BOUND FOR GLORY

Roald Hoffmann

From the beginning, chemistry was the craft of making substances change, or watching their spontaneous transformations. Ice turned into water, water could be made to boil. Grape juice or sugar cane mash turned into alcohol, and if one didn't intervene, it turned again, into vinegar. A colorless fluid from the gland of a Mediterranean sea snail, when exposed to air and sunlight, turned to yellow, then to green, and finally to a purple that could dye fast a skein of wool.

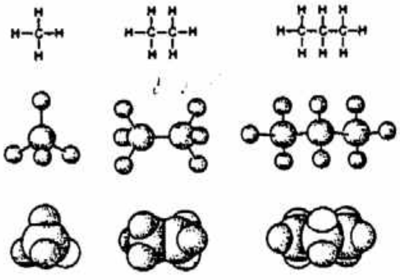
◄ A COMPUTER-GENERATED IMAGE OF A DRUG BINDING TO DNA

Today, chemistry is the science of molecules and their transformations. Over a period roughly coinciding with the history of *Scientific American*, the craft became a science, and instead of studying substances, chemists now think of molecules.

Molecules are made up of atoms. There are about 90 natural elements or kinds of atoms, 15 or so radioactive, humanly created ones. Some matter is truly atomic in its composition (helium or argon gas); some is made all of one atom, but with the atoms linked up in some simple or complex way (the iron atoms in iron metal; carbon in graphite or diamond).

But what a dull world it would be if there were only 105 things in it! Any square foot of this beautiful earth shows a far greater richness. The world is made of molecules—sugar, aspirin, DNA, bronze, hemoglobin—persistent groupings of atoms with reproducible colors, chemical properties, toxicity, which are a consequence not only of the identity of their atomic components, but also of the way those atoms are connected to each other.

That connection between atoms is called a bond. It's not a random coupling; there are rules to this cross between a donnybrook and a love affair. So carbon typically binds to four others and hydrogen forms a liaison (indeed, that's the French word for bond) with one. And then the game is on between the two, for one does not have CH (at least not much of it; that wouldn't satisfy carbon's constrained lust for bonding, and when CH is found it is a most reactive unstable species) but CH_4, methane. One can also form carbon-carbon bonds, and the constructive game begins in earnest with the hydrocarbon series: methane, ethane, propane, etc. The chain builds; its approach to infinity is that ubiquitous polymer, the most important plastic of our times, polyethylene.



◄ CHEMICAL FORMULA, "BALL-AND-STICK" MODEL AND "SPACE-FILLING" MODEL OF METHANE *(LEFT)*, ETHANE *(CENTER)* AND PROPANE *(RIGHT)*

Individual molecules are really tiny. Consider the sugar (glucose) molecule drawn to scale here. Just as a map might have a scale of 1:250,000, meaning that an inch on the map is 250,000 inches in reality, so we could say that these drawings are roughly 174,000,000:1, 1.74 inches on this page corresponding to 0.00000001 inches in the molecule. A single glucose molecule is much too small to be seen with the eye, or even with the very best optical microscope.

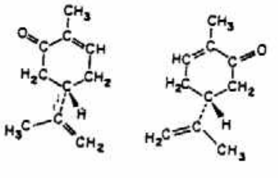
► A "BALL-AND-STICK" MODEL OF A GLUCOSE MOLECULE

Our knowledge of the atoms in a given molecule, of how they are connected to each other, and even of the molecule's three-dimensional shape, is largely indirect. We use various instruments, perturbing the molecules (often by light) and measure their responses. The ingenious way analytical chemistry knows without seeing is an incredible achievement of this century.

In the gas or seething liquid, an individual molecule is buffeted by collisions with other molecules. It travels, gives, deforms, yet remains a molecule with a

Look-alikes

Most chemical compounds look alike—90 percent are white crystalline solids. Yet some are beneficial, some harmful. In the realm of molecular differences, a particularly subtle but important one is chirality, or handedness. Some molecules exist in distinct mirror-image forms, related to each other as a left hand is to a right. Many, but not all, of the properties of such mirror-image molecules are the same—they have identical melting points, colors, etc. But some properties differ, often critically. This is, for instance, true of their interaction with other-handed molecules. Think of left feet meeting up with left or right shoes. So the enantiomers (for that is the name for the distinctly handed forms of a chiral molecule) may have drastically different biological properties. One may taste sweet, its mirror form tasteless. The mirror-image form of morphine is a much less potent pain reliever.



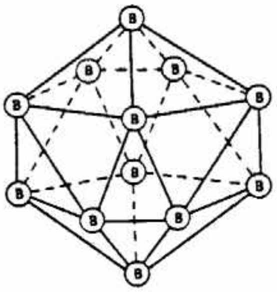
d- AND l-CARVONE

The illustration here shows d- and l-carvone. d-carvone can be isolated from caraway and dill seed, l-carvone from spearmint. And they are responsible for a good part of the taste and odor of these plants—they smell like caraway or spearmint—whether they are natural extracts or are made in the laboratory.

Our proteins, for instance the human smell and pain receptors, are like complex gloves; not always, but very often, they respond differently to handed molecules.

structure. The structural perspective is a fruitful world view, for we are builders from the beginning. You can build beautiful simple things, such as the inorganic $B_{12}H_{12}^{2-}$ ion, an icosahedron of borons, with twelve hydrogens pointing out.

Or you can build more complicated things. Below is a new, effective, immunosuppressant, FK-506.



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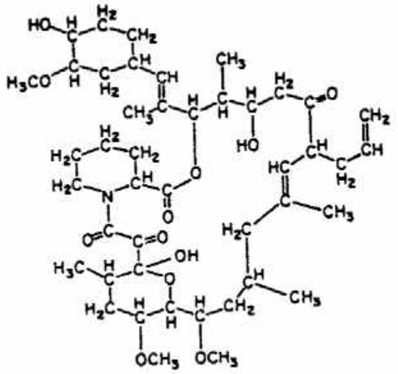
A MODEL OF AN ICOSAHEDRAL $B_{12}H_{12}^{2-}$ ION

Once you learn how to build it, you gain the power to fiddle with the design. If you can find out how this immunosuppressant fits the site that it binds to in a person's body, perhaps you can change a piece of the drug that seems to produce unwanted side-effects.



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THE IMMUNOSUPPRESSANT FK-506

Part of the definition of chemistry has survived from medieval times to today: chemistry is change. While the atoms in a molecule persist in their association with each other, the input of energy—heat, light, electricity—can induce a change. From collisions on that busy dance floor inside a flask emerge regroupings, new associations of atoms, new molecules.

Molecular dynamics, the study of molecules in motion or in chemical reactions, is one of the most exciting fields of modern chemistry. How to catch the fleeting molecules that come and go in a flame? What happens, in molecular detail, on the surface of a seemingly magic catalyst that reduces unwanted pollutants in the exhaust of a car (and what could replace the expensive rhodium in that catalyst)? Will a touted chlorofluorocarbon substitute in fact not harm the ozone layer?

Such questions are crucial to the vast chemical industry. Searching for the answers satisfies a basic human urge behind all science—curiosity. And the answers, which must be given in terms of how molecules interact with other molecules, will be essential for the comfort of people, and for the survival of the planet.