Chapter 33 Fats

33.1 The organic chemistry of biomolecules

The study of biology at the molecular level is called biochemistry. It is a branch of biology, but it is equally a branch of organic chemistry. Most of the molecules involved, the *biomolecules*, are bigger and more complicated than the ones we have so far studied, and their environment—a living organism—is a far cry from the stark simplicity of the reaction mixture of the organic chemist. But the physical and chemical properties of these compounds depend on molecular structure in exactly the same way as do the properties of other organic compounds.

The detailed chemistry of biological processes is vast and complicated, and is beyond the scope of this book; indeed, the study of biochemistry must be ***built upon*** a study of the fundamentals of organic chemistry. We can, however, attempt to close the gap between the subject "organic chemistry" and the subject "biochemistry."

In the remaining chapters of this book, we shall take up the principal classes of biomolecules: fats, carbohydrates, proteins, and nucleic acids. Our chief concern will be with their structures—since structure is fundamental to everything else—and with the methods used to determine these structures. Because biomolecules are big ones, we shall encounter structure on several levels: first, of course, the ***sequence of functional groups*** and the *configuration* at any chiral centers or double bonds; then, *conformation*, with loops, coils, and zig-zags on a grander scale than anything we have seen yet; finally, the arrangement of *collections of molecules*, and even of collections of these collections. We shall see remarkable effects due to our familiar intermolecular forces: operating between biomolecules; between biomolecules—or *parts* of them—and the solvent; between different parts of the same biomolecule.

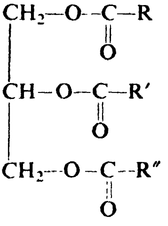
We shall study the chemical properties of these compounds observed in the test tube, since these properties must lie behind the reactions they undergo in living organisms. In doing this, we shall reinforce our knowledge of basic organic chemistry by applying it to these more complex substances. Finally, mostly in the last chapter, we shall look—very briefly—at a few biochemical processes, just to catch a glimpse of the ways in which molecular structure determines biological behavior.

33.2 Occurrence and composition of fats

Biochemists have found it convenient to define one set of biomolecules, the *lipids*, as substances, insoluble in water, that can be extracted from cells by organic solvents of low polarity like ether or chloroform. This is a catch-all sort of definition, and lipids include compounds of many different kinds: steroids (Sec. 15.16), for example, and terpenes (Sec. 8.26). Of the lipids, we shall take up only the *fats* and certain closely related compounds. These are not the only important lipids—indeed, every compound in an organism seems to play an important role, if only as an unavoidable waste product of metabolism—but they are the most abundant.

Fats are the main constituents of the storage fat cells in animals and plants, and are one of the important food reserves of the organism. We can extract these animal and vegetable fats—liquid fats are often referred to as *oils*—and obtain such substances as corn oil, coconut oil, cottonseed oil, palm oil, tallow, bacon grease, and butter.

Chemically, fats are carboxylic esters derived from the single alcohol, glycerol, $HOCH_2CHOHCH_2OH$, and are known as *glycerides*. More specifically, they are *triacylglycerols*. As Table 33.1 shows, each fat is made up of glycerides derived from many different carboxylic acids. The proportions of the various acids vary from fat to fat; each fat has its characteristic composition, which does not differ very much from sample to sample.



A triacylglycerol
(A glyceride)

With only a few exceptions, the fatty acids are all straight-chain compounds, ranging from three to eighteen carbons; except for the C_3 and C_5 compounds, only acids containing an even number of carbons are present in substantial amounts. As we shall see in Sec. 37.6, these even numbers are a natural result of the biosynthesis of fats: the molecules are built up two carbons at a time from acetate units, in steps that closely resemble the malonic ester synthesis of the organic chemist (Sec. 26.2).

