first verso page

ISAAC ASIMOV, Ph.D.

The World of NITROGEN

*ILLUSTRATED
WITH DIAGRAMS*

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To Robbie

ACKNOWLEDGMENT

To: Mrs. Joan Smith McLellan,
who prepared the formulas.

CONTENTS

SPECIAL NOTE

Those who have read my book THE WORLD OF CARBON may skip the preliminary section and begin directly with Chapter 1. Those who have *not* read THE WORLD OF CARBON, or who have read it but wish to refresh their memory, had better read the preliminary section first

PRELIMINARY SECTION

The substances that go to make up your body are quite different in several ways from those that go to make up a rock. The chemical compounds in you and in all living things, are, for the most part, fragile. If they are heated or subjected to sunlight or various chemicals for even a short time, they are often changed into forms no longer useful to the body. Rocks and metal, water and salt, air and glass can easily resist a harsh environment of a kind that would ruin our body chemicals.

Chemists, about a hundred and fifty years ago, consequently began to divide all chemical substances into two groups: *organic compounds* (those which occurred in living tissue) and *inorganic compounds* (those which occurred in the non-living air, sea and soil. It was noticed that, in most cases, substances in living tissue contained carbon atoms in their makeup, while inorganic substances did not. For that reason, organic chemistry is now considered to be the chemistry of those compounds which contain carbon, whether a particular compound occurs in living tissue or not. (If you have ever seen coal, you have seen carbon. Coal is made up almost entirely of carbon atoms.)

I wanted to write a book about organic chemistry; a book describing the important carbon-containing compounds. Consequently, I wrote *The World of Carbon.* The only trouble was that by the time I had finished the book, I had only had a chance to describe about half the compounds that needed describing.

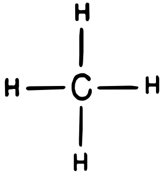
You may wonder why this should be when the book was concerned with the compounds involving, primarily, only one kind of atom. After all, there are 102 kinds of atoms altogether and I had earlier written a book about all of them (entitled *Building Blocks of the Universe*), even including a bit about carbon, and I managed to get all that into one volume. Why, then, the trouble here?

The fact of the matter is, you see, that there is more to the carbon atom than there is to all the other atoms put together. It's that very fact that makes life, as we know it, possible.

HOOKS AND INITIALS

To begin with, each carbon atom can be hooked to four other atoms by what are called *bonds*. The atoms to which carbon is most frequently attached in this way are those of hydrogen; a light, inflammable gas used to inflate balloons. A hydrogen atom, on the other hand, can only be attached to a single other atom. In other words, the carbon atom has four bonds, the hydrogen atom only one.

We can imagine a *molecule* (that is, a group of atoms held together by bonds) made up of a single carbon atom attached to four hydrogen atoms. Chemists represent carbon and hydrogen by *symbols* consisting of their initial letters, C and H, and write the bonds as little dashes. The result is a *formula*, thus:



$$\begin{array}{c} H \\ | \\ H-C-H \\ | \\ H \end{array}$$

Figure a—Methane

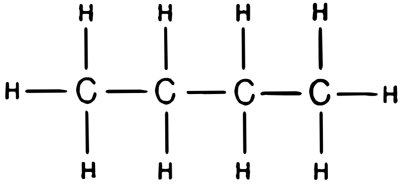
As you see, the carbon atom has its four bonds, each hydrogen atom its one bond. This formula represents a molecule of the gas, *methane*. Methane is an example of a *hydrocarbon*; that is, of a molecule made up of hydrogen and carbon atoms only.

It may seem to you that this is the only way in which carbon and hydrogen atoms can be arranged if we are to stick to the four-bond-one-bond arrangement. Actually, this is far from so and we come to the crucial point in organic chemistry and, in fact, in the chemistry of life.

The carbon atom can use its bonds to attach itself to other carbon atoms in almost any conceivable way. Complicated collections of carbon atoms, all bonded together, can be formed. No other atom of all the 102 known varieties can display even a fraction of this power.

For instance, imagine four carbon atoms attached in a straight line. The two middle carbon atoms will have two of their bonds occupied, while the end carbons will have only one occupied. The bonds that remain can then be attached to hydrogen atoms. But you needn't try to figure this out in your head. A formula shows it easily enough, which is one of the values of formulas:

Figure b—
Normal Butane



$$\begin{array}{ccccccccccc} & & H & & H & & H & & H & & \\ & & | & & | & & | & & | & & \\ H & - & C & - & C & - & C & - & C & - & H \\ & & | & & | & & | & & | & & \\ & & H & & H & & H & & H & & \end{array}$$

As you see, each carbon atom still has four bonds altogether, each hydrogen atom only one. This four-carbon compound, called *normal butane*, is still a hydrocarbon, but it is by no means the same compound as methane. It is made up of the same two elements, carbon and hydrogen, as methane is, but different quantities of each are present in the molecule. It happens, then, that methane is a gas at ordinary temperatures, and has a very low liquefying point; whereas butane, also a gas, can be liquefied in an ordinary household freezer. There are other differences, too.

Furthermore, there are differences even when the number of carbon and hydrogen atoms in the molecule are the same, but happen to be arranged differently. The four carbon atoms of normal butane need not be in a straight line. Suppose they are arranged in a T-shape, thus:

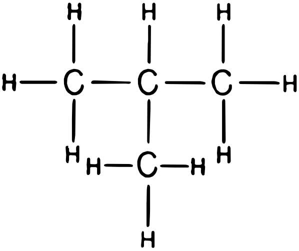
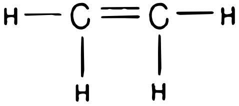


Figure c— Isobutane

This is *isobutane*. Like normal butane, the molecule of isobutane is made up of four carbon atoms and ten hydrogen atoms (count them). Because of the difference in atomic arrangement, though, the two compounds have somewhat different properties. Isobutane is harder to liquefy than normal butane, for instance.

When you think that the carbon chain can be almost any length, and branched in almost any way, you can see that by building molecules out of carbon and hydrogen only, you can have literally billions of different compounds. Perhaps you begin to understand the troubles I ran into trying to fit organic chemistry into one short volume.

Nor are we done with the versatility of the carbon atom. Two carbon atoms may be held together by two of their bonds (a *double bond*) or even three (a *triple bond*). Simple cases of this are shown in *Figures d* and *e*.



$$\mathrm{H-\underset{\displaystyle H}{\underset{|}{C}}=\underset{\displaystyle H}{\underset{|}{C}}-H}$$

Figure d—Ethylene

$$\mathrm{H-C\equiv C-H}$$

Figure e—Acetylene

The hydrocarbon with the double bond is *ethylene* and the one with the triple bond is *acetylene.* These are *unsaturated hydrocarbons* because they don't hold all the hydrogen atoms they would if some of the carbon bonds weren't wasted in that doubling and tripling.

In all the varieties of carbon chains that are possible, double bonds and triple bonds can be inserted almost anywhere and in almost any numbers. This increases still further the number of organic compounds possible.

RINGS AND SIDE-CHAINS

Then, too, who says the carbon atom must restrict itself to chains whether straight or branched? Carbon atoms may form rings. Most commonly the carbon atoms form rings made up of five or, especially, six atoms, like this:

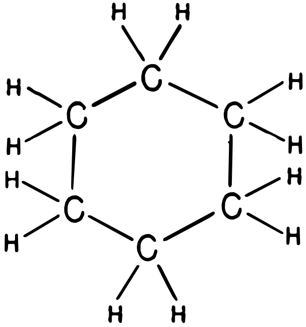


Figure f—Cyclohexane

This is *cyclohexane*, which has characteristics that are somewhat different from those of *normal hexane*, in which the carbon atoms form a straight line. A ring may have double bonds connecting its carbons, too. In fact, the most important ring of carbon atoms is one in which there are no less than three double bonds among the six atoms. This compound is *benzene* and its molecule looks like this:

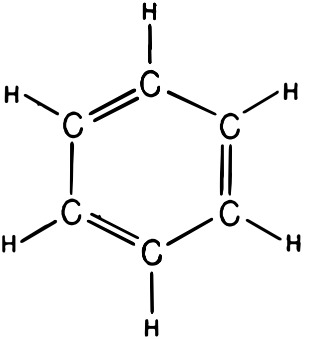


Figure g—
Benzene

Notice that the bond arrangement in the benzene ring of atoms is double bond / single bond / double bond and so on in alternation. This kind of bond alternation is referred to as *conjugated double bonds*. Compounds containing conjugated double bonds in their molecules are particularly stable; that is, they are less likely to undergo reorganizations of their atoms than are similar compounds without conjugated double bonds.

Chemists often write rings of carbon atoms simply as polygons, for the sake of brevity. For instance, the formula of cyclohexane would be written as a hexagon, while that of benzene would be a hexagon with three double bonds showing in the proper place, thus:

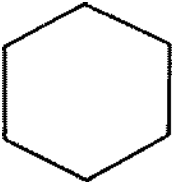


Figure h—
Cyclohexane (schematic)

Figure i—
Benzene (schematic)

Formulas like this look complicated to people who aren't used to them, but actually all you need do is remember two simple rules:

First, a carbon atom must be placed at each angle of the figure.

Second, any spare bonds not involved in forming the ring, must be attached to hydrogen atoms.

(If any atom other than carbon makes up part of the ring, or if any atom other than hydrogen is attached to the ring, those atoms are always shown in full even in the polygon formulas.)

Rings of carbon atoms can exist joined together in almost any number and arrangement, like the tiles on a bathroom floor, and in such compounds, the polygon short-cut formulas come in very handy. For instance, certain very important chemicals in the body contain atoms that are arranged into four connected rings. Such a ring system can be shown as follows:

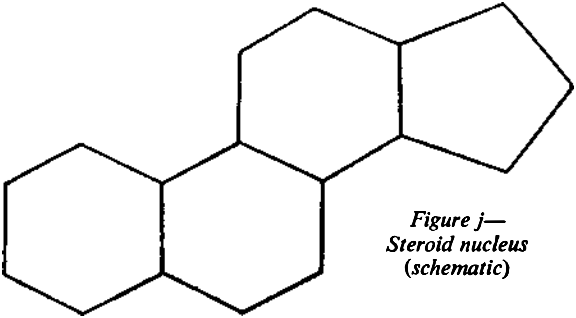


Figure j—
Steroid nucleus
(schematic)

(Notice that the ring in the upper right hand corner is a pentagon, not a hexagon. It has only five angles and is made up of only five carbon atoms.)

This four-ring combination is found in all *steroids*. (Examples of steroids include cortisone and the various sex hormones.) The steroids differ among themselves by the fact that different atoms or groups of atoms are attached to certain atoms in the rings. Atom groups attached to a ring are called *side-chains*. The various steroids differ, then, in the nature of their side-chains.

The side-chains are usually named after the compounds they resemble. A single carbon atom (with hydrogens bonded to it, of course) attached to a ring, or to any atom collection in fact, is called a *methyl* group, after methane. A two-carbon group is an *ethyl* group (after the two-carbon hydrocarbon, *ethane*.) A four-carbon group would be a *butyl* or an *isobutyl* group, depending on whether the four carbons are in a straight line or branched.

The major exception to this system of naming, involves the benzene ring. When a benzene ring is attached to a collection of atoms in a molecule, it is referred to as a *phenyl* group.

CHLORINE AND OXYGEN

All this, as yet, involves only the two types of atoms, carbon and hydrogen. But these are not the only ones commonly found in organic compounds. For instance, the chlorine atom, like the hydrogen atom, has one bond, and it can take the place of almost any hydrogen atom in almost any organic compound. (Chlorine, by the way, is a greenish, poisonous gas, but in combination with other elements it is necessary to life.)

Let's go back to our first formula, that of methane. It consisted of a carbon atom and four hydrogen atoms.

If three of those hydrogen atoms were replaced by chlorine atoms, the compound, *chloroform*, results:

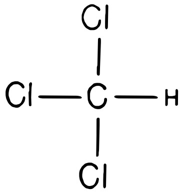


Figure k—Chloroform

Notice that the symbol for chlorine is Cl. The initial letter isn't enough because that has been used for the carbon atom. A second letter must be used to distinguish chlorine from carbon in formulas.

Next to carbon and hydrogen, however, the type of atom that most commonly appears in organic compounds is not chlorine but the oxygen atom, which is represented in formulas by its initial letter, O. (Oxygen occurs in the atmosphere to the extent of 20 percent and is necessary to life. We breathe in order to get it into our lungs, from where it is absorbed into the body.)

The oxygen atom has two bonds and these can be distributed in any one of several ways. For instance, one bond can be attached to a carbon atom and one to a hydrogen atom, giving the combination, C-O-H. Any compound that contains that particular combination of atoms is an *alcohol.*

The best-known alcohol and the one we usually mean when we say simply "alcohol" is *ethyl alcohol*, which contains the two-carbon ethyl group in its molecule as well as a *hydroxyl group* (OH):

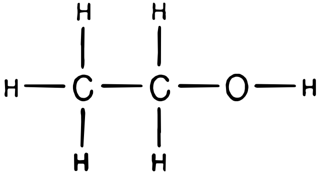


Figure l—Ethyl Alcohol

The number of alcohols is even more tremendous than the number of hydrocarbons, since in each hydrocarbon you can add a hydroxyl group to any point in the ring or chain. In fact, you can have more than one hydroxyl group present; you can have two, three, a dozen, hundreds.

When the hydroxyl group is attached to a benzene ring, a special alcohol called a *phenol* is formed. This brings up an important point.

The hydrogen atom that makes up part of the hydroxyl group has a very slight tendency to come loose. Any compound with such a tendency is an *acid*; the less the tendency, the weaker the acid. Ethyl alcohol is, therefore, an extremely weak acid, so weak that it can only be detected as such under special and unusual conditions. The hydroxyl group in a phenol, however, loses its hydrogen a little more easily, so that phenols are stronger acids than are ordinary alcohols. For that reason phenol is sometimes called *carbolic acid.*

The hydrogen lost by an acid is not really a whole hydrogen atom but only part of one. This part-hydrogen-atom is called a *hydrogen ion*. The missing piece of the hydrogen is still attached, as a kind of surplus, to the original acid molecule. Any atom, or group of atoms, that has had a sub-atomic piece torn loose, or has that piece as excess, is an *ion*.

Such ions, because of the part missing or in excess, carry an electric charge. If a part is missing, the charge is positive; if in excess, it is negative. Thus, when an acid loses a hydrogen ion, the hydrogen ion is positively charged, while what is left of the acid becomes a negatively charged ion.

Ions have properties that are quite different from those of the whole atoms to which they are related. A hydrogen ion is nothing like a hydrogen atom in its characteristics. As another example, sodium atoms form a poisonous highly active metal and chlorine atoms make up (in two-atom combination) a poisonous highly active gas; yet the *sodium ion* (positively charged) and the *chloride ion* (negatively charged) are harmless and even essential to life. In combination, they make up ordinary table salt.

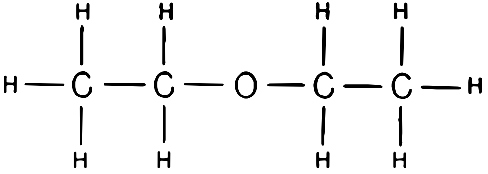
There are ions or molecules that have a tendency to add on hydrogen ions to themselves. Such substances are called *bases*. Notice that a base is the opposite of an acid. an acid gives up hydrogen ions; a base picks them up.

OXYGEN IN OTHER ROLES

Returning to the manner in which an oxygen atom might distribute its bonds, we find cases where both bonds are attached to carbon atoms, forming a C-O-C combination. Any compound with an atom combination in the molecule is an *ether*.

The best-known ether and the one we usually mean when we say simply "ether" is *diethyl ether*. This has a molecule in which the oxygen is attached to two ethyl groups, thus:

Figure m—
Diethyl Ether



$$H_3C-CH_2-O-CH_2-CH_3$$

Then, too, the oxygen atom might have both its bonds attached to a single carbon atom. Such a $C=O$ combination is called a *carbonyl group*. The carbon atom of the carbonyl group has two bonds remaining that can be distributed in several different ways. One, for instance, might be attached to a hydrogen and one to a carbon. The compound that results is an *aldehyde*. Or both bonds might be attached to carbon atoms, in which case the result is a *ketone*. Examples of each of these are:

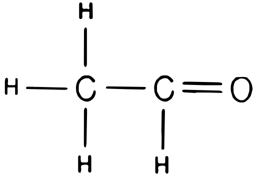
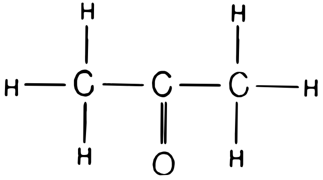


Figure n—Acetaldehyde

Figure o—Acetone



the former being *acetaldehyde*, the latter *acetone*.

Sugars (there are a number of different chemical substances that belong to this class) have molecules made up of chains of carbon atoms, one being part of a carbonyl group, and the rest having hydroxyl groups attached. A sugar is therefore both an aldehyde (or ketone) and an alcohol. Substances like starch have giant molecules made up of many sugar molecules hitched together by way of ether groups (COC).

One of the spare bonds of the carbonyl group may, on the other hand, be attached to an oxygen atom which, in turn, is most often hitched to a hydrogen atom by its other bond. The resulting combination (H—O—C=O) is called a *carboxyl group*. The hydrogen atom of a carboxyl group comes loose much more easily than does the hydrogen of a simple hydroxyl group. This, you may remember, is the mark of an acid. Organic compounds containing the carboxyl group are therefore noticeably acid in character and are, in fact, called *organic acids*.

The best known example of an organic acid is one in which the carboxyl group is attached to a methyl group, thus:

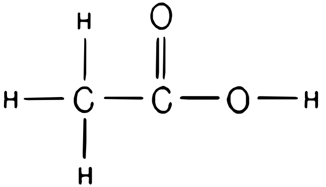


Figure p—Acetic acid

This is *acetic acid*, the compound that gives vinegar its taste and odor. Acids with much longer carbon chains make up part of the molecules of the fat in living creatures and are, for that reason, called *fatty acids*.

Naturally a carbon chain may have more than one of any of these combinations (carboxyl, hydroxyl, carbonyl or ether groups) strewn along in different places. There may be present some of one and some of another.

It frequently happens that two atom combinations can combine with one another, splitting out some atoms and forming a new type of combination. For instance, the carboxyl group of an organic acid and the hydroxyl group of an alcohol can combine as shown in the formula on the next page.

The new combination formed (C—O—C=O) is an *ester link* and compounds containing it are called *esters*. In forming an ester, as you see in the formula, an H—O—H group is split out. This represents a molecule of water. When two groups combine with one another, splitting out water (or some other small molecule), the process is known as *condensation*.

By adding water to the combined molecule, it is possible, often, to reverse the process, and break the combined molecule into its original components. This reversed process is called *hydrolysis*.

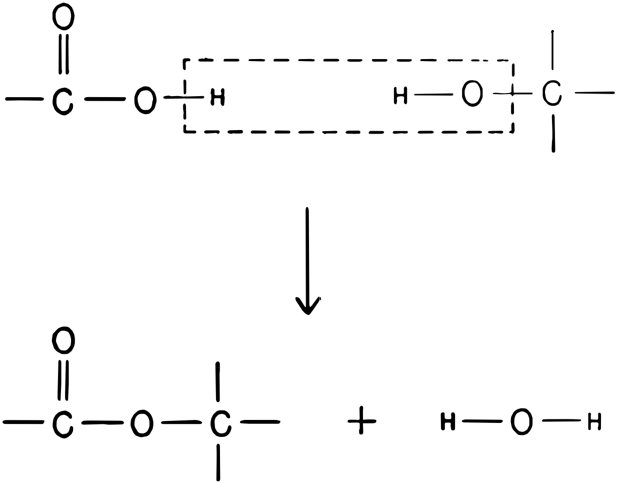


Figure q—Esterification

Well, then, in this preliminary chapter I have merely pointed out a few of the atom combinations that are possible in organic chemicals and that occur frequently. You can well imagine that if I tried to go into a little detail on each of these compounds and on several of their relatives as well, it would be only too easy to fill up a book on only the combinations I have mentioned so far. And that was, indeed, exactly what I did in *The World of Carbon.*

Yet the combinations so far described still leave out of consideration a number of interesting organic compounds, including some that are the most important of all. In order to discuss those others, it is necessary to introduce still another element, *nitrogen.* Because the remaining organic compounds to be discussed involve the nitrogen atom in almost every case, I am calling this second book on the subject, *The World of Nitrogen.*

1

Enter Nitrogen

TISSUE DECAY

Nitrogen is a gas, and the *nitrogen molecules* that compose it are made up of two nitrogen atoms apiece. Nitrogen occurs in the atmosphere, making up 4/5ths of it, in fact. As a gas, nitrogen combines with very few substances and is useless to most forms of life. We ourselves, for instance, breathe in quantities of nitrogen with every breath and then just breathe it out again. Some of it dissolves in our blood, but does nothing there.

Once nitrogen is forced to enter into combination with other atoms, it forms compounds that are essential to life. Plants and animals cannot force nitrogen to enter those combinations. There are certain bacteria in the soil that do have that ability, however. These are the *nitrogen-fixing bacteria*[1] and it is their presence in the soil that helps make other forms of life possible.

The nitrogen atom is capable of forming three different bonds and its symbol is just its initial letter, N. If a nitrogen atom is bonded to three hydrogen atoms, the result

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[1] The word "fixing" is an old-fashioned one. It refers to the change of a gas or liquid into a solid by some chemical means (not just by freezing). The agile molecules of gases or liquids are fixed in place, so to speak, and made to settle down, usually in the form of a new compound that happens to be solid at ordinary temperatures.

is a gas with a pungent and choking odor, called *ammonia*. Ammonia is, of course, an inorganic compound since its molecule contains no carbon atom. If at least one of the three nitrogen bonds is attached to a carbon atom, however, then we do have an organic compound. Such an organic compound is called an *amine*.

The simplest amine is one which contains only a single carbon atom. Its formula looks like this:

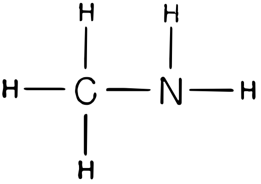

Figure 1—Methylamine

This is *methylamine*.

Methylamine is a gas with a strong, foul odor, like spoiled fish. Most of the simple amines have this unpleasant spoiled-fish odor, but have important industrial uses anyway. For one thing, amines can be used as starting materials for the manufacture of dyes and medicines. They can be used to prevent metals from corroding, so they are added to anti-freeze and other liquids which will make contact with metal.

Living tissue contains complicated substances whose molecules, after death, break down in a variety of ways to simpler molecules. This is usually the result of the chemical activity of *decay bacteria*. Small quantities of simple amines are formed from the complex nitrogen-containing compounds, particularly in fish. This is one of the reasons why decay results in bad odors.

Diamines (compounds carrying two amine groups) can also be formed during decay. For instance, a four-carbon or five-carbon chain with an amine group on each end can be formed. The four-carbon compound is called *putrescine* and the five-carbon compound, *cadaverine.* (These are among the most unpleasant names in chemistry.)

Such products of decay are lumped together as *ptomaines* and at one time they were thought to be very poisonous. Perhaps you have heard the expression "ptomaine-poisoning" in connection with people who have become sick as a result of eating spoiled food. Now we know that the ptomaines aren't as poisonous as had been thought. The responsibility for the poisoning must be laid at the door of other and more complicated products of bacterial action. The proper expression, which has displaced "ptomaine-poisoning" these days, is simply *food-poisoning*.

NERVES

More than one of the bonds of nitrogen can be attached to carbon atoms. When only one is, as in methylamine, the result is a *primary amine*. When two are, the result is a *secondary amine*. When all three are, the result is a *tertiary amine*. An example of a tertiary amine is *trimethylamine*, with a formula that looks like this:

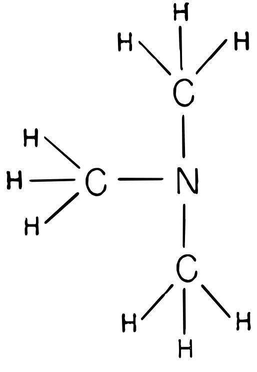

Figure 2—Trimethylamine

Under special conditions, a nitrogen atom can form a fourth bond which is just as strong as the other three, but has somewhat different electrical properties. A compound containing nitrogen attached to four other atoms (of which at least one is a carbon atom) is an *organic ammonium ion.* If nitrogen is attached to four different carbon atoms, it is a *quaternary ammonium ion.* The fourth bond is called a *co-ordinate bond* and is sometimes represented by a little arrow instead of just a dash.

To show you what I mean, look at these two formulas:

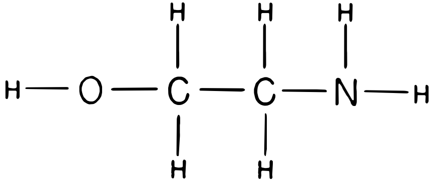

Figure 3—Ethanolamine

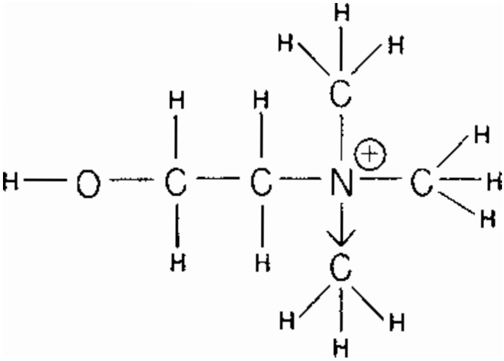

Figure 4—Choline

The top one is a two-carbon compound, with an amine group at one end and a hydroxyl group on the other. The amine group is an ordinary one and the nitrogen atom has three bonds. This compound is *ethanolamine.*

The lower compound is something like ethanolamine, except that it is a quaternary ammonium ion. The nitrogen atom is attached to four carbon atoms altogether. It is *choline.*[1]

Both ethanolamine and choline are extremely important to the body since they make up part of certain fat-like molecules.

