the atom directly bonded to the acetyl group.

***Types of Reactions in Palmitic Acid Biosynthesis***. The reactions in Figure (graphic 21.27) are analogous to reactions in previous chapters.

*Step (1): Acetyl-CoA + $CO_2$ → Malonyl-CoA*

"Aldol-type" reaction involving nucleophilic addition of an enolate ion ($^-CH_2C(=O)Y$) to carbon dioxide (O=C=O) (Chapter 18).

*Step (2): Malonyl-CoA → Malonyl-ACP*

Nucleophilic acyl substitution at C(=O)-Y (Chapter 16).

*Step (3): Malonyl-ACP + "acyl"-ACP → β-ketoacyl-ACP + $CO_2$*
Malonic ester synthesis (Chapter 18).

*Step (4): β-ketoacyl-ACP → β-hydroxyacyl-ACP*
C=O reduction to an alcohol (Chapter 17).

*Step (5): β-hydoxyacyl-ACP → α, β-unsaturated acyl-ACP*
Dehydration of a β-hydroxycarbonyl compound (Chapter 18).

*Step (6): α, β-unsaturated acyl-ACP → acyl-ACP*
Hydrogenation of a C=C bond (Chapter 11).

***Other Fatty Acids***. *Palmitic acid* ($C_{16}$) is the shortest fatty acid biosynthesized by humans and higher animals. **Elongase** enzymes convert it into higher saturated fatty acids. One *elongase* pathway uses the same sequence of steps as *palmitic acid* biosynthesis (Figure (graphic 21.27)) except *CoA* rather than *ACP* binds to all acyl groups. Another *elongase* pathway also uses *CoA* rather than *ACP*, but *acetyl-CoA* (rather than *malonyl-CoA*) provides the enolate-type ion in the chain-lengthening step (Step (3)). As a result, Step (3) in this second *elongase* pathway is a "Claisen-type" reaction (Chapter 18) instead of a "malonic ester-type" synthesis.

**Desaturase** enzymes dehydrogenate $CH_2CH_2$ groups in saturated or certain unsaturated fatty acids into *cis* CH=CH groups. [graphic 21.28] These "desaturase" reactions have specific restrictions on the values of "a" and "b" in the structures shown in Figure (graphic 21.28), and on the positions of new C=C double bonds with respect to existing C=C bonds. A major consequence is that many animals as well as humans cannot biosynthesize *linoleic acid* (a crucial precursor of *arachidonic acid* and hence *prostaglandins*). We and they must obtain it from external sources such as plant fats and oils in order to sustain proper metabolism.

***Fats, Oils and Phospholipids*** (21.2C)
The biosynthesis of fats, oils, and phospholipids requires not only fatty acids, but also the *glycerol* portion of these glycerides. [graphic 21.29] This comes from

*fructose* which organisms enzymatically convert to **dihydroxyacetone phosphate**. [graphic 21.30] *Dihydroxyacetone phosphate* (or its C=O reduction product **glycerol phosphate**) reacts stepwise with fatty acid acyl-CoA molecules to give *triglycerides* (fats and oils) or *phospholipids*. [graphic 21.31] The steps in which acyl-CoA's esterify OH groups are *nucleophilic acyl substitutions* at C(=O)-Y groups (Chapter 16). The formation of *dihydroxyacetone phosphate* from *fructose diphosphate* is a *retro aldol* reaction (Chapter 18).

***Waxes*** (21.2D)

Biosynthesis of waxes occurs by esterification of fatty acids or fatty acid acyl groups with long-chain alcohols (**fatty alcohols**). [graphic 21.32] *Fatty alcohols* come from reduction of fatty acids or fatty acid acyl groups. The *alkanes* found along with esters in waxes, such as beeswax, have an odd number of C's and result from decarboxylation of *fatty acids*.

***Prostaglandins*** (21.2E)

We mentioned earlier that *prostaglandin* formation in humans involves conversion of *linoleic acid* to *arachidonic acid* followed by its transformation into *prostaglandins* (see Figure (graphic 21.14)). *Arachidonic acid* arises from a pathway that uses *desaturase* and *elongase* enzymes. [graphic 21.33] Organisms store *arachidonic acid* as ester groups in phospholipids and release it as needed for prostaglandin synthesis. Its conversion to prostaglandins involves reactions with singlet $O_2$ (see Chapter 11/17) catalyzed by enzymes. [graphic 21.34]

***Terpenes*** (21.2F)

The $C_5$ *isoprene units* in terpenes arise in a multistep biosynthetic pathway. (1) Three acetyl-CoA molecules condense *via* a "Claisen-type" reaction followed by an "aldol-type" reaction to give the $C_6$ compound **β-hydroxy-β-methylglutaryl-CoA** (**HMG-CoA**). [graphic 21.35] (2) Reduction of the thioester group of *HMG-CoA* gives the $C_6$ compound **mevalonic acid** that is then converted to its pyrophosphate. (3) Decarboxylation of *phosphorylated mevalonate* anion gives the $C_5$ compound **isopentenyl pyrophosphate** that serves as the source of the $C_5$ isoprene units.

