Chapter 6

Here and There with the Hydroxyl Group

Vitamins and Eyes

HYDROXYL GROUPS can be attached to any kind of carbon chains or rings and an interesting variety of compounds occurs. There are terpene alcohols, for instance, in which a hydroxyl group is attached to the molecule of a terpene hydrocarbon.

An example is the ten-carbon compound, *menthol*, which occurs in peppermint oils. (In fact, its name comes from the Latin word for "mint.") If menthol is applied to the skin it creates a refreshing, cooling sensation. If it is dissolved in liquid petrolatum and sprayed into the nose or throat, it has a soothing effect on inflamed membranes. It is used in some cough drops and even some cigarettes, for that reason.

For a more important compound, let's go back to carotene. Carotene, you may remember, is a 40-carbon compound, built up out of eight isoprene units and containing a number of double bonds. Well, one of those double bonds is right in the middle of the chain.

Now the body can break the carotene molecule at that middle double bond. In the most common variety of carotene the two "half-molecules" formed in this way are identical. At the broken end of each "half-molecule" a hydroxyl group is formed. In place of the original 40-carbon carotene, there are now two 20-carbon alcohols.

This 20-carbon alcohol, built up out of four isoprene units, is *vitamin A*. Since the body can form vitamin A from carotene, carotene is sometimes called *provitamin A*. (The prefix "pro" in both Latin and Greek means "before.")

The human body makes use of vitamin A (or of compounds very like it) in the retina of the eye particularly, to help us see in dim light. Only small quantities are necessary for that purpose, but even these small quantities pose a problem. The body can't manufacture vitamin A out of simpler substances, the way it can most of the compounds in its tissues.[1] It can only make it out of carotene, and it can't make carotene out of any simpler substance, either. This means that the human diet must contain small quantities of either vitamin A or carotene or we will be in trouble. Foods such as milk, butter, and eggs contain vitamin A. Carrots, tomatoes, and some other vegetables contain carotene.

The body stores vitamin A in the liver if more is taken in than is required for immediate use. Then, if the diet is short in vitamin A for a time, the body uses what it has previously stored. If the storage continues, however, we do run out eventually. When we do, the human eye can no longer function as it should in dim light. The condition that results is known as *night blindness.* The moist membranes in the nose and throat, and particularly around the eye, become dry and scaly. This condition is known as *xerophthalmia,* from Greek words meaning "dry eyes." For this reason, the official chemical name for vitamin A is *axerophthol* (meaning "no dry eyes").

Vitamins and Bones

There is another alcohol that is a vitamin and this involves the steroid nucleus mentioned in Chapter 3. The most common steroid in the body is one which contains one double bond, three hydrocarbon side-chains at various points, and a hydroxyl group. I won't give the details of the formula, but here is the diagram of the steroid nucleus again so you can see exactly where the hydroxyl group is attached, where the double bond is, and where the side-chains are:

[1] There are a number of organic compounds which the body must have, for life and health, in small quantities, which it cannot make for itself. Over a dozen different kinds, in fact. These are the *vitamins,* and vitamin A is only one of them.