The ordinary fats and oils are made up of glycerides: That is, their molecules consist of glycerol (a three-carbon alcohol, with a hydroxyl group attached to each carbon) which is condensed with three fatty acids. Such fats and oils are known as *simple lipids.* (The word "lipid" comes from a Greek word meaning "fat.")

There are similar compounds, however, in which glycerol is condensed with two fatty acids only. This leaves the third hydroxyl group of glycerol free to condense with other substances, and it does. The atom combinations with which this third hydroxyl group combines often includes either ethanolamine or choline. Substances such as these are known as *compound lipids.*

The compound lipids are much more important to the body than the simple lipids are. The simple lipids are just energy reservoirs. If you go without food for a period of time, the body will use up its simple lipids to produce energy and you will lose weight. Then, when you start eating again, you will store simple lipids again and gain weight.

It is different with compound lipids. However long a

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[1] Actually no one bond of the nitrogen atom can be written with the little arrow. It could be any bond; I picked the one pointing downward at random. Modern theory, in fact, has it that when one bond has special electrical properties, the "specialness" spreads out over nearby bonds in a way that can't be shown easily on paper. The special character of the extra bond means also that it is really necessary to write a little plus mark (+) near the nitrogen to show that there is a missing electron there. Because of that, choline should really be referred to as *cholinium ion.* All these extra little points need not concern us in this book, however.

person goes without food, he will never use his compound lipids for energy. The body will die of starvation without using them. Apparently each cell has a supply of compound lipids that is necessary to its workings and can't be spared. This is particularly true of the cells of the nerves and the brain.

Egg yolk is very rich in compound lipids for the use of the developing chick. In fact, the best-known compound lipid is called *lecithin* (it contains choline as part of its molecule) from the Greek word for "egg".

Chemists still don't know exactly what it is that compound lipids do in the cell. Compound lipids may be an important part of the cell membrane. They certainly make up a good part of the myelin sheath that encloses nerve fibers.

Choline is important to nerves in another connection. The hydroxyl group of choline can condense with the carboxyl group of acetic acid to form an ester called *acetylcholine*. Small quantities of acetylcholine are formed from choline and acetic acid and are then hydrolyzed back again while a nerve is being stimulated. The making and unmaking of acetylcholine is somehow involved in the mechanism by which a nerve carries its message.

Nerves that make use of acetylcholine are *cholinergic nerves*; others are *adrenergic nerves*. They make use of small quantities of *Adrenalin* and *Noradrenalin*.[1] Noradrenalin has an amine group attached to a carbon chain with a hydroxyl-carrying benzene ring at the opposite end. Adrenalin has an additional methyl group attached to the nitrogen atom as well.

Adrenalin and noradrenalin are formed not only by the nerves themselves, but also by the inner portion

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[1] These are trade names. The proper chemical names are *epinephrine* and *norepinephrine*. The trade names are used much more commonly than the proper names even by most chemists.

(*medulla*) of the adrenal glands, which are situated just above the kidneys. Strong emotion, such as anger or fear, causes the adrenal medulla to form a bit of these compounds and send them out into the bloodstream. Instantly, the liver discharges glucose into the blood: the heart-beat speeds up; blood-pressure rises; other changes take place. In general, the body is put on an emergency basis, ready to fight or run as the case may be.

DYES

An amine group attached directly to a benzene ring makes up the molecule of *aniline*, thus:

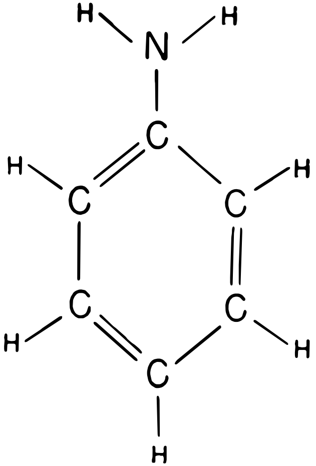

Figure 5—Aniline

Aniline is important to us not so much in itself but in what it leads to. Back in 1856, a chemistry student at the Royal (now Imperial) College of Science in London, named William Henry Perkin, was working with aniline. He was trying to make a substance called quinine out of it. (Quinine is a medicine used to combat the widespread disease, malaria). Perkin failed because quinine had a complicated molecule and at that time not enough was known of the structure of the quinine molecule, or about synthetic techniques either, to make it possible to succeed in that particular project.

However, Perkin's failure made him a rich man because, while treating aniline with various chemicals, he ended up with a purple substance which was eventually called *Aniline Purple*. Instead of ignoring it, Perkin saw its importance and developed methods for producing it in quantity. It was the first successful synthetic dye. (A *dye* is a colored substance that can be attached more or less permanently to textile materials.) Aniline Purple became quite the rage. The French called it *mauveine* and invented the word "mauve" to describe its color.

In fiction, chemists and other scientists often seem to be making great discoveries by accident. In real life, it doesn't happen so often, but it does sometimes and this is one of the cases. The most dramatic thing of all about the discovery, perhaps, is that Perkin was only eighteen when he made it.

Since then, hundreds of dyes of all sorts have been synthesized, many of them using aniline as a starting material. (Those that start with aniline are called *aniline dyes*). Their molecules are usually quite complicated and almost always include several benzene rings and several nitrogen atoms.

The nitrogen atoms may occur in the form of amine groups as in the dye, *fuchsin*, named from its fuchsia color. Others, the so-called *azo dyes* have the *azo group* as part of the molecule. The azo group consists of two nitrogen atoms connected like this: —N=N—.[1]

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[1] The term "azo" comes from the French name for nitrogen, "azote." This, in turn, comes from Greek words meaning "no life" because nitrogen is the part of the atmosphere which, unlike oxygen, does not support life.

Since aniline is obtained in quantity chiefly from coal tar (a black, tarry liquid obtained by heating coal strongly in the absence of air), the aniline dyes are often called *coal-tar dyes*. Some people are amazed that a black, ugly substance like coal-tar should give rise to such beautiful colors. Actually, it is only the aniline that gives rise to them, and aniline is colorless.

The organic chemist who builds up the aniline molecule into complicated dyes must know the molecular structures of the compounds he works with. He must also have an idea of the kind of atom arrangements that will produce color. Here is an example of the value of the type of formula I've been using in this book.

Perhaps an even more startling example of the value of knowing molecular structure involves the drug, cocaine. This is obtained from the leaves of a South American coca plant. Cocaine is a *local anesthetic*. That is, if it is injected, for example, into the gums near a nerve ending, that side of the jaw will lose all sensation for a period of time. A tooth can then be extracted without pain and yet without having to put the patient to sleep, either. The only trouble is that cocaine has certain undesirable effects, also. For instance, it can be habit-forming.

Chemists worked out the structure of the cocaine molecule and they set about trying to synthesize different parts of the molecule. They thought that perhaps they could make a simpler molecule that would still have the desirable properties of cocaine without the undesirable ones. (Furthermore, if they could make such a compound in the laboratory, they wouldn't have to depend on a South American plant for their supply.)

They made up a number of molecules modelled on cocaine. For instance, cocaine has a tertiary amine as part of its molecule and one of the carbon chains attached to that amine leads to a benzene ring. In one attempt, they kept that portion of the molecule and eliminated the rest. They made a few minor changes and had a new molecule they called *procaine*.

The anesthetic properties of procaine are only half as strong as those of cocaine, but the undesirable properties are weaker still. Procaine has replaced cocaine in dental work. You may have had injections of it yourself. If you don't recognize the name, perhaps you know the common trade-name for it, *Novocaine*.

Many other less common local anesthetics have also been synthesized using cocaine as a guide. This system has been tried for finding substitutes for other useful drugs with complicated molecules, too. It hasn't always worked, but enough has been done to make all chemists (indeed, all human beings) thankful for the formula system of describing chemical compounds.

WASTE PRODUCTS AND MIRACLE DRUGS

The nitrogen atom of an amine group may be attached to a carbon atom of a carbonyl group, like this:

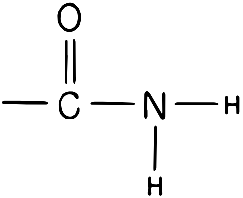

Figure 6—Amide Group

Any compound containing this atom combination (the *amide group*) is called an *amide*. (Don't get that mixed up with "amine.")

Notice that the carbon atom of the amide group still has one bond free. When that spare bond is attached to a second amine group, the compound, *urea*, results as shown in *Figure 7*.

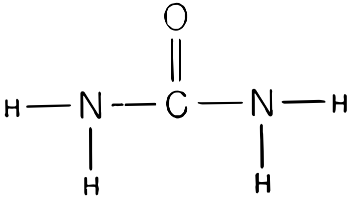

Figure 7—Urea

Modern organic chemistry started with urea, since it was the first organic material to be made in the laboratory. Urea is one of the important waste products of the human body. Those chemicals in the body with molecules made up of carbon, hydrogen, and oxygen atoms only (like sugar or fat) are converted to carbon dioxide and water. Both of these molecules can be dumped by the body easily. Carbon dioxide is a gas and is pumped out by the lungs while water can be lost through perspiration or as part of the urine or even (in the form of vapor) through the lungs.

What about chemicals in the body that contain nitrogen atoms? These must also be broken down upon occasion. If so, what does one do with the nitrogen atoms? The body has no way of turning it into nitrogen gas and getting rid of it through the lungs. The body could turn it into ammonia and get rid of that by way of the urine. Many sea-animals do exactly that. The only trouble is that ammonia is very poisonous. Sea-creatures can get away with it because they have a whole ocean into which to dump the ammonia. We do not.

A creature like man (or other mammals) living on land has no ocean to act as garbage-dump. Whatever nitrogen wastes he forms must accumulate for a while at least until he has a chance to get rid of it (just as your own household trash must be kept in trash-cans until the truck comes around for it.) For that reason, the nitrogen waste compound must be fairly non-poisonous.

A satisfactory compound for the purpose is urea. A sizable amount of it can accumulate, without harm, in the blood. As the blood passes through the kidneys, the urea is filtered out and eventually passes out of the body dissolved in the urine. (Urine contains many other waste products but none in anywhere near the quantity of urea. The word "urea" comes from "urine.")

Urea is an unglamorous compound with a simple molecule that has been known for a long time. There are other amides which are most glamorous indeed, which have quite complicated molecules and which were only recently discovered. These latter compounds are the *tetracyclines* (from Greek words meaning "four rings"). Sure enough, the molecules of these compounds are made up of four six-membered rings joined side by side. Attached to these rings are hydroxyl groups, methyl groups, amine groups and an amide group.

These tetracyclines are isolated from certain molds and have been found to be powerful germ-killers. They are examples of compounds that are formed by microscopic organisms and that are capable of killing other microscopic organisms. These are called *antibiotics*, from Greek words meaning "against life."

The antibiotics have been developed mostly since World War II and have advanced mankind greatly in the battle against germ infection. You have most likely received injections yourself of some antibiotic or other in past years, probably of one of the tetracyclines. The trade names are surely familiar to you. Tetracycline itself is often called *Achromycin*. A close relative, *oxytetracycline* (with an extra hydroxyl group on the rings) is called *Terramycin*, while *chlorotetracycline* (with a chlorine atom attached to the rings) is called *Aureomycin*.[1]

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[1] The "mycin" suffix of the trade names comes from the group of molds, the actinomycetes, from which the antibiotics are obtained.

HOLDING FLESH AND BLOOD TOGETHER

A molecule of sugar in which one of the hydroxyl groups is replaced by an amine group is called an *amino-sugar*. The most common of these is *glucosamine*. This has a molecule which looks like that of a simple six-carbon sugar called glucose except that a hydroxyl group near one end of the molecule is replaced by an amine group. Long molecules made up of glucosamine units hooked together (with two-carbon chains attached to the nitrogen atom of each unit) form the substance called *chitin*.

Chitin is a tough, horny, somewhat flexible substance which forms the outer shells of the group of animals called the arthropods. This includes insects, crabs, lobsters, shrimps and so on. These outer shells seem to clothe these creatures and, in fact, the word "chitin" comes from the name of an outer garment used by the ancient Greeks.

Chitin is the most thoroughly organic exoskeleton (that is, a skeleton on the outside of the body) in the animal kingdom. The molluscs (clams, oysters, snails and so on) also have an exoskeleton but in their case it is made up of calcium carbonate. This is an organic substance, in a way, since its molecules contain the carbon atom. However, it resembles the minerals[1] in properties much more closely than it resembles organic substances.

Vertebrates (including fish, amphibia, reptiles, birds and mammals) have endoskeletons (that is, skeletons within the body.) Such skeletons are even more efficient

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"Aureo" is from the Latin word for "gold" which refers to the golden color of aureomycin. "Achro", on the other hand, comes from Greek words meaning "no color." "Terra" comes from the Latin word for "earth" because the molds from which these helpful substances are obtained grow in the soil.

[1] In fact, calcium carbonate occurs as a common mineral and is called *limestone*.

in supporting the body and holding it together than are the exoskeletons of the lower animals.

Oddly enough, our skeletons are the most inorganic of the bunch. The chief component of our bones and teeth is a mineral that belongs to a group known as the hydroxyapatites, which have no carbon in them. Some carbonate is present in our bones, but not much.

Of course, our bones do contain some organic matter. Most of the organic compounds present consist of molecules made up of long chains of sugar acids (with molecules like those of the sugars, but with carboxyl groups added) and amino sugars. Such molecules are known as *mucopolysaccharides*. These are tough substances that are also flexible and can be sticky. In addition to being found in the bones, they make up much of the substance of ligaments and tendons, which hold muscles to bones and bones to one another.

The *mucins* that are secreted by cells in the intestines to lubricate the food and the food-canal contains mucopolysaccharides. Saliva contains some, for instance, and it is the mucin in saliva that makes it thick, stringy and slippery. *Synovial fluid*, which occurs in the joints and lubricates the ends of the bones where they meet so that you can move your arms and legs easily and without pain, also contain mucopolysaccharides.

Even the individual cells of the body are held together by a mucopolysaccharide "cement" called *hyaluronic acid.*

2

"Of First Importance"

A SET OF BUILDING BLOCKS

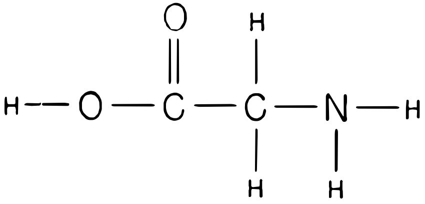
When a compound contains both a carboxyl group and an amine group in its molecule, it is an *amino acid.* An example is *para-aminobenzoic acid* (frequently abbreviated as *PABA*). Its molecule is made up of a benzene ring with an amine group and a carboxyl group attached at opposite ends. At one time, this compound was considered a vitamin and was even given a special vitamin name, "Vitamin H". However, that seems to be a mistake and you won't find "Vitamin H" in the listings any more.

The amino acids that are particularly important, however, are those in which the amine group and the carboxyl group are attached to the same carbon atom. These are called *alpha-amino acids.* About nineteen different amino acids of this kind occur almost everywhere in the body as part of more complicated molecules, usually. Several others occur here and there.

The simplest alpha-amino acid has a molecule that looks like the formula on the following page.

This compound is called *glycine.* The "glyc" prefix means "sweet" and glycine is indeed sweet to the taste.

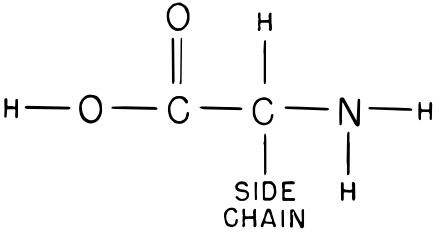
The other alpha-amino acids are like glycine except for one detail. The glycine molecules have two hydrogen atoms



$$\mathrm{H{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}{-}\underset{\underset{\displaystyle H}{|}}{N}{-}H}$$

Figure 8—Glycine

attached to the carbon atom in the middle of the formula. In the other alpha-amino acids, one of these hydrogen atoms is replaced by some sort of organic group. This organic group is called the *amino acid side-chain*. The molecule of such an alpha-amino acid would look like this:



$$\mathrm{H{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle \text{SIDE CHAIN}}{|}}{C}}{-}\underset{\underset{\displaystyle H}{|}}{N}{-}H}$$

Figure 9—Amino Acid (general formula)

In several cases, the amino acid side-chain is just a hydrocarbon group. For instance, in *alanine*, it is simply a methyl group. In *valine*, it is a three-carbon branched-chain hydrocarbon. In *leucine* and *isoleucine* they are four-carbon chains, both branched, but in slightly different ways. In phenylalanine, the *side-chain* includes a benzene ring.

In other cases, the side-chain is a little more complicated. For instance, in *serine* the side-chain is a methyl group to which a hydroxyl group is attached and in *threonine* it is an ethyl group with a hydroxyl attached to one of the carbon atoms. *Tyrosine* is like phenylalanine, except that the benzene ring in the side-chain has a hydroxyl group attached (so that there is a phenol group in the side-chain.)

Aspartic acid and *glutamic acid* both contain a second carboxyl group in the side-chain. *Lysine* contains a second amine group in the side-chain.

The carboxyl group, as I have explained previously, is a weak acid. The amine group, it so happens, is a weak base. The opposite properties of the weakly acid carboxyl group and the weakly basic amine group, both present in the same molecule, cancel each other. A molecule like glycine is therefore neither acid nor base and is a *neutral amino acid.*

If the side-chain contains a carboxyl group, that makes two carboxyl groups in the molecule altogether against only one amine group. The balance is in favor of acid properties. For that reason, aspartic acid and glutamic acid are *acidic amino acids*. (That is why the word "acid" is included in their names.)

Lysine has an amine group in the side-chain and the balance shifts toward basic properties. Lysine is a *basic amino acid.*

The amino acids so far mentioned[1] are all necessary to the body, but they're not all necessary in the diet. For instance, suppose that the complicated molecules in the food you ate contained glycine as part of the molecule, but no serine. The body could then make the serine it needs out of the glycine. In the same way, if glycine were missing but it had serine, it could make its own glycine out of serine. Amino acids which the body can make for itself out of other substances in the diet are called *non-essential amino acids*. Glycine and serine are examples.

However, there are some amino acids that must be

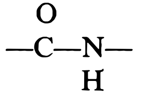
I have only mentioned twelve amino acids so far. The others possess atom groupings in their side-chains of kinds I have not yet discussed. I'll mention them later in the book.

present in the diet because the human body cannot make them out of other substances. The adult human being[1] for instance, cannot make his own valine, leucine, isoleucine, phenylalanine, threonine, or lysine. These amino acids are examples of *essential amino acids.*

STRINGING THE BUILDING BLOCKS TOGETHER

There are tiny quantities of various amino acids in the blood and other fluids of the body. For the most part, though, the amino acids condense with one another to form large molecules and it is these large molecules which occur in the body.

An amino acid can condense with another amino acid at either end; or at both ends, for that matter. Take the molecule of glycine, for instance. Its amine group can condense with the carboxyl group of a second amino acid while the carboxyl group on the other side of the glycine molecule is condensing with the amine group of a third amino acid. You can see how this works by looking at *Figure 10* (*see facing page*).



The $-\overset{O}{C}-\underset{H}{N}-$ combination of atoms that occurs in such condensed molecules (you'll find two of them in the formula on page 41) is a kind of amide group. Compare it with the formula of the amide group given in Chapter 1 and you'll see what I mean. When such a group involves amino acids, as in the case above, it is given a special name and is called a *peptide link*. Amino acids bound together by such links are called *peptides.*

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[1] Dietary requirements vary for different organisms. For instance, chicks cannot make enough glycine for their needs and must have some in their diets. Young rats, on the other hand, can make all the glycine they need.

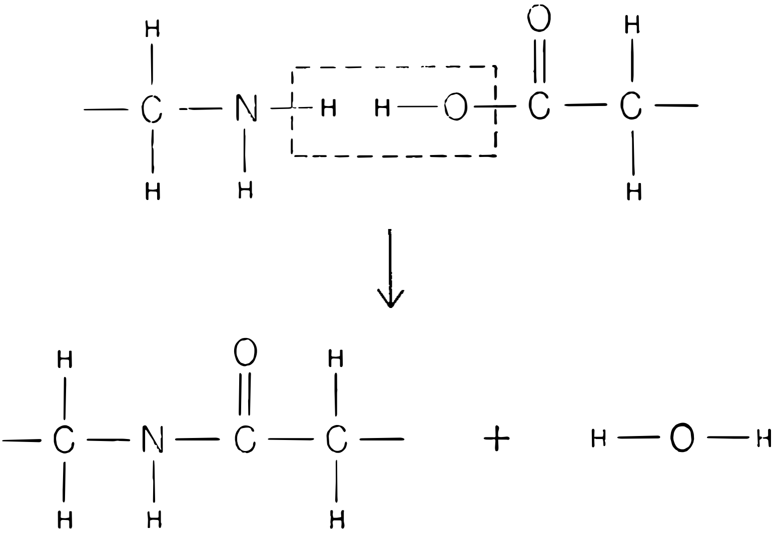

Figure 10—Peptide Condensation

If only two amino acids are hooked together the compound is a *dipeptide*; three form a *tripeptide* and so on. If a number of amino acids are in the chain and you're not sure exactly how many, the compound is a *polypeptide.*

Some of the hormones have polypeptide molecules. For instance, two hormones manufactured by the pituitary gland (a small gland just underneath the brain in the very center of the head) are polypeptides made up of exactly eight different amino acids. (They are *octapeptides.*)

Some of the antibiotics are also polypeptides. *Bacitracin*, for instance, is made up of eleven amino acids strung together by peptide links.

FIBERS

There is scarcely any limit to the number of amino acids that can be strung together. Thousands upon thousands may make up a single large molecule. When the number of amino acids making up a molecule is more than about a dozen, the molecule is that of a *protein*. The word comes from the Greek word meaning "primary" or "of first importance". That describes certain proteins very well as far as their position in the body is concerned.

Some protein molecules are nothing more than just a more or less straight string of simple amino acids. The best example of this involves the silkworm (which is a caterpillar and not a worm.) At a certain stage in its life the silkworm goes into a kind of hibernation during which its body machinery is completely altered. When the alteration is completed, it is no longer a caterpillar; it has become a moth.

During the hibernation, the caterpillar is completely helpless. To protect itself it ejects thin jets of fluid from certain glands. These jets harden at once into delicate fibers. It encloses itself in these fibers and the cocoon that results protects it till it is ready to break out once more into the world.

The fibers used to build the cocoon are what we call *silk*. The chief component of silk is a protein called *fibroin*. Its molecules consist of chains of about a hundred amino acids. Only the simpler amino acids occur frequently in the chain. Glycine, alanine and serine are the most common. (In fact, the word "serine" comes from the Latin word for "silk" since that is where it was first located.)

Such simple amino acid chains form *fibrous proteins* and there are generally tough strong substances that can stand a great deal of pull before snapping. Silk, for instance, is so strong that a fiber of it can stand more of a pull than can a metal wire of the same thickness. In addition, silk has a beautiful sheen and can form very sheer and filmy cloth. For that reason, silk has always been an item of luxury, since the days of the Roman Empire (and, of course, long before that in China, where growing silkworms for the sake of their cocoons was first invented.)

Since 1947 chemists have learned how to synthesize fibrous proteins, beginning with separate molecules of a single amino acid, or sometimes of two different amino acids. These artificial polypeptides resemble fibroin in many of their properties but, for various reasons, won't do as artificial silk.

A satisfactory artificial silk was synthesized as early as 1935, however. It was built up out of one type of molecule with an amine group at each end and another with a carboxyl group at each end. The two types of molecules hooked up alternately into long chains. The result was a fiber that is like silk except that it is even stronger. It is called *Nylon*.

In 1940, Nylon was first produced commercially and, what with World War II making it very difficult to import silk, the artificial fiber almost completely replaced the natural one. What's more, by the end of the war, women had decided that Nylon was better, anyway. Nowadays, a woman's stockings are practically never referred to as anything but "nylons" and other garments, too, both men's and women's, are made of Nylon.

Nylon is valuable not only for its beauty but for its strength, too. For instance, automobile tires, these days, frequently use Nylon linings to increase resistance to the shocks and strains of the road.

The human body contains a number of fibrous proteins, too. Hair is almost entirely made up of a fibrous protein called *keratin*. This protein also occurs in other outer portions of the body. It occurs in skin and fingernails. It also occurs in the claws, scales, feathers, horns and hooves of various animals. (The word "keratin" comes from the Greek word for "horn.")

Commercially, the most important type of hair is that grown by sheep. It is called *wool.* Wool fibers are weaker than those of cotton or silk but can be used to weave warm and light clothing of types that have been useful and popular for thousands of years.

