

Chemistry 630

Spring 2014

Instructor: Professor William D. Price

Texts:

Required: *Essentials of Computational Chemistry: Theories and Models*, 2nd or 3rd Edition, Christopher J. Cramer, John Wiley & Sons, Chichester, UK, **2002**. ISBN 0-471 485527 (paperback).

Required: *Exploring Chemistry with Electronic Structure Methods*. J. B. Foresman, A Eelen Frisch, 2nd ed.; Gaussian Inc.; Pittsburgh, PA, **1996**. ISBN 0-9636769-3-8.

Rec: *Gaussian 09 User's Reference*. Available on line.

Office: Science Bldg 482 Phone: 696-3156 e-mail: pricew@marshall.edu

Office hours: Monday & Wednesday Noon – 2:00 and by appointment.

"Let us remember, please, that the search for the constitution of the world is one of the greatest and noblest problems presented by nature." -- Galileo

"In so far as quantum mechanics is correct, chemical questions are problems in applied mathematics." -- Eyring, Walter & Kimball, 1944

"I think I can safely say that nobody understands quantum mechanics.

--R. Feynman

" A scientist is someone whose curiosity survives education's assaults on it."-- Sir Hermann Bondi

"If you get confused, logic out your dilemma." -- Picker X-Ray Corp. Digital Printer Manual, 1966

Although quantum mechanics is often viewed as an esoteric subject only of interest to theoretical physicists, it is the theory that permits us to understand many of the properties of matter that we observe every day, such as why glass is transparent and why copper conducts electricity and Styrofoam doesn't. Quantum technology is the technology of the present and of the future. Devices such as lasers, medical imaging devices like MRI and PET, and the atomic clocks that make the GPS possible, all depend on the quantum nature of matter. Quantum mechanics will drive cutting-edge technology for years to come.

Course Objectives:

The course teaches the art of quantum mechanical calculations from both the chemistry and physics point of view. It is a hybrid between a laboratory and a lecture course. A laboratory course emphasizes learning by doing; it is more important to learn how to run the equipment and to interpret the data than to learn how to design and construct that piece of equipment. Similarly, in this course, you will learn how to run various quantum codes correctly and how to interpret the output of the codes, but you will not necessarily need to know how each algorithm in the 100's of 1000's of lines of code works. Simultaneously, you will learn the theories behind the computer codes, so that you will be able to correctly interpret the output of the codes. You will also learn about the applications of computational quantum mechanical methods to better understand the potential and scope. Finally, you will gain insight into the current research and development of these methods to know where the field is going and what to expect in the future.

Goals of the Course:

Applications of electronic structure theory have become a standard and powerful tool in chemistry research. It is the goal of this course to teach students the abilities to:

- develop clear conceptual ideas and quantitative knowledge about methods of electronic structure theory,
- read the contemporary research literature with an understanding of applications of electronic structure theory,
- identify a problem in their current research that is amenable to study with electronic structure theory,
- write a proposal on the application of electronic structure theory on a problem specific to the student's thesis research,
- access research computing facilities and execute electronic structure computations with knowledge about input and output,
- understand the culture of the field of computational chemistry and judge your own work and the work by others in that context.

My intent is *not* to foster memorization of specific details within the field, but to provide the student with the background and resources necessary both to *apply* and to *assess critical* computational methodologies from a *chemistry* standpoint. There will be almost no emphasis on algorithms other than from a chemistry standpoint. Several classes will focus on discussion of recent applications and will **require** the prior reading of journal articles handed out in class.

Course Materials I. Webware & Software.

This course will have no meeting times or classroom experience, we will make use of the world-wide web as the only tool for instruction. The course includes hands-on molecular modeling as a major part of the learning activities. You will be working with word processing programs (WORD), spreadsheet programs (EXCEL), structure drawing software (WebMO, Molden, etc), and molecular modeling software (WebMO) to analyze and present your results. These packages are available on Marshall University Chemistry Department computers. Electronic structure calculation software (Gaussian 09, NWChem) will be accessed through the WebMO at the Marshall University Big Green website.

