Chapter 7

Varying the Combination

—And Still Champion

So FAR, the oxygen atoms in the organic compounds I have mentioned have always been part of hydroxyl groups. Let's change things a bit. Suppose both bonds of the oxygen atom were to be connected to carbon atoms. The combination would look like this: —C—O—C—. Any compound that contains this combination is an *ether*.

The most familiar ether is *diethyl ether*, with a molecule that looks like this:

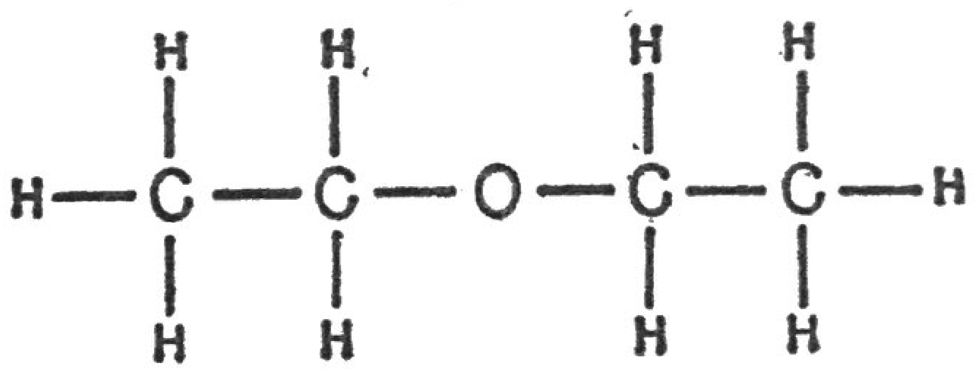


Figure 28—Diethyl Ether

The carbon atoms to which the oxygen atom is attached both belong to ethyl groups; hence the "diethyl" part of the name. Although there are many, many ethers, a chemist or doctor (or anyone else) who says simply "ether" always means diethyl ether.

Diethyl ether was discovered in 1544. At that time virtually nothing was known about organic chemistry. The thing that first amazed the early chemists was that any liquid should evaporate so easily and quickly. The boiling point of diethyl ether is only 34° C. (95° F.)—less than normal body temperature.

As I said earlier in the book, gases and vapors completely mystified the early chemists. To them, this new liquid just seemed to disappear into thin air. The Greeks had a word for the upper regions of the air, high above the lower atmosphere and its earthly corruptions. They called it "aether." In 1730, this vanishing compound which seemed to flee the earth was given the name "spiritus aethereus" (which, in English, means "ethereal spirit"). Eventually, this was shortened to "ether."

Furthermore, the two-carbon groups that were found to form part of the molecule (once chemists learned about atoms and molecules, that is) got their name "ethyl" from the same source. From that came the word "ethane" for the two-carbon hydrocarbon. It frequently happens in organic chemistry that one thing names another in chain fashion.

In some ways ethers have properties part way between alcohols and hydrocarbons, but they are considerably closer to the hydrocarbon. Diethyl ether is slightly soluble in water, but will mix much more easily with fatty substances, including the myelin sheaths of nerve cells.

That makes ether an anesthetic and, in fact, it is a good one. It was one of the first anesthetics used, and is completely American in its origin. In 1842, a Georgia doctor, Crawford Long, operated on a patient under ether. On September 30, 1846, a Boston dentist, W. T. G. Morton extracted a tooth from a patient under ether. Two weeks later, on October 16, 1846, Dr. J. C. Warren performed the first public operation on a patient under ether. That took place at the Massachusetts General Hospital, in Boston.

It was shortly after that that the term "anesthesia" was suggested by Oliver Wendell Holmes, the Boston doctor and poet, best known for his poems *Old Ironsides* and *The Wonderful One-Hoss Shay*.

For over a century, doctors have been experimenting with new anesthetics, and still diethyl ether is used more frequently than any other, particularly for long-drawn-out operations. It is still the champion. Other anesthetics may act more quickly, but diethyl ether is in some ways the safest; it is not as likely to affect heart and lung action as some other anesthetics.