The individual wool fibers have surfaces that are made up of tiny scales with rough edges. If pressed together, the fibers will cling and form a fuzzy mass called *felt.*

All hair is made up chiefly of keratin so that the cheapest felt hat and the most expensive chinchilla fur coat are much the same chemically.

Most animals cannot digest keratin. Unfortunately, the larvae (that is, the immature caterpillar-like forms) of certain moths and beetles can. Such insects lay their eggs in woollen clothes, in tapestries and carpets. The larvae eat the fibers and do much damage. One of the most important uses of modern insecticides is to fight these keratin-eating bugs.

DESSERTS

Another fibrous protein found in the body occurs in tendons, ligaments, bones, cartilage, and so on. It is called *collagen.*

Although most fibrous proteins are quite indigestible, collagen is a partial exception. As long as it stays collagen it is indigestible enough; however if it is heated (as in cooking), it changes at least partly into a gluey, soft substance. This new substance can be digested and utilized by the body. (In fact, the word "collagen" comes from Greek words meaning "giving birth to glue." When a horse is "sold to the glue factory," it is for the sake of the collagen in its hooves, which can be turned to glue.)

The collagen molecule is made up of several chains of amino acids held together in rather complicated fashion.

Strong heating will split apart the bundles into individual chains. The result is *gelatin.*

Gelatin is very soluble in water and very digestible. It has a very pleasant consistency when allowed to jell. It has no taste of its own but when various flavorings are added, gelatin makes a popular dessert. Gelatin is also used in ice cream to help give it smoothness and in marshmallow. It is also used in jellied meats.

However, despite its general pleasantness, gelatin has its shortcomings, and that will take a little explaining.

When a protein is digested, it is hydrolyzed into its separate amino acids in the stomach and intestines and the amino acids are then absorbed into the body. Once within the body, several things can happen to the amino acids. They can be broken down to carbon dioxide, water and urea. The energy that results can be used just as though it were fat or carbohydrate being broken down. Once the urea is split away, in fact, what is left of the amino acid molecules need not be broken down at once. It can be changed into glycogen or fat and stored away.

More important than that, though, is the body's ability to take amino acids and build them into proteins of its own; to build tissue, in other words. However, in order for the body to do this, the food protein it starts with must have enough of each of the essential amino acids (see page 40). The non-essential amino acids don't matter so much. The body can make them for itself. It is the essential amino acids that simply must be present in the diet in the right amounts.

Here's where gelatin falls down. It is missing in some of the essential amino acids almost altogether. It is therefore an *incomplete protein.* A man who tried to live on gelatin as the only protein in his diet would lose weight, sicken and eventually die. (However, when other proteins are also present in the diet, as they usually are, gelatin still makes a pleasant dessert. And, of course, it can always be used for energy.)

THE FRAGILE MOLECULES

The really complicated protein molecules of the body are the *globular proteins.* They are called so because at one time it was thought that while fibrous proteins had long thin molecules (like fibers), the globular proteins had molecules more like globes. Actually, it isn't as simple as that because globular proteins can also have fairly long, thin molecules. However, the name sticks.

The point about globular proteins is that, instead of being tough and strong like fibrous proteins, they are among the most fragile substances known.

Globular proteins have the amino acid chains in their molecules coiled and looped about in certain ways. These coils and loops are held in place by very weak bonds called *hydrogen bonds.* The working of globular proteins depends upon their molecules holding their shapes. Anything that will break the hydrogen bonds (gentle heat, almost any chemical, even just hard shaking) will cause the amino acid chains to flop into disorder. The protein loses its particular shape and can no longer fulfil its original function. The protein is then said to be *denatured.*

The proteins perform thousands of different tasks in the body. The secret of their versatility lies in the amino acids of which they are made up. The side-chains of these amino acids stick out from the polypeptide "backbone." Each protein has nineteen different amino acids (sometimes a few extra varieties, too). Some of these are present by the dozen, some by the hundred.

Every different kind of protein has its own arrangement of amino acids along the polypeptide chain; each has its own pattern of side-chains. Every protein with a particular side-chain pattern has its own particular set of properties.

The number of different patterns possible is tremendously high. It is possible for every protein molecule that ever existed to have a different pattern and still there would be no danger of exhausting the supply. In the last ten years, chemists have been trying very hard to determine the exact arrangement of amino acids that does occur in proteins. In the case of some of the simpler proteins, they have succeeded.

BLOOD AND FOOD

Some proteins have molecules that are made up of nothing but chains of amino acids. These are called *simple proteins*. Others may include as part of their molecules a bit of mucopolysaccharide or some compound lipid. These are called *mucoproteins* and *lipoproteins*, respectively.[1] The lipoproteins, in particular, are becoming very important to doctors nowadays. The number one cause of death in the United States today is *atherosclerosis*. This is a disease in which sterols and other fat-like molecules deposit in the walls of important blood vessels called arteries, and prevent the blood from circulating properly. Doctors are trying to find out if there is some connection between this disease and the quantity and kind of lipoproteins present in the blood.

The simple proteins are divided into two main classes: *albumins* and *globulins*. Albumins have the smaller molecules and are quite soluble in water. Globulins have molecules that are somewhat bigger and less soluble. Albumins are present in egg-white (in fact, the word "albumin" comes from the Latin word for "white"), in milk and in the liquid portion of blood (*blood plasma*).

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[1] Proteins made up of more than just amino acids are given the general name of *compound proteins*.

The blood plasma contains globulins as well as albumin, and clever methods have been worked out to separate the globulins from the albumin. What's more, the globulins can be separated into several groups. These are named after the letters of the Greek alphabet, as alpha-globulins, beta-globulins and gamma-globulins.

The *gamma-globulins* are the most important of these. They include molecules of *antibodies* manufactured by the body to counteract the influence of foreign proteins that get into the body somehow. The most important foreign proteins (that is, those the body does not make for itself) are those that belong to invading micro-organisms that cause disease. Once the body manufactures the proper antibodies to these proteins, the effect of the micro-organism is neutralized, and the sick person recovers.

In some diseases, such as smallpox, measles or mumps, the antibodies that are formed stay among the gamma-globulins of the blood for many years. That is why people who have had one attack of such diseases are generally *immune* to it afterward. That is also why some of these are "children's diseases." It isn't that children are particularly good at catching them; it's just that children haven't had a chance to make antibodies against them yet.

Smallpox has been largely wiped out in civilized countries by the practice of *vaccination.* In this process, a person is deliberately infected with a weakened virus (called a *vaccine*) that can only make him slightly sick. He develops antibodies against the weakened virus and these will also work against the full-strength virus so that he is immune to the disease at its worst. The same system, just about, is used in the *Salk vaccine* to guard people against poliomyelitis (infantile paralysis.)

Sometimes a person may form antibodies against harmless proteins such as those found in some kinds of plant pollen, or even in some kinds of food. Once such antibodies are formed, the person may react unpleasantly to the presence of these proteins. He is *allergic* to them.

He may break out in a rash or in hives if he eats the wrong kind of food. The membranes of his nose and throat may swell and fill with mucus at seasons when certain plant pollens are plentiful. This is *hay-fever*. He may even have trouble breathing, as in *asthma*.

In addition to the albumin and the globulins, blood plasma contains a protein called *fibrinogen*. When a wound causes bleeding, a series of rather complicated chemical changes takes place in blood. This ends by changing fibrinogen (which is soluble) into *fibrin*, which is an insoluble fibrous protein. The fibrin helps form a crust over the wound which we call a *scab*. In this way, loss of blood is prevented while the hurt tissues heal themselves and grow together.

Throughout the body, in every cell (and outside cells, too) there are thousands of different protein molecules that act as *catalysts*. That is, in their presence certain chemical reactions proceed briskly. Each different protein catalyst exerts its speed-up influence on one particular small group of reactions (often of only one reaction and no other). These protein catalysts are called *enzymes*. The body's chemical workings are controlled by the presence or absence of the various enzymes; or by how much of each is present.

Many of the globular proteins are *complete proteins*. That is, they contain reasonable quantities of all the essential amino acids. The most important proteins in the American diet are *casein* (which is the chief protein of milk and cheese[1]—in fact, cottage cheese is hardly more

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[1] Casein is rich in the amino acid, *tyrosine*. In fact, tyrosine was first discovered in cheese and its name comes from the Greek word for "cheese."

than just casein and water); *vitellin* (the chief protein of egg yolk); and *actomyosin* (the chief protein of meat.) These animal proteins are all complete. Plant proteins are not quite as satisfactory nutritionally as animal proteins but some (like those of most grains and of beans) are fairly good.

Casein is a particularly useful protein. In addition to its nourishing qualities, it can be used to make a strong glue. It can be added to certain paints to make them easier to mix with water. It can be made into a hard, ivory-like plastic that can be used for making buttons, and into an artificial fiber out of which clothing can be woven.

AMINO ACID SIDE LINES

The body doesn't use amino acids just to build proteins. Some amino acids have important side-lines. Tyrosine, for instance, is used as a building block for at least three important compounds. One is the hormone pair, epinephrine and norepinephrine, mentioned in Chapter 1. These have molecules resembling tyrosine with the carboxyl group knocked off and an additional hydroxyl group pinned onto the benzene ring. The body can make those changes without trouble.

If tyrosine is put through a series of rather more complicated changes, it ends up as a dark brown substance, with a large molecule, known as *melanin*. (The name comes from the Greek word for "black.") Melanin is found in human skin, eyes and hair. If a lot of it is present, skin and eyes are dark brown and the hair is black. With less melanin, the coloring is lighter. Hair may be light brown, or even blond. (Red hair is caused by the presence of another substance altogether.) Eyes may be light brown or even blue.[1] Skin may be only swarthy or even "flesh color." Negroes may have very much melanin and some Swedes (as an example) may have very little but all normal human beings have some.

As I said, though, the change from tyrosine to melanin is quite a complicated one. Many individual steps are involved. Whenever a change has many steps, each step usually has its own enzyme controlling it. In order that the change take place properly, a human being must be born with the ability to make every one of the necessary enzymes. Sometimes he isn't born with the ability.

For instance, occasionally a human being is born without one of the enzymes in control of the tyrosine-to-melanin change. That person, for lack of a single enzyme, cannot form melanin. His skin is very fair, his hair is white. There is no color in his eyes so that blood-vessels show through and make them look red. Such people are called *albinoes* (again from the Latin word for "white.")

There are a number of disorders caused by missing enzymes. Some are so slight that a person is never even aware of it. Others, such as albinism, which I just mentioned, are very noticeable. Some are more serious still.

For instance, in the normal human being, a certain amount of the phenylalanine in the diet is changed to tyrosine by the addition of one hydroxyl group to the benzene ring of phenylalanine. If a child is born without one of the enzymes in charge of this change, phenylalanine accumulates. Such a child is mentally retarded, every time. Fortunately, this happens quite rarely.

Disorders caused by missing enzymes or hormones (or

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[1] The blue of eyes is not due to a blue pigment but to the same melanin that causes brown eyes. In blue eyes, the melanin is present in tiny scattered particles that cause reflected light to appear blue, just as the tiny scattered dust particles in the air cause the sky to appear blue.

too much of them) are called *metabolic diseases*. Now that science has brought germ diseases under control, metabolic diseases are becoming much more important than they used to be.

Tyrosine has still another side-line. In another complicated series of changes, it can add a second benzene ring to the one it already possesses (with an oxygen atom sandwiched in between) and then attach two iodine atoms to each ring. The compound that results is *thyroxine*.

Thyroxine is a hormone which controls the overall speed with which the body produces energy. It is manufactured by a blob of tissue near the Adam's apple that is called the *thyroid gland*. This acts as an "iodine trap". Any iodine in our food gets into the blood and eventually is carried through the thyroid gland. The gland yanks it out of the blood and uses it to manufacture thyroxine.

Although the body needs very little iodine for this purpose, sometimes even that small quantity is not present in the diet. In that case, the body's machinery can go haywire, sometimes seriously. The thyroid gland may swell so that the neck bulges out. This condition is called *goiter*. This and other trouble can be prevented easily if a bit of iodine is added to a city's water reservoir, or if salt with a tiny bit of added iodine (*iodized salt*) is used on food.

MORE SIDE-LINES

Glycine is another versatile amino acid. One of its many jobs in the body is to help get rid of unwanted compounds This can be useful to physicians.

Suppose, for instance, that you accidentally swallow some benzoic acid; (its molecule consists of a benzene ring to which a carboxyl group is attached). It isn't particularly poisonous, but it's no use to the body, either.

The body gets rid of it by condensing it with glycine. The combined molecules is *hippuric acid*, which is quickly excreted through the urine. (The prefix "hipp" comes from the Greek word for "horse" since hippuric acid was first found in horse urine.)

Now this might not seem to be particularly important. After all, people practically never swallow benzoic acid by accident. These days, though, benzoic acid might be deliberately given to patients by doctors just so that hippuric acid might be formed. You see, the combination of glycine and benzoic acid takes place mainly in the liver because that is where the enzyme that controls the reaction is located. (It takes place in the kidneys, too, to a small extent).

Now, then, suppose that after the benzoic acid is given the patient, there is less hippuric acid in the urine than the doctor's experience tells him there ought to be. The most likely conclusion is that there is something wrong with the liver. The less hippuric acid appearing in a given time, the more diseased the liver. In this way, the doctor has found out something without having to operate on the patient. This is an example of a *liver function test*.

Still another amino acid, glutamic acid, guards us against a more serious type of poisoning. In Chapter 1 I explained that ammonia was too poisonous to be used as a waste-product and that the human body used urea for the purpose instead. Nevertheless, there are some reactions in the human body that do produce ammonia, and the body must have some way of taking care of it. The best way is to have some molecule snap up the ammonia as fast as it is formed.

The molecule that does the main amount of snapping-up is glutamic acid. It has a carboxyl group in its side-chain. This carboxyl group condenses with any ammonia molecule that may happen to be loose in the neighbourhood to form a non-poisonous amide group. The resulting compound is *glutamine.*

The brain is particularly sensitive to the presence of ammonia and there is a considerable quantity of glutamic acid and glutamine in the brain fluids, perhaps for that reason. Some people have wondered whether a too-high ammonia level might result in lowered intelligence and if feeding people glutamic acid might not make them more intelligent. Experiments have been tried, but the results are not clear cut, yet.[1]

Aspartic acid, with a molecule very similar to glutamic acid, will also snap up ammonia molecules. In this case, *asparagine* is formed. Asparagine was first discovered in asparagus, which accounts for its name and also for that of aspartic acid.

Serine, still another amino acid, can be used by the body to make ethanolamine. Both serine and ethanolamine form part of certain compound lipids called *cephalins.* This name comes from the Latin word for "head" since cephalins are found chiefly in the brain.

[1] Glutamic acid, with one of the hydrogen atoms of a carboxyl group replaced by sodium ion, is *sodium glutamate.* This has come into use, in recent years, as a way of giving food a meaty flavor by sprinkling it on like salt.

3

Life and Death

INTRODUCING THE B VITAMINS

When chemists first discovered that certain chemicals were needed in the diet in very small quantities, they had no idea what the structure of those chemicals might be. At first, some thought these chemicals were amines, so they called them "vitamines." The "vit" prefix comes from a Latin word meaning "life."

However, that turned out to be wrong. Some of the "vitamines" turned out to be amines indeed but others did not. The final "e" was therefore dropped to weaken the resemblance to "amine" and the name became *vitamin.*

The first attempt to separate the various vitamins was made about 1906 by American chemists. They showed that there were at least two vitamins, one of which was soluble in fat (they called this vitamin A) and the other soluble in water (vitamin B).

Of course, as time went on, things turned out to be much more complicated than that. Vitamin B proved to be not just a single vitamin but a whole group of vitamins, each with its own function in the body. Today, they are referred to as the *B Complex*. For a while, the different members of the B Vitamins were given numbers and called vitamin B_1, vitamin B_2 and so on. Sometimes, the individual members could exist in several different chemical forms so that names such as vitamin B_{12a} and vitamin B_{12b} resulted. As you see, this got complicated.

Once chemists worked out the structures of the vitamins, they began giving them names. On the whole, names are more satisfactory than letter-number-letter combinations and, especially where the B Complex is concerned, the old-fashioned system is going completely out of style.

The vitamins of the B Complex are all water soluble. They all contain at least one nitrogen atom in their molecules. They all occur in all cells of all forms of life.

The vitamins of the B Complex seem to form part of molecules which help certain enzymes of the body do their work. These helpers are called *coenzymes.* Coenzymes are needed by the body in only small quantities, but those small quantities are vital. The body can usually make at least part of the coenzyme but often the construction of some particular atom arrangement is beyond its powers. When this happens, the body must depend upon that atom arrangement being present, all prepared and ready, in the diet. It is this needed atom arrangement that represents the vitamin.

Plants can make all the types of atom arrangements that are needed in living tissue so we can usually rely on various plant foods for a number of our vitamins. Animals that eat plants will store certain vitamins for future use, usually in their livers. That is what makes liver a particularly valuable food.

Bacteria can also form the B Complex vitamins. The bacteria in our intestines can actually form some of them in amounts that are enough to satisfy our needs.

For now, I will only mention one of the B Complex vitamins, and that one is *pantothenic acid.*[1] It was first discovered in 1933 but its structure was not worked out

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The prefix "pan" comes from a Greek word meaning "all" because pantothenic acid occurs in small quantities in all cells. It is also until 1940. It turned out to be the condensation product of a hydroxy-acid, (a compound with a molecule containing both a hydroxyl group and a carboxyl group) and an amino acid.

The amino acid involved is rather unusual. Most of the amino acids in the body are alpha-amino acids, with the amine and carboxyl groups both attached to the same carbon atom. The amino acid in pantothenic acid is one of the rare *beta-amino acids*, in which the amine and carboxyl groups are attached to adjacent carbon atoms, thus:

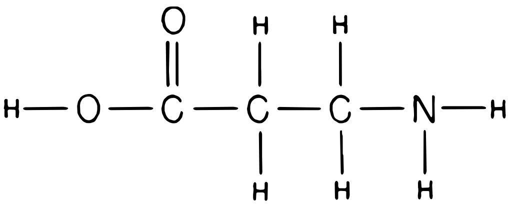

Figure 11—Beta-alanine

This particular one is called *beta-alanine*, because it is just like ordinary alanine except for the position of the amine group. In recent years, chemists are beginning to pay more attention to those unusual amino acids.

NITROGEN DOUBLES ITS BONDS

So far, all the nitrogen compounds I have discussed have contained nitrogen atoms attached to three different atoms

formed by bacteria in the intestines so that it is almost impossible for humans to suffer from a shortage of this vitamin. Sometimes scientists want to bring about a shortage deliberately, so they can study the effects. To do this, they begin by removing as much of the pantothenic acid as possible from the diet. Then they add to the diet some compound which will neutralize the effect of the vitamin formed by the bacteria. Such a vitamin-neutralizing compound is an *anti-vitamin* or a *vitamin antagonist.*

by one bond apiece. The nitrogen atoms can form double bonds, however, just as carbon atoms can. For instance, you can have an atom combination like this C=N—H. (The N—H group is referred to as an *imine group.*)

An example of an important compound that contains an imine group is *guanidine*, which has a molecule that looks like this:

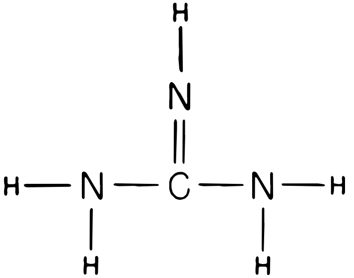

Figure 12—Guanidine

Guanidine is quite a strong base. Guanidine minus a hydrogen atom is called the *guanidine group* and any compound that contains the guanidine group as part of its molecule is also quite a strong base.

The most important such compound is *arginine*, which is one of the most common of the amino acids occurring in proteins. It has a guanidine group in its side-chain and that makes it the most basic of the amino acids.

Certain proteins are particularly rich in arginine. There are proteins called *protamines* in the sperm cells of such fish as salmon and herring. The molecule of protamine is small for a protein and may contain only 75 or so amino acids strung together. Of these amino acids, as many as 50 or 60 may be arginine. Proteins that are a bit more complicated occur in the sperm cells of other animals (including man) and in most other cells as well. These are the *histones* which, however, are still nearly half arginine.

In the body, arginine is the key compound in the production of urea. Part of the guanidine group is chopped off to form urea, leaving only an amine group behind in the side-chain. The compound that is left is called *ornithine*. The ornithine builds back to arginine and again part of the guanidine group is chopped off. Each time the chop-off action comes, a molecule of urea is produced. This process is known as the *urea cycle*. The cycle involves a number of reactions, each in the charge of a particular enzyme. The cycle takes place in the liver. (The liver is the busiest organ in the body as far as body chemistry is concerned.)

A somewhat simpler guanidine compound is creatine. This consists of a guanidine group and a carboxyl group attached to the same carbon atom. One of the hydrogen atoms of the guanidine group is replaced by a methyl group. Creatine is an important compound in muscle.

Still another guanidine compound brings us back to the antibiotics. In 1942, the Russian-born American scientist, Selman A. Waksman, isolated the first antibiotic from the family of molds that were later found to contain the tetracyclines. (This first antibiotic from this kind of mold was not a tetracycline at all, but something completely different.) It was named *streptomycin* and in 1952, Waksman received the Nobel Prize for his work.

In 1948, the structure of streptomycin was worked out. Its molecule was found to contain an inositol ring (a six-carbon ring with a hydroxyl group attached to each carbon atom) condensed to two quite unusual sugars[1]. The inositol ring has two guanidine groups attached to it.

It often happens that antibiotics contain as part of their molecule some unusual arrangement of atoms. For instance, one of the sugars in streptomycin is very similar to glucose, but has all its hydroxyl groups arranged in an opposite direction, as though it were a mirror image. Also, the inositol ring in streptomycin has a different arrangement of hydroxyl groups from that of the inositol rings that occur naturally in the body. These similar (yet different) components of

Of course, an antibiotic that interferes with the workings of a bacterial cell could interfere with human cells, too. Some possible antibiotics are useless because they do just that. Streptomycin is borderline. It can be used safely but only with considerable caution. The tetracyclines are safer and are therefore used much oftener.

NITROGEN TRIPLES ITS BONDS

All three of the bonds of a nitrogen atom can be attached to a carbon atom. If the fourth bond of the carbon atom is then attached to a hydrogen atom, the molecule that results looks like this:

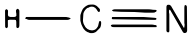

Figure 13—
Hydrogen Cyanide

This compound is hydrogen cyanide, which is an extremely poisonous gas. Hydrogen cyanide is a very weak acid and it is sometimes called *hydrocyanic acid* or *prussic acid.* (The last name comes from the fact that the cyanide group occurs in a dark blue iron-containing compound called Prussian blue.)

When a molecule of hydrogen cyanide loses a hydrogen ion, what is left behind is the *cyanide ion.* Cyanide ion is

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antibiotics seem to be able to put the chemical machinery of bacteria out of order. They resemble the natural compounds enough to take their place within the bacterial cell, and yet they are different enough not to be able to do the necessary work. It is like pushing a key that is not quite right into a lock, then trying to turn it and jamming the whole works. When a chemical reaction in a cell is stopped or slowed down, it is said to be *inhibited.* When this is done by a wrong compound which resembles the right compound and competes with it for a place in the cell, the process is called *competitive inhibition.* Anti-vitamins are usually quite similar to the vitamins whose actions they affect. This is another example of competitive inhibition.

most often found in combination with sodium ion or potassium ion, forming white solids called *sodium cyanide* and *potassium cyanide*. These are extremely poisonous compounds and need not be swallowed to kill. Enough can be absorbed through the membranes of the mouth to do the job.

Some states execute murderers by means of a "gas chamber". In such a chamber, potassium cyanide or sodium cyanide pellets are dropped into acid by some mechanical device after the prisoner has been placed inside the chamber and the chamber has been sealed. The acid changes the cyanide ions back to hydrogen cyanide. The vapors fill the air and in a short time the convicted man is dead.

When the cyanide group is attached to a carbon chain, the result is an *organic cyanide* or, as it is more commonly called, a *nitrile*. The nitriles are by no means as poisonous as the cyanides I mentioned earlier. For one thing, the cyanide group in the nitriles is attached firmly to the rest of the molecule. It doesn't come loose as the cyanide ion does.

An interesting synthetic fiber, in use since 1950, is made by hitching together (or *polymerizing*) molecules of an unsaturated nitrile. The result is a long chain of carbon atoms loaded with hydrogen atoms but with every other carbon atom having a cyanide group attached. The fiber is known as *Orlon*.

BANG!

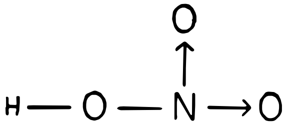
So far, the nitrogen atoms in compounds I have discussed were bonded either to hydrogen atoms or carbon atoms. Now it is time to consider compounds with nitrogen atoms bonded to oxygen atoms.

The nitrogen-oxygen combination is a hard one to bring about. It takes a great deal of energy to force these reluctant atoms together. For instance the nitrogen and oxygen in the atmosphere won't combine even with the urging of the heat energy of a forest fire.

There is a still stronger form of energy that will do it, however. That is the lightning bolt.

Each flash of lightning in a thunderstorm causes the nitrogen and oxygen in its neighbourhood to combine. The resulting molecules dissolve in the rain water and come to earth as *nitric acid*. Nitric acid is one of the very strong acids but it is present in rain water in such tiny amounts that it does no harm at all. In fact, it does good for it helps fertilize the ground.

