

Chemistry 478 — Molecular Modeling

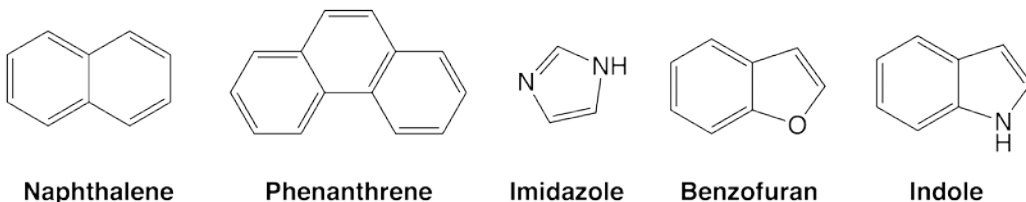
Laboratory #4 — Frontier Molecular Orbital Analysis of Regioselectivity

In this lab exercise you will perform extended Hückel and minimal basis set STO-3G calculations to generate frontier molecular orbitals, and then use FMO analysis to predict regioselectivity of three reactions: electrophilic aromatic substitution, Diels-Alder dimerization of acrolein, and nucleophilic addition of substituted benzoquinones. The Extended Hückel method is available in Gaussian 09, but not in Spartan. Hartree-Fock calculations with the STO-3G basis set can be run in either Gaussian or Spartan. The Avogadro program, which is already installed on all the lab computers, can display the orbitals generated by Gaussian 09.

Protocol

(1) As an initial exercise, generate the frontier orbitals for water using both an Extended Huckel theory (EHT) calculation and HF/STO-3G minimal basis set *ab initio* theory. The Gaussian 09 input file for EHT is provided in <http://dasher.wustl.edu/chem478/lab-04/> as **ehuckel.com**. To run the STO-3G computation, replace the **ExtendedHuckel** keyword (following #) with **HF/STO-3G** and copy the input file to some other name. Make sure that your Gaussian input file specifies production of a “checkpoint” **.chk** file (via the **%Chk** directive near the top of the file). The Gaussian 09 job can be run in a terminal window via the command: **g09 ehuckel >& ehuckel.log &**. After running Gaussian 09, the **.chk** file can be converted to a formatted version (**.fchk**) using the **formchk** utility (for example, via: **formchk ehuckel.chk**). This **.fchk** file can in turn be used as input to Avogadro for display of the molecule orbitals. In Avogadro, use the **Create Surfaces...** option from the **Extensions** menu to compute and display the orbitals. Copy pictures of the frontier orbitals into your lab report.

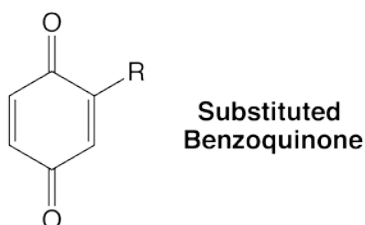
(2) Use frontier orbital analysis of Extended Huckel theory results to predict the preferred site of electrophilic aromatic substitution (nitration, for example) for the following molecules: naphthalene, phenanthrene, imidazole, benzofuran and indole. (Pick any two of them for your report, and then do the others if you have the time/interest.) Is the HOMO or the LUMO of the aromatic molecule the one controlling the substitution site? Look up the experimental site of nitration for each of these molecules and compare with your calculations. For at least one of the aromatic molecules, perform additional STO-3G and AM1 calculations, and compare the frontier orbitals across the levels of theory.



(3) There are two reasonable dimer products from the Diels-Alder dimerization of acrolein (both use the C=C bond as the “dieneophile”). Use frontier orbital arguments to predict the

preferred regioselectivity of dimerization of acrolein ($\text{H}_2\text{C}=\text{CH}-\text{CHO}$). Find and use a quantitative FMO-based formula that can be used to predict the “strength” of the bonds formed in making the alternative dimerization products.

(4) Early in his career, Ken Houk (a well-known applied quantum theorist, now at UCLA) studied a number of organic reactions in terms of FMO theory. Following work from Houk’s group, predict the site of nucleophilic addition to substituted benzoquinones. Consider three classes of substituents: electron-donating, conjugating and electron-withdrawing. Using $-\text{CH}_2^-$, $-\text{CH}=\text{CH}_2$ and $-\text{CH}_2^+$ as models for these three substituent types, run calculations (you may use either EHT or HF/STO-3G) to rationalize the site of attack by nucleophilic reagents in terms of FMO theory.



Questions

(1) How do the orbital energies and coefficients for water differ between EHT and STO-3G? Rationalize the differences.

(2) What do your calculations on water say about the concept of “rabbit ear” lone pairs in the water molecule? See if you can find direct experimental evidence that supports your MO results regarding the lone pairs.

(3) Organic chemists often debate the electron donating vs. withdrawing effect of a methyl substituent. In fact, FMO-based arguments suggest there is no single correct answer—that methyl substituents are often σ -withdrawing and π -donating. For example, the acidity order of amines increases with increasing methyl substitution, as does the basicity order: $\text{Me}_3\text{N} > \text{Me}_2\text{HN} > \text{MeH}_2\text{N} > \text{NH}_3$ for both acidity and basicity! Provide a frontier orbital explanation for this example. Use some simple calculations to support your answer.

(4) Consider the total charge density of each of the electrophilic aromatic substitution substrates above. Do the sites of greatest atomic charge density agree with the FMO-based sites of substitution? Explain why the FMO analysis gives better predictions than simple analysis of the total density.

(5) Is the acrolein dimer predicted by FMO analysis consistent with traditional “valence bond” arguments from basic organic chemistry? For “typical” Diels-Alder reactions, which is orbital generally plays a important role for the diene, the HOMO or the LUMO? What about the dienophile? In terms of FMO theory, what is an “inverse electron demand” Diels-Alder reaction?