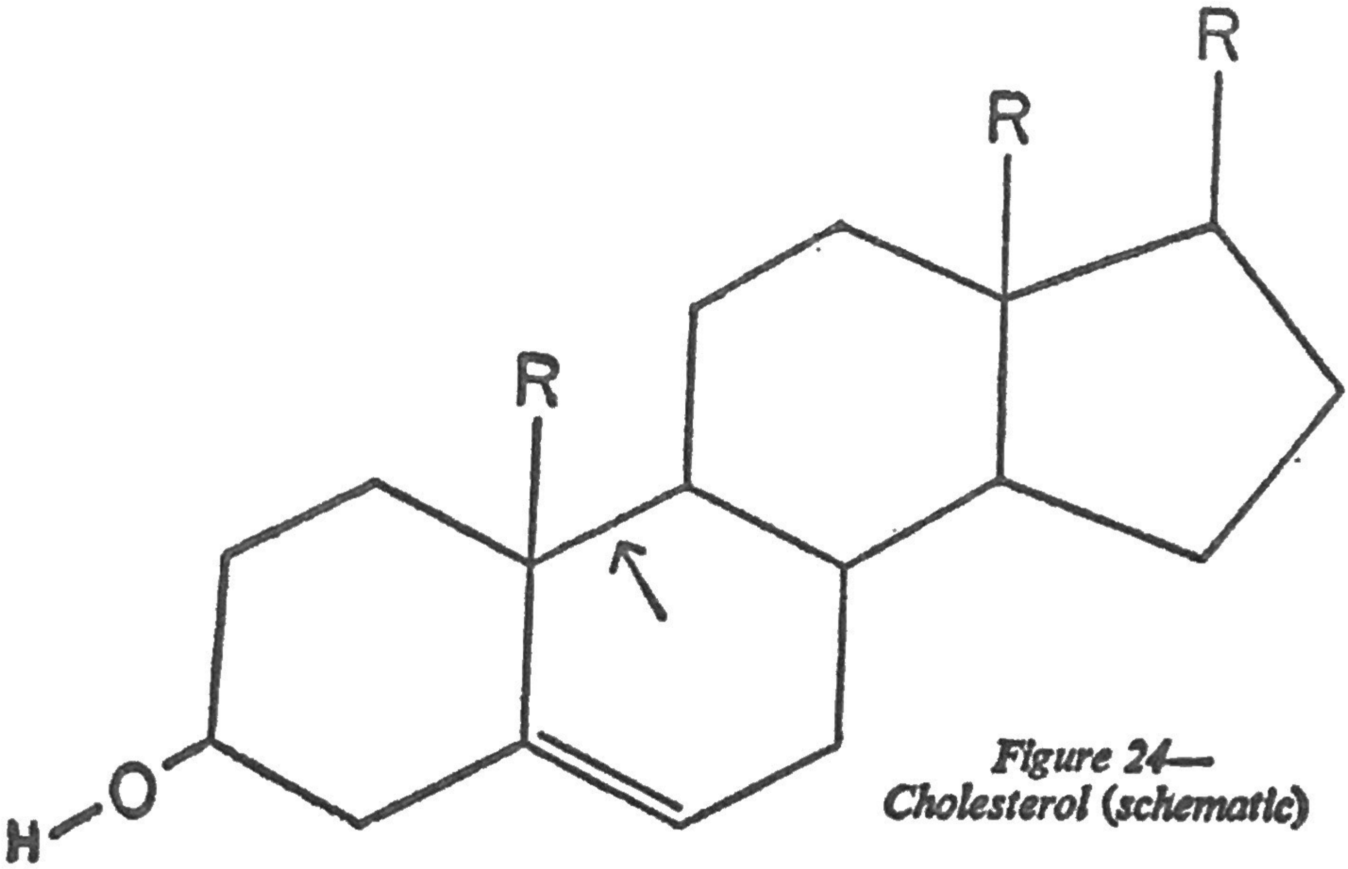

Figure 24—
Cholesterol (schematic)

The R stands for the hydrocarbon side-chains.[2] The arrow will be explained later.

Any steroid that contains a hydroxyl group is called a *sterol*. This word comes from a Greek word meaning "solid" because the sterols were the earliest (or one of the earliest) known alcohols that happened to be solid at room temperature. Once the chemical structure was worked out, then other compounds with similar structure but without the hydroxyl group were given the name "steroid" meaning "sterol-like." (The suffix "oid" comes from the Greek and means "similar to.")

The particular sterol that is common in the body and has the formula shown above is *cholesterol*. The prefix "chole" comes from the Greek word for "liver bile." This is a digestive fluid manufactured by the liver and poured into the intestine.

The name is a good one, because the liver bile happens to contain a good deal of cholesterol. In fact, it contains more than is good for us sometimes. The bile is stored in the gall bladder and becomes particularly thick and concentrated

[2] Sometimes the organic chemist wants to show that there is a carbon chain or ring attached to a certain spot in a molecule but finds the details of the chain unimportant at the moment. When that happens, he saves time by just writing R to represent the group.

there. Cholesterol is not very soluble and if enough of it accumulates in the gall bladder, it will come out of solution in the form of little crystals. The crystals may join together and, in time, may grow big enough to block the narrow duct that leads from the gall bladder to the intestine. These *gall stones,* which are almost pure cholesterol, can give rise to considerable pain and an operation may be required for relief.

You mustn't think of cholesterol as just a trouble-maker, though. Only a small number of people have gall-stone trouble. Every human being, on the other hand, has a great deal of cholesterol in the brain and nervous system. Almost half the solid matter in the brain is cholesterol. It forms an important part of the insulating myelin sheaths about the nerves. It is also used by the body to manufacture vital chemicals that are needed in small amounts.

