4   **Computational Molecular Modeling**

4.1 Introduction

Computational molecular modeling is an area of chemistry that uses modern computer resources to help chemists rationalize experimental data, provide mechanistic insights, and to relate molecular structure to stability. With improvements in computer software and hardware, chemists are able to predict and explain with greater accuracy the properties of increasingly sophisticated molecules.

The ultimate aim of the CHEM 344 molecular modeling component is to provide a deeper insight into the experimental results generated and the concepts covered in the lab. The current chapter is devoted to exercises aimed at familiarizing you with some of the basic concepts of molecular modeling and providing practice in performing calculations. As the semester progresses, you will be required to perform similar calculations *on your own* in order to answer post-lab questions related to most laboratory experiments. It is thus in your interest to become confident and competent in using WebMO. The information and exercises contained within this chapter serve as an excellent resource.

4.2 Reference Section – WebMO

In order to use WebMO, you will need to access the program *via* the UW-Madison Chemistry Department Cluster website (https://phoenix.chem.wisc.edu/) using a Java-equipped web browser. Click the WebMO button located on the list of options on the left and login with the username and password sent to your wisc.edu email address. After you login, you will be at the WebMO Job Manager from which you can create jobs, monitor their progress, and organize previously run jobs ("job" is a general term for various types of calculation). One of the co-creators of the WebMO software package is Prof. J. R. Schmidt, a theoretical chemist here at UW-Madison.

In order to create a new job, select **New Job** > **Create New Job** which will open a blank file for you to generate your input molecular geometry.

4.3 Reference Section – Build Molecule

The molecule builder has an intuitive click and drag style interface. The default starting atom is carbon; other atoms, rings, or fragments may be selected by selecting **Build** from the menu or by typing the letters for an element on the keyboard. The most useful parts of the molecule builder involve the **Adjust**, **Clean-up** and **Symmetry tools**. A full explanation of these features can be found by selecting **Help > Index** or by hitting **F1**.

Using the correct molecular symmetry (point group) for any molecule that you submit will make your calculations faster and, more importantly, provides a more accurate answer. An understanding of point group symmetry is beyond the scope of CHEM 344 but an appropriate symmetry point group will always be suggested for your calculations by WebMO or the Lab Manual. For more information, check out the following link: http://en.wikipedia.org/wiki/Point_groups.

Build Molecule

Status «
- besselman
- webmo
- unlimited
- unlimited
- 0 jobs

Progress
- Job manager
- Build molecule

Build a new molecule using the WebMO editor, or import an existing molecule from a file. Additionally, you can export the molecule to a variety of file formats.

- Choose engine
- Job options
- Submit job

- Editor help

File Edit Tools View Build Adjust Clean-Up Symmetry Help

Rotate – Allows you to rotate the molecule; you cannot build in rotate ~~mode~~.

Build – Allows you to build molecules; you cannot rotate or move the molecule in build ~~mode~~.

Adjust – Allows you to adjust the bond lengths, bond angles, and dihedral angles.

Clean up – Allows you to clean up the structure drawn using two different methods.

Symmetry Point Group – Displays the current molecular symmetry.

Current Selected Mode

Continue – Accepts the structure as drawn and takes you to the job setup sequence.

Build Mode - C (click = add atom; drag = add bond; click & drag = add atom & bond; letter = change atom)

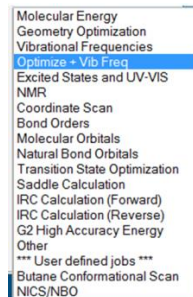Import Molecule   Export Molecule

When a molecule is built and cleaned up, it can be useful to symmetrize the molecule. At the simplest level, the appropriate molecular symmetry prevents WebMO from displaying an error message regarding the symmetry. When the **Continue** button is pressed for structures which WebMO determines to be almost symmetric, but symmetrize has not been selected, the message "*Molecule is nearly (but not exactly) symmetric. Continue without symmetrization?*" is displayed. Having the correct symmetry will also give you a little extra confidence that you built the structure as indicated by the exercise in the lab manual. Finally, the computational time is reduced by allowing Gaussian09 to make use of symmetry to cut down the number of electrons it must account for. You will learn about symmetry point groups in future chemistry courses, but for the purposes of CHEM 344 it is sufficient to match the molecular symmetry point group displayed in the Build Molecule window to that suggested in the lab manual.