Problem 33.1 *n*-Heptadecane is the principal *n*-alkane found both in a 50 million-year-old shale and in the blue-green algae, primitive organisms still existing. When blue-green algae were grown on a medium containing stearic-18-^{14}C acid, essentially all the radioactivity that was not left in unconsumed stearic acid was found in *n*-hepta-

Table 33.1 Fatty Acid Composition of Fats and Oils

Fat or Oil	Saturated Acids, %							Unsaturated Acids, %					
								Enoic				Dienoic	Trienoic
	C_8	C_{10}	C_{12}	C_{14}	C_{16}	C_{18}	$>C_{18}$	$<C_{16}$	C_{16}	C_{18}	$>C_{18}$	C_{18}	C_{18}
Beef tallow			0.2	2-3	25-30	21-26	0.4-1	0.5	2-3	39-42	0.3	2	
Butter	1-2[a]	2-3	1-4	8-13	25-32	8-13	0.4-2	1-2	2-5	22-29	0.2-1.5	3	
Coconut	5-9	4-10	44-51	13-18	7-10	1-4				5-8	0-1	1-3	
Corn				0-2	8-10	1-4			1-2	30-50	0-2	34-56	
Cottonseed				0-3	17-23	1-3				23-44	0-1	34-55	
Lard				1	25-30	12-16		0.2	2-5	41-51	2-3	3-8	
Olive			0-1	0-2	7-20	1-3	0-1		1-3	53-86	0-3	4-22	
Palm				1-6	32-47	1-6				40-52		2-11	
Palm kernel	2-4	3-7	45-52	14-19	6-9	1-3	1-2		0-1	10-18		1-2	
Peanut				0.5	6-11	3-6	5-10		1-2	39-66		17-38	
Soybean				0.3	7-11	2-5	1-3		0-1	22-34		50-60	2-10
											C_{20} $>C_{20}$		
Cod liver				2-6	7-14	0-1		0-2	10-20	25-31	25-32 10-20		
Linseed				0.2	5-9	4-7	0.5-1			9-29		8-29[b]	45-67[c]
Tung										4-13		8-15	78-82[d]

[a] 3-4% C_4, 1-2% C_6.

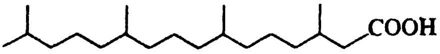
[b] Linoleic acid, *cis,cis*-9,12-octadecadienoic acid.

[c] Linolenic acid, *cis,cis,cis*-9,12,15-octadecatrienoic acid.

[d] Eleostearic acid, *cis,trans,trans*-9,11,13-octadecatrienoic acid, and 3-6% saturated acids.

decane. By what kind of chemical reaction is the hydrocarbon evidently produced? Of what geological significance is this finding?

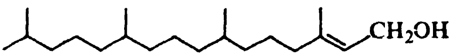
Problem 33.2 (a) Acetate is not the only building block for the long chains of lipids. From a 50 million-year-old shale (see Problem 33.1)—as well as from modern organisms—there has been isolated 3,7,11,15-tetramethylhexadecanoic acid,



3,7,11,15-Tetramethylhexadecanoic acid

What familiar structural unit occurs here?

(b) The long side chain of chlorophyll (p. 1004) is derived from the alcohol *phytol*, which is cis-7(R),11(R)-3,7,11,15-tetramethyl-2-hexadecen-1-ol. The acid in (a)



cis-7(R)-11(R)-3,7,11,15-Tetramethyl-2-hexadecen-1-ol
Phytol

was found to be a mixture of two diastereomers: the 3(S),7(R),11(R) and 3(R),7(R),11(R). Of what biogenetic significance is this finding?

Besides saturated acids, there are unsaturated acids containing one or more double bonds per molecule. The most common of these acids are:

$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
Oleic acid
(*cis*-isomer)

$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$
Linoleic acid
(*cis,cis*-isomer)

$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$
Linolenic acid
(*cis,cis,cis*-isomer)

The configuration about these double bonds is almost invariably *cis*, rather than the more stable *trans*.

Unsaturation *with this particular stereochemistry* has an effect that is seemingly trivial but is actually (Sec. 33.8) of vital biological significance: it lowers the melting point. In the solid phase, the molecules of a fat fit together as best they can; the closer they fit, the stronger the intermolecular forces, and the higher the melting point. Saturated acid chains are extended in a linear fashion—with, of course, the zig-zag due to the tetrahedral bond angles—and fit together rather well. *trans*-Unsaturated acid chains can be similarly extended to linear conformations that match saturated chains rather well (Fig. 33.1) But *cis*-unsaturated acid chains have a *bend* at the double bond, and fit each other—and saturated chains—badly. The net result is that *cis* unsaturation lowers the melting point of fat.

While we synthesize fats in our own bodies, we also eat fats synthesized in plants and other animals; they are one of the three main classes of foods, the others being carbohydrates (Chap. 35) and proteins (Chap. 36). Fats are used in enormous amounts as raw materials for many industrial processes; let us look at some of these before we turn our attention to some close relatives of the fats.