The formula of nitric acid is as shown here:



$$H - O - \overset{\overset{\displaystyle O}{\uparrow}}{N} \rightarrow O$$

Figure 14—Nitric Acid

Nitric acid is an inorganic compound.[1] There are no carbon atoms present.

Nitric acid minus its hydrogen atom forms what is called the *nitrate group*. Nitric acid minus the hydroxyl group is the *nitro group*. Both groups can be attached to a carbon chain. In the former case, we have an *organic nitrate*. In the latter case, we have a *nitro compound*.

The most famous organic nitrate is *glyceryl trinitrate*, which consists of a molecule of glycerol (see page 27) with a nitrate group in place of each of the three hydroxyl groups.

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[1] Although an oxygen atom forms two ordinary bonds, it is satisfied if it is at the receiving end of a single *coordinate bond*. The coordinate bond is the bond with special electrical properties mentioned first near the beginning of Chapter I in connection with choline. It is represented by a little arrow as shown.

The importance of glyceryl trinitrate is that it is always teetering on the edge of a breakup. It is hard to get nitrogen and oxygen atoms to hook up. Once they are forced together, they break apart again at the least excuse. A bit of heat in the form of a spark is enough to break them apart, often; sometimes just a sharp blow will do the trick.

If the nitrate group is attached to a carbon chain, then, when it breaks up, the oxygen atoms being turned loose will combine with the carbon and hydrogen atoms in the neighborhood. In this way, a great deal of energy is liberated very quickly. The hot gases (carbon dioxide, water vapor, nitrogen and a little bit of left-over oxygen) expand outward with great force. The result is an explosion.

Glyceryl trinitrate is one of the most powerful explosives. A mild tap will set it off and it must be prepared and handled with the greatest care. You are probably more familiar with it by its more common name of "nitroglycerine." (This name is quite wrong since the molecule contains nitrate groups, not nitro groups.) By either name, however, it is the "soup" that safecrackers use in movies and in crime novels (and, for all I know, in real life, too.)

Despite the danger of manufacturing explosives (and there have been horrible accidents), they are an important product of our chemical factories. Their importance in war and for death is easy to see. However, they are also important in peace time and for a better life. Coal could scarcely be mined fast enough to keep our modern factories going, if the seams weren't blasted apart with explosives. Modern highways are blasted through hills, and tunnels under mountains or rivers must be blown open by explosives to begin with.

Just the same, chemists try to make the explosives as safe to handle as possible.

A Swede named Alfred Nobel, for instance, was engaged in the manufacture of glyceryl trinitrate a hundred years ago. An explosion killed his younger brother and thereafter he dedicated himself to making the danger of similar accidents less. He tried freezing the stuff but that wasn't good enough.

Finally, in 1862, Nobel discovered that glyceryl trinitrate could be absorbed by a certain kind of porous earth called kieselguhr. This would absorb up to three times its own weight of glyceryl trinitrate and still remain dry. Once glyceryl trinitrate was absorbed, it was no longer sensitive to blows and shocks. It could be handled almost as though it were so much sand.

The kieselguhr with the glyceryl trinitrate in it could be molded into sticks of convenient size and wrapped in waxpaper. Such sticks are called *dynamite*. A stick of dynamite is set off by means of a percussion cap or *detonator* which contains a small quantity of some compound very sensitive to shock.[1] When it goes off, the force of its explosion is enough to set off the dynamite. The detonator can be set off by a long fuse or by an electric spark produced by a distant battery. (When dynamite goes off, distance is important.)

During World War II, housewives were urged to save used fat, bacon drippings and so on. These were collected and broken down for the sake of the glycerol that could be produced from them. The glycerol was needed for explosives.

Other compounds with a number of nitrate groups attached to the molecule are also explosive. Cellulose, the chief substance in wood, is made up of giant molecules

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[1] Some of the detonators are inorganic compounds, but one of the most important is *mercuric fulminate*, an organic compound which contains nitrogen atoms attached to single oxygen atoms, instead of to three as in organic nitrates.

consisting of thousands of simple sugar molecules hitched together. There are three hydroxyl groups attached to each glucose unit in its long molecule. These can all be replaced by nitrate groups to form *cellulose trinitrate.* If you start with cotton (which is almost pure cellulose) you end with something that hasn't changed in appearance, A common name for the result is therefore *guncotton.* Also, because of the general confusion between nitrate groups and nitro groups in industrial establishments, it is often called *nitrocellulose.*

THE BETTER SIDE

Explosives can be useful for reasons that have nothing to do with explosions.

Glyceryl trinitrate, for instance can be very useful to people suffering from the disease, angina pectoris. This is a disease of the arteries that feed the heart. The walls of these arteries are thickened and hardened, the heart's blood supply is cut down and the patient gets attacks in which he feels agonizing pain in the shoulders and arms. At such times, breathing the vapors of glyceryl trinitrate causes the walls of the arteries to relax. More blood gets through them to the choking heart and the pains cease.

Similar help can be gotten from the compound, *amyl nitrite.* Its molecule consists of a five-carbon chain with a *nitrite group* attached to the end carbon.[1]

A close relative of guncotton has surprising non-explosive uses, also. Cellulose can have only two of the three hydroxyl groups on each glucose unit replaced by nitrate groups. In this way, *cellulose dinitrate* is formed.

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[1] The nitrate group, as I have already said, contains nitrogen attached to three oxygen atoms. The fulminate group contains nitrogen attached to one oxygen atom. Well, the nitrite group lies between these. It contains nitrogen attached to two oxygen atoms.

This is much less dangerous than cellulose trinitrate. The common name for cellulose dinitrate is *pyroxylin.*

Back in the 1860s, a prize was offered to anyone who would find a substitute for ivory in the manufacture of billiard balls. In 1869, an American named John Wesley Hyatt, found the answer in pyroxylin. He mixed the pyroxylin (which is itself a brittle substance) with a bit of camphor and ethyl alcohol. The resulting mixture became soft when heated and could then be molded into any shape, including that of billiard balls. The heat evaporated the alcohol, but left the camphor behind, When the mass cooled down, it was a hard and perfectly good billiard ball.

Hyatt won the prize. More important, he had invented the first synthetic plastic. He called it *celluloid.*

For a while, celluloid was used for a great many things. For instance, it could be used in the manufacture of photographic film. However, celluloid, although not explosive, still had many nitrate groups in its molecule. That made it very inflammable and once it caught fire, it burnt very quickly. As a result, it was replaced whenever possible by less dangerous substances. Modern photographic film, for instance, is made up of much less inflammable cellulose acetate in which the sugar hydroxyl groups are condensed with molecules of acetic acid, not nitric acid.

There is another bright side to explosives. Nobel, who made his fortune in explosives, died in 1896 and left nine million dollars to set up a fund out of which, each year, prizes amounting to about $40,000 each are awarded to people who have helped advance chemistry, physics, medicine, literature and peace.

People sometimes think it ironical that the inventor of dynamite should establish a prize for advancing peace. However, this is quite the wrong way to look at it. Nobel was a humanitarian who would have been happy to see his explosives used only in peaceful constructive ways. Their use in war is none of his doing.

MORE BANG!

Nitro groups (remember the difference between nitro groups and nitrate groups) are most commonly found attached to benzene rings. The simplest case is *nitrobenzene*, the molecule of which consists of one nitro group attached to the benzene ring. It is poisonous, but not explosive.

If more than one nitro group is attached to a benzene ring, there is an increasing chance that the compound will be explosive. An example is *trinitrophenol*, which has a molecule consisting of a benzene ring to which a hydroxyl group and three nitro groups are attached. The three nitro groups encourage the hydrogen of the hydroxyl group to come loose as a hydrogen ion. For that reason, trinitrophenol is a stronger acid than phenol. This shows up in the common name for trinitrophenol, which is *picric acid.*

Picric acid is a yellow, very bitter solid (its name comes from a Greek word meaning "bitter"). When nitric acid comes in contact with proteins or with something that contains proteins (as, for instance, the human skin) nitro groups are added to the phenol group present in the side-chain of the amino acid, tyrosine. Compounds related to picric acid are formed and the protein (or the skin) turns yellow. After a while the yellow color on the skin turns a dirty gray-brown but it doesn't come off until that part of the skin wears off. You'll often read in books of a chemist's "acid-stained fingers." Well, this is what they mean.

If the hydroxyl group in picric acid were a methyl group, the compound would be *trinitrotoluene*. This is an excellent explosive. (Picric acid is only a rather mediocre one.) In fact, trinitrotoluene is the most important wartime explosive there is. You have probably heard of it frequently under the common name made up of the initial of the chemical name,—*T*ri*N*itro*T*oluene—*TNT*.

So far only one nitro compound has ever been found in any form of living tissue. That one is an antibiotic obtained, as usual, from a mold. This is *chloramphenicol*, also known by its trade-name, *Chloromycetin*. It is a little on the toxic side and not as popular a medicine as the various tetracyclines.

The name "chloramphenicol" is rather odd in one way. The "chlor" part shows it contains chlorine atoms, the "am" refers to an amide link which it contains; the "phenic" to a benzene ring; and the "ol" to the hydroxyl groups. Everything is mentioned but the nitro group and that, after all, is the one really unusual thing about the compound.

4

The Smell of Brimstone

SKUNKS AND ENERGY

The *sulfur* atom is a close relative of the oxygen atom in its chemical properties. However, sulfur doesn't resemble oxygen in the least in appearance. Oxygen is a colorless gas but sulfur is a yellow solid.

Sulfur has a bad reputation as far as odor is concerned. The devil is often supposed to smell of brimstone. (Brimstone is an old-fashioned name for sulfur.) Actually, sulfur itself doesn't smell at all, but when it burns, sulfur atoms combine with oxygen atoms to form sulfur dioxide. That has an unpleasant and choking odor. Sulfur dioxide often occurs among the gases coming out of cracks in the earth in volcanic regions. That is probably why sulfur and the smell of it burning is associated with underground regions and with the devil.

What our medieval ancestors couldn't guess, though, is that there are organic compounds containing the sulfur atom that smell so badly that the "smell of brimstone" is perfume in comparison.

For instance, suppose we take the molecule of ethyl alcohol and replace the oxygen atom with a sulfur atom. (The sulfur atom can form two bonds with other atoms, just as the oxygen atom does. The chemical symbol for sulfur is simply its initial letter, S.)

With sulfur replacing the oxygen, instead of an O—H group there is an S—H group. The S—H group is called a *thiol group*. (The prefix "thi" comes from the Greek word for "sulfur" and a number of sulfur-containing compounds have "thi" somewhere in the name for that reason.) The —S—H group is also frequently called the *sulfhydryl group*, from the name of the elements that make it up.

A compound containing a sulfhydryl group is called a *mercaptan*. Ethyl alcohol with a sulfur atom replacing the oxygen atom becomes *ethyl mercaptan*.

The simple mercaptans smell just about as bad as anything can smell. It is perfectly horrible. *Butyl mercaptan* (a sulfhydryl group attached to a four-carbon chain) isn't quite as bad as ethyl mercaptan but it's still the compound that makes the skunk smell as he does. The fluid he shoots out when angry contains butyl mercaptan.

Believe it or not, even this smell can be made useful. Small quantities of mercaptans are added to the natural gas piped into houses. In that way, a gas leak can be smelled at once and something can be done about it. It is certainly better to endure a bit of a bad smell than to be poisoned unaware.

More complicated molecules may contain a sulfhydryl group and yet have no odor. This is fortunate since some of these molecules occur in our body. One is an amino acid called *cysteine*, which has a small side-chain to which a sulfhydryl group is attached.

Cysteine makes up part of many proteins, particularly of enzymes. The sulfhydryl groups on enzymes (sticking up out of the cysteine units) are usually essential to the enzyme workings. Any chemical which will hook on to those sulfhydryl groups and change their chemical nature will ruin the enzymes. Compounds containing such elements as copper, lead, arsenic and mercury do exactly that. That is at least one reason why such compounds are poisonous to us if we take them internally even in small quantities. We can't continue living if the molecules that control our chemical machinery are put out of action.

To fight against the effects of such poisoning, doctors often try to supply the patient with other substances containing sulfhydryl groups. Milk and egg-white, for instance, contain proteins carrying those groups. If the poison is still in the stomach, it will be tied up harmlessly by the *antidote* and prevented from attacking the proteins of our own tissues.

Cysteine can condense with two other amino acids, glutamic acid and glycine, to form a tripeptide called *glutathione*. This is also important in the action of certain enzymes and is probably the most important small peptide in our bodies.

One of the ways in which the sulfhydryl group works is probably by condensing with a carboxyl group, in the following way:

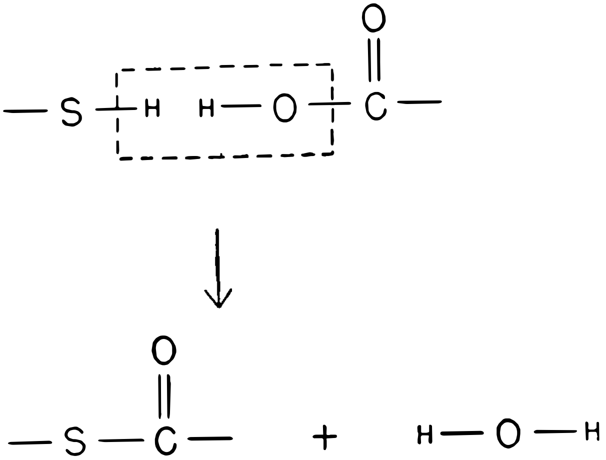

Figure 15—Acyl-Mercaptan Formation

The atom combination that results (a sulfur atom attached to a carbonyl group) is called an *acyl-mercaptan group.*

Such an atom combination is an example of a high-energy group, because when it is hydrolyzed an unusual amount of energy is released. Chemists now think that when carbohydrates and fats are oxidized to release energy, the energy is stored first in the form of acyl-mercaptan groups.

BLADDER STONES AND RADIATION SICKNESS

Two sulfhydryl groups can condense with one another in the following way:

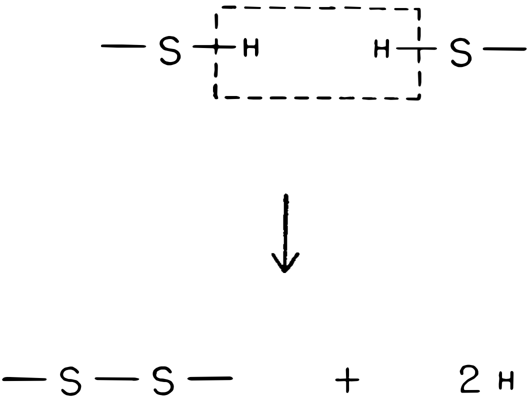

Figure 16—Disulfide Group Formation

This is different from the acyl-mercaptan condensation. What is being eliminated here is not a molecule of water but a molecule of hydrogen. This is an example of a *dehydrogenation.* The atom combination that results, —S—S—, is called a *disulfide group.*

When two cysteine molecules react with one another in this fashion, they end up held together by the disulfide group that is formed. The result is a double-headed amino acid: an amine group and a carboxyl group on both sides; and a disulfide group in the middle.

This double-headed amino is called cystine[1] and it occurs in protein quite commonly. Of all the amino acids to be found in proteins, cystine is the least soluble in water. That fact is responsible for its discovery. You see, it sometimes happens that a person may suffer from a disorder in which a number of amino acids leak out of his body through his kidneys. It's not a serious leakage and the person would never know there was anything wrong if it weren't that one of the amino acids was cystine.

Cystine is the insoluble amino acid while the others that leak into the urine in this condition are quite soluble. As a result, there is sometimes more cystine in the urine of such people than the urine can hold. The cystine settles out in the form of little crystals that may group together into a "stone." Such stones generally end in the bladder and can be quite uncomfortable.

It was in one such stone that a British chemist named W. H. Wollaston discovered cystine in 1810, and, in fact, the name comes from the Greek word for "bladder". Cystine was the first of the amino acids of proteins to be discovered but actually chemists did not find out that

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[1] Cystine and cysteine are pronounced just about alike and that is too bad. Chemistry teachers go to all sorts of lengths to pronounce them differently so that the students will know which we mean. You may wonder why names are not changed if they seem unsuitable but that is easier said than done. Hundreds of books and thousands of research papers (a research paper is a report of original experiments) have been written using the terms cystine and cysteine. We couldn't go back and change the words wherever they've been mentioned. And if we picked new names and said, "From now on use these", we would still have to teach the old ones also so that people who read those books and papers would know what it was that was being discussed.

it occurred in proteins (and not just in bladder stones) till 1899.

The ability of cysteine to change easily to cystine may possibly be important to us of the atomic age. You see, the invisible radiations given off by an exploding atomic bomb strike the water molecules in tissues as they pass through the body. The water molecules are torn into fragments called *free radicals.* These fragments are very active and tear away at any molecule which they bump into. If they happen to bite into some protein molecule essential to the cell's chemistry, that particular cell may be weakened or even killed. If the exposure to radiation has been great enough, so many cells are weakened or killed that *radiation sickness* results and that sometimes ends in death.

Suppose, however, that there is an extra supply of cysteine in the body. The free radicals are likely to be used up attacking the plentiful sulfhydryl groups. The sulfhydryl groups also react easily and are converted to the harmless disulfides. The sulfhydryl group is offered to the free radicals, so to speak, in order to keep them away from more important compounds. Animals that have been injected with cysteine just before or just after exposure to radiation are less likely to get radiation sickness. As yet, this is a rather weak defense against atomic dangers, but it points the way, perhaps, to better solutions.

PERMANENT WAVES

Cystine is very important in the protein molecule since it can be used to hold two amino acid chains together. The amine group and carboxyl group on one side of the disulfide link can form part of one amino acid chain. The amine group and carboxyl group on the other side can form part of another. The disulfide link in between connects the two chains and holds them together.

The protein that contains more of these disulfide links than any other is keratin, the protein of skin and hair. It is because the amino acid chains of keratin are held together so tightly that keratin is strong and tough. That is why it can be made into hair and fingernails and why skin is such good protection for the body.

In our world of today, a large industry has grown up based on breaking and remaking the disulfide links in keratin.

You see, most people happen to have straight hair while most women seem to prefer wavy or curly hair. Unfortunately, you can't bend a hair and have it stay bent. It springs back as soon as you let go. (For that matter, if you take a curly hair and pull it out straight, it curls up again as soon as you let go.)

Let's see why this is. Suppose you had a dozen fairly stiff rubber rods that were all tied together tightly. Now imagine the whole group bent into a U-shape. The rods along the outside U would have more distance to cover than the ones on the inside. They would have to stretch. The rods on the inside of the U, on the other hand, would be squeezed together, or compressed. If you let go of the bundle of rods, they would spring back to the original straight position where none were either stretched or compressed. Straightness would be the position of least strain.

Suppose, though, that you had the same bundle of rods, not tied together but loose. If these were bent into a U, each rod could slide against the others and find its natural position. Now imagine the rods, in this natural U position tied together tightly and released. The bundle could no longer straighten out because to do so some of the rods would have to stretch and some to compress.

The bent U-shape would now be the position of least strain.

The situation in hair resembles what I have just described. The individual rods are the amino acid chains of keratin and the tying together is done by the disulfide links. If you want to change the hair from straight to curly (or from curly to straight, for that matter), it is necessary to break the disulfide links, put the hair into a new position, let the amino acid chains find their natural place and form the disulfide links again.

This is exactly what is done in permanent waving. The hair is curled and treated with chemicals. (Beauty parlors use heat but there are "home permanents" which don't require heat.) The treatment breaks the disulfide links into two sulfhydryl groups. The amino chains come apart and slide along past one another into a new position matching the curve of the hair. The disulfide-breaking chemicals are then neutralized by other chemicals. The disulfide links are formed again and now the hair must stay curled. It will not straighten again.

ONIONS AND BLISTERS

The oxygen atom in any type of organic compound can be replaced by a sulfur atom. So far, I have changed alcohols into mercaptans in this way. Ethers can be changed into *thioethers* (or, as they may be called, *organic sulfides*). Instead of the atom combination C—O—C, there is now C—S—C.

Again, there is a change for the worse in some ways. The most familiar organic sulfide is shown in *Figure 17* opposite.

The sulfur atom is connected on both sides to an ethylene group which is minus a hydrogen atom. An ethylene minus a hydrogen is called a *vinyl group* and so the compound is *divinyl sulfide.* (The "vin" prefix comes from the Latin word for "wine" since the vinyl group is easily prepared from ethyl alcohol.

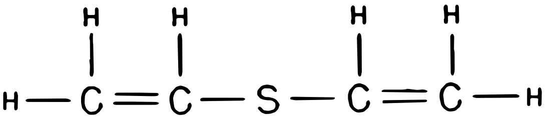

Figure 17—Divinyl Sulfide

Now it is divinyl sulfide that gives onions their taste. This is both good and bad. I'd hate to think of cooking without onions and a little onion on hamburger or steaks or in salads is delightful. Of course, it is not quite so delightful when a person is talking to you immediately after having eaten some onions.

The same is true of another sulfide called *diallyl sulfide.* Its molecule has the sulfur atoms attached to a pair of three-carbon chains with a double bond in each. A three·carbon chain with a double bond is called an *allyl group* from the Latin word for "garlic". That should give it away. Diallyl sulfide is what gives garlic its odor.

A relative of these compounds is much more unpleasant, It is *dichlorodiethyl sulfide.* In it, the sulfur atom is attached to a pair of ethyl groups, to each of which a chlorine atom is attached. This compound is commonly called *mustard gas.*[1]

Mustard gas was just about the most effective of the poison gases used in World War I. It is not only poisonous to breathe, but just its contact with skin is dangerous. Such contact causes the formation of large blisters. (A blistering gas is called a *vesicant.*) What's more, despite

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[1] It's supposed to be called that because it has an odor like mustard, but I've smelt some and it smells like garlic to me.

its name, mustard gas is a liquid and its vapors are 5½ times as heavy as air, so it is a clinging gas that may contaminate a low-lying region for weeks.[1]

It is a pleasure to switch to a thioether that is not only odorless and tasteless, but is essential to life. Again, an amino acid is involved; one with a thioether group in the side-chain. This is *methionine.*

The sulfur atom in methionine is attached to a methyl group on one side and to the rest of the amino acid on the other. The methyl group is rather loosely held and can be easily transferred to other compounds. It is called an *active methyl.* One of the reasons methionine is important in the body is that it is a source of a methyl group which the body can use as a small building block in finishing off some of the complicated molecules it makes.

If there is enough methionine in the diet, the body can use its sulfur atom to make whatever cysteine and cystine it needs. Cysteine and cystine are not essential in the diet for that reason. The body cannot do the reverse. It cannot make methionine out of cysteine or cystine, so methionine is essential in the diet.

However, if there is an ample supply of cysteine or cystine in the diet, you can get along on less methionine, since you don't have to waste any methionine just to make cystine. Cystine therefore has a *sparing action* on methionine.

Certain giant molecules are complicated organic sulfides. For instance, there is a type of artificial rubber called *polysulfide rubber.* (Its trade name in America is *Thiokol*). Its molecule is made up of an ethylene group, a sulfur

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[1] If the sulfur atom in mustard gas is replaced by a nitrogen atom (carrying an additional chlorinated chain since the nitrogen atom can form three bonds, rather than only two) the compound that results is a *nitrogen mustard.* These have been important in the study of cancer.

atom, an ethylene group, a sulfur atom and so on. Polysulfide rubbers resist rubbing off against the road (*abrasion*, that is) even better than natural rubber does. A thin coat of polysulfide rubber can be spread over tires to preserve the tread.

MORE SMELL; MORE TASTE

The carbonyl group can also have its oxygen atom replaced by a sulfur atom. The atom combination C=S is a *thiocarbonyl group*. The simplest compound with such a combination is *carbon disulfide*, whose molecule contains two sulfur atoms and one carbon atom. It looks like this: S=C=S.

Carbon disulfide is a low-boiling liquid. Its boiling point is 46° C. (113° F.). It is an extremely good solvent for fatty substances and is used for this reason in industry. However, it has three disadvantages.

First, it is one of the most easily inflammable of all organic compounds. Using it always means a fire hazard is present.

Second, it mixes so easily with fatty substances that if it is breathed it gets into the fatty tissue about the nerves. Too much exposure to it will bring on nervous disorders for that reason.

Third, it has a perfectly horrible odor. The chemistry books insist that pure carbon disulfide has a faintly pleasant smell. They say that the reason that ordinary carbon disulfide smells so is that small quantities of mercaptans are present as impurities. That may be so, but in that case, I've never come across pure carbon disulfide yet, and neither has anyone I know.

Carbon disulfide reacts with alcohols and replaces the hydrogen of the hydroxyl group with a kind of atom combination that is shown in *Figure 18* overleaf.

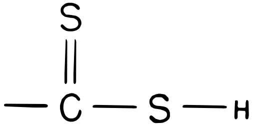


Figure 18—
Xanthate Group

Compounds containing such a group are called *xanthates*. Cellulose treated in this way becomes water soluble. A solution of cellulose xanthate is known as *viscose*, which is used in the manufacture of rayon.