Course Activities

I. Lectures. Recorded lectures and powerpoint slides are available at science.marshall.edu/pricew/COMP_CHEM_2014/lectures.html. View by dates are posted on this site.

II. Exercises Specific Exercises: I will select from various sources or generate and distribute, electronic form, problems relating to specific topics covered in recorded lecture. There are quite a few useful computational chemistry related web sites on the WWW. We will make attempts to harvest whatever knowledge can be gained from such sources. A collection of interesting sites will be added to the Course Web Site. Suggestions of sources are welcome.

- 1) Due Feb 7: http://www.computationalscience.org/ccce/Lesson1/Lab1_WebMO.pdf
- 2) Due Feb 14: http://science.marshall.edu/pricew/computational/ASSIGN_2/lab2.html
- 3) Due Feb 21: http://www.computationalscience.org/ccce/Lesson3/Lab3_WebMO.pdf
- 4) Due March 7: http://www.computationalscience.org/ccce/Lesson5/Lab5_WebMO.pdf

- 5) Due March 28: http://www.computationalscience.org/ccce/Lesson7/Lab7_WebMO.pdf
- 6) Due May 2: Attached Below

III. Term Project (proposal due Feb 7, final report due April 25): The term project is your chance to gain practical experience with the tools of computational chemistry. If possible, you are encouraged to select a project related to your research interests, since this will give you more direct experience with how computational chemistry methods can assist your own work. However, if you are studying something like the denaturation of DNA, this is probably not feasible... However, you should speak with me and there may be some approximations you can make to investigate some part of a larger problem.

Please prepare a class project proposal to turn by FEBRUARY 7. I will review the proposed projects (which can be fine-tuned later) to make sure they sound feasible.

Your project should use methods of computational chemistry to help answer a chemically interesting question.

You may opt to use any of the computational chemistry methods discussed in class, including molecular mechanics (force field) methods, semiempirical methods, and *ab initio* electronic structure methods. As a rough guideline, *ab initio* methods should be reserved for systems with about 20 atoms or fewer, while semiempirical and molecular mechanics methods might be feasible for systems of up to a few dozen atoms. The molecular mechanics and semiempirical methods are available in TINKER and MOPAC, respectively, while GAUSSIAN09 will be used for the *ab initio* computations.

Some suggestions for possible projects are given below:

- a. Structures and relative energies of different conformations of a molecule.
- b. Energetics of a reaction (reaction enthalpy and activation barriers: energies of reactants, products, and transition states).
- c. Thermodynamic properties of a molecule (including heat of formation).
- d. Absorption and/or emission spectra of a molecule.
- e. Charge density of a molecule and its implications for reactions governed by electrostatic effects.
- f. Substituent effects on structures and/or energetics.
- g. Vibrational frequency predictions to explain spectra.
- h. Rotational constant predictions to explain spectra.
- i. Candidate molecules for unusual bonding, etc.

Examinations and Grading. The Greek philosopher Socrates argued that “the unexamined life is not worth living.” Accordingly, there will be two 1-hour-examinations (100 points each), periodic exercises (300 points), term project (200 points), and a final webpage presentation (100 points) for a total of 700 points. The tests will contain but are not limited to lecture and homework material. In tests you are expected to abstract from the latter and apply your knowledge to different scenarios. Tests will also include the materials studied in exercises and during hands-on computer instructions.

Grading Scale:

A	90 - 100 %	D	60 - 69 %
B	80 - 89 %	F	≤ 59 %
C	70 - 79 %		

Academic Honesty. Academic honesty is fundamental to activities and principles of a university. All members of the academic community must be confident that each person's work has been responsibly and honorably acquired, developed, and presented. Any effort to gain an advantage not given to all students is dishonest whether or not the effort is successful. The academic community regards academic dishonesty as an extremely serious matter, with serious consequences that range from probation to expulsion. When in doubt about plagiarism, paraphrasing, quoting, or collaboration, consult the course instructor. Proven academic dishonesty will be reported to the Provost for Academic Affairs and the student's Dean.