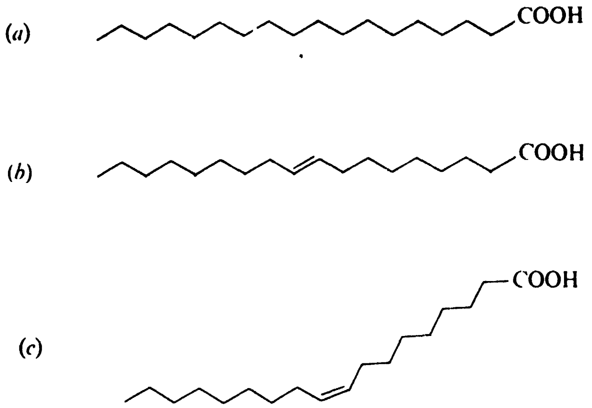
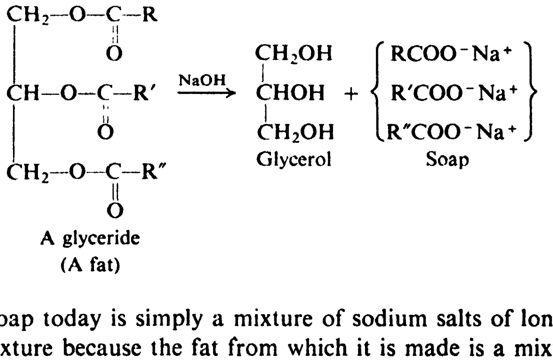


Figure 33.1. Extended chains of fatty acids: (*a*) saturated, (*b*) *trans*-unsaturated, (*c*) *cis*-unsaturated. Note bend in (*c*).

33.3 Hydrolysis of fats. Soap. Micelles

The making of soap is one of the oldest of chemical syntheses. (It is not nearly so old, of course, as the production of ethyl alcohol; man's desire for cleanliness is much newer than his desire for intoxication.) When the German tribesmen of Caesar's time boiled goat tallow with potash leached from the ashes of wood fires, they were carrying out the same chemical reaction as the one carried out on a tremendous scale by modern soap manufacturers: *hydrolysis of glycerides.* Hydrolysis yields salts of the carboxylic acids, and glycerol, $CH_2OHCHOHCH_2OH$.



$$\begin{array}{l}\mathrm{CH_2{-}O{-}\underset{\underset{O}{\|}}{C}{-}R}\\ |\\ \mathrm{CH{-}O{-}\underset{\underset{O}{\|}}{C}{-}R'}\\ |\\ \mathrm{CH_2{-}O{-}\underset{\underset{O}{\|}}{C}{-}R''}\end{array} \xrightarrow{NaOH} \begin{array}{l}\mathrm{CH_2OH}\\ |\\ \mathrm{CHOH}\\ |\\ \mathrm{CH_2OH}\end{array} + \left\{\begin{array}{l}\mathrm{RCOO^-Na^+}\\ \mathrm{R'COO^-Na^+}\\ \mathrm{R''COO^-Na^+}\end{array}\right\}$$

A glyceride
(A fat)

Glycerol

Soap

Ordinary soap today is simply a mixture of sodium salts of long-chain fatty acids. It is a mixture because the fat from which it is made is a mixture, and for washing our hands or our clothes a mixture is just as good as a single pure salt. Soap may vary in composition and method of processing: if made from olive oil, it is *Castile soap*; alcohol can be added to make it transparent; air can be beaten in to make it float; perfumes, dyes, and germicides can be added; if a potassium salt (instead of a sodium salt), it is *soft soap*. Chemically, however, soap remains pretty much the same, and does its job in the same way.

We might at first expect these salts to be water-soluble—and, indeed, one can prepare what are called "soap solutions." But these are not true solutions, in which solute molecules swim about, separately and on their own. Instead, soap is dispersed in spherical clusters called **micelles**. each of which may contain hundreds of soap molecules. A soap molecule has a polar end, COO^-Na^+, and a non-polar end, the long carbon chain of 12 to 18 carbons. The polar end is water-soluble, and is said to be *hydrophilic* (water-loving). The non-polar end is water-insoluble, and is said to be *hydrophobic* (water-fearing); it is, of course, soluble in non-polar solvents. Molecules like these are called *amphipathic*: they have both polar and non-polar ends and, in addition, are big enough for each end to display its own solubility behavior. In line with the rule of "like dissolves like," each non-polar end seeks a non-polar environment; in this situation, the only such environment about is the non-polar ends of other soap molecules, which therefore huddle together in the center of the micelle (Fig. 33.2). The polar ends project outward into the polar solvent, water. Negatively charged carboxylate groups stud the surface of the micelle, and it is surrounded by an ionic atmosphere. Repulsion between similar charges keeps the micelles dispersed.