In some cases, small differences between bonds on opposite sides of the molecule or slight twists of dihedral angles can prevent WebMO from identifying symmetry elements within a molecule. If you believe that a molecule is drawn correctly according to the instructions in the lab manual, but the symmetry is not being properly recognized, you can adjust the symmetry tolerance. This tool can be found by selecting **Symmetry > Symmetrize Molecule.** Adjust the tolerance to

Symmetrize Molecule

Detect
Tolerance: 0.18
Detect Symmetry

Symmetrize
Point Group: C2v
Symmetrize

Exact Point Group: Cs
Approximate Point Group: C2v

OK   Cancel

a larger value and click the **Detect Symmetry** button. In order to accept a new detected symmetry, click the **Symmetrize** button. This will adjust the structure to fit the new (approximate) symmetry point group.
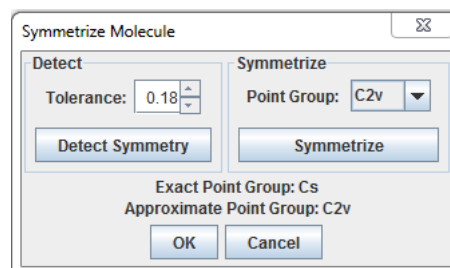
4.4 Reference Section – Computational Engine, Cluster Queues, Common Job Types

WebMO is a user-friendly and intuitive front-end program that provides access to all of the tools and job types that are available in research level computational software systems. Gaussian 09, the program that performs the calculations, is a program typically used by researchers to run routine or high-level computational jobs. We will be submitting jobs to the "chem344" queue which sets aside a large number of processors on the departmental computer cluster for our exclusive use. This is pretty cool!

```
Molecular Energy
Geometry Optimization
Vibrational Frequencies
Optimize + Vib Freq
Excited States and UV-VIS
NMR
Coordinate Scan
Bond Orders
Molecular Orbitals
Natural Bond Orbitals
Transition State Optimization
Saddle Calculation
IRC Calculation (Forward)
IRC Calculation (Reverse)
G2 High Accuracy Energy
Other
*** User defined jobs ***
Butane Conformational Scan
NICS/NBO
```

In CHEM 344, you will be using the following job types: **Geometry Optimization, Vibrational Frequencies, Optimize + Vib Freq, NMR, Coordinate Scan, Molecular Orbitals (MO), Natural Bond Orbitals (NBO), Transition State Optimization,** and others.

Geometry Optimization – Calculates an optimized, energy minimized geometry or structure for an input geometry or structure.

Vibrational Frequencies – Calculates the infrared vibrational frequencies of a molecule.

Optimize + Vib Freq – Calculates the optimized geometry and the vibrational frequency for a molecule in one combined job of the previous two job types. This will be your most common job type.

NMR – Calculates the chemical shifts of the atoms in an input geometry. For the protons and carbon nuclei, the ^{1}H and ^{13}C NMR chemical shift values are calculated relative to TMS.

Coordinate Scan – A specific bond distance, bond angle, or a dihedral angle in the molecule is scanned such that all other parts of the molecule are optimized, while that coordinate is systematically varied.

Molecular Orbitals (MO) & Natural Bond Orbitals (NBO) – Generates the molecular orbitals, electron density, atomic charges, and the natural hybrid and bond orbitals of a molecule using NBO 6.0, a program developed by UW-Madison theoretical chemist Prof. Frank Weinhold. NBO displays the orbitals in a clear, user-friendly manner.

Transition State Optimization – Calculates an optimized geometry for a molecular structure that possess exactly one negative or imaginary vibrational mode. Such a molecule represents a transition state (an energy maximum on the potential energy surface or reaction coordinate diagram).
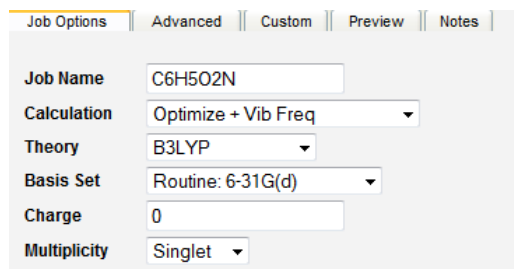
4.5 Reference Section – Level of Theory and Basis Sets

Access to sophisticated computational tools means that we can run fairly simple calculations (such as **Hartree-Fock** or "**HF**") to more complicated and more accurate methods (such as **CCSD(T)**). The details of these computational methods or levels of theory are not important in CHEM 344 because the appropriate level of theory to use for a particular calculation will always be stated in the lab manual.

Basis sets are the mathematical functions that describe the orbitals of an atom. In general the more basis functions or orbitals used, the better the result of the calculation. An appropriate basis set will always be stated, and typically will be **6-31G(d)** and **6-311+G(2d,p)**.

Both the **level of theory** and **basis set** <u>must</u> be reported for any calculated value. If values obtained from separate calculations are to be compared then the level of theory and basis set used for each calculation must be identical.

The conventional notation for reporting the method of a calculation is **theory**/**basis set**. A **B3LYP**/**6-31G(d)** calculation indicates that the calculation was performed using the **B3LYP** theory with the **6-31G(d)** basis set. Both the level of theory and basis set must be selected for every calculation on the **Job Options** tab.