Exercise 6 - Transition States

Chemical Reactions and Transition States

Chemical reactions occur by the rearrangement of nuclear configurations from the reactant state to the product state. For polyatomic molecules, there is an enormously large number of possible rearrangement paths that take reactants to products. Reactant molecules that have lots of energy could follow a path that involves high-energy configurations, reactants with less energy will follow a path that involves configurations with lower energy. A complete description of a chemical reaction dynamics would include all these paths. However, such a complete description is challenging because of the need to map out a multidimensional potential energy surface. Instead, a simplified approach, termed the transition state theory, is commonly employed.

The simplest versions of the transition state theory assume that reactants behave like very tired mountain climbers who are trying to get from one valley to another and have to cross a mountain range. Such mountain climbers will seek out the easiest path, one that avoids steep climbs and raises minimally in altitude. They will seek out a gorge that takes them over the ridge. Like a group of tired mountain climbers, the reactant molecules in the transition state theory will follow a unique path that connects the reactant basin and the product basin. The highest point on this path is the col, or saddle point that separates the reactant basin from the product basin. The saddle point is the point of highest energy along the reaction path and is also the point of lowest energy in the

direction perpendicular to the reaction path (lowest point of the ridge that separates reactants and products).

Optimization of Transition States

Transition states correspond to saddle points on the potential energy surface. Strictly speaking, a transition state of a chemical reaction is a first order saddle point. Like minima, the first order saddle points are stationary points with all forces zero. Unlike minima, one of the second derivatives in the first order saddle is negative. The eigenvector with the negative eigenvalue corresponds to the reaction coordinate. Transition state search thus attempts to locate stationary points with one negative second derivative. The basic recipe is: identify the reaction mode and maximize energy along this mode while minimizing energy in all other directions. One reason why transition state optimization is more difficult than the search for a minimum is that a successful search should start off in a region where the reaction coordinate already has a negative curvature. In other words, search for a transition state should start near the transition state.

Here are some recipes to locate transition state structures for chemical reactions:

Manually build a guess structure and optimize it using first and second derivatives. This approach is also called eigenvector following because the search will follow the eigenvector with a negative eigenvalue. If the starting structure has one and only one negative second derivative then the search will converge to the closest saddle point. If the starting structure has several negative eigenvalues, the search either fails or follows the direction with the largest negative eigenvalue. The main shortcoming of methods that require second derivatives is high computational cost and in practice algorithms that calculate the Hessian once and then update it during the search (Requested by **Opt=CalcFC in Gaussian**) are faster than methods that calculate the Hessian at each step. Starting with a guess transition state structure is often successful for simple reactions for which chemical intuition provides reasonable transition state guesses. For example, transition states for S_N2 reactions involving alkyl halides can be located using this approach because we know that the transition state has penta-coordinate nature with the incoming nucleophile and the leaving group roughly in line.

Build the structures of the reactant and the product and use a synchronous transit-guided quasi-Newton approach to generate an initial guess and optimize it to the transition state. If the

interpolation is carried out along the straight line that connects reactants and products, the method is called the linear synchronous transit (LST). If the interpolation is carried out along the parabola that connects reactants and products, the method is called the quadratic synchronous transit (QST2). By default, the initial guess will be a structure exactly halfway between the reactants and the products complex. This approach works well for bimolecular reactions where structures of the reactant complex and the product complex can be specified. However, QST2 fails for many unimolecular isomerization reactions because the interpolation between the reactant and the product gives a poor guess structures.

Build the structures of the reactant complex, the product complex, and guess for the transition state, and use a synchronous transit-guided quasi-Newton approach (QST3) to optimize the transition state. This approach is more robust than QST2 as it overcomes problems due to poor interpolated guess structures. The advantage of transit-guided quasi-Newton approaches over the eigenvector following method is that a full evaluation of second derivative matrix is not needed. Thus, QST2 and QST3 can be employed with methods such as CCSD(T) for which analytic second derivatives are not available.