Like most anesthetics except chloroform, diethyl ether is a fire and explosion hazard. Furthermore, if it is allowed to stand, it adds additional oxygen atoms to its molecule to form unstable compounds which can explode even if left undisturbed.

To prevent this, ether intended for anesthetic purposes is carefully purified and stored in small, sealed cans. A piece of iron wire is also included in the can because iron slows down the formation of the explosive compound. Even so, once a can of ether has been open for longer than 24 hours, it is not used for anesthesia.

Diethyl ether has a strong smell which, in small quantities, is not unpleasant. Now that iodoform is no longer used, ether is the most familiar "hospital smell."

Because diethyl ether will dissolve fatty substances very easily, it is useful to chemists. They add it to a mixture of substances and let the mixture soak (or they shake the mixture well, or use a special device called a "Soxhlet extractor" to hasten the process). The fatty part of the mixture will dissolve in the ether. The rest will not. If the ether is then poured off, the fat will be poured off with it. What is left behind is a *fat-free residue.*

Diethyl ether can be easily evaporated because of its low boiling point. A flask of the ether with the fat dissolved in it need merely be placed in a container of hot water. The ether bubbles away[1] and leaves the fat behind. The whole process is called *ether extraction.*

Diethyl ether is a little too inflammable to use in the large quantities that industry would require. Somewhat more complicated ethers called *cellosolves* are used as industrial solvents. They have molecules that contain hydroxyl groups as well as ether combinations.

Tears and Plastics

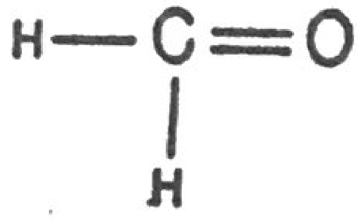
What if both bonds of the oxygen atom are attached to the same carbon atom? A combination like this is formed: $C{=}O$. This combination is the *carbonyl group.* Compounds containing it are *carbonyl compounds.*

[1] Because ether is so inflammable, it is always evaporated in a special closed area with a fan to suck away the vapors as they are formed. Such a well-ventilated and closed area is called a *hood.* Chemists always use hoods where inflammable or poisonous vapors are being formed during the course of a chemical reaction.

The carbon atom of the carbonyl group has two bonds available for further use. If one of those bonds is attached to a hydrogen atom, the resulting combination is H — C = O. Any compound having this combination is an *aldehyde.*

The simplest aldehyde is one in which both spare bonds of the carbonyl group are attached to hydrogen atoms. The resulting molecule looks like this:

Figure 29—Formaldehyde



It is called *formaldehyde.* If you will compare this molecule with that of methyl alcohol in Chapter 5, you will see that methyl alcohol minus two hydrogen atoms is formaldehyde. Any aldehyde can be produced by taking two hydrogens away from an alcohol (that is, by *dehydrogenating* the alcohol). In fact, that is how the word "aldehyde" arose. It is an abbreviation of "*al*cohol *dehyd*rogenated."

Formaldehyde is a gas with a very strong and irritating odor, which you won't forget once you've smelled it. It irritates the membranes of the eyes, nose, and throat. Get a whiff and your eyes will smart and tear. A substance that will make your eyes tear in this way is known as a *lachrymator* from the Latin word for "tears."

Under the proper conditions, formaldehyde will polymerize into large molecules to form *paraformaldehyde.* This is a solid substance that is easily shipped from place to place and is much more pleasant to handle than the tear-making formaldehyde gas. If paraformaldehyde is heated gently, formaldehyde is formed at once and can then be used.

One of the reasons formaldehyde is so irritating is that it combines easily with proteins, which are the most important compound in all living tissue. By doing so, it hardens tissue and kills it. It also kills any microorganisms that might be present.