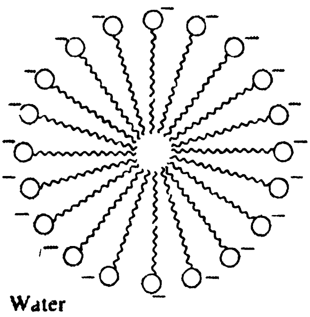


Figure 33.2. Soap micelle. Non-polar hydrocarbon chains "dissolve" in each other. Polar –COO groups dissolve in water. Similarly charged micelles repel each other.

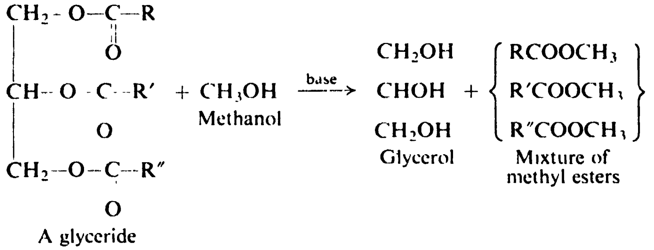
Now, how does a soap clean? The problem in cleansing is the fat and grease that make up and contain the dirt. Water alone cannot dissolve these hydrophobic substances; oil droplets in contact with water tend to coalesce so that there is a water layer and an oil layer. But the presence of soap changes this. The non-polar ends of soap molecules dissolve in the oil droplet, leaving the carboxylate ends projecting into the surrounding water layer. Repulsion between similar charges keeps the oil droplets from coalescing; a stable emulsion of oil and water forms, and can be removed from the surface being cleaned. As we shall see, this emulsifying, and hence cleansing, property is not limited to carboxylate salts, but is possessed by other amphipathic molecules (Sec. 33.5).

Hard water contains calcium and magnesium salts, which react with soap to form insoluble calcium and magnesium carboxylates (the "ring" in the bathtub).

33.4 Fats as sources of pure acids and alcohols

Treatment of the sodium soaps with mineral acid (or hydrolysis of fats under acidic conditions) liberates a mixture of the free carboxylic acids. In recent years, fractional distillation of these mixtures has been developed on a commercial scale to furnish individual carboxylic acids of over 90% purity.

Fats are sometimes converted by transesterification into the methyl esters of carboxylic acids; the glycerides are allowed to react with methanol in the presence of a basic or acidic catalyst. The mixture of methyl esters can be separated by



fractional distillation into individual esters, which can then be hydrolyzed to individual carboxylic acids of high purity. Fats are thus the source of straight-chain acids of even carbon number ranging from six to eighteen carbons.

Alternatively, these methyl esters, either pure or as mixtures, can be catalytically reduced to straight-chain primary alcohols of even carbon number, and from these can be derived a host of compounds (as in Problem 18.10, p. 604). Fats thus provide us with long straight-chain units to use in organic synthesis.

33.5 Detergents

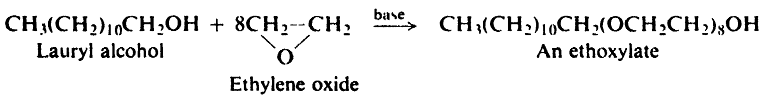
Of the straight-chain primary alcohols obtained from fats—or in other ways (Sec. 32.6)—the C_8 and C_{10} members are used in the production of high-boiling esters used as *plasticizers* (e.g., octyl phthalate). The C_{12} to C_{18} alcohols are used in enormous quantities in the manufacture of *detergents* (cleansing agents).