Sterols and sunshine make an interesting combination. When exposed to the ultra-violet rays of the sun, one of the rings of the steroid nucleus breaks. The bond that breaks is the one to which I have pointed an arrow in the cholesterol formula. When this happens to certain sterols (not all), molecules of *vitamin D* result.

Now the body can make its own sterols, but it can't break the bond that must be broken to form vitamin D. That's why children must have vitamin D in their diet, as well as getting a certain amount of sunlight. It is for this reason that vitamin D is sometimes called the "sunshine vitamin." It isn't in sunshine, of course, but sunshine helps produce it out of sterols that are in the skin.

Vitamin D helps in the proper formation of bones, in growing children. Since the chief element in bone is calcium, vitamin D has been named *calcifero*[8] from Greek words meaning "calcium carrying." Youngsters who are deficient in vitamin D can develop soft bones which are easily bent or deformed and which then remain that way permanently. This condition

[8] Vitamins were discovered by means of nutritional experiments years before chemists had worked out their structure. For that reason, they were called by letters of the alphabet. Once the structures were worked out, they were given actual names. On the whole, chemists consider it better practice to use the names rather than the letters.

is known as *rickets*. It is more likely to happen among children who are born in the winter or in northern latitudes because it is then that sunlight is particularly weak and least likely to form the vitamin D.

Rickets, xerophthalmia, and other *vitamin deficiency diseases* are much less common in the civilized world (particularly in the United States) than they used to be. First, scientists discovered that vitamins existed and learned the foods in which they were to be found. In this way, a healthful diet could be worked out. Secondly, chemists learned the structure of vitamins and learned how to make some synthetically.[4] The result is that a large quantity of vitamin pills and concentrates are for sale on the counters of any drug store. Probably every reader of this book has taken vitamin pills at one time or another. Here is another example of the way knowledge of structural formulas has helped the health of mankind.

However, it should not be assumed that because a little of something is good, a lot of it is better. The two vitamins we have just discussed, vitamin A and vitamin D, can actually harm the body if taken in too great a quantity. (Disorders caused by too many vitamins are called *hypervitaminoses*.) In these days of vitamin pills (especially for children with overenthusiastic mothers) there is actually more danger of people taking too much vitamin preparation than too little.

Sweetness

Must we confine ourselves to one hydroxyl group per molecule? Chemists, indeed, have found it impossible (except in rare cases) to put more than one hydroxyl group on a single carbon atom. Such an arrangement is unstable. The atoms rearrange themselves at once into more stable combinations. However, you can have a hydroxyl group on different carbon atoms in a molecule. You can even have one on every carbon atom in a molecule.

[4] You mustn't suppose that a synthetic substance is inferior to a natural substance, or just a kind of substitute. If the structure of a molecule is known and that molecule is made in the laboratory, the product is identical with the natural one. The only difference is the place of manufacture; the laboratory instead of living tissue.

The simplest case of this is a two-carbon compound with two hydroxyl groups:

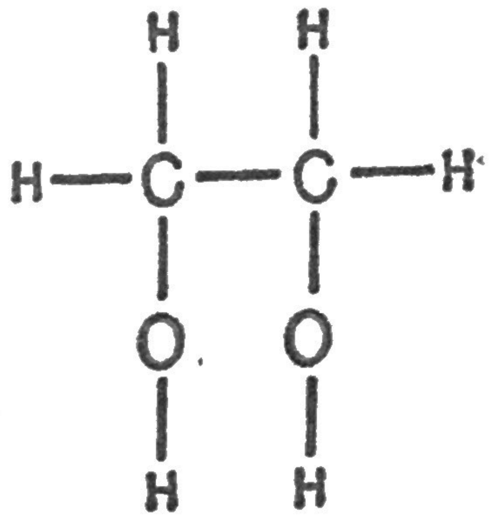

Figure 25—Ethylene Glycol

This compound is *ethylene glycol.* Any compound with two hydroxyl groups on adjacent carbon atoms is called a glycol, but when the word "glycol" is used all by itself, it is generally intended to mean ethylene glycol.

The presence of a number of hydroxyl groups in a compound makes a molecule more soluble in water and gives it a higher boiling point than similar compounds with fewer hydroxyl groups. It also often causes a compound (for no reason we know) to be sweet-tasting. For instance, ethylene glycol tastes as sweet as sugar. The very name "glycol" comes from a Greek work meaning "sweet."