Job Options	Advanced	Custom	Preview	Notes

Job Name	C6H5O2N
Calculation	Optimize + Vib Freq
Theory	B3LYP
Basis Set	Routine: 6-31G(d)
Charge	0
Multiplicity	Singlet

4.6 Reference Section – Understanding Output Files

Geometry Optimization & Transition State Optimization – These optimizations find points that correspond to the local energy minimum (Geometry Optimization) and local energy maximum (Transition State Optimization) on the potential energy surface (the reaction coordinate). The molecule can be inspected visually and bond lengths, bond angles, and dihedral angles can be measured with the **Select tool**.

The output file for each calculation contains a repetition of the command line or route, followed by a table of the geometry optimization steps. Below this you can also view the Stoichiometry, Symmetry, Basis Set, Calculated Energy, Rotational Constants, Dipole moment, Partial Charges, etc. **Always use the energy immediately following the Basis Set**; it will be listed as **RHF**, **UHF**, **RB3LYP**, or **UB3LYP** depending on the calculation performed (R refers to "restricted" and is the prefix for a closed shell molecule *i.e.* all electrons are paired; likewise, U refers to "unrestricted" and is the prefix for an open shell species such as a radical in which one or more electrons are unpaired).

Route	#N B3LYP/6-31G(d) OPT FREQ Geom=Connectivity
Geometry Sequence	

Step	Energy
0	-222.663767569
1	-222.700706056
2	-222.708109672
3	-222.712464698
4	-222.712479715
5	-222.712482802
6	-222.712482802
7	-222.712482802
Animation speed	5
Loop	None

|	
Stoichiometry	CN_2O
Symmetry	C2V
Basis	6-31G(d)
RB3LYP Energy	-222.712482802 Hartree

The absolute energy of an output molecular structure will be reported in the unit Hartrees/particle. This value must be converted to kcal/mol using the following conversion factor:

1 Hartree/particle = 627.509 kcal/mol. (For reference, 1 kcal/mol = 4.184 kJ/mol.)

You must report absolute energy values in kcal/mol and Hartrees/particle in your laboratory report.
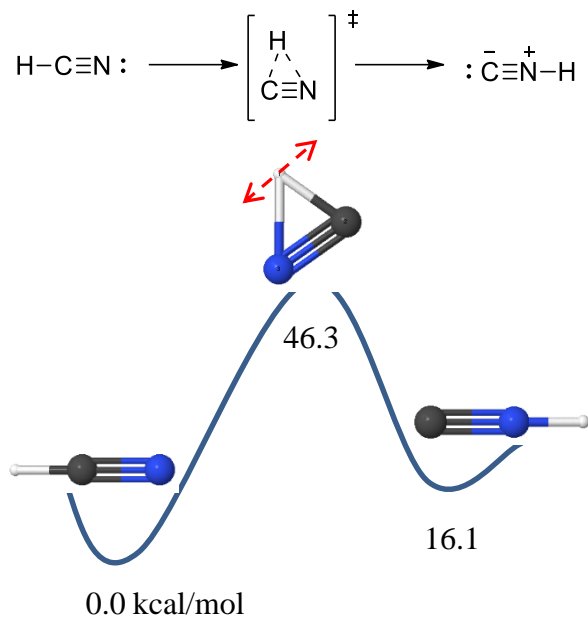
You must report relative energy values in kcal/mol and NOT Hartrees/particle in your laboratory report.

Vibrational Frequencies – The important part of a harmonic vibrational frequency calculation is the list of vibrational or IR frequencies which can be animated by clicking the movie icon. WebMO displays an idealized, simulated gas-phase IR spectrum of the molecule. Displayed below is an infrared or IR spectrum of 4′-butoxyacetophenone from 0 to 4000 cm^{-1} calculated at the **B3LYP**/**6-31G(d)** level.
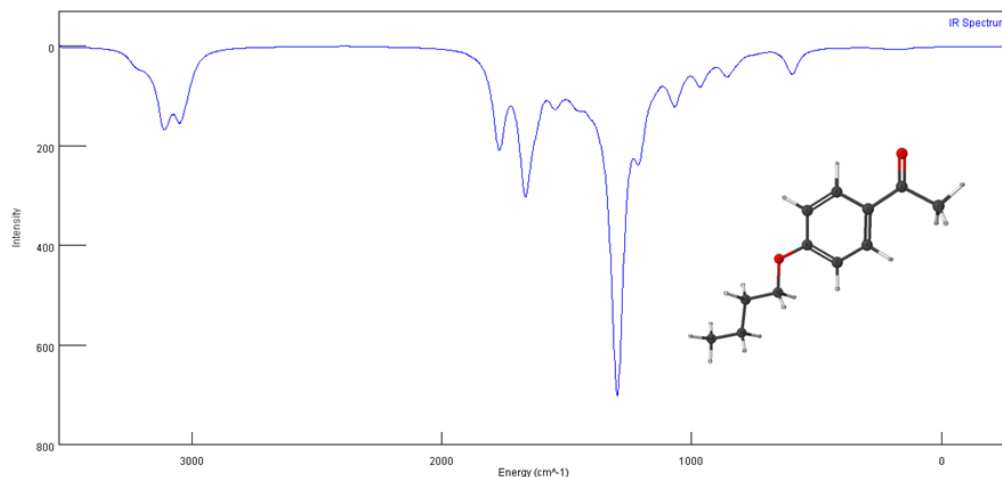