Formaldehyde is therefore used to preserve tissues, organs, and even whole organisms. Not only does it prevent decay

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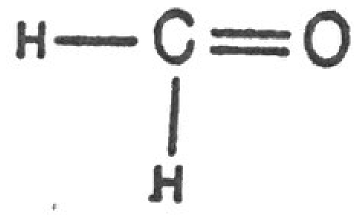

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Formaldehyde is therefore used to preserve tissues, organs, and even whole organisms. Not only does it prevent decay but it makes the tissue as stiff as a board and easy to handle. Pure formaldehyde is not used, since that is a gas at ordinary temperatures. Instead, a 40 percent solution of formaldehyde in water is used. This solution is called *formalin.* Zoology laboratories in colleges and anatomy laboratories in medical schools always smell of formaldehyde because specimens for dissection are preserved in it. (Formaldehyde is also used in embalming fluids.)

Formaldehyde molecules will combine with phenol molecules under the proper conditions to form a polymer. This polymer, like many organic polymers, has a glassy appearance and is rather brittle. Such polymers are called *resins.*[2] Resins will generally soften on heating. Certain high-boiling substances can be added to the resin to make it soften even more easily. Softened resin can be molded into any desired shape and is then called a plastic. The substance that helps change a resin into a plastic is called a *plasticizer.*

Plastics, after being molded, will become hard upon cooling and will keep their new shape. Some plastics will become soft again when heated and can then be molded into another shape. These are *thermoplastics.* (The prefix "thermo" comes from a Greek word meaning "heat.") Polyethylene, which I mentioned in Chapter 2, is an example of such a plastic.

Other plastics, after being heated and molded, and then cooled, set permanently into shape. If they are heated again, they may char but they will not soften. These are *thermosetting plastics.* The thermosetting plastics are particularly hard and strong, but they tend to be brittle.

Phenol-formaldehyde polymers can be made into thermosetting plastics. The first plastic of this type was developed by the Belgium-born chemist, L. H. Baekeland in 1905. He named the plastic *Bakelite.* Although one of the older plastics,

[2] *Natural resins* are the gummy sap of certain trees, usually evergreens. *Rosin* from the sap of the pine tree is the most familiar example. *Myrrh,* which was one of the gifts of the wise men to the Christ-child, is obtained from the sap of certain trees that grow in Arabia and Ethiopia. *Amber* is a hardened resin once formed by an evergreen growing in the Baltic Sea area that is now long extinct. Amber is mined and was much valued in the ancient world as a semi-precious substance. Ornaments are still made of it.

it is also one of the strongest and is still used widely in industry. Plastics in general have grown amazingly in importance. Since the end of World War II, the production of resins and plastics has tripled.

If the two hydrogen atoms of formaldehyde are replaced by two chlorine atoms, the compound that results, *phosgene,* has a much improved odor. In fact, it has a delightful, flowery smell. I smelled a very little bit of it once and I can vouch for that. However, I would much prefer to smell formaldehyde because one good breath of phosgene means death! It causes the lungs to fill with fluid and makes breathing impossible. Phosgene was one of the poison gases used in World War I.

When carbon tetrachloride is used to put out fires, especially fires from electric short-circuits, small quantities of carbon tetrachloride may be changed to phosgene. This is something to be very careful about. Carbon tetrachloride extinguishers should not be used on electrical fires.

Intermediates

In all aldehydes other than formaldehyde, the carbonyl group is attached to only one hydrogen atom. The fourth and last bond of the carbon atom is attached to another carbon atom. As an example, take the two-carbon aldehyde, whose molecule looks like this:

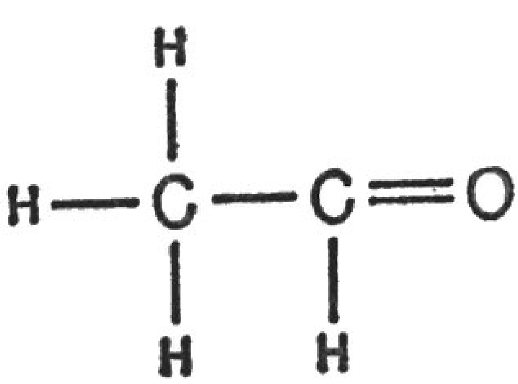

Figure 30—Acetaldehyde

This is *acetaldehyde.* (The official name, using Geneva rules, is *ethanal,* just as formaldehyde should be called *methanal.* The "al" suffix signifies an aldehyde.)