A more complicated thiocarbonyl compound is *phenylthiourea*. The molecule of this compound is like that of urea except that a sulfur atom has replaced the oxygen atom. Moreover, a benzene ring is attached to one of the amine groups. One of the interesting things about this compound is its taste. It is supposed to be a very bitter compound; many people insist it is. Yet it turns out that other people (of whom I am one) cannot taste it at all. They find it completely tasteless. In this way, the phenomenon of *taste-blindness* was discovered. People can be taste-blind to other compounds also.

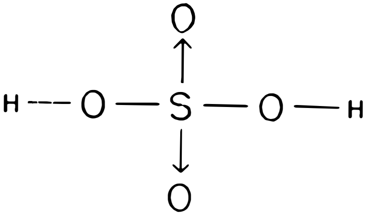
This is not just a chemical curiosity. The ability to taste or not taste certain compounds is inherited, usually in a simple way. People who are interested in the way heredity works are therefore very interested in taste-blindness.

ANOTHER KIND OF ACID

Like nitrogen, the sulfur atom can form part of a strong inorganic acid. The name of the acid is *sulfuric acid*, and its formula is shown in *Figure 19* opposite.

As you see, the sulfur atom is capable of possessing two co-ordinate bonds in addition to its two usual bonds.

If the sulfuric acid molecule loses one of its hydrogens as a hydrogen ion, what is left is the *bisulfate ion*. If it



$$H-O-\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}-O-H$$

Figure 19—Sulfuric Acid

loses both hydrogens as hydrogen ions, what is left is the *sulfate ion.*

Bisulfate groups are sometimes attached to mucopolysaccharide molecules. A mucopolysaccharide called *heparin* carries a number of such groups in its molecule; on the average of five for every two sugar units. Heparin is present in many types of tissue and its action is to slow up the clotting of blood. Surgeons use heparin preparations sometimes to prevent blood from clotting during an operation and interfering with their work.

The sulfuric acid molecule with one hydroxyl group missing is a *sulfonic acid group.* There is one compound involving such a group which occurs in living tissue. This is *taurine* (the name comes from the Latin word for "bull" since it was first found in the liver bile of bulls.) The molecule of taurine is made up of a two-carbon chain with an amine group on one carbon and a sulfonic acid group on the other.

Certain synthetic sulfonic acid compounds have detergent action and have come into use as a substitute for soap. These detergents have become particularly popular since World War II. They are generally more expensive than soap but their great advantage is that they work well in hard water. As a result, the production and use of soap has been cut just about in half since 1945 and now more synthetic detergent is produced than soap. Mostly, the synthetic detergents are used in washing clothes, dishes and hair. For washing the human skin, bar-soap still holds its own.

THE GRANDADDY OF THE MIRACLE DRUGS

Now if you look at the formula of sulfuric acid and imagine one hydroxyl group gone and the other replaced by an amine group, what you have left is this:

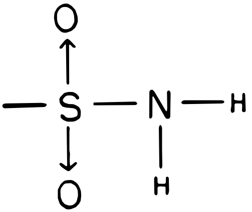


Figure 20—Sulfonamide Group

This is the *sulfonamide group.*

The most important compound containing this group is *sulfanilamide.* The molecule of sulfanilamide is made up of a benzene ring with an amine group attached at one end and a sulfonamide group attached to the other.

Sulfanilamide has had a strange history. It was first synthesized in Germany in 1908. For twenty-five years after that, however, it was only used as a starting material out of which to make various dyes. One such dye was called *Prontosil.*

In 1932, a German chemist named Gerhard Domagk found that Prontosil could cure certain bacterial infections in mice. (In 1939, he got the Nobel Prize in Medicine for that.) By 1935, Prontosil was a "miracle drug"—the first one.

It was quickly discovered that in the body Prontosil was broken up into two pieces, one of which was sulfanilamide and that it was the sulfanilamide that had the germ killing ability. So people forgot about Prontosil and concentrated on sulfanilamide.

The reason why sulfanilamide works seems to be this:

There is a compound called *folic acid*, which is essential to the working of all cells, including those of bacteria. Some bacteria make their own folic acid out of several simpler compounds. One of these simpler compounds is *para-aminobenzoic acid*.

Para-aminobenzoic acid has a molecule which resembles that of sulfanilamide. Both molecules are made up of a benzene ring with an amine group at one end and a second group at the other. In para-aminobenzoic acid, the second group is a carboxyl group; in sulfanilamide, it is a sulfonamide group.

Apparently, some bacteria can't tell these two compounds apart. If sulfanilamide molecules happen to be in the neighbourhood, the bacteria will snap them up and make it part of a folic acid molecule. The trouble with that (for the bacteria) is that a folic acid molecule containing sulfanilamide won't work. The bacterial cell that is stuck with it can't grow or multiply. Its chemical machinery is stalled.

There are some bacteria, however, that don't make their own folic acid, but pick the compound up ready-made from their surroundings. Such varieties of bacteria are not affected by sulfanilamide. It is a general rule that a particular drug will only affect particular germs.

The use of drugs, even "miracle drugs", is not the final answer to disease even for those germs against which it works. Sulfanilamide may kill off most germs of a particular type but there is always a chance that a few bacteria may escape. These few may happen to have a set of enzymes that can get around the drug. Perhaps they can manufacture folic acid in a way that doesn't involve para-aminobenzoic acid. Perhaps they can use folic acid with sulfanilamide in it. Perhaps they can do without folic acid or use a substitute.

In any case, these few bacteria will not be killed by sulfanilamide. They will be the only ones that will survive in the body of that particular variety of bacteria. After a while, if they multiply dangerously and the doctor tries another dose of sulfanilamide, he may find that this second dose will have no effect at all. The bacterial strain has grown *resistant.*

For this reason, it is necessary to keep developing new drugs. A second drug may attack bacteria that have grown resistant to the first drug, or which were never affected by it in the first place.

A whole series of drugs similar to sulfanilamide have been developed. They differ from sulfanilamide in that one of the hydrogen atoms of the sulfonamide group has been replaced by some combination of atoms. For instance, it can be replaced by atoms which change the amine part of the sulfonamide group into a guanidine group. The *sulfaguanidine* that results can be given by mouth in greater quantity than sulfanilamide without giving rise to undesirable reactions.[1]

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[1] Almost all drugs that will kill bacteria will also kill human beings. Some drugs are just as poisonous to humans as to germs and are therefore too *toxic* to use. A useful drug is one that kills bacteria when added in a dose that is not sufficient to kill the patient. The proper dose is not an easy thing to determine. Some patients are more easily affected by a particular drug than other patients are. Such patients are *sensitive* to the drug. These may have an allergic reaction and even be killed by an amount of drug completely harmless to almost anyone else. Some patients may become sensitive during the course of treatment. A drug won't hurt them at first and then suddenly become very bad for them. The taking of drugs is definitely something you should consult a physician about as much as possible. There are even people to whom a dose of aspirin might be fatal, just as there are some people who can be killed by a bee-sting.

Sulfanilamide and its close relatives are called the *sulfonamide drugs*, or, more familiarly, the *sulfa drugs*. Since World War II, use of the sulfa drugs has fallen off because of the new antibiotics that have been developed.[1]

SWEETER THAN SWEET

If a benzene ring has a carboxyl group and a sulfonamide group attached to adjacent carbons, the two groups can easily be made to condense with one another. The compound that results is *saccharin* and its usefulness was discovered by accident.

Saccharin was first prepared by an American chemist named Ira Remsen in 1879. The story goes that he got a speck or two of it on his fingers and when he happened to place his hand on his lips, he was amazed at the sweet taste. The compound got its name, almost at once, from the Latin word for "sugar".

Saccharin is about 550 times as sweet as sucrose. That is, a teaspoonful of it will sweeten 550 cups of coffee as much as a teaspoon of ordinary sugar will sweeten one cup. (Why? No one knows.)

Saccharin is prepared in small tablets which may be added to tea or coffee. It is useful to those people who like their drinks sweet but don't want to eat sugar because they have to watch their calories or because they have diabetes.

You see, sugar is put through chemical changes in the body and if its energy isn't needed at the moment, it is stored as fat. Saccharin is not used by the body at all and

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[1] The sulfa drugs are not antibiotics because they are not formed by microorganisms. The sulfa drugs are strictly synthetic, made up in the chemical laboratory, and do not occur in any type of living tissue.

is just eliminated through the kidneys. The only thing it leaves us to remember it by is its sweetness.[1]

Saccharin, or compounds like it (there are several artificial sweeteners known, some many times more potent even than saccharin), are also used in the manufacture of low-calorie beverages.

Actually, there is always a certain danger that chemicals added to food (*food additives*) to improve its taste, appearance, or to keep it from spoiling or to improve its cooking qualities, may do some damage to the body in the long run. The chemists of the food industry and of the Food and Drug Administration, check on all compounds carefully for this reason. The result is that only three or four hundred out of all the hundreds of thousands of organic compounds known are used in food.

5

A Variety of Atoms

ENERGY!

There is still an element, not yet mentioned, that occurs in a wide variety of organic compounds. That is *phosphorus*. It is an element that is essential to life. Its occurrence in living tissue is always in the form of some variety of *phosphoric acid* in combination with other substances.[1]

The chemical symbol for phosphorus is just the initial letter, P. The formula for phosphoric acid is:

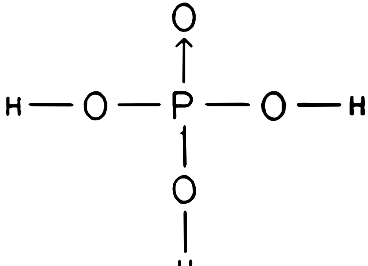

Figure 21—
Phosphoric Acid

The phosphorus atom, as you see, is similar to the nitrogen atom. Like the nitrogen atom, it can form three ordinary bonds and one coordinate bond.

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[1] Phosphoric acid is another of the strong inorganic acids. It is not quite as strong, however, as nitric acid and sulfuric acid.

A molecule of phosphoric acid can lose one, two, or all three of its hydrogen atoms as hydrogen ions. In the first case, what is left behind is a *primary phosphate ion*; in the second case, a *secondary phosphate ion*; in the third, a *tertiary phosphate ion*. (Inorganic phosphates make up most of the bones and teeth.)

Almost any hydroxyl group of an organic compound can be replaced by some kind of phosphate group to form an *organic phosphate*. Starting in 1905, chemists began to realize that almost all the chemical changes that take place in living tissue involve organic phosphates somehow.

For instance, suppose we consider the way that glucose is gradually broken down to carbon dioxide and water. The very first thing that happens is that glucose is converted to a glucose phosphate.

Some organic phosphates (depending on the exact arrangement of atoms) liberate a rather more-than-average amount of energy when the phosphate group is hydrolyzed off. These are *high-energy phosphates*. An example is *creatine phosphate* (which is creatine with a phosphate group attached to one of the nitrogen atoms in its molecule).

When sugars, fats or proteins are broken down for energy, the energy is transferred to acyl-mercaptan bonds that are built up in the process. The acyl-mercaptan energy is used to manufacture high-energy phosphate groups. Finally, the high-energy phosphate groups supply the immediate energy needs of the body.

Phosphate groups occur in some proteins. Casein (the protein of milk) and vitellin (the protein of egg-yolk) contain primary phosphate groups. They are called *phosphoproteins*, for that reason. The phosphate groups occur in place of the hydroxyl group on the side-chains of some of the serine units in the protein.

Some of the very important compound lipids such as lecithin and cephalin contain secondary phosphate groups. For this reason, they are frequently called *phosphatides.*

It is possible for two phosphate groups to condense to form a *pyrophosphate group* (also called a *diphosphate group*). The resulting combination looks like this:

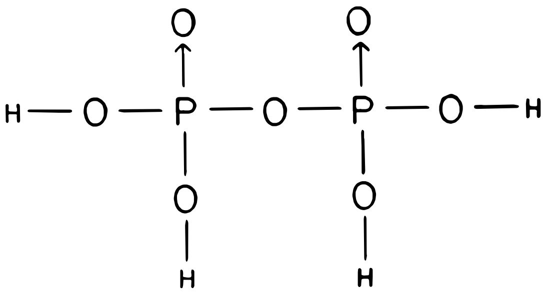

Figure 22—Pyrophosphoric Acid

Three phosphate groups can condense to form a *triphosphate group.* All compounds containing a diphosphate group or a triphosphate group are high-energy phosphates. In fact, the most important high-energy phosphate in the body is *adenosine triphosphate.* (Chemists have to use this name so often that they save time by usually referring to it simply as *ATP.*)

Adenosine triphosphate and creatine phosphate were first studied in muscle. To start a muscle contraction one of the phosphate groups of adenosine triphosphate breaks off, leaving *adenosine diphosphate* (*ADP*) behind. The energy released is used by the muscle in contracting. The adenosine diphosphate is changed back to adenosine triphosphate by the action of creatine phosphate. This gives up its phosphate group for the purpose and becomes simply creatine. There are many more changes that take place, too, but I won't go into the matter any further here.

So far, all the organic phosphates I have mentioned have been most useful to the body; essential, in fact. But there are some bad actors, too.

There are some phosphates that are violently poisonous. They interfere with the enzymes that control the workings of acetylcholine in the nerves. This means they slow up or even stop nerve impulses altogether. Paralysis sets in after a matter of minutes, and death follows. Some of these compounds are used as pesticides. There have also been speculations as to the possible use of such *nerve gases* in a future war. They would be terribly deadly. They need not even be breathed to kill, but can be absorbed through the skin and eyes.

THE MAGIC BULLET

The arsenic atom resembles the nitrogen and phosphorus atoms, but unlike them, it is not essential to life. In fact, all its compounds are more or less poisonous. Some are very poisonous.

The poison gas, *Lewisite*, (first developed by an American chemist named W. Lee Lewis in 1917) has a molecule with two carbons attached by a double bond. To one of the carbon atoms is attached a *dichlorarsine group* (consisting of an arsenic atom to which two chlorine atoms are attached). Another chlorine atom is attached to the other carbon atom.

Lewisite has the poisonous qualities of the arsenic compounds combined with the blistering qualities of mustard gas. It is worse than mustard gas but never got to be used in World War I. Just as it was being shipped over to France, the Armistice was signed. Large quantities of it had to be sealed up and dumped in deep parts of the ocean. It was the only way people could think of getting rid of it.

Even the savage arsenic has its better side, though. It occurred to a German doctor named Paul Ehrlich to try to find some arsenic compound which was only weakly poisonous to humans but which would still be considerably poisonous to at least some bacteria. He tried organic arsenic compound after organic arsenic compound. When he finally found one that worked, in 1909, one of the names given it was 606 because it was the six hundred and sixth compound he had tried. The names most often used are *arsphenamine* and the German trade name, *Salvarsan.*

The molecule of arsphenamine is built around two arsenic atoms held together by a double bond. Each arsenic atom has a third bond available and each is attached to a benzine ring. Both benzene rings carry a hydroxyl group and an amine group.

Some years ago, a motion picture was made about Dr. Ehrlich's discovery and it was called *The Magic Bullet.* That was the phrase, you see, that Ehrlich used to explain what it was he was searching for. He was looking for a chemical that would act like a magic bullet, passing harmlessly through the human body but seeking out some germ and hitting it bulls-eye.

Arsphenamine isn't what we would call a "wonder drug" today. For one thing, it only works on one type of micro-organism; the one that causes a disease known as syphilis. We expect a "wonder drug" of the modern type to attack a wide variety of germs. In fact, arsphenamine these days has been put out of business by the antibiotics, which do the job more quickly and more safely.

After the success of arsphenamine, doctors thought for a while that if they looked hard enough, they might find a magic bullet for each different dangerous germ. They didn't succeed though. Nothing else showed up for 25 years, until Prontosil and the sulfa-drugs. Those weren't magic bullets, but "magic shrapnel," so to speak, for they spread out and destroyed a variety of different germs.

METALS JOIN THE PARADE

Nor do phosphorus and arsenic exhaust the list of the kinds of atoms that may exist in organic compounds. Organic compounds can occur containing any of the atoms that form compounds.[1]

In living tissue, for instance, there are organic compounds (usually quite complicated ones) that contain atoms of *iron*, *copper*, *zinc*, *molybdenum*, *magnesium*, *manganese*, or *cobalt* in their molecules. Small quantities of each of these metals are therefore essential to life. Organic compounds containing metal atoms are called *metal-organic compounds.*

Compounds containing gold and silver atoms have been used as medicines. Partly, I think, this is because doctors in the days before chemistry developed into a real science thought that such precious metals must surely be good for the body. An example of a modern drug that does contain a gold atom and really is useful is *gold thioglucose.* Its molecules resemble glucose except that one of the hydroxyl groups is replaced by a combination made up of a sulfur atom and a gold atom. It is used in certain diseases such as rheumatoid arthritis.

A more familiar metal-organic compound is *merbromin.* This has a rather complicated molecule with three benzene rings, to which are attached, among other things, two bromine atoms and a mercury atom. You are probably more familiar with it under its trade name, *Mercurochrome.* It has a mild antiseptic action and for a while was quite popular as a substitute for the more stinging iodine. A

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[1] There are six elements, the inert gases, that form no compounds at all, with carbon or with any other element.

simpler mercury-containing antiseptic is *merthiolate.* Its molecule is made up of only one benzene ring to which are attached, among other things, a nitro group and a mercury atom. In both compounds, a hydroxyl group is also attached to the mercury atom.

6

A Variety of Rings

A STRANGER IN THE MIDST

At the beginning of the book, I said that carbon atoms could hook up to form rings. The only types of rings I have mentioned particularly, however, were those that were made up only of carbon atoms. Ring compounds, generally, are called cyclic compounds. If the ring contains only carbon atoms and no other kind, the substances are called *carbocyclic compounds*.[1]

But it is also possible that a ring of atoms may occur in which at least one of the atoms is not a carbon atom. A compound with molecules containing such rings is a *heterocyclic compound*. (The prefix "hetero" comes from a Greek word meaning "different".) The different atom, the stranger in the midst, is a *hetero-atom*. Usually, the hetero-atom is either oxygen, sulfur or nitrogen.

The two most common rings with an oxygen hetero-atom are shown on facing page.

The ring on the left, made up of four carbon atoms and an oxygen atom is *furane*, and the one on the right, made up of five carbon atoms and an oxygen atom is *pyrane*.

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[1] They may also be called *homocyclic compounds* or *isocyclic compounds*. The prefix "homo" comes from a Greek word meaning "same" and the prefix "iso" comes from a Greek word meaning "equal".

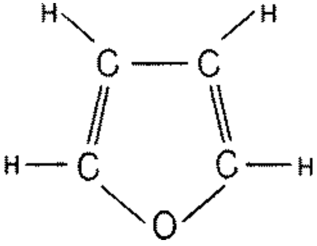

Figure 23—Furane

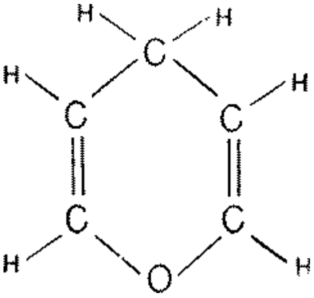

Figure 24—Pyrane

Notice the double bonds in the ring. Heterocyclic rings often contain two or three double bonds, which are usually conjugated. Such conjugated double bonds make the ring more stable, but rings without double bonds occur also.[1]

The most familiar simple compound containing one of these rings is *furfuraldehyde* (also called simply *furfural*) which is obtained from corncobs or from bran (the outer husks of grain kernels such as oats and rice). Its molecule contains the furane ring with an aldehyde group attached to one of the carbons next to the oxygen atom in the ring. The Latin word for bran is "furfur" and that is where furfuraldehyde and furane both get their names.

Despite its unglamorous origin, furfuraldehyde is one of the important starting materials for Nylon which, as you know, can be very glamorous indeed.

But the most important thing about these two heterocyclic rings is that carbohydrate molecules are actually made up of them. There are six carbon atoms in such simple sugars as glucose and galactose and these atoms are generally shown in a straight line. That, actually, is not

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[1] There is this same situation in carbocyclic compounds. Benzene, with three conjugated double bonds is very stable, but cyclohexane, without any double bonds, also exists.

quite correct. In reality, the carbon chain of both glucose and galactose bends. The oxygen atom of one of the hydroxyl groups in the compound hitches up to the aldehyde carbon at one end so that a pyrane ring is formed. There are no double bonds and there are hydroxyl groups at each position, but the ring itself is made up of five carbon atoms and an oxygen atom and that is the "skeleton" of a pyrane ring.

Other sugars may, in the same way, form a furane ring. Sucrose, the common table sugar we use every day, has a molecule that is made up of a pyrane ring hooked to a furane ring by an ether linkage. Starch and cellulose are made up of long chains of pyrane rings. In fact, furfuraldehyde is obtained from husks and bran because of the pyrane and furane rings in the carbohydrate molecules contained in those substances.

Do you wonder then why sugar molecules are usually written with the carbon atoms in a straight chain? The answer is that the furane and pyrane rings of the sugar molecules break very easily so that the chemical properties of the sugars are much what you would expect of straight-chain compounds. In fact, at first, chemists assumed they really were straight chain and only gradually became aware of the ring form.[1]

If the oxygen atom in furane is replaced by a sulfur atom, the compound *thiophene* is the result. Thiophene has the properties that are very similar to benzene. When benzene is isolated from petroleum, the same process will

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[1] In general, heterocyclic compounds that have rings that are easily broken are often not treated as heterocyclic. For instance, saccharin, which I mentioned at the end of Chapter 4, is really a heterocyclic compound, with two hetero-atoms, one nitrogen and one sulfur. In the rest of the book, however, I will deal with compounds whose rings are not easily broken and which may therefore be considered as "true" heterocyclic compounds.

also separate thiophene[1] so that unless special care is taken, benzene will always have a bit of thiophene in it as an impurity. Before 1882, chemists did not realize this. In fact they worked out a test[2] for benzene that was really a test for the thiophene impurity in the benzene and for years they noticed nothing wrong.

Finally, in 1882, a German chemist named Victor Meyer was demonstrating this test to his class. He used a sample of benzene that had been prepared, not from petroleum, but from pure benzoic acid. It was one of the rare occasions when a benzene sample did not have any thiophene in it. Victor Meyer ran through the test and nothing happened! (Since Victor Meyer was a chemist of importance and since German scientists usually are fully aware of their importance, he must have been very embarrassed and the class must have enjoyed it greatly.) Fortunately, Meyer didn't let it go. He tackled the problem of what was wrong with the test and discovered thiophene. (There's a moral

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[1] Some simple heterocyclic compounds occur in petroleum along with the ordinary hydrocarbons. Thiophene is the most important of these.

[2] A chemical *test* is a method by which one can prove that a certain kind of atom or atom grouping is present in an unknown substance even if it is only present in small quantities. Usually, such a test consists in the addition of a small quantity of a chemical, or mixture of chemicals, to the unknown substance, then applying heat or making the mixture acid or doing something else that will help a reaction take place. Then, if the atom grouping you're after is actually present, it combines with the chemicals you've added with very noticeable results. Usually, a bright color develops. If the atom grouping is absent, nothing happens. For instance, in the socalled "test for benzene" which I just mentioned, an unknown liquid is shaken with some strong sulfuric acid and then a little bit of a chemical called isatin is added. If benzene were present, the mixture would turn bright blue; otherwise, it would stay colorless. — The only thing is that it was the thiophene impurity that was doing the reacting with isatin and the thiophene that was giving the test; not the benzene.

to this. In scientific research pay strict attention to experiments that seem to go wrong. Those are just the experiments that may turn out to be the most worth-while.)

COLORS AND STILL MORE VITAMINS

Heterocyclic rings can be joined to ordinary benzene rings so that a two-ring compound (or an any-number-ring compound) results. If a pyrane ring is joined to a benzene ring, the result is *benzpyrane*, which looks like this:

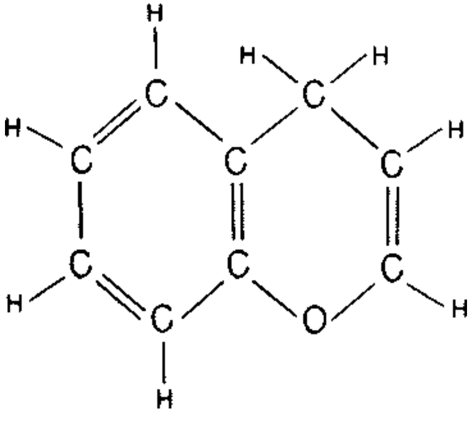

Figure 25—Benzpyrane

Certain compounds that occur in plants have benzpyrane rings. For instance, there is *coumarin*, the molecule of which is like that of benzpyrane except that one of the carbon atoms next to the oxygen hetero-atom is part of a carbonyl group. Coumarin has one of the pleasantest smells in existence. You can smell it in freshly-cut hay so that you might say coumarin has the smell of "country air."

Yet even from a substance as pleasant as coumarin, something unpleasant may come. If hay is allowed to stand in the dampness and spoil, some of the coumarin molecules may double up to form *dicoumarin*. Dicoumarin interferes with the way in which Vitamin K works and prevents blood from clotting. An animal eating spoiled hay, with dicoumarin in it can get a disorder that will result in its bleeding to death.

A benzpyrane ring with three methyl groups and a hydroxyl group attached to the benzene ring, and a long hydrocarbon side-chain attached to the pyrane ring makes up a molecule of one of the *tocopherols*. This is a fat-soluble vitamin, usually called *Vitamin E*.