Although the synthetic detergents vary considerably in their chemical structure, the molecules of all of them have one common feature, a feature they share with ordinary soap: they are amphipathic, and have a large non-polar hydrocarbon end that is oil-soluble, and a polar end that is water-soluble. The C_{12} to C_{18} alcohols are converted into the salts of alkyl hydrogen sulfates. For example:

$$\underset{\text{Lauryl alcohol}}{n\text{-}C_{11}H_{23}CH_2OH} \xrightarrow{H_2SO_4} \underset{\text{Lauryl hydrogen sulfate}}{n\text{-}C_{11}H_{23}CH_2OSO_3H} \xrightarrow{NaOH} \underset{\text{Sodium lauryl sulfate}}{n\text{-}C_{11}H_{23}CH_2OSO_3^-\ Na^+}$$

For these, the non-polar end is the long chain, and the polar end is the $-OSO_3^-Na^+$.

Treatment of alcohols with ethylene oxide (Sec. 17.13) yields a *non-ionic* detergent:

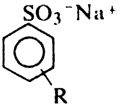


$$\underset{\text{Lauryl alcohol}}{CH_3(CH_2)_{10}CH_2OH} + 8CH_2\text{—}CH_2 \xrightarrow{\text{base}} \underset{\text{An ethoxylate}}{CH_3(CH_2)_{10}CH_2(OCH_2CH_2)_8OH}$$

Ethylene oxide

Hydrogen-bonding to the numerous oxygen atoms makes the polyether end of the molecule water-soluble. Alternatively, the ethoxylates can be converted into sulfates and used in the form of the sodium salts.

Perhaps the most widely used detergents are sodium salts of alkylbenzenesulfonic acids. A long-chain alkyl group is attached to a benzene ring by the action



of a Friedel-Crafts catalyst and an alkyl halide, an alkene, or an alcohol. Sulfonation and neutralization yields the detergent.

Formerly, polypropylene was commonly used in the synthesis of these alkylbenzenesulfonates; but the highly-branched side chain it yields blocks the rapid biological degradation of the detergent residues in sewage discharge and septic tanks. Since about 1965 in this country, such "hard" detergents have been replaced by "soft" (biodegradable) detergents: alkyl sulfates, ethoxylates and their sulfates; and alkylbenzenesulfonates in which the phenyl group is randomly attached to the various secondary positions of a long straight chain (C_{12}–C_{18} range). (See Problem 17, p. 403.) The side chains of these "linear" alkylbenzenesulfonates are derived from straight-chain 1-alkenes (Sec. 32.6), or chlorinated straight-chain alkanes separated (by use of molecular sieves) from kerosene.

These detergents act in essentially the same way as soap does. They are used because they have certain advantages. For example, the sulfates and sulfonates retain their efficiency in hard water, since the corresponding calcium and magnesium salts are soluble. Being salts of strong acids, they yield neutral solutions, in contrast to the soaps, which, being salts of weak acids, yield slightly alkaline solutions (Sec. 18.10).

33.6 Unsaturated fats. Hardening of oils. Drying oils

We have seen that fats contain, in varying proportions, glycerides of unsaturated carboxylic acids. We have also seen that, other things being equal, unsaturation in a fat tends to lower its melting point and thus tends to make it a liquid at room temperature. In the United States the long-established use of lard and butter for cooking purposes has led to a prejudice against the use of the cheaper, equally nutritious oils. Hydrogenation of some of the double bonds in such cheap fats as cottonseed oil, corn oil, and soybean oil converts these liquids into solids having a consistency comparable to that of lard or butter. This *hardening* of oils is the basis of an important industry that produces cooking fats (for example, Crisco, Spry) and oleomargarine. Hydrogenation of the carbon–carbon double bonds takes place under such mild conditions (Ni catalyst, 175–190°, 20–40 lb/in.^{2}) that hydrogenolysis of the ester linkage does not occur.

Hydrogenation not only changes the physical properties of a fat, but also—and this is even more important—changes the chemical properties: a hydrogenated fat becomes *rancid* much less readily than does a non-hydrogenated fat. Rancidity is due to the presence of volatile, bad-smelling acids and aldehydes. These compounds result (in part, at least) from attack by oxygen at reactive allylic positions in the fat molecules; hydrogenation slows down the development of rancidity presumably by decreasing the number of double bonds and hence the number of allylic positions.

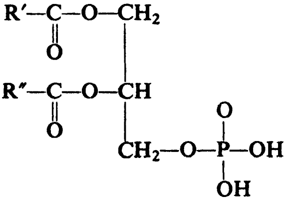
(In the presence of hydrogenation catalysts, unsaturated compounds undergo not only hydrogenation but also isomerization—shift of double bonds, or stereochemical transformations—which also affects physical and chemical properties.)

