
INTRODUCTION

An *atom*, for present purposes, consists of a positively charged nucleus plus negatively charged electrons that are distributed about the nucleus in a more or less spherical cloud. Important properties of atoms as far as chemistry is concerned are largely determined by the charges and masses of these particles. One might, therefore, conclude that problems in chemistry are really problems in electrostatics (or electrodynamics). While in a sense that is true, at the practical level it is convenient to approach the problem in a different way.

To a first approximation, a *molecule* may be regarded as a simple assemblage of atoms. The details of that assemblage may be largely understood from the familiar laws of classical mechanics and electrostatics, and such a model is now usually referred to as a *molecular mechanics model*. A more proper solution to molecular problems uses quantum mechanics (which automatically includes electrostatics as well). But this more sophisticated (and harder to understand) method is not needed for the most part for understanding practical chemical problems. Much of the time it is found that molecular mechanics is adequate for solving the problem at hand.

Within its area of applicability, molecular mechanics has two definite advantages over quantum mechanics. These are related and depend upon how hard we look at a particular problem. The first advantage is what we might call “intuitive.” With a

molecular mechanics formulation of a molecule at hand, the chemist can often look at a problem and decide that a certain change will lead to a certain result in a qualitative (or semiquantitative) sense. It is normally much more difficult to look at a quantum mechanical problem and come to a similar conclusion in a simple and direct way.

Part of the difficulty with quantum mechanics is that its quantitative application to the solution of a problem is usually much more demanding mathematically and computationally than the corresponding molecular mechanics application. If one wants “chemical accuracy” in solving a problem for a small molecule, the quantum mechanical calculation may require something like 10^4 times as much computation time as the equivalent molecular mechanics calculation. For problems involving rather small systems, this may not pose much of a difficulty, but this ratio increases rapidly with molecular size. For problems involving larger systems, the quantum mechanical solution may require shortcuts or approximations at the practical level, which often interfere with the attainment of the desired accuracy.

The application of quantum mechanics to chemical problems involves solving equations that describe laws of nature. At our current level of understanding, that is just the way it comes out. If one wants to implement exactly those laws of nature, one solves those equations. There are a lot of choices as to how one might go about that, but overall it is clear what has to be done.

On the other hand, molecular mechanics gives us a *model* that describes the molecular system. Our model attempts to reproduce the results of the laws of nature, but there is really unlimited flexibility in just how one may go about that. The most important things about a model are: The model must not violate any laws of nature or fundamental principles, and the model should give results to the desired accuracy in a relatively simple and easy way while being as intuitive as possible.

The invention of actual physical models of molecules has been ascribed to A. W. Hofmann. He is said to have built these models by taking a croquet set, drilling holes in the croquet balls, and using pieces of the croquet handles to connect those balls into large ball-and-stick models that he used in a lecture demonstration given at a meeting of the Royal Institution of Great Britain, Friday, April 7, 1865, entitled “On the Combining Power of Atoms.”¹ In this lecture Hoffman discussed the laws governing chemical combinations from the atomic point of view and introduced the concept of valency. However, at that time (1865) chemistry was considered to be two dimensional, and Hofmann’s models were also two dimensional. These ball-and-stick models subsequently evolved into smaller (and three-dimensional) desktop models that we still use today.

The earliest three-dimensional molecular models known to the present author were those constructed by van’t Hoff in connection with his stereochemical work² (1874). These models (which the author has had the privilege of holding in his hands) were constructed of orange-colored cardboard triangles approximately one inch along an edge, which were glued together to form tetrahedra. With assemblages of these tetrahedra, van’t Hoff described the geometries of simple molecules, as is now so well known. In the early 1890s, Sachse illustrated the boat-and-chair structures of cyclohexane as three-dimensional models of essentially the Hofmann type.³

While the ball-and-stick models are quite useful for understanding in a three-dimensional sense, how various parts of a molecule interact with one another, or with

other molecules, in trying to refine this model, a few other things were noted. The most important thing was that atoms have a physical volume. That is, they occupy space and hence bump into one another. The *space-filling* model was thus developed and was quite useful for understanding steric effects. But this space-filling model still has deficiencies. Perhaps the most conspicuous deficiency is that an atom is not very well represented by a hard sphere. Atoms are, on the contrary, better represented by soft spheres that exert weak attractive forces on one another at longer distances, which then become strongly repulsive at short distances (van der Waals description).