This is a very low-boiling liquid. It boils at 20° C. (68° F.). However, if acetaldehyde is treated with strong acid, the individual molecules hook up in groups of three, forming a ring. This new cyclic compound is *paraldehyde.* In this form, the substance does not boil till a temperature of 122° C. is reached, so that it can be easily shipped from place to place, bottled, and so on. By treating paraldehyde with weak acid, the single acetaldehyde molecules are formed again and are given off as vapor on gentle heating.

Acetaldehyde is an example of a compound that is formed in the human body but is never present except in very small quantities, because as soon as it is formed, it is changed to something else. Compound A is turned to acetaldehyde and then acetaldehyde is turned into compound B. Because acetaldehyde lies in between these two compounds, it is called a *metabolic intermediate.*[3] Although large quantities of it may be formed and then broken down in the body, the amount present at any one time is very small.

One compound that is turned into acetaldehyde by the body is ethyl alcohol. Other simple alcohols are turned into compounds more poisonous than acetaldehyde which is why ethyl alcohol is least harmful. Still acetaldehyde is bad enough. In most people, the acetaldehyde is quickly changed into something else. Some individuals, however, have body chemistries that are a little slow in changing the acetaldehyde once it is formed. In their bodies, acetaldehyde quickly mounts up, and even a small amount of liquor has unpleasant effects.

There are drugs which interfere with the body's handling of acetaldehyde. If these are given to a person who overindulges in alcohol, his next drink will turn out to be a very unpleasant one as the acetaldehyde builds up in his body. A few experiences like that and he may swear off liquor and mean it. Of course, this sort of trick, like any other interference with body chemistry, had better be carried out only on a doctor's advice and under his supervision.

Sleep and Flavor

Paraldehyde is an example of a *sedative.* The word comes from a Latin word meaning "calm" and that is the purpose of

[3] The term, *metabolism,* is the name given to all the chemical reactions that take place in living tissue.

a sedative; to relieve nervousness and tension; to make calm. A small quantity of paraldehyde can be given in water and ten or fifteen minutes afterward, the patient is calmed to the point where he has fallen asleep. (A sedative that calms a person to the point of sleep is called a *hypnotic,* from a Greek word, meaning "put to sleep.")

A more effective compound is *chloral* which has a formula like that of acetaldehyde, except that the three hydrogen atoms on the methyl group are replaced by three chlorine atoms. When chloral is dissolved in water, a water molecule adds on to each chloral molecule to form *chloral hydrate.* Chloral hydrate will put a patient to sleep more promptly than paraldehyde will.

These compounds have their disadvantages, however. They have a terrible taste and they irritate the stomach. Furthermore, they can act too quickly and too strongly. Chloral hydrate may be used to prepare what is commonly known as a "knockout drop" or a "Mickey Finn." These days, milder and less harmful sedatives are usually used.

Incidentally, when a sedative such as chloral hydrate is used a number of times, a person may get used to it. He may get to like the calmness and the relief of tension that comes after he has taken it. He may, in fact get to feeling very tense and nervous if he doesn't take a sedative every once in a while. He becomes an "addict."

Addiction to any drug is dangerous and must be avoided. That is one reason why sedatives should not be taken except under a doctor's direction. Another reason is that any sedative, if taken in a carelessly large amount, may make the sleep too deep and turn it into death.

Many aldehydes are quite pleasant one way or another. Some have pleasant odors and are used in perfumes. Others have pleasant tastes and are used in flavors.

Citral, for instance, is a ten-carbon aldehyde, built up of two isoprene units. It has a strong lemon odor and is used in lemon flavorings.

Benzaldehyde is an example of an aromatic aldehyde. That is, its molecule consists of an aldehyde group attached to a benzene ring. Benzaldehyde has a strong almond odor and is used in flavorings and in perfumes.

The most familiar of the aldehydes of this sort also has a benzene ring in its molecule. In addition to an aldehyde group attached to the ring, however, there is also a hydroxyl group and a small ether group. This compound is *vanillin* and it is, of course, the compound that gives vanilla flavoring its pleasant taste. Other aldehydes smell of cinnamon, of lilacs, and so on.