Linseed oil and tung oil have special importance because of their high content of glycerides derived from acids that contain two or three double bonds. They are known as **drying oils** and are important constituents of paints and varnishes. The "drying" of paint does not involve merely evaporation of a solvent (turpentine, etc.), but rather a chemical reaction in which a tough organic film is formed. Aside from the color due to the pigments present, protection of a surface by this film is the chief purpose of paint. The film is formed by a polymerization of the unsaturated oils that is brought about by oxygen. The polymerization process and the structure of the polymer are extremely complicated and are not well understood. The process seems to involve, in part, free-radical attack at reactive allylic hydrogens, free-radical chain-reaction polymerization similar to that previously described (Secs. 6.19 and 32.3), and cross-linking by oxygen analogous to that by sulfur in vulcanized rubber (Sec. 8.25).

Problem 33.3 In paints, tung oil "dries" faster than linseed oil. Suggest a reason why. (See Table 33.1.)

33.7 Phosphoglycerides. Phosphate esters

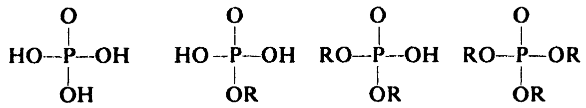
So far, we have talked only about glycerides in which all three ester linkages are to acyl groups, that is, triacylglycerols. There also occur lipids of another kind, phosphoglycerides, which contain only two acyl groups and, in place of the third, a *phosphate* group. The parent structure is *diacylglycerol phosphate*, or *phosphatidic acid.*



Phosphatidic acid
(A phosphoglyceride)

Phosphoglycerides are, then, not only carboxylate esters but phosphate esters as well. Just what are phosphate esters like? It will be well for us to learn something about them since we shall be encountering them again and again: phospholipids make up the membranes of cells (Sec. 33.8); adenosine triphosphate lies at the heart of the energy system of organisms, and it does its job by converting hosts of other compounds into phosphate esters (Sec. 37.3); nucleic acids, which control heredity, are polyesters of phosphoric acid.

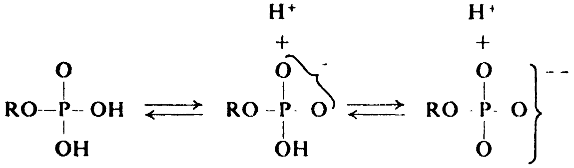
To begin with, phosphates come in various kinds. Phosphoric acid contains three hydroxy groups and can form esters in which one, two, or three of these have been replaced by alkoxy groups. Phosphoric acid is highly acidic, and so are the



$$\mathrm{HO{-}\overset{\overset{\displaystyle O}{|}}{\underset{\underset{\displaystyle OH}{|}}{P}}{-}OH} \qquad \mathrm{HO{-}\overset{\overset{\displaystyle O}{|}}{\underset{\underset{\displaystyle OR}{|}}{P}}{-}OH} \qquad \mathrm{RO{-}\overset{\overset{\displaystyle O}{|}}{\underset{\underset{\displaystyle OR}{|}}{P}}{-}OH} \qquad \mathrm{RO{-}\overset{\overset{\displaystyle O}{|}}{\underset{\underset{\displaystyle OR}{|}}{P}}{-}OR}$$

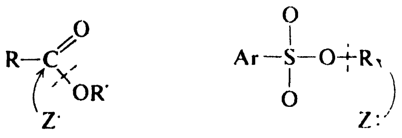
Phosphoric acid Phosphate esters

monoalkyl and dialkyl esters; in aqueous solution they tend to exist as anions, the exact extent of ionization depending, of course, upon the acidity of the medium. For example:

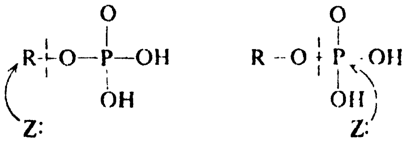


Like other esters, phosphates undergo hydrolysis to the parent acid and alcohol. Here, the acidity of —OH attached to phosphorus has several effects. In the first place, since acidic phosphate esters can undergo ionization, there may be many species present in the hydrolysis solution. A monoalkyl ester, for example, could exist as dianion, monoanion, neutral ester, and protonated ester; any or all of these could conceivably be undergoing hydrolysis. Actually, the situation is not quite that complicated. From the dissociation constants of these acidic esters, one can calculate the fraction of ester in each form in a given solution. The dependence of rate on acidity of the solution often shows which species is the principal reactant.

