

Molecular Modeling in Organic Chemistry

Chemists have been using molecular models of one kind or another for more than a century. Building representations of molecules in three dimensions helps to illuminate both the structure and function of a compound. With the advent of computers, molecular modeling has become an even more important tool for both chemists and biochemists. Complex mathematical formulae can be applied to atomic parameters resulting in pictures that accurately depict the relative bond lengths and geometry of a molecule. Additional output can provide quantitative information about a variety of properties such as charge distribution and stability. These modeling programs also allow scientists to build molecules that are unstable and therefore inaccessible in the laboratory, such as reaction intermediates and transition state molecules. Biological compounds can be modeled on the computer along with pharmaceutical candidates to study potential interactions between the molecules. Applications such as these illustrate why this powerful tool has now become ubiquitous in science.

The theoretical basis for the molecular modeling calculations that you will use starts with the Schrödinger equation. The Schrödinger equation derives from the assumption that nuclei will repel nuclei, electrons will repel electrons and nuclei will attract electrons. While the Schrödinger equation actually cannot be solved for molecules (other than the hydrogen molecule, H_2), certain approximations can be made. These include:

- wavefunctions that result from a combination of many electrons are a sum of the products of the one electron wavefunctions
- from the point of view of electrons, nuclei are stationary
- molecular orbitals are represented as linear combinations of atom-centered basis functions

When the above approximations are applied to the Schrödinger equation, the results lead to the Hartree-Fock molecular orbital models. The number and kind of atom-centered basis functions can change, and this will determine the length of time required to produce the model as well as its accuracy.

To learn more about molecular modeling, read Chapter 8, Computational Chemistry, in your textbook, *Laboratory Techniques in Organic Chemistry*.

Molecules used in Experiment 1, Part 2. Solubility Tests

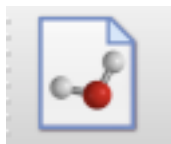
Acetic acid	$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{C}-\text{OH} \end{array}$
Acetone	$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{C}-\text{CH}_3 \end{array}$
Benzoic Acid	$\begin{array}{c} \text{O} \\ \parallel \\ \text{HC}=\text{C}-\text{C}-\text{OH} \\ \parallel \quad \parallel \\ \text{HC} \quad \text{CH} \\ \parallel \quad \parallel \\ \text{HC} \quad \text{CH} \\ \parallel \quad \parallel \\ \text{H} \quad \text{H} \end{array}$
Ethanol	$\begin{array}{c} \text{H}_2 \\ \\ \text{H}_3\text{C}-\text{C}-\text{OH} \end{array}$
Hexane	$\begin{array}{c} \text{H}_2 \quad \text{H}_2 \\ \quad \\ \text{H}_3\text{C}-\text{C}-\text{C}-\text{CH}_2-\text{CH}_3 \\ \\ \text{H}_2 \end{array}$
Methanol	$\text{H}_3\text{C}-\text{OH}$
Resorcinol	$\begin{array}{c} \text{HO}-\text{C} \quad \text{C}-\text{OH} \\ \parallel \quad \parallel \\ \text{HC} \quad \text{CH} \\ \parallel \quad \parallel \\ \text{H} \quad \text{H} \end{array}$
Toluene	$\begin{array}{c} \text{HC}=\text{CH} \\ \parallel \quad \parallel \\ \text{HC} \quad \text{C}-\text{CH}_3 \\ \parallel \quad \parallel \\ \text{HC} \quad \text{CH} \end{array}$
Water	$\begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{H} \end{array}$

Instructions for finding the dipole moment and atomic charges in organic molecules using the program Spartan

1. Pull down the File menu and select **New Build**. The Organic Model Kit will appear.
2. Click on the desired atom and hybridization in the grid, or click on the Group or Ring button to select a functional group or ring system.
3. Click in the middle of the Spartan screen. The atom, group or ring should appear.
4. To continue to build the molecule, choose atoms and/or groups as necessary and click at the ends of the desired bonds.
5. Once the backbone of the molecule has been built, select the hydrogen atom and add hydrogens as necessary to complete the molecule.
6. At any time during the building process, you can rotate the molecule. Simply place the cursor near the molecule, then click and drag the mouse. You'll need to rotate the molecule to be sure all the bonds have atoms connected to them.
7. Note that atoms and bonds can be erased by selecting **Delete** from the Build menu, then clicking on the atom or bond.
8. Under the Build menu, choose **Minimize**.
9. Under the Build menu, choose **View**.
10. Under the Setup menu, choose **Calculations...** In the dialog box that appears, select **Equilibrium Geometry** with **Hartree-Fock/3-21G**. The Total Charge should be **Neutral**. Click on **Submit**.
11. A Save dialog box appears. If necessary, give the molecule a name, then click on **Save**. You may replace any previously saved files that have the same name.
12. A dialog box will tell you that the calculation has begun. Click on **OK**.
13. It may take a few minutes for the calculation to be completed, depending on the complexity of the molecule. A dialog box will appear telling you when the calculation is finished. *Do not continue on to the next step until this box has appeared!*
14. When the calculation is complete, click on **OK**.
15. Under the Display menu, select **Properties**. A box appears that lists several properties of the molecule. The relevant property for this exercise is the dipole moment. Record the number of debyes for the dipole moment in your notebook. Click in the box next to Display Dipole Vector, then close the Properties box. A yellow vector will appear on the molecule showing you the direction of the dipole.
16. Under the Model menu, choose **Configure...** In the box that appears, click in the circle next to Electrostatic Charge, and click **OK**. A number will appear next to each atom, which indicates the "charge" on the atom.
17. You may want to sketch the molecule in your notebook, along with a dipole vector and some of the most important charges on the atoms.
18. Before building another molecule, pull down the File menu and select **Close**. You do not need to save the changes. If you do not Close the file, the molecule will appear on the screen the next time you choose View, obscuring your next molecule.
19. For molecules with one or more hydroxyl groups (—OH), build the molecule a second time. Click on the bond between the oxygen atom of the hydroxyl and the carbon atom. Hold down the Option key, and drag the mouse. The molecule will rotate around the highlighted bond. Position the hydrogen of the hydroxyl so that it is as far away from other atoms in the molecule as possible. Then, follow steps 8 through 18. See if the dipole moment changes.

The following buttons correspond to the commands indicated.

Build New =



Delete =



Minimize =



View =



Calculations =



Close file =