Most of the experiments with tocopherols have been conducted on animals such as rats and mice. In these animals, the substance is necessary in the diet since without it, the females do not bear young. In fact, the word "tocopherol" comes from Greek words meaning "to bear children." The human requirement[1] for vitamin E has not been determined. We don't even know for sure that vitamin E affects the child-bearing ability of humans at all, though I'm sure it would do no harm to have some in the diet just to be on the safe side.

If a benzene ring is attached by one end to a benzpyrane ring, a whole series of compounds (depending on the exact groups attached to the various rings and the position of attachment) is produced. These are called the *anthocyanidins*[2] and the *flavones*. These compounds are respon-

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Experiments on diet are conducted on animals much more frequently than on human beings. You can probably see why that is. Animals can be under continuous watch; their diet can be controlled by force; if they are small, they don't eat as much. For that reason, it happens that we know a great deal about the vitamin, mineral and amino acid requirements of rats and not nearly so much about the same requirements of human beings.

[2] In plants the anthocyanidins and flavones are found in combination with sugars such as glucose. These are called *anthocyanins*.

sible for the coloring of many flowers. In fact, the word "anthocyanidin" comes from Greek words meaning "blue flower" and "flavone" comes from a Greek word meaning "yellow".

When the fluid in the cells of a flower-petal is a bit basic, some of the anthocyanidins are indeed blue, as the name suggests, and the resulting color is that found in corn-flower and delphinium. If the fluid is a bit acid, the same anthocyanidins are red in color and you can see the result in roses and peonies.

Color isn't all that these compounds are good for. Some have been considered to have vitamin properties. For instance, one of the symptons of a disease called scurvy is the unusual fragility of the small blood vessels called capillaries. They break easily and there is bleeding, about the gums particularly. Since a bruise is caused by broken blood vessels beneath the skin, a person with scurvy bruises very easily.

Now ascorbic acid (vitamin C) in the diet cures most of the symptoms but there are occasions when capillaries continue to leak blood a bit too easily, even when the body contains plenty of ascorbic acid. (The capillaries, in other words, are too permeable to blood.) Another vitamin seemed to be needed and it was called vitamin P. (The P stands for permeability.)

Compounds that behave as though they were vitamin P are certain flavones, of which the best known are *rutin* and *hesperidin*. They are found in the peel of citrus fruits, particularly lemons, in buckwheat and in other places. After considerable optimism about these compounds in the late 1940s, chemists are still uncertain as to their value, or even if they are vitamins.

There is one flurry in advertisements these days, however, that you may have noticed. Some "anti-cold tablets" are appearing which have "citrus bioflavonoids" in them.

These are our flavone friends. In combination with ascorbic acid, the advertisers say, they have a beneficial effect on colds. Unfortunately, the advertisers seem to be a bit over-optimistic. Recent clinical studies do not bear them out.

A pyrane ring fused to two benzene rings, one on each side, is found as part of the molecule of a compound known as *fluorescein.* When base is added to a solution of fluorescein, a part of the ring opens up and a fluorescent[1] green color is produced. A little bit of this basic variety of fluorescein will color a lot of water. Fluorescein can be used to locate leaks in water pipes for this reason. Where the water leaks out, it will be easily detected if it has fluorescein in it whereas otherwise it might go completely unnoticed.

During war-time, it was frequently used as a *dye-marker.* Men who were stranded on rubber life-rafts in mid-ocean would watch for search-planes circling overhead. When one showed up, they would rip open a water-proof bag containing basic fluorescein and dump the reddish powder into the ocean. A large patch of water would turn a fluorescent green almost at once. The pilot in the plane high above might miss the little speck of the life-raft, but he would almost certainly see the patch of green water. Many an airman and sailor owes his life to fluorescein.

THE COLOR OF BLOOD

The compounds with a nitrogen hetero-atom are more

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[1] Some compounds, when exposed to light, absorb it, and then give it off again in a different color. This is called *fluorescence* and it is from that that fluorescein gets its name. A fluorescent color is more glowing and "alive" than a color which is just the result of reflection. Fluorescent paints are frequently used to mark rear bumpers of cars or trees on the side of the road. Some years ago, there was a fad among youngsters which consisted of wearing articles of clothing colored with fluorescent dyes.

numerous and complicated than those with oxygen or sulfur hetero-atoms.

I'll begin by writing the structural formulas of two rings with nitrogen hetero-atoms that resemble furane and thiophene. They look like this:

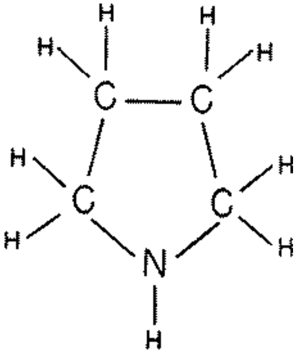

Figure 26—Pyrrolidine

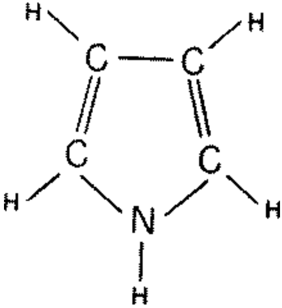

Figure 27—Pyrrole

The one on the left is *pyrrolidine* and the one on the right is *pyrrole*. The only difference is that pyrrole has two double bonds and four hydrogen atoms while pyrrolidine has no double bonds and eight hydrogen atoms.

Of the compounds with a pyrrolidine ring in the molecule, *proline* is the most important. Its molecule has a carboxyl group attached to one of the carbon atoms next to the nitrogen hetero-atom. This means that there is both a carboxyl group and an —N—H— group attached to the same carbon atom. An —N—H— group is an *imino group* and proline is an *imino acid*. Proline occurs in proteins and behaves just as do the amino acids I've already mentioned earlier. It is therefore included in the list of natural amino acids even though it is really an imino acid.

Proline occurs particularly in the protein, collagen.

Collagen also contains *hydroxyproline*, which is like proline except that a hydroxyl group is also attached to the pyrrolidine ring. Hydroxyproline does not occur, to speak of, in any protein besides collagen.

As for pyrrole, its importance lies not so much in itself as in a still more complicated ring system made up of a group of pyrrole rings. For instance, four pyrrole rings can be joined by one-carbon connecting links to form a still larger ring. I will show you the skeleton of the ring only. If I put in all the atoms, it would make for considerable confusion. I think you can get the general idea of the shape of the molecule from the following:

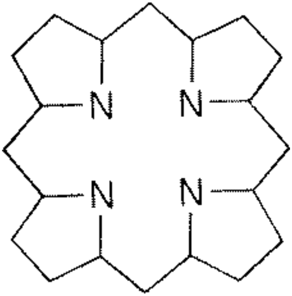

Figure 28—Porphin Skeleton

This ring of rings is called a *porphin ring*.

The porphin ring is quite a stable affair because of all the conjugated double bonds (eleven of them) and there are many compounds that contain the porphin ring as part of the molecule. Such compounds are called *porphyrins*. Because of all the double bonds, the porphyrins are generally deeply colored. The word "porphyrin" comes from the Greek word for "purple".

In our bodies, the most important porphyrin is *protoporphyrin IX*. This contains eight side-chains, one attached to each of the exposed angles of the four pyrrole rings. The side-chains include four one-carbon groups, two two-carbon groups and two three-carbon groups. These eight groups can be attached to the porphin ring system in no less than fifteen different ways. Each different arrangement would result in a different compound.

A German chemist, named Hans Fischer, figured out which arrangement is the one that occurs in our body and this is the way he did it. He listed all fifteen possible arrangements, divided his sixty students into fifteen groups of four, and gave each group the formula of one of the arrangements. Each group synthesized that particular arrangement (and the synthesis was a tremendous job in itself). The properties of each compound as it was prepared was compared with that of the natural protoporphyrin.

The arrangement which Fisher had labelled "nine" turned out to be the right one and that is why our protoporphyrin has the IX after its name. The "proto" prefix comes from the Greek word meaning "first" and testifies that this particular variety of porphyrin is of first importance.

Protoporphyrin IX, in the body, is combined with an atom of iron. This atom is located in the center of the ring and is connected with all four nitrogen atoms. Such an iron-porphyrin combination is called *heme*. The iron has two other bonds it can use. One of them can be attached to a protein.[1] In the most common case, the protein is one called *globin*. The combination of heme and globin is called *hemoglobin*.

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[1] Several of the side-chains on the porphyrin ring of heme also combine with the protein so that the heme and protein are attached firmly in at least five different places. When a compound like heme, not made up of amino acid units, is firmly attached to a protein molecule, it is called a *prosthetic group*. "Prosthetic" comes from the Greek word for "addition."

Hemoglobin is the compound that occurs in the red blood cells and which gives blood its color. (The word "heme" comes from the Greek word for "blood".) Hemoglobin itself is blue in color as you can see if you look at the veins that travel just under the skin on the back of your hands or the inner surface of your wrists.

However, as hemoglobin passes along the thin membranes of the lungs it picks up oxygen molecules from the air within the lungs. These oxygen molecules are attached to the iron atom by the iron atom's sixth and last bond. In this way *oxyhemoglobin* is formed, and oxyhemoglobin is the familiar bright red that is associated with blood.

Once the blood travels through the rest of the body, the oxyhemoglobin gives up its oxygen gradually to the cells and becomes hemoglobin again. It returns in that form through the veins which are blue in color for that reason.

When you bleed, the color of blood is always bright red, even if you are bleeding from a vein, since the blood combines with oxygen as soon as it is exposed to air.

Without hemoglobin carrying our oxygen, we couldn't live very long. Carbon monoxide (with a molecule made up of one carbon atom and one oxygen atom) will also hang on to hemoglobin. It will hang on so tightly that oxygen molecules can't find room on the molecule. That is why a small quantity of carbon monoxide in the air can be fatal.

Once the cell has picked up oxygen from the oxyhemoglobin of the blood, there are special enzymes within the cell to handle that oxygen. These enzymes are called *cytochromes.* These also contain heme in their molecules, but the protein part is different from globin. Cyanide ion interferes with the working of the cytochromes and that is why small quantities of cyanide ion can be fatal.

It is because we need hemoglobin and cytochromes to live that iron is one of the *essential minerals.* A shortage of iron results in a form of *anemia* (from Greek words meaning "no blood"). Anemics are not able to handle oxygen properly in their bodies and are pale, listless and tired.

THE COLOR OF GRASS

The porphyrin ring can attach itself to metals other than iron. In fact, a compound in plant tissue on which almost all life depends has a molecule made up of a porphyrin ring to which an atom of magnesium is attached. (The porphyrin ring is different in the details of its side-chains from the one in protoporphyrin IX.) The magnesium-porphyrin combination is *chlorophyll* and it is the green compound that gives color to the leaves and stalks of plants. (The name "chlorophyll" comes from the Greek words for "green leaf".)

Chlorophyll makes it possible for the green plant to absorb the energy of sunlight and use it to split water molecules into hydrogen and oxygen. The hydrogen combines with carbon dioxide (which the plant absorbs from the air) to form carbohydrates. The oxygen is turned loose in the atmosphere.

Since carbohydrate is formed (that is, synthesized) through the action of light, the process is known as *photosynthesis.* The prefix "photo" comes from the Greek word for "light."

As a result of photosynthesis, the energy of sunlight is converted into chemical energy and stored as carbohydrate.[1] The plant lives on this stored carbohydrate and

[1] From carbohydrate, the plant can form fat also. By adding simple nitrogen compounds, which it absorbs from the soil, the plant can make proteins. In general, the green plant can make all the compounds it needs in its tissues from carbon dioxide, water, and inorganic compounds of the soil. Such an organism is called *auto-*

so do the animals that eat plants and the animals that eat animals that have eaten plants and so on. It all comes down to the plant in the end—which lives on the energy of sunlight.

Furthermore, it has happened that plants have died and been covered first with swamp water, then with soil and rock. Their tissues have been converted after long ages to petroleum and to coal. So when we use those for energy, we are still living on the action of the chlorophyll molecules of millions of years ago.

Photosynthesis performs another vital function, too. Animal life gets energy out of the carbohydrate, fat and protein of their food by combining it with oxygen and forming carbon dioxide and water. If that were the only process that went on on earth, the atmosphere would eventually be loaded with a fatal quantity of carbon dioxide.

However, during photosynthesis, the plant uses up the carbon dioxide as fast as it is formed and by breaking up the water molecule, it restores oxygen to the atmosphere. What we breathe, as well as what we eat, we owe to the green plant.

A very unusual compound, with a structure that has been worked out only in the last few years, is *cyanocobalamine*. This is a deep red substance with a molecule made up of a porphyrin-like ring[1] with complicated side-chains. The central atom is one of cobalt (a metal very similar to iron) and this fact proved quite a sensation when it was

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trophic. Some bacteria are autotrophic, too. Animals, fungi, viruses and most bacteria must live on organic compounds originally formed by plants. There are *heterotrophic*. Man is heterotrophic, of course.

[1] It is not quite a porphyrin because in cyanocobalamine one of the carbon bridges of the ring is missing. Two of the pyrrole rings are connected directly to each other.

discovered. Cyanocobalamine is the only natural organic compound containing cobalt in its molecule.[1]

Cyanocobalamine has vitamin activity and it is also called *vitamin* B_{12}. It is essential to the body's manufacture of hemoglobin and that is why, by the way, that cobalt is one of the essential minerals required in small amounts in the human diet.

Now a shortage of hemoglobin in the blood gives rise to the disease known as *anemia*. I've already mentioned one kind of anemia caused by a shortage of iron in the diet. That kind of anemia is a simple one to treat. Pills containing iron compounds need be swallowed and that's all there is to that.

The hemoglobin shortage that comes about as the result of a shortage of cyanocobalamine is much more dangerous. In fact, the disease is called *pernicious anemia*, because it used to be invariably fatal. In 1926, two American doctors named G. R. Minot and W. P. Murphy discovered that certain extracts they prepared from liver could correct the disease. (The vitamin is stored in the liver, you see.) In 1934, they received the Nobel Prize for this discovery.

In 1948, the chemical responsible for this was isolated from liver and found to be cyanocobalamine.

Cyanocobalamine is required in very small amounts by the body. Only a thousandth as much is required as of any other vitamin. Furthermore, it is formed by bacteria in the intestines. For this reason, people with

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[1] The "cobal" stem in "cyanocobalamine" stands for "cobalt" with the "t" left out to improve the sound. There are amine groups in the molecule, too, of course. The "cyano" prefix indicates the presence of a cyanide group, too. This is not dangerous, however, because the cyanide group is bound tightly to the molecule and doesn't break loose as cyanide ion. Besides, the vitamin is present in such small quantities that there wouldn't be enough cyanide to do damage even if it did break loose.

pernicious anemia aren't really suffering from any shortage of the vitamin in their food. Instead, their trouble is that they are lacking a substance known as *intrinsic factor* which is needed to help them absorb the vitamin. In the absence of intrinsic factor, they can't get any good out of cyānocobalamine unless an extra large supply is present in their diet.

MIND DRUGS AND MORE DYES

When a pyrrole ring is condensed with a benzene ring, the compound that results is *indole*. Its molecule looks like this:

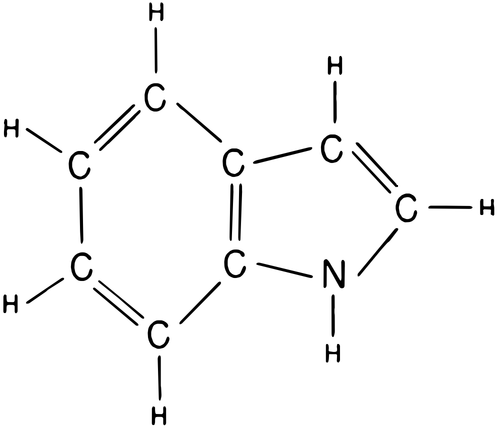

Figure 29—Indole

An indole ring with a methyl group attached is *skatole*. Both indole and skatole have a very foul odor and are responsible for much of the bad smell of our solid wastes, or *feces*. The word "skatole", in fact, comes from the Greek word meaning "feces."

These two compounds are formed in the intestines by the action of bacteria on one of the amino acids that occur in proteins. This amino acid is *tryptophan*, which has the indole ring in its side-chain. It is odorless and is one of the amino acids we must have in our diet. Bacteria always manage to get to some of the tryptophan molecules before they can be absorbed and form indole and skatole out of them. These are useless to the body and are not absorbed. They are just eliminated with the feces.[1]

Out of tryptophan, the body makes an important compound which has only been studied in the last few years. Put a hydroxyl group on the indole ring of tryptophan and remove the carboxyl group in the molecule and the result is a compound known as *serotonin.*

Serotonin is found chiefly in the brain and nerves and, apparently, has something to do with the way the brain cells work. Normally, it is quickly broken down by an enzyme called *amine oxidase.* Certain known chemicals will interfere with the workings of amine oxidase and will cause serotonin to pile up in the brain. This results in all sorts of mental quirks. Hallucinations and temporary mental disorders can be produced.

Drugs have also been discovered which work along these lines in an opposite direction. They calm tensions and fears and therefore are known as *tranquilizers.* They have become quite popular in the last few years.

Two indole rings joined together at the carbon atoms next to the nitrogen hetero-atom (with a couple of hydroxyl groups tacked on to the rings) make up a molecule of a deep blue substance called *indigo.* The name "indigo" comes from "Indicus", the old Latin name for "India" since it was from India that the ancient Romans got the substance. From indigo, by the way, comes the name "indole."

Indigo is one of the few natural substances which is a good dye. As such, it was extremely valuable in the days

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[1] Bacterial change brought about in food or tissue which results in the formation of foul-smelling (and often poisonous) substances is termed *putrefaction.*

before modern synthetic dyes. Whole plantations were given over to the plants that produced indigo. Nowadays, chemists have learned to synthesize indigo more cheaply than the plants could be grown and indigo plantations have gone out of business.

A dye with a molecule like that of indigo but with two bromine atoms attached is *Tyrian purple*. The inhabitants of ancient Tyre obtained the dye from a purple snail. They kept the secret closely and sold the dye for high prices. This was one of the reasons the Tyrians were so prosperous. The dye was so expensive, in fact, that it was used only for royal garments. By the time the Middle Ages began, the secret of the dye was lost. And now, of course, even though it has been rediscovered, it is no longer important. There are any number of synthetic dyes of the same color that are cheaper and better.

A less common type of pyrrole-benzene combination is one that looks like this:

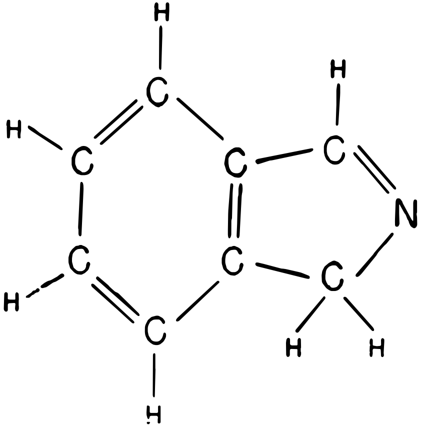

Figure 30—Isoindole

This compound is isoindole and if you compare its formula with that of indole you will see that the only difference is that the nitrogen atom is in a different place.

The isoindole ring, like the pyrrole ring, can connect up to form a larger ring made up of four of the smaller ones. The small rings are connected by nitrogen bridges rather than carbon bridges, however. The final molecule is *phthalocyanine*, a brilliant greenish-blue compound.

A copper atom easily joins the molecule in the center, being connected to the four nitrogen atoms of the isoindole rings. The resulting *copper phthalocyanine* is a pure blue in color. ("Cyanine" comes from a Greek word meaning "blue".) In fact, it is the best blue dye for use in color printing because it has so little red or yellow in it.

Copper phthalocyanine has no less than nineteen conjugated double bonds in the molecule. This accounts not only for the color but also for its stability. It is most unusually stable for an organic compound. It can be heated to 500° C. without harm and will withstand the strongest chemicals.

Other phthalocyanines are coloured differently. Lead phthalocyanine is yellowish-green. Copper phthalocyanine, with some fourteen or sixteen chlorine atoms attached to the ring system, is a pure and brilliant green and so on.

7

Medicine and Poison

THE FIRST DRUGS

The earliest medicines were extracts prepared from various parts of certain plants. People found, more or less accidentally, that these parts had powerful effects on the body. A bit of it could sometimes cure a disorder or, sometimes, kill a person.

This happens because certain plants contain in their seeds, leaves, bark or roots, compounds known as *alkaloids*. These alkaloids are heterocyclic compounds (often with complicated ring systems) which contain at least one nitrogen as a hetero-atom.

These alkaloids apparently don't play any part in the chemical machinery of the plant. They just seem to be there, doing nothing. Some people have suggested that the alkaloids are produced by plants as a defense against animals. After all, plants are completely helpless organisms, for the most part. Animals can eat them at will. The plants can't run and they can't fight. However, they can produce poisons and once they've done that, animals learn to stay away. Fortunately for animals (including us) only a small percentage of the plants of the world have learned this trick.

An example of a familiar alkaloid is *strychnine*. The molecule of strychnine contains no less than seven rings arranged in a complicated way. The molecule contains two nitrogen atoms, both of which are parts of pyrrolidine rings. It also contains an oxygen atom which is part of a pyrane ring.

Strychnine is found in the seeds of the orange-like fruit of an East Indian tree called nux vomica.[1] Strychnine is probably familiar to all of you because, in detective stories, strychnine is one of the favorite ways of poisoning a victim. Actually, it may not be so easy to manage this as the mystery thrillers might have you think. Strychnine is one of the most bitter compounds known. An ounce of strychnine can still be tasted after it has been dissolved in eight thousand gallons of water. There are few ways of masking the taste well enough to make the victim take it.

Strychnine acts by stimulating the nervous system and, in that way, causing the muscles to contract more vigorously. In very small quantities, strychnine could have a desirable tonic effect. This is especially so where a patient may be suffering from an overdose of sedative so that his nervous system has been depressed almost to the point of his death. A bit too much strychnine, however, stimulates too strongly and sends the muscles into convulsions and rigor. (A muscle in rigor stays tightly contracted.) Strychnine poisoning is a very painful kind of death.

Physostigmine is a compound with a molecule less complicated than that of strychnine. Its molecule contains three rings, two of which are pyrrolidines. It is found in the Calabar bean, which is the seed of an African tree.

Physostigmine interferes with the breakdown of acetylcholine just as the nerve gases do. It has the same poisonous effect in overdose. It can be used beneficially, though, as

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[1] Along with strychnine, there is also formed a very similar alkaloid called *brucine*. Usually, a plant that forms alkaloids forms a number of very closely related ones.

eyedrops. In the disease glaucoma, the fluid within the eyeball increases its pressure abnormally. The increase in pressure is painful and can reach the point where blindness results. Eye-drops containing physostigmine will reduce the pressure and save the vision.

THE NON-CATCHING DISEASE

A heterocyclic ring consisting of five carbon atoms and a nitrogen atom looks like this:

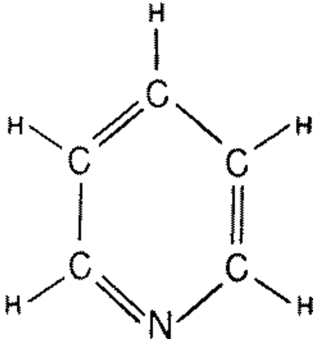

Figure 31—Pyridine

It is called *pyridine* and, as you see, looks just like benzene except for that nitrogen atom. It is even more stable than benzene. Pyridine is one of the rings that can be attached to the sulfanilamide molecule to form a useful drug, *sulfapyridine*.

An important pyridine-ring compound is *nicotinic acid*. This has a molecule in which a carboxyl group is attached at the second carbon from the nitrogen hetero-atom. Nicotinic acid is one of the B vitamins and is a necessary part of at least three different coenzymes. The body cannot make enough nicotinic acid for its needs so it depends on getting small quantities of it in the diet.

Before introducing nicotinic acid into the coenzymes, the body changes it to *nicotinamide* by changing the carboxyl group to an amide group Nicotinamide in the diet is, of course, just as useful, if not more so, than nicotinic acid itself is. When two similar molecules have similar vitamin action, they are called *vitamers.* Nicotinic acid and nicotinamide are vitamers.

The three coenzymes of which nicotinamide is part are often called simply *Coenzyme I, Coenzyme II and Coenzyme III* (though they also have more complicated names). They are associated with dozens of enzymes which control the dehydrogenation (see page 72) of a large number of different compounds.

If nicotinic acid and nicotinamide are absent from the diet, the body cannot make coenzymes I, II and III (though it can make all the rather large coenzyme molecule except for the nicotinamide portion). Without the coenzymes, dozens of reactions in the body slow down. The whole chemical mechanism starts grinding and limping.

The disease that results is called *pellagra,* from Italian words meaning "rough skin," because the skin gets rough and inflamed. There are also many other unpleasant symptoms.

At one time pellagra was fairly common in southeastern United States where the poorer people lived on a rather monotonous diet made up mostly of cornmeal. Cornmeal is not only poor in nicotinic acid; it is also poor in the amino acid, tryptophan. Intestinal bacteria, it seems, can convert tryptophan to nicotinic acid. A person whose diet contains tryptophan can always absorb some of the nicotinic acid the bacteria form. It may not be enough to meet all his needs but at least it helps out.

