

Experiment #11: Molecular Mechanics Modeling

Pre-Lab Preparation

1. Study the following overview of molecular mechanics calculations and the experimental section.
2. Carry out pre-lab preparations as described in Chapter 11, section 11.6A, or as called for by your instructor. Your preparations will obviously be somewhat different than for laboratories involving wet chemical procedures, but make sure that, when you sit down at the computer, you are ready to begin work.

A Brief Overview of Molecular Mechanics

Molecular mechanics calculations are commonly used to predict equilibrium molecular geometries or conformations. Mathematical expressions are used to represent various components of the bonding interactions (bond stretching, bond bending, and torsional interactions) and non-bonding interactions (van der Waals and electrostatic) that influence molecular geometry. Using these expressions, the total energy of a molecule, in a given conformation, is calculated. The simplest interactions to model are the bond stretching and bending energies. In a molecular mechanics calculation, atoms are treated as hard spheres interconnected by springs that represent the bonds, and thus stretching and bending can be quantified mathematically by Hooke's Law [equations (1) and (2)]. Energies calculated in this way will be lowest when bond lengths and angles are close to normal values and will increase as bonds are distorted from their normal equilibrium values (i.e., as strain is introduced).

$$E_{\text{stretch}}(r) = \frac{1}{2} k_{\text{stretch}} (r - r_{\text{eq}})^2 \quad (1)$$

r = bond length, r_{eq} = ideal (equilibrium) bond length, k_{stretch} = stretching force constant

$$E_{\text{bend}}(\alpha) = \frac{1}{2} k_{\text{bend}} (\alpha - \alpha_{\text{eq}})^2 \quad (2)$$

α = bond angle, α_{eq} = ideal, equilibrium bond angle, k_{bend} = bending force constant

Analogous expressions may be formulated to approximate the torsional and non-bonded interactions as well, and the total energy of the molecule is then given by equation (3).

$$E_{\text{total}} = \sum_{\text{bonds}} E_{\text{stretch}} + \sum_{\text{bond angles}} E_{\text{bend}} + \sum_{\text{torsion angles}} E_{\text{torsion}} + \sum_{\text{noncovalent interactions}} E_{\text{noncovalent}} \quad (3)$$

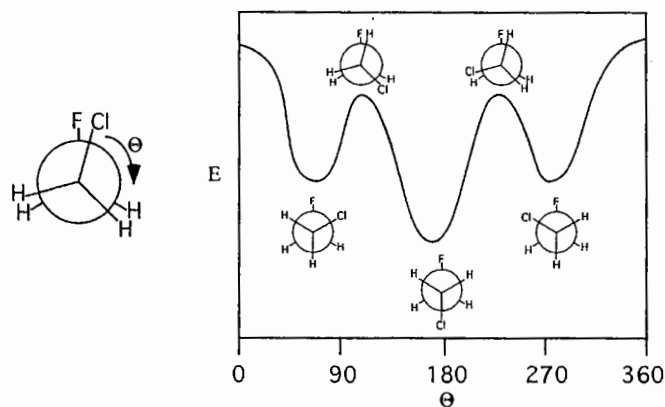
The conformation of the molecule that leads to the lowest overall energy is taken to be the equilibrium geometry. Development and testing of mathematical expressions that result in models best describing the experimentally measured properties of actual molecules represents an ongoing area of research.

Molecular mechanics calculations involve an iterative process of energy calculation, perturbation of the molecular conformation, and recalculation of total energy, continuing until a minimum energy conformation is obtained. This process may be outlined as follows.

1. Enter the atomic coordinates of the starting structure into the program. This is often achieved through a graphical interface, enabling input by simply providing the structure of the molecule. In this step, the atom types (carbon, hydrogen, etc.) are set and initial values for bond lengths, bond angles, and dihedral angles are established.
2. Calculate the energy of the structure.
3. Change the structure (e.g., by altering a bond length or angle) and recalculate the energy. If the energy is lower, the model has taken a step in the right direction, toward a minimum energy (equilibrium) structure.
4. Repeat step #3 until the lowest energy conformation is found. Such a structure is said to be *minimized*. Each round of structural change/calculation is called an *iteration*.

This procedure will result in a minimized structure. This *may* represent the lowest energy structure possible, a so-called *global minimum*. However, it is also possible that the structure is merely a *local*

minimum, lower in energy than any of its closely related conformations, but higher in energy than the global minimum. The energy diagram for the rotation of the carbon-carbon bond in 1-chloro-2-fluoroethane provides a simple illustration of this point – the global minimum occurs at a dihedral angle of 180° , while local minima are present at rotations of 60° and 300° .