These aldehydes do not dissolve in water but do dissolve in ethyl alcohol. It is for this reason that perfumes and flavoring extracts contain alcohol.

Nobody knows why things smell or taste as they do. It would be nice and simple for the chemist if all aldehydes smelt the same and we could say: "Aha, that is the smell of the aldehyde group." The trouble is they don't all smell the same. They don't even all smell pleasant. Remember formaldehyde.

Diabetes and Perfumes

When the two spare bonds of the carbon atom of a carbonyl group are both attached to other carbon atoms, the resulting compound is a *ketone*. The simplest one is *acetone,* where the two bonds are both attached to methyl groups, thus:

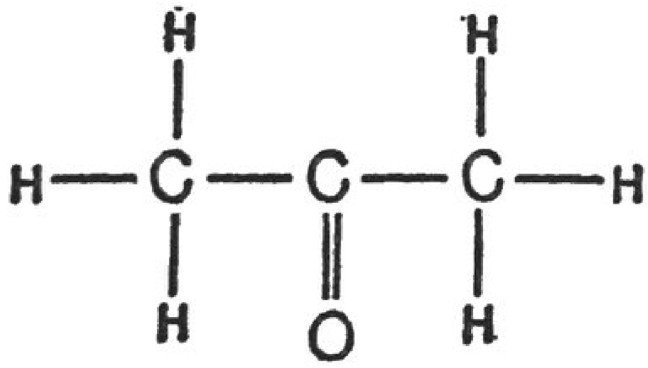

Figure 31—Acetone

The word "ketone" comes from "acetone" and so does the "one" suffix that is the Geneva sign for ketones. The official name for acetone is *propanone,* since it is a three-carbon compound like the hydrocarbon propane.

Acetone will mix with water in all proportions. At the same time, it will dissolve a number of organic compounds that water will not. This makes it very useful as an industrial solvent. Its low boiling point of 56° C. is also helpful.

Acetone, like acetaldehyde, may occur in the body in small quantities. Acetone is not a metabolic intermediate but is formed as the result of a *side reaction*. Compound A, for instance, may usually be converted to Compound B in the body. A very small fraction of it may be, however, converted to Compound C. This minor fraction is the side reaction. Acetone results from such a side reaction.

In the condition known as *diabetes*, there is a shortage in the body of the hormone, insulin. In the absence of insulin, some of the usual chemical changes in the body don't take place properly. It's as though some of the wheels or gears of a machine began to stick. What was previously a side reaction becomes more important as the proper reaction "sticks."

In diabetes, acetone is one of the substances that accumulates in the body because of the improper working of the machinery. It shows up in the urine and, in advanced cases, it leaks into the lungs, and gives the diabetic what is called an "acetone breath." (The odor of acetone is rather pleasant, to be sure, but it is a bad thing to have on your breath if it means advanced diabetes.)[4]

Fortunately, diabetes these days can be treated quite effectively by supplying insulin prepared from the insulin-producing organs of domestic animals. This does not cure the disease but it relieves the symptoms and allows the chemical machinery of the body to continue normally.

Acetone brings to mind another form of unpleasantness. If one of the hydrogen atoms in the acetone molecule is replaced by a bromine atom, the result is *bromacetone*. This is a strong lachrymator, which means, as I said earlier, a tear-producer.

Bromacetone, and other bromine-containing compounds, were used in tear-bombs and tear-shells in World War I. Soldiers with their eyes smarting and blinded with tears are pretty helpless. Even in peacetime such compounds are used

[4] Diabetes is an example of a *metabolic disorder*. There are a number of these but diabetes is the most common and therefore the greatest health problem. Diabetes develops during the course of life, sometimes in youth but more often in middle age. Other metabolic disorders are *inborn* or *congenital*. That is, they result from some chemical defect existing in the body from the moment of birth.

by police as *tear gas* to force trapped criminals to surrender and to put down riots without loss of life.

For a noxious gas[5] to be effective, it must be heavier than air. Formaldehyde is noxious enough, for instance, but it is just about as heavy as air. If one army tried to use it against another, the smallest wind would waft it away (perhaps back across the army using it) and break up the gas clouds.