In carboxylates, we remember, attack generally occurs at acyl carbon, and in sulfonates, at alkyl carbon, with a resulting difference in point of cleavage. In



hydrolytic behavior, phosphates are intermediate between carboxylates and sulfonates. Cleavage can occur at either position, depending on the nature of the alcohol group.

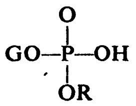


C—O cleavage P—O cleavage

Here again the acidity of phosphoric acids comes in. Cleavage of the alkyl-oxygen bond in carboxylates is difficult because the carboxylate anion is strongly basic and a poor leaving group; in sulfonates such cleavage is favored because the weakly basic sulfonate anion is a very good leaving group. Phosphoric acid is intermediate in acidity between carboxylic and sulfonic acid; as a result, the phosphate anion is a better leaving group than carboxylate but a poorer one than sulfonate. In these esters, phosphorus is bonded to four groups; but it can accept more—witness stable pentacovalent compounds like PCl_5—and nucleophilic attack at phosphorus competes with attack at alkyl carbon.

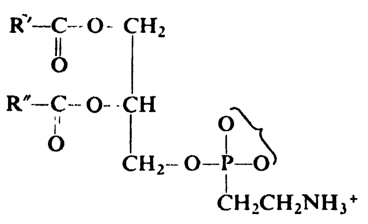
In acidic solution, phosphate esters are readily cleaved to phosphoric acid. In alkaline solution, however, only trialkyl phosphates, $(RO)_3PO$, are hydrolyzed, and only one alkoxy group is removed. Monoalkyl and dialkyl esters, $ROPO(OH)_2$ and $(RO)_2PO(OH)$, are inert to alkali, even on long treatment. This may seem unusual behavior, but it has a perfectly rational explanation. The monoalkyl and dialkyl esters contain acidic —OH groups on phosphorus, and in alkaline solution exist as anions; repulsion between like charges prevents attack on these anions by hydroxide ion.

In most phospholipids, phosphate is of the kind

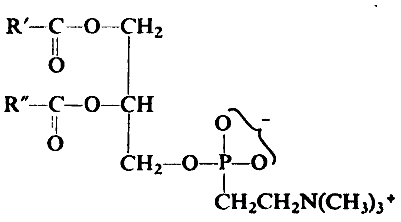


$$GO-\overset{\displaystyle O}{\underset{\displaystyle OR}{P}}-OH$$

in which G is the glyceryl group—with its two carboxylates—and R is derived from some other alcohol, ROH, most often *ethanolamine*, $HOCH_2CH_2NH_2$, or *choline*, $HOCH_2CH_2N(CH_3)_3^+$. Since the remaining —OH on phosphorus is highly acidic, the ester exists mostly in the ionic form. Furthermore, since the alcohol ROH usually contains an amino group, the phosphate unit carries both positive and negative charges, and the phospholipid is—at this end—a ***dipolar ion***. On hydrolysis, these phosphates generally undergo cleavage between phosphorus and oxygen, $P \nmid O{-}R$.



Phosphatidyl ethanolamine
(Ethanolamine phosphoglyceride)



Phosphatidyl choline
(Choline phosphoglyceride)

Problem 33.4 Consider hydrolysis of $(RO)_2PO(OH)$ by aqueous hydroxide, and grant that for electrostatic reasons attack by OH cannot occur. Even so, why does not attack by the nucleophile water lead to hydrolysis? After all, water *is* the successful nucleophile in acidic hydrolysis. (*Hint:* See Sec. 20.18.)

33.8 Phospholipids and cell membranes

The fats are found, we said, in storage fat cells of plants and animals. Their function rests on their chemical properties: through oxidation, they are consumed to help provide energy for the life processes.

The phospholipids, on the other hand, are found in the membranes of cells—all cells and are a basic structural element of living organisms. This vital function depends, in a fascinating way, on their physical properties.

Phosphoglyceride molecules are amphipathic, and in this respect differ from fats--but resemble soaps and detergents. The hydrophobic part is, again, the long fatty acid chains. The hydrophilic part is the dipolar ionic end: the substituted phosphate group with its positive and negative charges. In aqueous solution, as we would expect, phosphoglycerides form micelles. In certain situations, however—at an aperture between two aqueous solutions, for example--they tend to form bilayers: two rows of molecules are lined up, back to back, with their polar ends projecting into water on the two surfaces of the bilayer (Fig. 33.3). Although the polar groups are needed to hold molecules in position, the bulk of the bilayer is made up of the fatty acid chains. Non-polar molecules can therefore dissolve in this mostly hydrocarbon wall and pass through it, but it is an effective barrier to polar molecules and ions.