The most important use of ethylene glycol has nothing to do with its sweetness. Ethylene glycol freezes at —17° C. Water, as I've said several times, freezes at 0° C. Now it is almost always true that a mixture of two substances will freeze at a lower temperature than either substance separately. If six parts of ethylene glycol are mixed with four parts of water, the mixture doesn't freeze till a temperature of —49° C. is reached.

I've already mentioned the use of denatured ethyl alcohol as an anti-freeze. Well, adding ethylene glycol to the water in an automobile radiator will also prevent it from freezing in the winter. There is an important difference, though, in favor of the ethylene glycol.

Ethyl alcohol boils at 78° C. but ethylene glycol boils at 197° C. When the liquid in a car's radiator warms up as the engine works, it gets warm enough to evaporate the ethyl alcohol but it never gets warm enough to evaporate much of the ethylene glycol. What little evaporation there is, takes place very slowly. Ethylene glycol is a *permanent anti-freeze.*

An even more important *polyhydroxyl compound* (that is, one with many hydroxyl groups) is *glycerol.* This is a three-carbon compound with a hydroxyl group on each carbon atom:

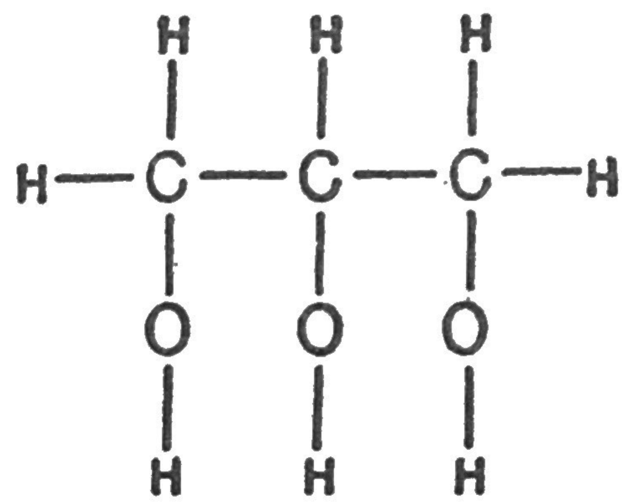

Figure 26—Glycerol

(Sometimes the compound is called "glycerine" but chemists prefer to keep the "ol" suffix.)

The name glycerol also comes from the Greek word meaning "sweet" and glycerol is, in fact, sweet, just as glycol is. Glycol is rather poisonous, but glycerol is completely harmless to the body. You can eat al the glycerol you want. Sometimes you do, in fact. Glycerol is added to cream-centered candies to increase the smoothness of the cream without taking away any of its sweetness. It also prevents the cream from drying out. It doesn't evaporate itself (its boiling point is far too high for it to evaporate at room temperature) and it holds on to water tightly and keeps it from evaporating also.

Because of this "keep-moist" property of glycerol (which chemists refer to as *hygroscopic*), it may be added to tobacco. It keeps the tobacco from drying out and allows it to burn evenly and slowly. Glycerol is also found in lotions used for rough or chapped skin.

As far as the human body is concerned, the most important thing about glycerol is that its molecule combines with other substances to make up the fats and oils of living organisms.

Important in a similar way is a six-carbon ring with a hydroxyl group attached to each of the six carbon atoms, and with no double bonds present. This compound is called *inositol.* It makes up part of the molecules of certain complicated substances found mostly in brain and nerves.

First Victory Over Infection

Before doctors were aware of the existence of germs, any kind of serious wound or surgery was likely to be fatal. Even if the patient could endure the pain (there were no anesthetics, you know) and survived the bleeding and the shock, bacterial infection would set in to finish the job.

In the middle 1800s, the French chemist Louis Pasteur first advanced the germ theory of disease. He proclaimed, and proved, that disease and infections were caused by microscopic organisms.[5] To prevent infection, then, it is necessary to kill these tiny creatures. (Incidentally it is interesting to note that the germ theory of disease, which is the greatest single advance ever made in medicine, was not the work of a physician, but of a chemist.)