Scan the reaction path or slice of a potential energy surface to identify saddle points. This is very robust approach that eventually will lead to transition state, but because it requires a large number of calculations, it is also time-consuming. The scanning approach is effective when there is only one reaction coordinate, as in the case of transitions between conformational isomers. For example, to locate the transition states for the internal rotation in hydrogen peroxide, the HO-OH dihedral angle can be scanned in 20-degree increments to identify maxima along this internal rotation path. The scanning approach becomes less effective as the number of geometric variables that change as the reaction occurs increases. However, mapping out potential energy surfaces is sometimes valuable as it allows the identification alternative reaction paths.

It is clear from the above discussion that the choice of the method depends largely on the nature of the problem. Furthermore, because transit-guided quasi-Newton approaches use approximate guess Hessians that might differ significantly from the true Hessian, it is important to perform full second order derivative calculation (**Freq** keyword in Gaussian) to verify that the structure from QST2 or QST3 optimization is indeed a transition state with one and only one negative eigenvalue.

In practice, it is often faster to pre-optimize the transition state with an affordable method. For example, if one is interested in the CCSD/cc-pVTZ transition state structure, it is a good idea to

first find the transition state at a MP2/cc-pVTZ level. This has two key advantages. First, the relatively fast MP2/6-311+G(d) optimization most likely yields a structure that is a good starting point for the more coupled cluster expensive optimization. Second, the Hessian at the MP2/6-311+G(d) level can be used as the initial guess Hessian for the CCSD/cc-pVTZ optimization. (**Opt=ReadFC** keyword in Gaussian.)

Tutorial

The Menshutkin Reaction: Gas Phase Reaction Path

The reaction between tertiary amines and alkyl halides is known as the Menshutkin reaction. This reaction provides an useful route to quaternary ammonium salts. The Menshutkin reaction involves nucleophilic substitution of halide by the nucleophilic amine and can be thus classified as an S_N2 process. The Menshutkin reaction converts two neutral reactants into a pair of charged products while the more familiar S_N2 displacements involve an anionic nucleophile and an anionic leaving group. A computationally efficient model for the Menshutkin reaction is a reaction between ammonia and methyl chloride.

The transition states of Menshutkin reactions can be located readily using synchronous transit-guided quasi-Newton approach (QST2) approach. One of the features of S_N2 reactions in the gas phase is the formation of a reactant complex before the transition state is reached. The reactant complex in the Menshutkin reaction is stabilized by dipole-dipole interactions and dispersion attraction. In case of an energetically favorable back-side attack, the incoming nucleophilic nitrogen is almost in-line with the leaving halogen group. The products of the Menshutkin reaction are a pair of oppositely charged ions that are attracted to each other via Coulombic forces that are balanced by the exchange repulsion. Thus, in the gas phase, a product complex where the halide is near the methyl group is expected to form. The structures of such reactant and product complexes are suitable starting points for QST2 search for the transition state.

Using MOLDEN, build structures of the reactant complex and the product complex for a reaction between ammonia and methyl chloride. Save these structures as **reactant.dat** and **product.dat**. Close MOLDEN and use Unix command **cat (cat reactant.dat product.dat > nh3_ch3cl_qst2_ts_search.dat)** to combine these two files into one input file. Edit the input file to add appropriate computational directives (**HF/3-21G Opt=QST2** is suitable for a quick pre-

optimization) and separate the two molecule definitions by an empty line. The structure of the input file thus is:

```
%Mem=16MW
%Chk=nh3_ch3cl_ts_qst2_search.chk
# HF/3-21G Opt=QST2
```

Menshutkin reaction between NH₃ and CH₃Cl: Reactant complex

0 1

[Reactant Complex Z Matrix]

Menshutkin reaction between NH₃ and CH₃Cl: Reactant complex

0 1

[Product Complex Z-matrix]

Submit this calculation. After completion (the calculation should finish in a few minutes) examine the convergence of optimization with MOLDEN. The transition state located by QST2 method at HF/3-21G level has the C-Cl distance of 2.416 and the C-N distance of 1.948.

Build a guess transition state for the Menshutkin reaction between ammonia and methyl chloride using MOLDEN. Write this guess structure out as **nh3_ch3cl_hess_ts_search.dat** and edit the input to add directives for optimization at the HF/3-21G level using analytical second derivatives at the initial point (**Opt=(TS,CalcFC)** in Gaussian). Perform calculation and compare the structure obtained via this approach to the structure obtained with the synchronous transit-guided quasi-Newton approach.

