CH241 Experiment #4, Week of October 29, 2018

Molecular Modeling Part II

Introduction: In this lab you will continue to refine your computational modeling skills using Spartan while exploring several key concepts discussed in class and comparing the results with known experimental data. As always, the goal here is not to simply get the "right" or "expected" answer, but to gain an appreciation for the techniques that organic chemists employ to solve problems.

Review your notes from Molecular Modeling I (Experiment #2) to reacquaint yourself with the programs and basic commands so that you can be self-sufficient this week. For all parts except Part V this week, you should geometry optimize using the Semi-Empirical/AM1 method after building the appropriate molecule.

Part I. Substituted cyclohexanes

In this part, you will explore the relative stabilities and chirality of several substituted cyclohexanes. Be sure to rotate the structures around and draw Newman projections as needed to see the interactions that might stabilize or destabilize each individual conformer. The cyclohexane template provided under the "Rings" menu can be useful for building structures.

- Build both chair conformations of methylcyclohexane and record their energies. Using the difference in the energies, calculate the amount of each species present at equilibrium. Repeat this calculation for *tert*-butylcyclohexane. Refer to problem 5.11 and section 7.4a in your text if you are unsure how to proceed. For your calculations, assume $\Delta G \sim \Delta E$, and set them up so that K = [equatorial]/[axial].
- Build both chair conformations of *cis*-1,3- and *trans*-1,3-dimethylcyclohexane. As before, record their energies and compute the equilibrium ratios of the conformers for each compound. Note how these structures are related to each other and determine whether each structure is chiral.

Part II. Investigating relative acidities

As you might expect, a hydrogen atom in a stronger acid has a greater partial positive charge than one in a weaker acid. In other words, a stronger acid has a more "electron poor" hydrogen than a weaker one. In this exercise, you will assess the acidity of various compounds by examining their charges.

- Compare acidities of ethane, ethylene, and acetylene by building these three compounds. After each calculation is done, record the value of the charge on the hydrogen atom for each compound (use the "Electrostatic" charge values).
- Build acetic acid, trifluoroacetic acid, and trichloroacetic acid to explore the effect of substituents on acidity. Submit the calculations as before and record the charge value on the carboxyl hydrogen atom for each compound.
- To compare the acidity of alcohols versus phenols, repeat the same calculations for ethanol and phenol and record the appropriate values for each.

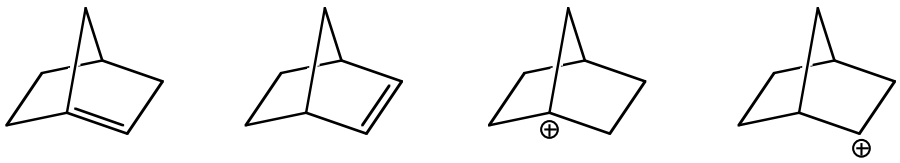
Part III. Relative stabilities of cations

You have learned in class that carbocation stability is strongly correlated with the number of carbon substituents attached to the cationic carbon center. In this section, you will explore whether your calculated energies for various butyl carbocations are consistent with what you have learned.

Build models of the 1°, 2°, and 3° butyl cations. Be sure to specify that each molecule has a positive charge before submitting its job. Record the energy for each cation.

Part IV. Bridgehead alkenes and cations

Now you get to explore whether computation allows you to predict the types of strain energies that you have learned about for bridged bicyclic molecules, such as the compounds below that are related to norbornane. Build the four species shown below and record the energy for each. Also record the three C-C-C bond angles around the positively charged carbon in the bridgehead cation. For the bridgehead alkene, record the two H-C=C-C dihedral angles.



Part V. Model of ibuprofen and acetominophen

Build and do a "quick" minimze of (*S*)-ibuprofen and acetaminophen, but do not submit calculation jobs for them. Use the program functions to check if you have built the compound structures and stereocenter correctly.

Pre-laboratory Preparation (Don't forget to cite sources!)

1. Record the pKa values and structures of ethane, ethylene, acetylene, acetic acid, trifluoroacetic acid, trichloroacetic acid, ethanol, and phenol.

2. The formula for equilibrium calculations is $\Delta G = RT\ln K$, where R = 2 cal/degree-mol, T is the temperature in kelvin, and K is the equilibrium constant. Calculate the amounts at equilibrium at 25 °C of two compounds differing in energy by ΔG = 2.8 kcal/mol.

3. Draw the structures of (*S*)-ibuprofen and acetominophen.

What Should Be In Your Notebook?

1. An entry of the title, date, and page number in your table of contents.
2. An entry of the title and date on the first page of your experiment.
3. All the items that you were asked to record for each individual part of this lab.

What Should Be In Your Laboratory Report?

Use the **Experiment 4 Report Form** to write your lab report.

Remember to:

1. Submit an electronic copy to CH241Lab@colby.edu by the date your report is due.
2. Submit a hardcopy in lab on the due date (start of lab).