In 1865, a Scottish surgeon, Joseph Lister, found a practical way to kill germs. He used chemicals. While treating a patient with a compound fracture of a bone (that is, a fracture where the bone had broken through the skin), he applied a chemical known as *phenol* to the wound. (A solution of one ounce of phenol in three quarts of water will kill most bacteria in five minutes.) He continued to apply it daily and the patient recovered without infection.

This was the beginning. Phenol itself turned out to be too

[5] "Germ" is the name given to any tiny object bearing life. A seed, for instance, is a kind of germ. The embryo plant of a wheat seed is called "wheat-germ." Disease can be caused by a variety of germs. Some diseases are caused by bacteria which are microscopic one-celled plants, or fungi, which are somewhat more complicated plants. (Often, bacteria are classified among the fungi.) Disease can also be caused by protozoa, which are microscopic one-celled animals, or by viruses, which are too small to be seen at all by ordinary microscopes, and which are neither plants nor animals. Nowadays, all these creatures are referred to as *microorganisms.*

irritating and damaging to tissues to use generally. It was mixed with other substances. Other chemicals which would kill germs even more easily and damage the patient less were discovered. Even so, the strength of the newer antiseptics is still measured as the *phenol coefficient;* that is, as how much stronger than phenol the particular antiseptic is.

Lister was the originator of antiseptic surgery. Nowadays, doctors wash their hands and arms thoroughly before operations, wear masks, and sterilize their instruments before using them. Germs just aren't given a chance.

The molecule of phenol is made up of a benzene ring to which a hydroxyl group is attached, thus:

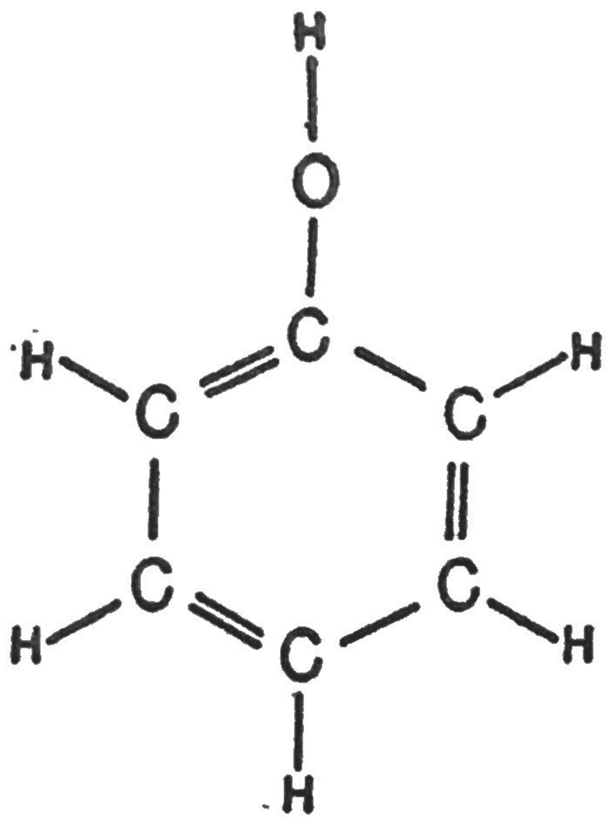

Figure 27—Phenol

Generally, any compound containing a hydroxyl group attached to a benzene ring is called a phenol, but the name is applied particularly to the compound shown in the formula.

Phenol was discovered in 1834 in coal-tar. At that time, coal-tar was used mostly to produce illuminating gas, and the prefix "phen" comes from a Greek word meaning "to illuminate."

An example of a more complicated phenol is *urushiol,* in which there are two hydroxyl groups attached to the benzene ring, as well as a 15-carbon chain. Some of you may have come in contact with urushiol and, if so, you have surely regretted it, because urushiol is the poison in poison ivy.

Acids and Hormones

Phenol is sometimes called *carbolic acid.* In order to explain that, I must first explain what an acid is. Certain compounds occasionally lose part of a hydrogen atom that ordinarily forms part of their molecules. They don't lose a whole hydrogen atom, but just a part of it. The part lost is called a *hydrogen ion.*[6]

Compounds that allow hydrogen ions to break away from their molecules are *acids.* If the hydrogen ions come off the compound very easily so that a lot of them are present at one time, the compound is a *strong acid.* If the hydrogen ions come off with difficulty so that only a few of them are present at any one time, the compound is a *weak acid.* The hydrogen ion has a sour taste and is very active. It will attack and corrode metals of various kinds. Strong acids are therefore dangerous. Chemists handling them must do so carefully to avoid damaging not only chemical equipment, but clothes, skin, or eyes.