Before 1915, people thought pellagra was a germ disease but in that year, a doctor named J. Goldberger had the daring thought it might be the fault of diet. After all, pellagra didn't seem to be catching and people who were lucky enough to own a cow or had enough money to buy milk didn't get pellagra somehow. (Milk is a good source of the vitamin, we now know.)

Goldberger experimented with convicts, feeding six on a very restricted diet, and five others on a diet that allowed more variety and included milk. It was very difficult to keep the six restricted-diet convicts from breaking the rules, as you can well imagine, since living on a very limited diet can grow unbearable. Goldberger managed, however, and sure enough the six convicts with limited diets all got pellagra; the other five did not. The secret of pellagra was out. It could be cured by proper diet.

In 1937 the chemical in food that prevented pellagra was finally identified. It was nicotinic acid (or nicotinamide).

Nicotinic acid gets its name from an alkaloid that is found in the leaves of the tobacco plant. The alkaloid is *nicotine*.[1] The molecule of nicotine consists of a pyridine ring with a pyrrolidine ring attached by one corner. When the two rings are broken apart by chemical treatment, one carbon atom of the pyrrolidine ring is left behind as a carboxyl group and nicotinic acid is the result.

The American Medical Association has been concerned that the similarity in names might get people to thinking

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[1] In general, alkaloids have names with the suffix "ine". Most often, the rest of the name is taken from the Latin name of the group of plants in which the alkaloid is found. For instance, the group of plants to which tobacco belongs is "Nicotianum". Strychnine comes from a plant group with the Latin name "strychnos" and so on.

that there was a vitamin in cigarettes and that cigarette-smoking was therefore good for the health and would prevent pellagra. They have therefore suggested that nicotinic acid be called *niacin* and that nicotinamide be called *niacinamide.* If you look at the label of some box of vitamin pills or of cereal food, you will probably find niacin, rather than nicotinic acid, on the list of vitamins contained.

Nicotine, by the way, is quite poisonous, as most alkaloids are. Most of it is destroyed during smoking, but about a quarter of it gets drawn into the throat or lungs with the smoke. It doesn't seem to do serious harm there, though the same amount taken into the stomach might make you sick indeed, or even kill you.

Another vitamin with a pyridine ring in its molecule is *pyridoxine.* In the molecule of this compound, the pyridine ring has four groups attached: a hydroxyl group, a methyl group and two hydroxymethyl groups.[1] One of the hydroxymethyl groups can be replaced by an aldehyde group to form *pyridoxal*, or a methylamine group to form *pyridoxamine.* It is pyridoxal that actually forms part of a coenzyme called *pyridoxal phosphate* (in which a phosphate group is attached to the molecule, as you can tell from the name). However, pyridoxine and pyridoxamine are easily converted by the body to pyridoxal so all three compounds are vitamers. They are sometimes referred to as *vitamin* B_6.

THE SOUTH AMERICAN MEDICINE

If a pyridine ring is condensed with a benzene ring, the result is *quinoline*, with a molecule that is shown in *Figure 32* opposite.

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[1] A hydroxymethyl group is a methyl group which has had one of its hydrogen atoms replaced by a hydroxyl group.

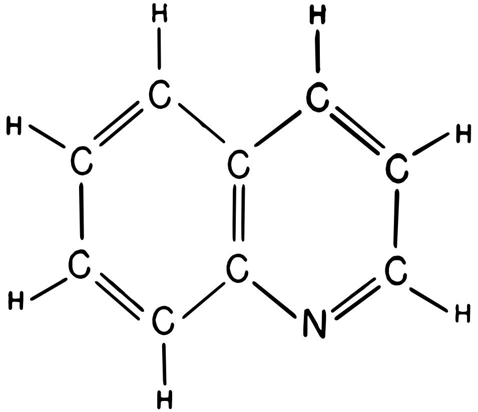

Figure 32—Quinoline

The name "quinoline" comes from an alkaloid known as *quinine*, a drug with a most useful history. Quinine has been used to cure malaria (or at least to suppress its worst symptoms). Even today, malaria is probably the most serious disease in the world. In India alone, at least a million people each year die of malaria and there is no telling how many of the rest are seriously weakened by it. Malaria is spread by certain mosquitoes. By wiping out breeding-places for mosquitoes and by using insecticides, malaria can be controlled. Still, in the less developed and more crowded portions of the earth, particularly in warmer climates, malaria remains a major danger.

When the Spaniards first arrived in Peru, they found that the natives chewed the bark of a particular tree to help them get over malaria attacks. (The word "quinine" comes from a Peruvian Indian word meaning "bark.") The Spaniards tried it and it worked. In 1639, it was used to treat the Countess de Chinchon, wife of the Spanish Viceroy of Peru. Hence, the tree from which the bark came was named the cinchona tree, and another alkaloid found in the bark, very similar to quinine but only one-fifth as active, is called *cinchonine*.

Quinine has a quinoline ring in its molecule. This is attached to another double ring of rather complicated structure, which we don't have to worry about.

With time, the South American source was used up, but the trees had been transplanted to East India and had flourished there. By World War I, almost all the supply came from Java. Germany, cut off from the sea by the British blockade, had to find a substitute drug against malaria (a synthetic *antimalarial*, in other words).

Certain synthetic compounds with molecules containing quinoline rings showed promising results. One of these is *plasmochin*. Its molecule is almost (not quite, though) like that of quinine in which the other double ring has been cut open and made straight-chain. Here is another case in which a synthetic drug was designed by using the natural substance as a guide and simplifying it.

In World War II, America faced the same problem, because the quinine supply was cut off by the Japanese occupation of the East Indies. To make it worse, American troops were fighting in tropical climates where malaria was a greater danger than it usually was in the United States itself.

Drugs of the plasmochin type were not available in America during World War II. Instead we used *quinacrine* (better known by its trade name *Atabrine*) It contains a three ring molecule: a pyridine ring fused to two benzene rings, one on each side, as shown in *Figure 33* opposite.

This three-ring molecule is *acridine*. In quinacrine there is a long side-chain attached to the middle ring. It's the one that looks like that quinine double ring cut open.

Actually, the synthetic anti-malarials are better than quinine in some ways and certainly cheaper. Like silk,

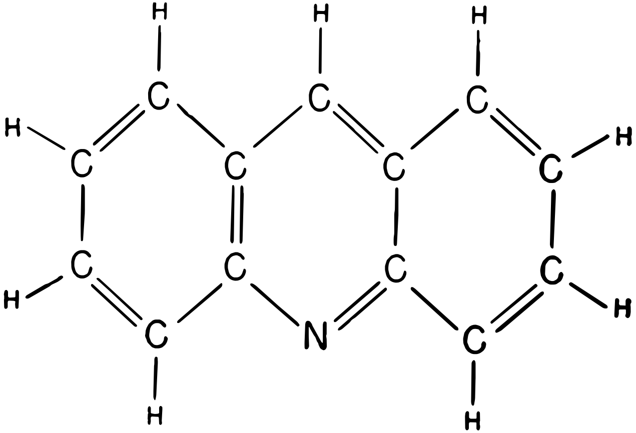

Figure 33—Acridine

quinine came back after World War II to find that Americans had learned to do without it.

DRUGS FROM FUNGI

There is a fungus known as *ergot* that grows on rye. This fungus manufactures a number of alkaloids of unusually complicated structure. These are quite poisonous and there have been cases, even quite recently, of people eating bread made out of spoiled rye and developing a serious disease called *ergotism.* The symptoms include mental disorders.

If the ergot alkaloids are used very cautiously, they can produce muscle contractions that can be helpful. The muscles of the uterus are particularly affected. (The uterus is the organ in the woman which holds the unborn child.) Ergot is sometimes used to hasten childbirth for that reason, but it is a dangerous drug and is usually used only as a last resort and even then only with great caution.

The ergot alkaloids can all be hydrolyzed in part. When this is done, a fragment of the molecule, called *lysergic acid*, is liberated. This has a four-ring molecule, including two nitrogen atoms. One of the nitrogen atoms is part of a quinoline ring; the other part of an indole ring. Starting with lysergic acid, chemists have converted a carboxyl group attached to the quinoline portion of the compound into amides of various sorts. They found that the resulting compounds sometimes had even greater activity than the natural ergot alkaloids. One in particular, *lysergic acid diethylamide*, has been useful.

Lysergic acid, and all the compounds related to it, have an indole ring in the molecule. This makes it somewhat similar in structure to serotonin which also has that indole ring. Amine oxidase, the enzyme which breaks down serotonin, can pick up lysergic acid diethylamide instead if that drug happens to be around. That ties up the enzyme which can then no longer work on serotonin. This means that serotonin builds up in the brain and queer things happen.

By injecting lysergic acid diethylamide into a person, hallucinations can be made to appear to that person, as well as symptoms of a serious mental disorder called *schizophrenia*. For the first time now, chemists hope they are on the track of understanding the chemistry of a mental disease. You can see the importance of this if I tell you that more than half the people in hospitals in the United States are sufferers of schizophrenia.

Another alkaloid with a complicated ring system of which indole is a part, is *reserpine*. It comes from the root of plants known as Rauwolfia. Part of its molecule looks like an indole ring attached to a pyridine ring (*see facing page*), but there are more rings and various side-chains in the molecule. It also has a mental effect, but of the reverse type. It possesses a calming or quieting

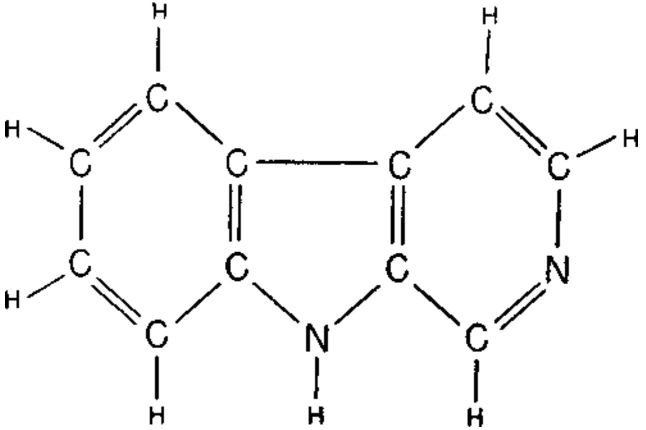

Figure 34—Pyridinoindole

effect without bringing on sleep and was the first of the tranquilizers.

THE MOST DANGEROUS DRUGS

Pyridine and benzene rings can be fused in another way, like this:

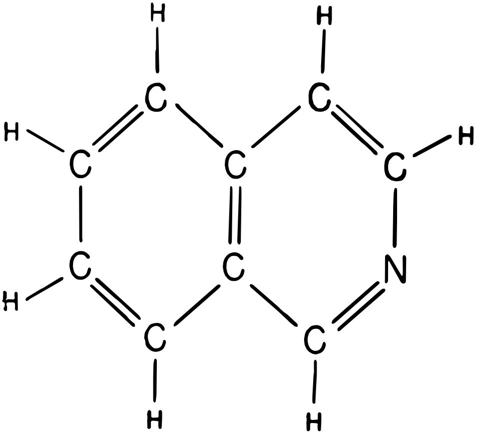

Figure 35—Isoquinoline

This is *isoquinoline*. If you compare the formula with that of quinoline, you will see that the nitrogen atom is in a different place.

The most important isoquinoline compounds are those that occur in the unripe fruit of certain poppies. The dried juice of this fruit is called *opium* (from a Greek word meaning "juice") and the plant is called the opium poppy.

Opium contains about two dozen different alkaloids, including some of the most important known to man. In the days before modern anesthetics and sleeping pills, opium was used to relieve pain and discomfort. Sometimes, it was just taken to make one feel good and forget the troubles of life. A person could get into the habit of doing that but perhaps that was no worse than getting into the habit of taking a little whisky in order to forget your troubles.

However, once chemists took to purifying the alkaloids in opium, "drug addiction" became quite a dangerous thing. The pure alkaloids took a stronger grip on a person and made him less able to let go. They also did more harm than the original poppy juice.

The most important alkaloid in opium is *morphine* (from the Greek word for "sleep") which is one of the most powerful sedatives and pain-relievers known. It is used by doctors to relieve pain despite its dangers. By using it only when necessary and even then only with great care, the dangers are decreased.

Still, opium poppies are grown in far greater quantities than are necessary to satisfy the needs of the medical profession. The excess is sold (at high prices) to the miserable people who have become addicted to drugs. One of the ways in which the different nations of this world have successfully pulled together is in their efforts to control this illegal drug trade. The greatest efforts never seem to work completely, however, and drug addiction remains a great health menace.[1]

The ring system of morphine is quite complicated. Five rings are involved but the isoquinoline ring system is part of it.

Codeine also occurs in opium. (The name comes from the Greek word for "poppy head.") It has the same formulas as morphine except that a methyl group is added to the ring system. It is not as powerful a pain-reliever as morphine is, but on the other hand it is less likely to cause drug addiction.

Quite the opposite is *heroin*, which is not a natural alkaloid at all, but a synthetic product. It is morphine condensed with two molecules of acetic acid. Heroin is more powerful than morphine, more likely to cause addiction, and does more damage. In fact, heroin is probably the most dangerous drug there is.

On the other hand, chemists have built up a synthetic molecule keeping some of the features of the morphine structure. The result is *meperidine* (more commonly called *Demerol*). It was first produced in Germany in 1939. Demerol is less potent than morphine, to be sure, but it is also much less dangerous.

In fact, Demerol can be used in helping people who are trying to get over addiction to morphine. If such addicts

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[1] Some famous types of drug addiction don't involve opium alkaloids. There are compounds in a plant known as Indian hemp (also called marijuana and hashish) to which people can become addicted. The use of these compounds causes temporary mental disorders such as hallucinations and queer illusions as to the speed at which time is passing. The same effects can be achieved by the compounds in a small cactus of the Southwest called mescal. The Indians use mescal in their religious ceremonies sometimes because its queer mental symptoms seem to take them out of the ordinary world into a supernatural one. The effects of such drugs may be the same as that of lysergic acid diethylamide.

are forced to break off short and swear off morphine all at once, they get what are known as *withdrawal symptoms.* These are very hard to bear and can drive the victim back to the drug even against his will. Demerol will ease these withdrawal symptoms and still allow the addiction to wear off.

A somewhat different example of an isoquinoline drug is *curare.* This, like rubber and quinine, is another example of the chemical discoveries of the primitive South American Indians.

Curare is gotten from plants that belong to the same group as those from which strychnine is derived, but the alkaloids in curare have the opposite action from that of strychnine. The curare alkaloids relax the muscles and are used in small doses by doctors for just that purpose. A trace too much, however, means death. The Indians, in fact, used it as a very effective arrow poison.[1]

SHARING THE NITROGEN

Sometimes the nitrogen atom in a heterocyclic compound is part of two different rings in a way that cannot be drawn easily on paper. Seen from the side, such a molecule looks like the letter Y. Seen from above, such a ring might look like this (I'll include only the carbon and nitrogen atoms) (*see following page*):

The C—N—C combination in the middle is the stem of the Y, while the C—C on one side and the C—C—C on the other would be the two forks at the top of the Y.

If you imagine a methyl group on the nitrogen atom

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[1] At one time, detective stories often used "mysterious South American poisons" to kill people with. These were inspired by curare. Now that the chemistry of curare is being worked out, mysterious South American poisons have gone out of fashion.

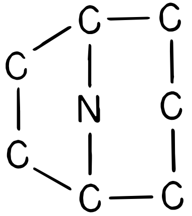

Figure 36—
Tropane Skeleton

and then fill in hydrogen atoms all around for the spare bonds, the result is a molecule of *tropane.*

A variety of alkaloids with the tropane ring occur in a number of plants, such as one called belladonna. These alkaloids have the ability to cause the iris of the eye (the colored part) to contract. As a result, the pupil grows large. There was a time when ladies of fashion used the juice of the belladonna root to give themselves large pupils deliberately because they thought the dark eyes that resulted made them look more glamorous and beautiful. ("Belladonna" is Italian for "beautiful lady".) Of course, tinkering with the eyes that way interfered with vision but women who are planning to look beautiful will do queer things sometimes.

Doctors use these alkaloids in the same way these days, but for a more sensible reason. They put drops containing a bit of these alkaloids into the eyes when they want to look inside the eyeball and learn some facts about its structure so they can correct vision defects. The most common belladonna alkaloid used for this purpose is *atropine.*

Another alkaloid with a molecule containing the tropane ring system is *scopolamine.* This drug has mental effects. It causes a kind of delirium. People asked questions while in this delirium are liable to answer truthfully (since telling lies takes considerable mental effort). They are even likely to say things in the course of delirious babbling which are true but which they would not say if they had their wits about them. Sometimes scopolamine is called *truth serum* for this reason.

Still another of the tropane alkaloids is *cocaine*. It comes from the leaves of certain South American coca trees, hence its name. Once again this is a discovery of the South American natives. They chewed the leaves of the coca tree for the sake of the good feeling it gave them. When cocaine entered medical practice, it was as a local anesthetic. The "good feeling" it brought about can cause drug addiction which is one reason why substitutes were looked for and found in the manner I described earlier in the book.

8

More Than One

A DOUBLE DOSE OF HETERO

There are ring systems that contain more than one hetero-atom. For instance, there is a five-membered ring which contains both a nitrogen atom and a sulfur atom, thus:

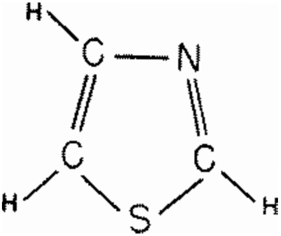

Figure 37—Thiazole

It is called *thiazole.*

One of the compounds that contains such a ring is one that has grown familiar to all of us in the years since World War II. I'm talking about *penicillin.*

The story of this important compound is another example of the discovery-by-accident that happens every once in a while in science. Back in 1928, an English doctor, Alexander Fleming, was growing germ cultures in shallow containers called Petri dishes. Some of these cultures had been accidentally contaminated with the spores of common bread mold. (The scientific name of this mold is *Penicillium notatum.*)

Instead of throwing the cultures away as "spoiled" (as I probably would have done without a second thought), Fleming stopped to look at them. He noticed that about each mold spore there was a clear area in which germs did not grow. Evidently, there was something (which later turned out to be penicillin) in the mold which stopped bacterial growth. He reported this and the reward of his careful observation was that in 1945, he received the Nobel Prize (and also that he saw many lives saved because of that observation).

By 1939, English chemists were isolating crude preparations of penicillin from the mold. In 1941, it was first used on patients and was very successful. During World War II, working out its structure was made a high-priority project in England and America. By 1945, the job was done.

Its molecule contains the thiazole ring, as I have said, fused to a four-carbon ring. Two methyl groups and a carboxyl group are attached to the thiazole ring and an amide group is attached to the four-membered ring.

The amide group can be connected to various groups. For each group that is attached, a different penicillin is formed, each with somewhat different properties. The penicillin usually used by doctors and sold in drugstores contains a benzene ring attached to the amide group by way of a one-carbon bridge. It is called *penicillin G.*

The sulfonamides were used ten years earlier than penicillin, but the sulfonamides were strictly synthetic substances. Penicillin is produced by a living organism and is an antibiotic, the first to be developed. Unlike some of the useful antibiotics discovered later, penicillin is almost completely harmless to human beings. Large doses of millions of units[1] can be used.

ALLERGIES AND EGG-WHITE

A ring-system can contain more than one hetero-atom of the same type. For instance, a five-membered ring, with two nitrogen atoms placed as follows:

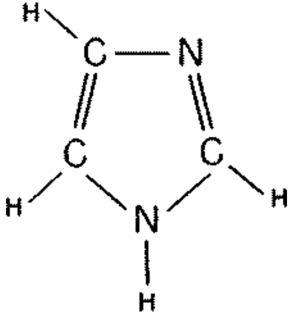

Figure 38—Imidazole

is called *imidazole.*

The most important compound containing this ring is the amino acid, *histidine*, which has an imidazole ring in its side-chain.

If the histidine molecule has its carboxyl group removed, what is left is *histamine.* Histamine occurs in the body in small quantities and has a powerful effect on various organs. For instance, it expands the small blood vessels so that blood pressure drops. On the other hand, it contracts the small tubes in the lungs and makes breathing

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[1] Compounds such as vitamins and antibiotics have powerful effects on the body in very small quantities. Measuring the weight of the doses of such compounds would cause doctors to work with ridiculously small figures. Instead, an ounce of pure penicillin G is set equal to 47,250,000 units. These units are convenient to work with. Two and a half units per ounce of blood will control germs that are susceptible to penicillin. (Not all germs are, of course.)

harder. It causes the stomach to secrete digestive juices at a more rapid rate.

All these effects can have their uses, if they occur in the proper way and at the proper times. However, it is possible that too much histamine is formed in the body under certain conditions. When this happens, the effects are those noticed by people with hay-fever and certain other allergies.

One way to control the discomfort of allergic symptoms is to dose the patient with some compound that will neutralize the effects of histamine. These neutralizing compounds, called *antihistamines* are tertiary amines with rather complicated molecules. Their molecules generally contain at least two or three rings and heterocyclic combinations are often included.

Some years ago, there was a fad for using antihistamine drugs to combat colds. Colds show some of the same symptoms that hay fever does, so it was thought that what would ease the symptoms in one case would do the same in the other. It didn't work, though. Colds are quite different from hay-fever and what helps one doesn't necessarily help the other.

An imidazole ring fused to a benzene ring is *benzimidazole*. Benzimidazole rings form part of the complicated structure that makes up the molecule of vitamin B_{12}.

An imidazole ring fused to a thiophene ring, thus:

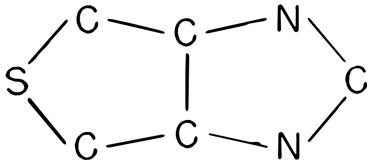

*Figure 39—
Biotin Ring System*

makes up a ring system that forms part of *biotin*, one of the B vitamins. If biotin is absent from the diet of rats, a skin-inflammation results and originally the Germans called biotin, *vitamin H.* The "H" stood for "Haut" which is the German word for "skin."

Biotin is one of those vitamins which are present in small quantities in almost every food[1] It is also manufactured by bacteria in the intestines. It is not likely, therefore, that anyone would ever be short of the vitamin. In fact, chemists found it very difficult to find a way of making rats short of the vitamins so they could observe the results of biotin-shortage.

Raw egg-white came to their rescue. Raw egg-white contains a protein called *avidin* which combines with biotin and keeps it from performing its function. Rats fed raw egg-white developed a disease called *egg-white injury*, which turned out to be the fault of a biotin shortage.

The same could be done in the case of human beings. If you like eggs, however, don't stop eating them because of this. Cooking eggs in any fashion destroys the avidin and you are safe.

SLEEPING-PILLS AND POLISHED RICE

The most important six-membered heterocyclic ring with two nitrogen hetero-atoms is shown on following page, and is called pyrimidine.[2]

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[1] Biotin is a good example of the difficulties a chemist may have to face sometimes in isolating a bit of pure compound from tissue. In 1936, a German chemist named Fritz Kögl started with 550 pounds of dried yolks of duck eggs and after tremendous work ended up with just about a twenty-five thousandth of an ounce of pure biotin.

[2] There are two other positions the nitrogen atoms can take in the ring. They can be next to each other (in which case the compound is *pyridazine*), or at opposite ends of the ring (in which case it is *pyrazine*). All together, the three types of rings are called *diazines.* Sulfonamide drugs exist in which a pyrazine ring is added to the

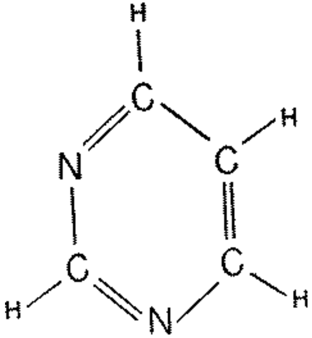

Figure 40—Pyrimidine

One important compound that contains the pyrimidine ring is *barbituric acid.* In barbituric acid, three of the carbon atoms of the pyrimidine ring are part of carbonyl groups. The fourth carbon has two hydrogen atoms attached. These hydrogen atoms can be replaced by various types of side-chains and the result is a group of compounds known as the *barbiturates.*

The best-known barbiturate is one in which both hydrogen atoms are replaced by ethyl groups, giving *diethyl barbiturate.* This is more commonly called by its trade-name, *Barbital.* Another, with one side-chain an ethyl group and the other a benzene ring is *phenylethyl barbiturate*, or *Phenobarbital*, to use its trade name.

The barbiturates are the most widely-used of the "sleeping pills." Barbital and Phenobarbital, in the proper dose, will put a person to sleep in half an hour to an hour and keep him sleeping for from four to twelve hours. Other barbiturates may act more rapidly and wear off more rapidly.

molecule of sulfanilamide. The final product is *sulfapyrazine.* The pyrimidine ring can also be added but in that case the product is called *sulfadiazine.* Sulfadiazine has fewer harmful side-effects than the other sulfonamides. (The pyrazine ring, by the way, occurs in mauveine, the first of the aniline dyes.

The barbiturates have their dangers. An overdose can turn sleep into death. One reads about such accidents only too often in the newspapers and this again shows the dangers of dosing one's self with pills, however useful they may be at the proper time.