Energy diagram for rotation of carbon-carbon bond in 1-chloro-2-fluoroethane, displaying global minimum at 180° and local minima at 60° and 300°

Thus, molecular mechanics calculations must be used with care. Two safeguards can improve the chances of obtaining a global minimum. First, restart the calculation from a drastically different conformation to see if the same minimized energy structure is obtained. If it is, there is a good chance it represents the global minimum. Second, use common sense, checking the structure to see if the bond lengths and angles appear reasonable. If they do not, this is a good indication that the structure represents only a local minimum. Finally, remember that the results of the computations are only models and these models are only as good as the method you used to calculate them. It is best to test any modeling program by using it to calculate the structure (bond lengths and angles) of a known compound before using it in an attempt to predict the unknown properties of a new compound.

Experimental Procedure

There are a variety of molecular modeling programs available for use on personal computers. The following experimental description is for Mac SPARTAN Plus v. 1.2.2 (Wavefunction, Inc., Irvine,

California, USA). Minor modifications are required when using PC SPARTAN Plus v. 2.0. If you are using a different version or different modeling program, refer to the instruction manual and/or receive information from your instructor regarding its usage.

CIS- AND TRANS-STILBENE

1. Build and minimize a model of *trans*-stilbene by carrying out the following steps.

Choose **New** from the File menu.

Using the Builder menu, construct *trans*-stilbene. Important hint: If you start with a completely planar structure, the program will find only a local minimum. Begin with a nonplanar structure in order to facilitate location of the global minimum.

Minimize the structure in the Builder Menu (**Minimize** button); click **Done** when complete.

Choose **Calculation** from the **Setup** menu.

In the dialog box, choose Task = Geometry Optimization, Level = Sybyl, Charge = 0, Multiplicity = 1 and leave Options blank.

Choose **Submit** in the Setup menu.

Wait until the energy minimization is complete.

Explore the different display modes in the *Model* menu.

Record the energy (found in the *Output* submenu of *Display*) of the minimized structure for *trans*-stilbene. (The energy should be less than 7.)

Under *File* menu, choose **Close**.

2. Repeat the above process for *cis*-stilbene. Again, the energy of your minimized structure should be less than 7.

ISOMERS OF 4-METHYLCYCLOHEXENE

3. Following the same steps, build and minimize both isomers of 4-methylcyclohexene. Make sure that you have found the lowest energy conformation for each isomer. Record the final energies of the two isomers.

1,4-BIS(1-HYDROXYCYCLOHEXYL)-1,3-BUTADIENE

4. Build and minimize 1,4-bis(1-hydroxycyclohexyl)-1,3-butadiene. Record the final energy.

- By exploring the minimized structure, locate the longest atom-to-atom distance in the molecule. Record the identity of the atoms and the distance.

5,10,15,20-TETRAPHENYLPORPHYRIN DIANION

- Build and minimize 5,10,15,20-tetraphenylporphyrin dianion (no hydrogens on any of the central nitrogen atoms, leading to a charge = 2-). In order to ensure that all of the ring atoms are sp² hybridized, use the phenanthryl ring system as your basic building block, then edit appropriately. This will take some effort; consult with your instructor if you have problems. (Some programs may provide a pre-formed porphyrin ring structure. If so, consider yourself lucky and continue with the exercise, adding the four phenyl rings to the structure.) Record the final energy.
- Examine the minimized structure to determine if the porphyrin ring (ignoring the four phenyl substituents) is planar. (It should be.)
- Measure and record the torsional angle between the porphyrin plane and each of the attached phenyl rings.

Post-Lab Questions and Exercises

- What were your calculated energies for *cis*- and *trans*-stilbene? Do the relative energies of these two isomers make sense?
- What were your calculated energies for the isomers of 4-methylcyclohexene? Do the relative energies of these two isomers make sense?
- What is the longest atom-to-atom distance in 1,4-bis(1-hydroxycyclohexyl)-1,3-butadiyne? Which atoms are separated by this distance?
- What was your calculated energy for 5,10,15,20-tetraphenylporphyrin? Was your minimized porphyrin ring system planar?
- What were your measured torsional angles between the porphyrin plane and each of the attached phenyl rings in your minimized structure of 5,10,15,20-tetraphenylporphyrin? Why do you think the phenyl rings adopt this orientation?

Experiment Development Notes

This module was developed at the University of Oregon. It is easily adaptable to other computational packages, and clearly lends itself to student exploration of other molecules and other capabilities of the program. If your computational package includes other capabilities and time allows, a number of other interesting explorations can be carried out. For example, one can use AM1, a semi-empirical electronic structure calculational method, to simulate infrared spectra.