Homework

Level 1

Manually build the transition state for the reaction between ammonia and methyl chloride and optimize it at the HF/3-21G, HF/6-31G, HF/6-31+G(d,p), MP2/6-31+G(d,p), and B3LYP/6-31+G(d,p) levels. Build structures of the two separated reactants and optimize these at the same levels. Build structures of the two separated product and optimize these at the same levels. Perform frequency analysis for each of the structures at each level to verify the minima and

saddle points. Calculate reaction energy, reaction enthalpy, and reaction free energy in the gas phase at each level. Calculate activation energy, activation enthalpy, and activation free energy in the gas phase at each level. Discuss which levels of theory seems to be reliable in describing this reaction. *Hint: using at least Cs symmetry is appropriate and will speed up calculations.*

Level 2

Perform a reaction path scan along the reaction coordinate for a Menshutkin reaction between N-methylamine and methyl chloride using a method and basis set that seems reliable and efficient based on Level 1 calculations. In the scan, decrease the distance between the nucleophilic nitrogen and the electrophilic carbon in 0.2 angstrom steps from 3.5 angstroms to 1.5 angstrom. The relaxed potential energy scan can be performed in Gaussian using the **Opt=Z-matrix** directive. Locate and verify (i.e. perform frequency calculation) the transition state and the reactant complex along this path. Calculate the energy difference, enthalpy difference, and the free energy difference between the reactant complex and the transition state. *Hint: using at least Cs symmetry is appropriate and will speed up calculations.*

Level 3

Compare the activation barriers in the Menshutkin reaction of methyl chloride with four different nucleophiles: ammonia, N-methylamine, N,N-dimethylamine, and quinuclidine (1-Azabicyclo[2.2.2]octane) using MP2/6-311+G(d,p) energies at HF/6-31+G(d,p) optimized geometries. Also, calculate the gas phase proton affinity for these four bases at the same level. Is there a correlation between the gas phase proton affinity and the gas phase nucleophilicity?

You may use a computational chemistry program of your choice. If you prefer using Windows, then PC Gamess is a good choice (however, you still want to build your molecules in MOLGEN).

Transition States

Verification of Transition States

Transition states correspond to first order saddle points on the potential energy surface. A characteristic feature of a transition state is that one and only one of the second derivatives in the transition state is negative. The eigenvector with the negative eigenvalue corresponds to the reaction coordinate. Thus, the transition state can be verified by the analysis of Hessian eigenvalues that are

printed in the output and by the visualization of vibrational normal modes with programs such as MOLDEN.

1. Extract the optimized Z-matrix from the QST2 optimization that you performed earlier. You can use the command **tail -50 outputfile** to show the last 50 lines that include the optimized Z-matrix
2. Perform the frequency analysis (Freq=NoRaman) for this transition state. The frequency calculation must be performed with the same method and basis set as the optimization.
3. Open the output file of the frequency calculation with the MOLDEN and display vibrational frequencies **Norm. Mode**

Solvation Effects on Transition States

Common Homework for All Levels: Extra credit

Solvation can change the structures and relative energies of transition states. Thus, to study reactions in solution, transition states should be reoptimized in the presence of appropriate solvent model. We will use Polarizable Continuum (PCM) model to reoptimize transition states.

- a) Modify the input file for the transition state optimization to add the keyword for solvent calculation (**SCRF=PCM** keyword in Gaussian) and optimize the transition state at the HF/6-31+G(d,p) level (**Opt=(TS,CalcFC)** keyword in Gaussian). Once the calculation has finished, perform frequency analysis to verify that the structure is indeed the transition state. Compare the structure of the transition state in water and in the gas phase.
- b) Modify the input files for the starting materials and products to add the keyword for solvent calculation (**SCRF=PCM** keyword in Gaussian) and optimize these structures at the HF/6-31+G(d,p) level (**Opt** keyword in Gaussian). Calculate the reaction energy and the reaction activation energy in the solution phase and compare these values with the gas phase values.
- c) Provide the rationalization for the observed solvent effects.