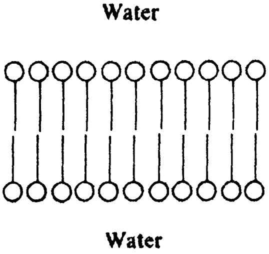


Figure 33.3. A phospholipid bilayer. Hydrophobic fatty chains held together by van der Waals forces. Hydrophilic ends dissolve in water.

It is in the form of bilayers that phosphoglycerides are believed to exist in cell membranes. They constitute walls that not only enclose the cell but also very selectively control the passage, in and out, of the various substances—nutrients, waste products, hormones, etc.—even from a solution of low concentration to a solution of high concentration. Now, many of these substances that enter and leave the cells are highly polar molecules like carbohydrates and amino acids, or ions like sodium and potassium. How can these molecules pass through cell membranes when they cannot pass through simple bilayers? And how can permeability be so highly selective?

The answer to both these questions seems to involve the proteins that are also found in cell membrane: embedded in the bilayer, and even extending clear through it. Proteins, as we shall see in Chap. 36, are very long chain amides, polymers of twenty-odd different amino acids. Protein chains can be looped and coiled in a variety of ways; the conformation that is favored for a particular protein molecule depends on the exact sequence of amino acids along its chain.

It has been suggested that transport through membranes happens in the following way. A protein molecule, coiled up to turn its hydrophobic parts outward, is dissolved in the bilayer, forming a part of the cell wall. A molecule approaches: a potassium ion, say. If the particular protein is the one designed to handle potassium ion, it receives the ion into its polar interior. Hidden in this hydrophobic wrapping, the ion is smuggled through the bilayer and released on the other side.

Now, if the transport protein is to do its job, it must be free to move within the membrane. The molecules of the bilayer, while necessarily aligned, must not be locked into a rigid crystalline lattice—as they would be if all the fatty acid chains were saturated. Actually, some of the chains in the membrane phospholipids are unsaturated and these, with their *cis* stereochemistry and the accompanying bend (Fig. 33.1), disrupt the alignment enough to make the membrane semiliquid at physiological temperatures.

Here, we have had a glimpse of just one complex biological process. Yet we can begin to see how the understanding of biology rests on basic chemical concepts: van der Waals forces and ion–dipole bonds; polarity and solubility; melting point and molecular shape; configuration and conformation; and, ultimately, the sequence of atoms in molecular chains.

Problem 33.5 The degree of unsaturation of the membrane lipids in the legs of reindeer is higher in cells near the hooves than in cells near the body. What survival value does this unsaturation gradient have?

PROBLEMS

1. From saponification of cerebrosides, lipids found in the membranes of brain and nerve cells, there is obtained *nervonic acid.* This acid rapidly decolorizes dilute $KMnO_4$ and Br_2/CCl_4 solutions. Hydrogenation in the presence of nickel yields tetracosanoic acid, n-$C_{23}H_{47}COOH$. Vigorous oxidation of nervonic acid yields one acid of neutralization equivalent 156 ± 3 and another acid of neutralization equivalent 137 ± 2. What structure or structures are possible for nervonic acid?

2. When peanut oil is heated very briefly with a little sodium methoxide, its properties are changed dramatically—it becomes so viscous it can hardly be poured—yet saponification yields the same mixture of fatty acids as did the untreated oil. What has probably happened?

3. On oxidation with O_2, methyl oleate (methyl 9-*cis*-octadecenoate) was found to yield a mixture of hydroperoxides of formula $C_{18}H_{34}O_4$. In these, the —OOH group was found attached not only to C–8 and C–11 but also to C–9 and C–10. What is the probable structure of these last two hydroperoxides? How did they arise? Show all steps in a likely mechanism for the reaction.

4. Although alkaline hydrolysis of monoalkyl or monoaryl phosphates is ordinarily very difficult, 2,4-dinitrophenyl phosphate, $2,4\text{-}(NO_2)_2C_6H_3OPO_3H_2$, does react with aqueous base, and with cleavage at the phosphorus–oxygen bond. Suggest an explanation for this.