An example of terpene biosynthesis is that leading to the $C_{30}$ terpene **squalene**. [graphic 21.36] *Isopentenyl pyrophosphate* combines with **dimethylally pyrophosphate** (formed by allyic rearrangement of isopentenyl pyrophosphate) to give **geranyl pyrophosphate** ($C_{10}$). It in turn combines with another *isopentenyl pyrophosphate* to give **farnesyl pyrophosphate**. Two *farnesyl pyrophosphate* molecules subsequently dimerize to give *squalene*. The formation of *geranyl* or *farnesyl pyrophosphate* involves electrophilic addition of a C+ (from ionization of a -C-O-P-P group) to the terminal C of the $CH_2$=C of *isopentenyl pyrophosphate*. [graphic 21.37] In contrast, dimerization of *farnesyl pyrophosphate* occurs *via* formation of an intermediate cyclopropane structure that subsequently opens to *squalene via* rearrangements of carbocationic intermediates. [graphic 21.38]

***Steroids*** (21.2G)

Steroids have *cholesterol* as their common biosynthetic precursor (see Figure (graphic 21.21)). Cholesterol forms from *squalene via* the intermediate *lanosterol* (see Figure (graphic 21.20)). The first step of the three step biosynthesis of *lanosterol* is epoxidation of squalene. [graphic 21.39] A cascade of cycloaddition reactions leads to a carbocation that subsequently rearranges and loses a proton to give *lanosterol*. The conversion of *lanosterol* to *cholesterol* involves a 19-step sequence of reactions.

## Chapter Review

### *Structures of Lipids*

(1) Lipids include fats, oils, fatty acids, waxes, glycerophospholipids, prostaglandins, terpenes, and steroids. They are biosynthesized from acetyl-CoA, generally soluble in organic solvents, but relatively insoluble in water. (2) Fats, oils, and glycerophospholipids are esters of glycerol and long chain saturated or unsaturated (*cis* C=C) carboxylic acids, with even numbers of C's, called fatty acids. (3) Waxes are esters of fatty acids and fatty alcohols. (4) Soaps are fatty acid carboxylates, and detergents are long alkyl chain sulfonates, but they are not lipids. (5) Prostaglandins, $C_{20}$ carboxylic acids containing a $C_5$ ring and two adjacent substituent chains, are biosynthesized from the $C_{20}$ unsaturated fatty acid arachidonic acid (4 C=C). (6) Terpenes contain $C_5$ isoprene units with "head" to "tail" C-C bonds. (7) Steroids have a characteristic structure that is based on a skeleton of four fused rings (A, B, C, D).

### *Biosynthesis of Lipids*

(1) Acetyl-CoA ($CH_3C(=O)$-CoEnzyme A), the biosynthetic precursor of all lipids, forms by catabolism of carbohydrates, or proteins, as well as fats and oils. (2) Palmitic acid ($C_{16}$) arises from a repeated reaction sequence involving stepwise carbonyl condensation reactions of $C_2$ fragments originally from acetyl-CoA. (3) Higher saturated and unsaturated fatty acids (including *arachidonic acid*) arise *via* reactions of existing fatty acids with elongase and desaturase enzymes. (4) Fats, oils, and phospholipids originate from reactions of fatty acid-CoA's and dihydroxyacetone phosphate formed from fructose. (5) Waxes arise by esterification of fatty acid derivatives and fatty acid alcohols (reduction products of fatty acids). (6) Prostaglandins form *via* enzymatic reactions of arachidonic acid with singlet oxygen. (7) Terpenes arise from electrophilic addition reactions of dimethylallyl pyrophosphate ($C_5$) and isopentenyl pyrophosphate ($C_5$) from decarboxylation of mevalonic acid ($C_6$). Mevalonic acid comes from stepwise condensation reactions involving three acetyl-CoA's. (8) Epoxidation of squalene followed by a series of cyclizations gives lanosterol that is subsequently transformed to cholesterol, the precursor to steroid hormones.