When a hydrogen atom it attached to a carbon atom, there is practically no chance at all of a hydrogen ion breaking loose. When a hydrogen atom is attached to an oxygen atom, as in a hydroxyl group, there is a slight chance of a hydrogen ion breaking loose. Ethyl alcohol is therefore an extremely

[6] An atom is made up of a small nucleus in its center (which contains a number of particles bunched together) and anywhere from one to a hundred other particles, called electrons, distributed throughout the rest of the atom. Sometimes an atom (or group of atoms) splits away from a molecule leaving one or more electrons behind. The atoms are then, of course, short those electrons. The rest of the molecule has one or more extra electrons. Atoms or groups of atoms with missing electrons or with extra electrons are called *ions.* Ions have properties that may be quite different from those of the original atom. For instance, the sodium atom and the chlorine atom are both dangerous to life. The sodium ion (one electron missing) and the chloride ion (one electron extra) are not only harmless, but essential to life.

weak acid; so weak, in fact, that only chemists can detect its acidity.

When the hydroxyl group is attached to the benzene ring, however, the chance of a hydrogen ion breaking off is increased to the point where the acid properties are noticeable; still very weak, but noticeable. And that is why phenol is sometimes called carbolic acid.

A compound similar to phenol is *cresol.* This is phenol with a methyl group also present on the benzene ring. It is a stronger antiseptic than phenol, cheaper and easier to handle. Household antiseptic cleaners, such as Lysol, contain cresol or similar compounds. It is the cresol that gives them their odor.[7]

Tannins are plant products with rather complicated molecules. These contain two or more benzene rings, each with two hydroxyls attached. They are, therefore, *polyphenols.* The tannins combine with substances in the skin and hide of animals, hardening and toughening them. Hides, treated with tannins, are "tanned" and are converted to leather.

Tannins will also harden skin which has been burned and lessen the pain of the burn. That is why tea-leaves (which contain tannins) are sometimes soaked and placed over a burn. (Incidentally, milk or cream added to coffee or tea combines with some of the tannins soaked out of the tea-leaves or coffee-beans. It is the tannins that give those beverages some of their bitter taste and milk or cream makes them less bitter, for that reason.)

An interesting phenol with medical importance is *diethylstilbestrol,* also called simply *stilbestrol.* Its molecule contains two phenol groups connected by a two-carbon bridge.[8] Stilbestrol is an example of a substitute hormone.

[7] The most common household antiseptic is, of course, tincture of iodine. Lately, a "colorless iodine" has been put on the market. It can be put on cuts without leaving brown splotches on the skin. This is not really iodine but an *iodo-alcohol* (that is, a compound containing both iodine atoms and hydroxyl groups). "Colorless iodine" has a molecule made up of three carbon atoms, with a hydroxyl group attached to one and iodine atoms attached to each of the other two.

[8] I will occasionally talk about "bridges" connecting rings. That's the easiest way to describe that particular situation without drawing formulas, and I am trying to keep the formulas in this book

Hormones are chemicals that are produced in the body by certain small organs called *ductless glands.* These are discharged into the blood in very small quantities and have a powerful effect on the chemical machinery of particular parts of the body. It is as a result of hormone activity, for instance, that a boy or girl changes into a man or woman at adolescence.

Hormones are sometimes used by doctors to help relieve a patient of some disorder. To get enough of certain hormones out of the small quantities present in domestic animals is a long, tedious process. The doctor ends with very little and that very little is very expensive.

However, it is possible to manufacture some of the hormones synthetically in the laboratory. It is even possible, sometimes, to manufacture some other compound, with a molecule easier to put together than that of the hormone, which will have the same effect as the hormone. Stilbestrol is the most successful example. It was first introduced in Europe in 1939 as a substitute for female sex hormones. It is easier to synthesize than female sex hormones, and, in some ways, it actually works better.

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to a minimum. Two rings connected by a two-carbon bridge would look like this: ring-C-C-ring. A one-carbon bridge would be ring-C-ring. Two rings may even be connected at one corner, and that could be written ring-ring. This is not the same as a fused ring where the two rings are not connected at one corner but along one side. If you have trouble following this, I'm rather glad. It may help convince you that formulas are sometimes easier to understand than words.