We also know from classical mechanics that if we have two weights held together by a spring, the system can vibrate. And there are extensive consequences from that vibrational motion, which can be well described by classical mechanics. Thus we have Hooke's law, and vibrational frequencies, and the model of a molecule that is considered as an analog of a classical system, where the atoms and bonds are similar to weights and springs. And as the system becomes more complex (many weights connected by many springs), classical mechanics deals with it very well. Such a description of a molecule allows one to calculate the vibrational spectra (Raman and infrared) of that molecule. With that information one can proceed to calculate thermodynamic properties of molecules. Thus, with these refinements, the classical mechanical model of a molecule moves up from the rigid ball-and-stick model to the soft sphere vibrating model that is normally used in molecular mechanics today.

WHAT, EXACTLY, IS A MOLECULAR STRUCTURE?

In order to understand a structure, we have to understand a lot of component pieces. Listed in order of importance, it would seem that what we have to know would be as follows:

1. The numbers and kinds of atoms present
2. The connectivity of the atoms
3. The stereochemistry
4. The internal coordinates of the molecule*
5. The **F** matrix of the molecule

*It takes three coordinates to describe the location of an atom, say in a Cartesian coordinate system. If a molecule contains N atoms, it will take $3N$ coordinates to describe their locations. The *internal coordinates* (of which there are $3N - 6$ for a molecule containing N atoms, except for linear molecule, where there are only $3N - 5$), namely the bond lengths, bond angles, and torsion angles, define the structure of the molecule completely. The *external coordinates* (of which there are 6, or 5 if the molecule is linear) define the location and orientation of the molecule in space. The *Cartesian coordinates* of a molecule specify the location of each atom in the molecule in a Cartesian coordinate system. These Cartesian coordinates include both the internal and the external coordinates of a molecule. The Cartesian coordinates of the molecule can be converted into internal coordinates in a straightforward and unique way, and the internal coordinates can be converted into Cartesians by deciding where to locate the molecule. Hence, knowing either set of the coordinates is equivalent to knowing both sets, as far as the structure is concerned.

An understanding of these items tells us with increasing accuracy the structure of the molecule. It is essentially in historical order. The earliest chemists who thought about molecular structure worried only about the numbers and kinds of atoms that were present in the molecule. Next, with the discovery of isomerization, they worried about the connectivity, and they thought that took care of the problem. However, as the three-dimensional nature of molecules became clear, it was realized that stereochemistry was an essential extension of the connectivity, and it had to be considered as well. And in classical organic chemistry, having that much of the information about a molecule meant that the structure was known and understood.

However, once it was realized that structures could be determined quantitatively using the tools of X-ray and electron diffraction and microwave spectroscopy, it was recognized that there was in fact more to the problem. Conformational analysis showed us that there were three-dimensional aspects of the structure that had to be considered beyond classical stereochemistry, if one were fully to interpret experimental results, mostly spectroscopic and thermodynamic results, that were structure dependent. Hence, it became necessary to know the internal coordinates of the molecule, including the torsional coordinates that define the conformations. Finally, since the molecules do not have a rigid motionless structure such as our ball-and-stick models, the structures and, in particular, interconversion rates between conformations are temperature dependent. So this means that one must understand the potential energy surface of the molecule, not just the minimum energy points, if one is to fully understand the structure. Hence, the little list above gives both the historical development of the theory of structure and also the increasingly quantitative progression of just what we mean by structure.

If we have an atom in a Cartesian coordinate system, it will take three coordinates to describe its location. If we have N atoms in a coordinate system, it will take $3N$ coordinates to describe their locations. It doesn't matter if the atoms are bound together or not. Hence the exact geometry of any molecule including its spatial location and orientation can be described by $3N$ coordinates.

The molecule can translate, rotate, and vibrate. To discuss the translation and rotation of the molecule, we need only describe the location of the center of mass of the molecule in the coordinate system and the orientation of the molecule with respect to the coordinates. We can do this with the aid of three coordinates for translation and three for rotation. (The special case of a linear molecule will not be discussed here.) These six coordinates simply define where we are positioning the molecule and how we are orienting it, and they have nothing to do with the structure of the molecule.