Actually, the most effective noxious gases are not really gases, but liquids. Bromacetone, for instance, boils at 127° C. Such liquids stay put wherever they are scattered by the bomb carrying it. It is the vapors of these liquids that then do the dirty work. The bromacetone vapor is four times as heavy as air so it blows away quite slowly. And as it blows away, more is formed from the liquid.

But enough of that. Some ketones, especially those with rings in their molecules, are much more pleasant to talk about. In *ionone* and *irone* molecules, the carbonyl group is attached to a methyl group on one side and to a more complicated hydrocarbon group, containing a six-carbon ring, on the other. These smell of violets.

A carbonyl group can actually form part of a ring and such a compound is a cyclic ketone. The best-known example is *camphor,* in which the carbonyl group forms part of a six-carbon ring. Camphor is an important plasticizer. It is not uncommon to be able to smell camphor in plastic objects such as combs.

Very unusual cyclic ketones are *muskone* and *civetone.* Muskone occurs in *musk,* which is produced in a small gland near the abdomen of the male musk deer. This creature lives in Central Asia, mostly in the Himalaya region. Apparently the deer uses the musk (which has a powerful scent) to attract the female musk deer, but it also attracts the hunters. Thousands of the deer are killed each year, just for their precious musk. For every 100 deer killed, some 7½ pounds of musk are obtained. This amount of musk contains about an ounce of muskone.

[5] The term "noxious" refers to anything that is very unpleasant. It includes poisonous compounds, but also compounds that are blinding, or nauseating, or choking, or sneeze-producing.

The unusual thing about muskone is that the carbonyl group forms part of a ring containing sixteen carbon atoms. When this was discovered, chemists were quite amazed because until then they had been convinced that rings with more than six carbon atoms were quite unstable and not very likely to exist in nature.

Civetone occurs in similar secretions in a gland of the African civet cat. Civetone is like muskone but it goes one better. It is part of a seventeen-carbon ring. Both muskone and civetone (especially the latter) smell rather disgusting when present in quantity. If only a small amount is added to a perfume the effect is pleasant. This is another example of the rule that if a little of a chemical is good, a lot isn't necessarily better.

Actually, perfumery is an art rather than a science. There is no way of predicting odor and perfumes must be blended by trial and error. Even after a blend of compounds has been developed with a most pleasant fragrance, there are problems. The compounds all vaporize easily (or else they would have no odor as a rule). On a warm skin, they will vanish soon, too soon.

Compounds must therefore be added to slow down the vaporization without stopping it. Muskone and civetone do this. They make the perfume clinging and long-lasting, and also strengthen the odor.

Another substance which improves perfume in this way is *ambergris,* a bad-smelling secretion produced by sick whales. Quantities of it are sometimes found in whales or are even cast up on shore. Despite its unappetizing origin and appearance it is immensely valuable because of its use in perfumes.

Perfumes can be diluted in alcohol-water mixtures to form cologne or toilet water. These are cheaper but, of course, don't last as long.

More Vitamins; More Hormones

When two carbonyl groups form part of a six-carbon ring, which also contains two double bonds (so that there are four conjugate double bonds altogether), the result is a *quinone.* The most common quinone is *para-quinone:*