Certain pyrimidine compounds occur as part of important tissue compounds which I am reserving for discussion in the last chapter of the book. The three most important are *uracil*, *thymine*, and *cytosine*. In uracil, the pyrimidine ring has two hydroxyl groups attached; in thymine, two hydroxyls and a methyl group; in cytosine, a hydroxyl and an amine group.

If a pyrimidine ring is attached to a thiazole ring by way of a one-carbon bridge, the ring system that results is found in *thiamine*, one of the B vitamins.

It is one of the longest-known vitamins, too, as you could perhaps tell by its other name of *Vitamin* B_1. As long ago as 1890, a Dutch scientist, named C. Eijkmann, was interested in a disease known as *beri-beri*. It afflicted people in what was then called the Dutch East Indies, where he was stationed, and in other parts of the Orient. It affected the nervous system, and the same disease in fowls was called *polyneuritis*.

Eijkmann discovered that people so afflicted had diets that consisted mostly of polished rice; that is rice from which the husks, or bran had been removed. If the husks, or "rice-polishings" were added to the diet, the beri-beri disappeared.[1] The rice-polishings contained thiamine. In 1929, Eijkmann received the Nobel Prize for his work.

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[1] The East Asians polish their rice for the same reason we polish our wheat. The husks contain fat which goes rancid on storage. The starchy part of the grain is easy to store because it keeps almost indefinitely. It is only since we've learned about vitamins that we've come to value whole-wheat bread and even so, we have found that it is easier to add vitamins to white bread, than to try to store whole wheat flour in quantity.

In 1933, an American chemist named R. R. Williams first isolated the pure vitamin from rice husks. He used a ton of rice husks and ended with less than a fifth of an ounce of thiamine.

COFFEE AND GOUT

If a pyrimidine ring is fused with an imidazole ring, the result is a two-ring combination carrying four nitrogen hetero-atoms altogether, like this:

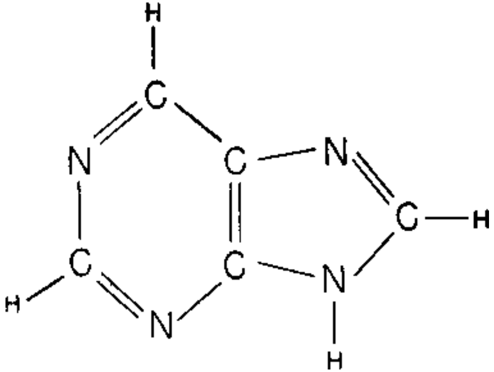

Figure 41—Purine

Such a combination is called *purine*.

To the average person, the best-known compound with a purine ring in its molecule is *caffeine*, an alkaloid that occurs in the coffee bean and in tea leaves. Its molecule has two hydroxyl groups attached to carbon atoms in the purine ring and a methyl group attached to each of the three nitrogen atoms. Caffeine acts as a stimulant and is the reason for the "pick-up" effect of tea and coffee.

More important, really, however, are two purines that occur in the same tissue components I mentioned earlier in connection with the pyrimidines; the components I'm reserving for the last chapter. One of these is *adenine*, the molecule of which consists of a purine ring to which an amine group is attached. The other is *guanine*, which has a molecule made up of a purine ring to which an amine group and a hydroxyl group are attached.

When the body is done with these adenine and guanine units and wishes to get rid of them, it converts them to *uric acid*. The molecule of uric acid is made up of a purine ring to which three hydroxyl groups are attached. Getting rid of uric acid is a problem because it must be excreted by way of the urine (hence its name) and it is only very slightly soluble in water. Most mammals get around this by changing the uric acid further. They break open the larger ring of the purine combination and form *allantoin*. Allantoin is more than ten times as soluble as uric acid and presents no problem.

Unfortunately, man and the various apes are among the very few mammals who do not possess the enzyme that brings about this change of uric acid to allantoin. Man is stuck with uric acid and must get rid of it in the urine, little by little, as best he can. In most cases, he manages, somehow. Occasionally, though, the urine of some individual may be overloaded and uric acid will settle out to form still another variety of kidney stone.

Worse still, there are some unfortunate people in whom the uric acid settles out in the joints for some reason. Usually, it is the joint of the big toe that starts the trouble. The result is an agonizingly painful disease known as *gout*.

TWO LAST VITAMINS

If a pyrimidine ring is fused with a pyrazine ring, the result is shown in *Figure 42* overleaf.

Such a compound is called *pteridine*. Such a ring system was found to form part of the molecules of the pigments in the beautifully-colored wings of moths and butterflies.

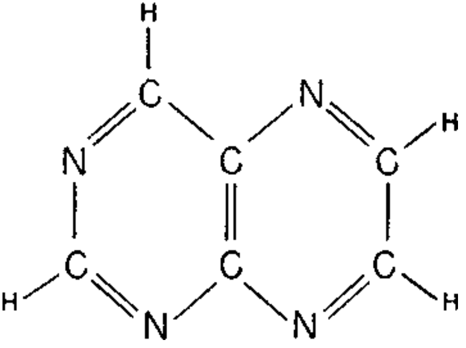

Figure 42—Pteridine

The scientific name for those insects is Lepidoptera. The word "pteridine" is derived from the last five letters of that name.

The pteridine ring system has greater importance to us, however, than any number of butterfly wings, however beautiful. A pteridine ring (with an amine group and a hydroxyl group attached to the pyrimidine part) when condensed with para-aminobenzoic acid and glutamic acid forms *pteroylglutamic acid*. This is more commonly called *folic acid* from the Latin word for "leaf" since it was first found in leaves. Folic acid is another of the B-vitamins that are necessary to the working of every cell.

I have already mentioned folic acid in connection with the workings of the sulfonamide drugs. Sulfanilamide gets picked up by some bacteria instead of para-aminobenzoic acid. A misshapen folic acid results that the bacterial cell can't use. Bacterial growth stops and the patient's condition improves.

Chemists deliberately manufacture certain compounds that are similar to folic acid but not exactly like it. For instance, if the hydroxyl group on the pteridine ring is changed to an amine group, the compound that results is *aminopterin*. If fed to the human, the cells pick it up and try to use it instead of folic acid. They fail and the chemical operations of the cell are jammed up. Aminopterin belongs to a class of compounds called *folic acid antagonists.*

Some folic acid antagonists have been found which damage cancerous cells more than they do normal cells. Chemists and doctors have worked hard to find a particular compound which, in the proper dose, will kill at least some kinds of cancer. This kind of treatment seems to do some good in cases of leukemia, but like all cancer treatments so far, it's not really satisfactory. Chemists and doctors are still looking.

This leaves just one vitamin I have not yet mentioned. It is another of the B vitamins and its molecule involves a pteridine ring system with a benzene ring fused on also. This makes a three-ring system that looks like this:

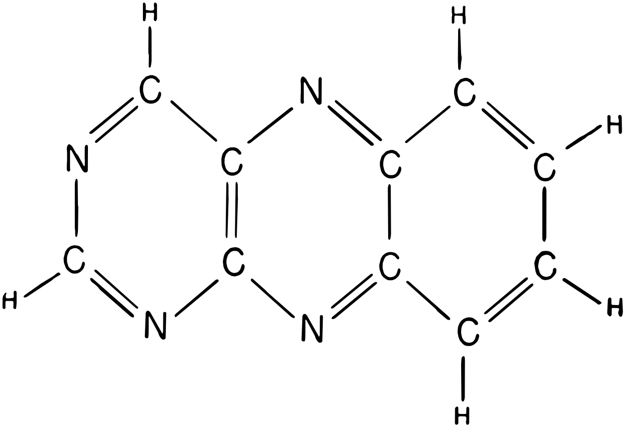

Figure 43—Isoalloxazine Ring System

Molecules containing such a ring system are *isoalloxazine* derivatives. More frequently, they are called *flavins*, from the Latin word for "yellow", since that is their color.

The isoalloxazine derivative that is a vitamin has two methyl groups on the benzene ring and two hydroxyl groups on the pyrimidine ring. The pyrazine ring in the middle carries a five-carbon sugar alcohol called *ribitol* attached to one of the nitrogen atoms. The total combination is called *riboflavin*. A more old-fashioned name is *vitamin* B_2.

In the body, riboflavin forms part of somewhat more complicated compounds which are coenzymes. Enzymes that make use of these are sometimes referred to as *flavoenzymes*. The flavoenzymes catalyze the same sort of reactions that enzymes making use of nicotinamide coenzymes do. A shortage of vitamin B_2 can cause just as serious symptoms.

9

Life, at Last

SUGAR PLUS HETERO-ATOM

When a nitrogen hetero-atom is condensed with a sugar or sugar alcohol, the result is a *nucleoside.* I just gave you an example at the end of the previous chapter. Riboflavin is made up of an isoalloxazine ring system condensed with ribitol by way of a nitrogen hetero-atom. Riboflavin is therefore, an *isoalloxazine nucleoside.*

If a phosphate group is attached to the sugar or sugar alcohol of a nucleoside, the result is a nucleoside phosphate, or a *nucleotide.* For instance, one of the coenzymes built up by the body out of riboflavin is simply that molecule with a phosphate group attached to the ribitol side chain. The name for this coenzyme is *flavin mononucleotide.*

Now a number of the most important key compounds in the body are nucleotides and most of them involve the five carbon sugar, *ribose.* The formula for ribose is shown on following page.

The coenzymes built up by the body out of nicotinamide for instance, contain the nicotinamide attached to a ribose. A phosphate group is also attached to the ribose. For this reason, and since nicotinamide is built up of a pyridine ring, these coenzymes are sometimes referred to as the *pyridine nucleotides*.

The most important nucleotides of all are those that

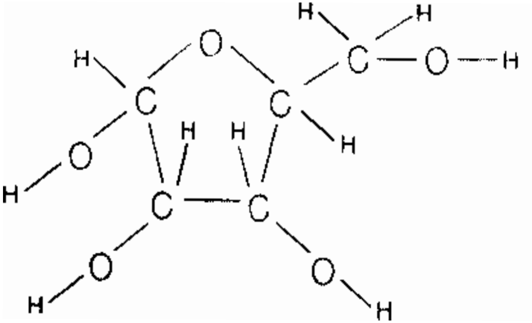

Figure 44—Ribose

contain a purine or a pyrimidine as part of the molecule. The purine, adenine, for instance, will condense with ribose to form the nucleoside, *adenosine*. Its formula is:

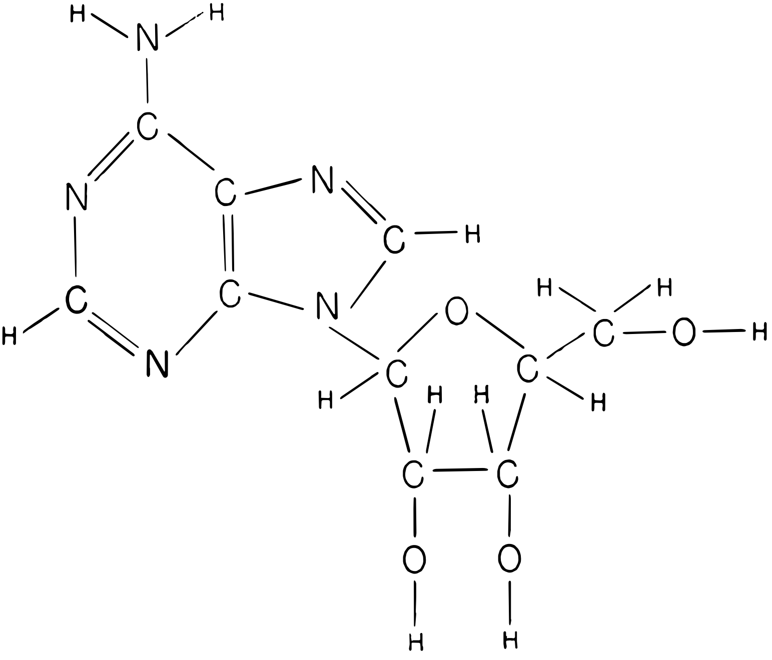

Figure 45—Adenosine

If a phosphate group is also attached to the ribose, the result is adenosine phosphate or, as it is more commonly called *adenylic acid.* Adenylic acid occurs in a number of the coenzymes built up out of nicotinamide and riboflavin. Such molecules are actually made up of two nucleotides joined tail-to-tail, so to speak, by way of the two phosphate groups. The name of one coenzyme made up of a riboflavin phosphate and an adenylic acid is *flavin adenine dinucleotide.* The "di" prefix shows that two nucleotides are involved.

Adenosine is an example of a purine nucleoside. A typical pyrimidine nucleoside is *uridine*, which is made up of the pyrimidine, uracil, with a ribose attached (*see following page*).

Uridine forms part of a coenzyme called *uridinediphosphoglucose.* This catalyzes reactions involving some of the simple sugars.

A nucleoside can have more than one phosphate group attached. For instance, three phosphate groups can be attached, all in a row, to the adenosine molecule and then we have a molecule of *adenosine triphosphate.* The bonds between two phosphate groups are high-energy and so adenosine triphosphate is an example of a high-energy phosphate (see Chapter 5), probably the most important in the body. Other purines and pyrimidines can form such high-energy compounds, also. Uracil forms part of *uridine triphosphate*, and so on.

A NEW KIND OF CHAIN

Just as amino acids can form chains and become polypeptides, so nucleotides can form chains and become *polynucleotides.*

The amino acids in a polypeptide chain differ in the

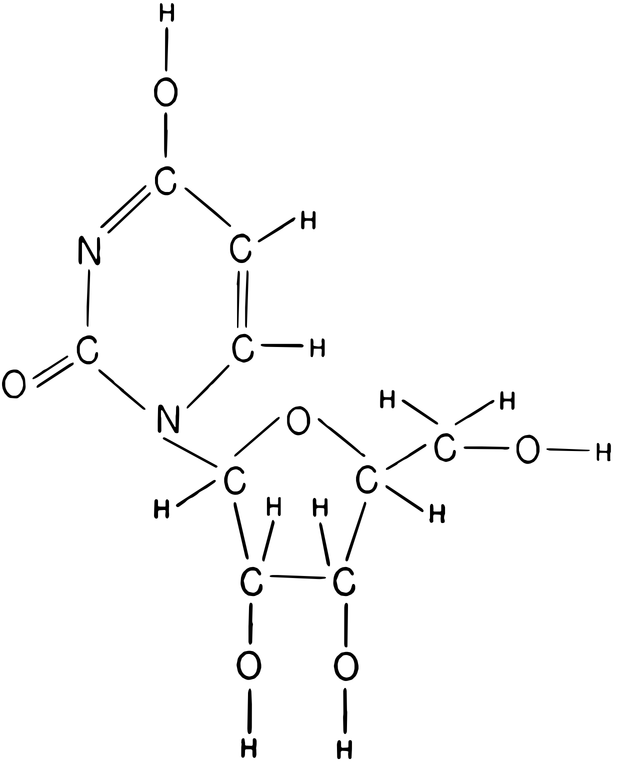

Figure 46—Uridine

nature of their side-chains. The nucleotides in a polynucleotide chain differ in the nature of the purine or pyrimidine portion. An individual nucleotide of a polynucleotide chain may contain either one of two purines, adenine and guanine, or either one of two pyrimidines, cytosine and uracil.

A polynucleotide chain therefore has four different heterocyclic portions attached in almost any possible order. Each different order makes a different compound so you can see that there are uncounted millions of possible polynucleotides, just as there are uncounted millions of possible proteins.

Polynucleotide chains as they occur in living tissue are called *nucleic acids.* There are two major varieties of nucleic acids. The one I have just described contains a ribose unit in each nucleotide and so it is an example of a *ribonucleic acid.*

There is another variety, though, in which each nucleotide contains a sugar-like ribose except that it has one less oxygen atom in its molecule. This is *deoxyribose,* whose molecule is:

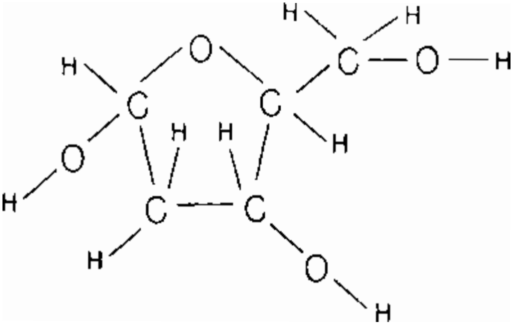

Figure 47—Deoxyribose

Nucleic acids containing deoxyribose are *deoxyribonucleic acids.* Molecules of deoxyribonucleic acid do not contain uracil as one of the two pyrimidines. They contain thymine instead, which is uracil with a methyl group attached. Ribonucleic acid is frequently abbreviated as *RNA*; deoxyribonucleic acid as *DNA.*

Both types of nucleic acid occur in every living cell. Each type has its own special location. A cell, you see, consists of a droplet of living matter enclosed by a membrane. Within this bag of life is a still tinier drop separated off by another membrane. The inner membrane houses the *cell nucleus*. Between the two membranes is the *cytoplasm.*

Ribonucleic acid is found in the cytoplasm and deoxyribonucleic acid in the nucleus. Deoxyribonucleic acid was the first of the two to be discovered and for a time, chemists had the impression that this type of compound occurred only in the nucleus. That is how the name "nucleic acid" arose, and then such names as "nucleotide" and "nucleoside".

In the cell, the nucleic acids are always combined with protein to form single molecules (and very large ones, too, containing millions of atoms) containing both types of compounds. The combination is called *nucleoprotein.* There are *ribonucleoproteins* in the cytoplasm of the cell and *deoxyribonucleoproteins* in the cell nucleus.

THE SUPERVISORS

So far in the book, I have mentioned a number of compounds that are found in living tissue, but none has been alive in itself. What is it in living tissue, then, that is alive? The answer is, of course, no one thing.

No one individual on a football team can win a game if he is alone on the field against the opposing team. No one musician in a symphony orchestra can play an entire symphony by himself. No one soldier in an army can win a battle entirely on his own.

However, there is one man on a football team that directs matters and gets the credit for victories and the blame for defeats. That man is the coach. In the same way, the conductor is responsible for the success or failure of an orchestra and the general bears the weight of decision for an army.

Naturally, the coach does not win the game with his own muscles. He is not even on the field. Nor does the symphony conductor play an instrument nor the general carry a rifle. But these men supervise; they make the decisions.

A cell is like this. It takes all the substances present, in proper relation among themselves, to make the cell alive. But somewhere in the cell are compounds that give the orders, so to speak. They are the supervisors.

Now the chemical workings of a cell depend on the kind of enzymes it contains, and how much it contains of each. If an enzyme is missing, a particular reaction does not take place and that may result in great changes. Human beings can suffer from gout because a single enzyme is missing. An albino lacks coloring in skin or hair because he is missing a single enzyme.

Because of this, chemists have been particularly interested in the way in which enzymes are formed in the cell. They know the kind of reactions that will allow amino acids to be condensed into a peptide chain. They know enzymes that catalyze such reactions. What they wonder about, though, is how the cell manages to have the amino acids arranged in the exact order that will produce a particular enzyme.

It seems almost certain now that this is done by using some molecule as a model. It is as though you put a jig-saw puzzle together by having each piece fit into a slot in a sheet of cardboard that would only hold that piece and no other. Once all the individual pieces were put into the proper slots, the jig-saw puzzle would be complete automatically.

Apparently, it is nucleoprotein that acts as the mold for the fitting in of amino acids in the proper order. In the cytoplasm, the ribonucleoprotein acts as the framework for small particles called *mitochondria*. Within the mitochondria are a number of enzymes, apparently formed by the ribonucleoproteins. Within the nucleus, the deoxyribonucleoprotein makes up small thread-like objects called *chromosomes*. These, too, act as models for enzyme production.

Well, then, if the nucleoproteins act as models for enzyme production, what forms the nucleoproteins? The answer is that the nucleoproteins themselves do. Each nucleoprotein molecule can, at the proper time, catalyze the production of another nucleoprotein molecule exactly like itself! This is known as *autoreproduction*.

This process can best be seen when a cell divides. Each chromosome catalyzes the formation of another chromosome like itself. When the two new cells are formed, each has a complete set of chromosomes, identical with each other. In that way cells inherit the chemical workings of the parent cell.

Of course, it may happen that occasionally a chromosome reproduces itself imperfectly. One of the new cells then has a slightly different chromosome which will produce slightly different enzymes or, perhaps, not be able to produce some particular enzyme at all. This is called a *mutation*.

Chemists have not yet worked out the exact way in which a nucleoprotein autoreproduces or in which it catalyzes the formation of an enzyme. A number of theories have been advanced but all are still pretty shaky. Nor are the chemists certain if the deoxyribonucleoprotein forms ribonucleoprotein or vice versa.

However, one fact seems established: the nucleoproteins are to the cell what the coach is to the team, the conductor to the orchestra, the general to the army. They are the supervisors of life.

THE LIVING MOLECULES

The importance of nucleoproteins shows up clearly if we consider bits of living matter that are simpler than the average cell.

The human being (and other animals, too, of course) begins life as a single cell, the *fertilized ovum.* This grows and divides within the mother's body, obtaining nourishment from the mother's blood stream, until it is large enough to come out into the world.

The fertilized ovum begins in the union of two cells. The unfertilized ovum, or *egg cell*, is formed by the mother. It contains half the usual number of chromosomes in human cells. The *sperm cell* is formed by the father. It, too, contains only half the usual number of chromosomes. When the two cells combine to form a fertilized ovum, the final combination possesses a full set of chromosomes, half from the mother, and half from the father.

The egg cell is a large cell. The human fertilized ovum is only the size of a pinhead but it is the largest cell in the human body. It is large because it must contain a certain amount of food to start the embryo on its way and last it until it is far enough along to begin absorbing nourishment from the mother's blood stream.[1]

The sperm cell is a tiny little thing, on the other hand. It is nothing but a droplet of life equipped with a microscopic tail. It swims furiously toward the egg cell in order to enter it. If it fails to make it, it dies in a matter of hours. Because it must reach the egg quickly, it is a cell that has been stripped to its absolute essentials. (After all, you

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[1] Animals which lay eggs must supply the young with all the food they will need to develop to where they are capable of independent life. A hen's egg is only a single cell and is as large as it is because it must contain a three weeks' supply of food for the young chick. For that matter, an ostrich egg is only one cell.

wouldn't expect a man running a hundred-yard dash to wear an overcoat.) For this reason, the sperm cell is almost entirely deoxyribonucleoprotein and nothing else. It is just a packet of chromosomes pressed as tightly together as possible.

In a way, then, the father is contributing only a group of supervisors to the fertilized ovum. Nothing more. Yet the child's chemical machinery is inherited from mother and father. This is proof that the chemical supervisor, the nucleoprotein, is the essential part of the cell, the very essence of life.

If sperm deoxyribonucleoprotein is studied closely, it turns out that the nucleic acid part of the molecule is fully as complicated as nucleic acid occurring anywhere else in the body. The protein portion, however, is a histone, which is a rather simple protein, as proteins go. The proteins in the chromosomes of the other cells of the body are more complicated than that. In the sperm cells of certain fish, such as salmon and herring, the protein portion of the deoxyribonucleoprotein is a protamine, which is almost nothing more than a series of arginine molecules strung together. Yet there, too, the nucleic acid part is present in full.

It appears as though, in the sperm cell, there is such necessity to keep the burden as light as possible that all the unessential parts of the nucleoprotein molecule itself are cut away. These unessential parts come from the protein, which certainly makes it look as though the nucleic acid is more important than the protein.

There is more evidence for this, if we consider small particles of life, much smaller than cells, called *viruses*. These invade cells and multiply within the cell, often killing it. They are parasites on cells just as some bacteria are parasites on organisms. In fact, there are viruses that are parasites on bacteria.

Viruses come in a variety of sizes. Some are almost as large as small bacteria and are quite complicated in chemical makeup. Others are extremely small and seem to be made up of single nucleoprotein molecules.

Viruses may almost be looked upon as an invading army of foreign chromosomes. Once they get into a cell, they impose their own supervisory activity upon it, making the cell's own chromosomes helpless in some way. The virus causes the cell to do nothing but create more virus molecules, until finally the cell has been converted into nothing but virus. The virus would continue in this way and kill the infected animal unless the animal can protect itself by forming antibodies against the virus.

Chemists have now learned something about the structure of the viruses, particularly of some, the *bacteriophages*, which are viruses that infect bacteria. The bacteriophages are made up of deoxyribonucleoprotein.[1] The protein portion is on the outside of the virus, acting as a shell or skin. The nucleic acid portion is on the inside of the molecule and is arranged in a double twist, like the two banisters of a circular stairway.

When a bacteriophage molecule attaches itself to a bacterial cell, the protein shell of the virus remains on the outside. Only the nucleic acid enters the bacterial cell! Once within the bacterium, the virus nucleic acid forces the production not only of itself, but also of the virus protein. So it is the nucleic acid portion of the nucleoprotein that is the real supervisor, that is the nearest thing to life.

Of course, how a nucleic acid can use itself as a model to construct a particular protein molecule is still a mystery, but there seems no doubt that this is what it does.

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[1] Some of the smallest viruses, which infect plants, are made up of ribonucleoprotein. Both varieties are capable of autoreproduction.

It is research in this direction that may finally give us the key secrets of the chemistry of life. And at this point, where the world of carbon and nitrogen merges with the world of life, it seems a good place to end the book.

THE END

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("n" denotes footnote)