Thus, there are $3N - 6$ coordinates that represent vibrational degrees of freedom of the molecule, and they are necessary to define its structure. If we want to know its structure, what we have to determine are the $3N - 6$ coordinates that define the positions of all of the atoms when the molecule is in its ground state. If the molecule is a little bit complicated, there may be several different stable structures (conformations). In that case we will wish to know the structures of all of the conformations. We will also need to know their relative energies so that we can calculate a Boltzmann distribution among them. Also, we frequently wish to know the torsional barriers on the potential surface that separate these structures from one another.

Calculations that are now to be described are usually done in Cartesian coordinates, but they can be done in internal coordinates (which has the advantage that there are six fewer coordinates needed). However, since we can translate from one set of coordinates to the other in a unique way, in principle it makes no difference which set we use. Conceptually, it's much easier to understand what is happening if one thinks in terms of internal coordinates, and that's what we will do here.

To determine a molecular structure, the problem to be solved then is to find that point on the potential energy surface where the energy is at a minimum. And if there are several such points, we want to find them all. And if we are interested in transition states, we want to find also saddle points, which are in effect minima in all directions except one, and in that direction they are maxima.

The mathematics here is pretty straightforward, although it was impossibly tedious except for very simple cases before computers were available. With computers of current availability, the problem can be solved in typical cases for molecules containing up to 100 atoms or so, in a short time, typically of the order of seconds or minutes. The problem is always solved by successive approximations, so the time required is dependent on how good a structure one uses to start. And the problem can be solved for systems containing many thousands of atoms, although it may take quite a while.

How does one solve the problem? First, it should be said that there is an extensive literature available that answers this question. I will give a somewhat superficial overview here. If one wishes the answer to this question from the viewpoint of physics, the book *Molecular Mechanics* by Machida^{4a} is recommended. Other descriptions can be found in *Molecular Mechanics* by Burkert and Allinger^{4b} and elsewhere.^{4c} In general, what one wishes to do is to find that structure (the atomic positions) where the energy of the system is at a minimum. That is, one wants to find the point on the potential surface where the derivatives of the energy with respect to each of the coordinates is equal to zero. This will, for a system of N atoms, consist of solving $3N - 6$ simultaneous equations. These equations can ordinarily only be solved not by using a "closed" method but by successive approximations. The usual way to carry out these calculations is by utilizing matrix algebra. There are many details here that are of interest for those who develop methods for actually solving this kind of problem. However, here we will only say that such methods exist, are well known, and one can read about them elsewhere if interested.⁴ For our purposes here, it will be sufficient to describe the force constant matrix, commonly referred to as the \mathbf{F} matrix, which is a general description of the simultaneous equations to be solved, and to understand in a chemical sense what kinds of things make up the elements of this matrix. Our classical model system contains weights and springs, and at the energy minimum the net force acting on each atom must be zero. That is, the system is stationary at the energy minimum. There is one difference between that model system and an actual molecular system in that the atoms are never actually at rest at the energy minimum position, but they vibrate about that position in a prescribed way. The problem can best be dealt with by first finding the energy minimum and then adding the vibrational information to the minimum energy solution.

In the force constant matrix, there appear terms that are associated with each of the degrees of freedom in the molecule. If these degrees of freedom are the internal

coordinates, then the force constants associated with each of those degrees of freedom are what we have to know to put into the force constant matrix.

The **F** matrix of a molecule is part of the description of the molecular structure. If we want to know the structure as a function of temperature, we have to know the thermodynamics, and for that we have to know the **F** matrix. So here we consider that what is described by the **F** matrix is an essential part of the structure.

Finally, we certainly do want to know the heat of formation of the molecule. The heat of formation of a molecule is probably better thought of as a property, rather than as part of the structure. This is a fundamental quantity, arguably the most important property of a molecule, and if we are interested in actual chemistry (i.e., interconversions between molecules), then we need to understand heats of formation. To be able to calculate and understand those, we want to understand bond energies as the component parts of those heats of formation.

So these are some of the basic things that we will want to learn to help us to understand molecular structure. And there are fundamentally two different ways that we can study these things: by experiment (Chapter 2) and by theory using computational methods (Chapter 3). We will use both of these tools to study organic molecules in the remainder of this book.

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