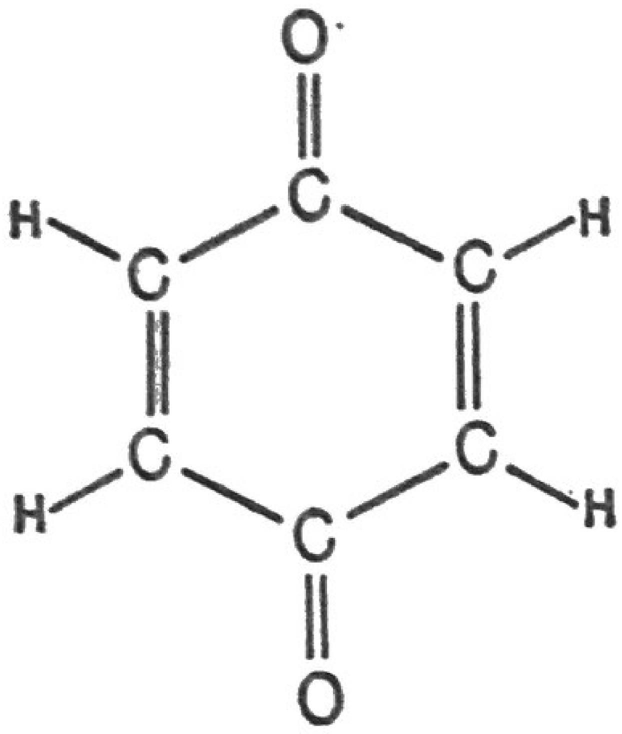

Figure 32—Para-Quinone

The four conjugated bonds give the compound a yellow color. Some of the more complicated quinones are important starting materials for the development of dyes, partly because of their color.

Anthraquinone has a molecule made up of the para-quinone combination shown above with a benzene ring fused on each side of it. If two hydroxyl groups are present on one of the benzene rings of anthraquinone, *alizarin* (also called *Turkey red*) results. This is a red compound one can obtain from the root of a plant known before the days of modern chemistry[6] and it was therefore very valuable. The name, alizarin, comes from an Arabic word meaning simply "the extract," which shows how important the Arabs considered it. They didn't feel it necessary to say which extract—just *the* extract.

To us moderns, however, a far more important quinone is *vitamin K*. Its molecule is built up out of *naphthoquinone*, which is made up of a para-quinone combination with a benzene ring fused on only one side. In vitamin K, the other

[6] Remember that in order to be a good dye, it is not enough that a compound be colored. The compound must also have the ability to combine tightly with the surface of a fabric so that it will not be washed out by water. The color has to be brilliant and not easily faded or changed by the action of air and sun. These are not easy requirements to meet.

side of the naphthoquinone carries a methyl group and a long twenty-carbon chain.

Vitamin K is important to the body because it is used at some point in the clotting of the blood. In the case of accidental bleeding, the blood clots and forms a hard crust at the point of bleeding, thus plugging the leak. If vitamin K is lacking, the machinery of clotting is interfered with, and even a scratch would lead to death by bleeding. (The letter K in the vitamin's name stands for "Koagulation," which is German for "clotting.")

Actually, we don't have to worry about being short of vitamin K. This is one of a number of vitamins which is continually being manufactured by the bacteria that live in our intestines on the food passing by. They make enough for themselves and for us, too. It's a kind of rent they pay for the living quarters and food that we supply.

New-born infants are the only human beings that don't have bacteria swarming in their intestines. Under modern hospital care it takes about three days for the little bugs to establish themselves in the babies. Those three days are a danger period because during that time the infants' bodies do not have the necessary clotting properties, and bleeding could be fatal. For this reason, the mother is usually given vitamin K just before childbirth and enough of it leaks into the baby's bloodstream to protect it. (Of course, for children born outside hospitals under less antiseptic conditions, the danger period of vitamin K deficiency is much shorter.)

Some steroids have carbonyl groups as part of their ring system and are therefore cyclic ketones. A number of the most important hormones are included. Both male and female sex hormones come under this heading. The chief female sex hormone is *estrone*. This consists of a steroid nucleus with one of the carbon atoms in the upper right ring part of a carbonyl group. On the lower left ring is a hydroxyl group.

The chief male sex hormone is *testosterone*. It is formed the opposite way. Its carbonyl group is on the lower left ring and its hydroxyl group is on the upper right.

The adrenal glands (little organs just above each kidney) produce a large number of hormones. All of these have molecules containing the steroid nucleus with one or more carbonyl groups as part of the ring system and one or more hydroxyl groups attached. The most familiar one to the general public is *cortisone*. Its steroid ring system contains three carbonyl groups and two hydroxyl groups.

Cortisone is one of the "wonder drugs" we have heard so much about in recent years. Most of its fame is in connection with its uses in treating some kinds of arthritis. A new adrenal hormone, with very powerful effects on the body, has been discovered recently. It is called *aldosterone* and is unusual because in addition to the carbonyl and hydroxyl groups on the steroid nucleus, it also has an aldehyde side-chain.