Of critical importance is the understanding that molecules that represent an energy minimum (reactant, product, or intermediate) will have all real and positive infrared vibrational frequencies; in contrast, geometries that represent an energy maximum (a transition state) will have a negative or imaginary vibrational frequency.

For example, in the isomerization of HCN (hydrogen cyanide) to HNC (hydrogen isocyanide) shown on page *4-8*, a **B3LYP**/**6-31G(d)** optimization of the transition state and subsequent frequency calculation reveals a negative vibrational mode of **-1146.6173 cm^{-1}**. This negative (imaginary) frequency corresponds to a rocking motion in which the hydrogen is passed from the carbon atom to the nitrogen atom and can be viewed by clicking on the movie icon adjacent to the vibrational frequency value. The transition state is 46.3 kcal/mol higher in energy than the reactant and 30.2 kcal/mol higher in energy than the product. Thus, HCN is 16.1 kcal/mol more stable than HNC (at the **B3LYP**/**6-31G(d)** level of theory).

$$H-C{\equiv}N\colon \longrightarrow \left[\begin{array}{c} H \\ \diagdown \diagup \\ C{\equiv}N \end{array} \right]^{\ddagger} \longrightarrow \ \colon\!\overset{-}{C}{\equiv}\overset{+}{N}-H$$

46.3

16.1

0.0 kcal/mol

Natural Bond Orbitals (NBO) – These calculations allow you to view a range of useful images of orbitals and maps based upon the electron distribution. Several of these are shown below.
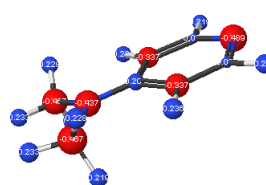
Bond Dipole Moment (μ), Partial Charges, and Natural Population Analysis – The calculation output displays the dipole moment in units of Debye (D), the direction of which can be viewed as a blue vector overlaying the structure by clicking on the magnifying glass next to the value. Additionally, the NBO charges are displayed in a list entitled "**Natural Population Analysis (NPA)**." You should always use the **NPA** charge values rather than those in the "**Partial Charges**" list as NPA values are more accurate. Either of these charge values can also be displayed overlaying the molecular structure. The atoms are coded **red (-)** or **blue (+)** indicating the sign of the charge. Shown below are 2 different depictions of the charge distribution in the heterocyclic compound 4-dimethylaminopyridine (4-DMAP) calculated at the **B3LYP**/**6-31G(d)** level of theory.
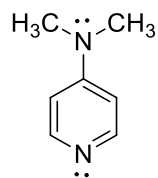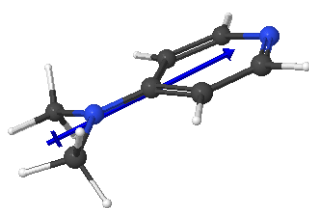
4-DMAP   dipole moment, μ = 4.54 D   NBO – Natural Population Analysis

Electrostatic potential – The electrostatic potential map is a quick method for determining the charge distribution in a molecule. It can be found at the end of the **Molecular Orbitals** list under **Electrostatic Potential**. The default image is opaque as shown below, but it can be modified to reveal the underlying molecular structure by right-clicking and choosing **opacity > transparent**.
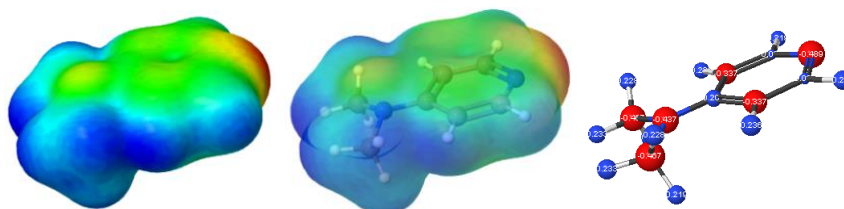
electrostatic potential map of 4-DMAP in opaque and transparent modes

When comparing multiple structures, it is important to standardize the color scheme so that the colors correspond to the same charge values in different files (i.e. so that you are comparing "apples to apples"). This can easily be done by right-clicking and choosing **preferences**, un-checking the **Auto scale range** and then setting the **Mapped values** to the same minimum and maximum values for each molecule of interest.
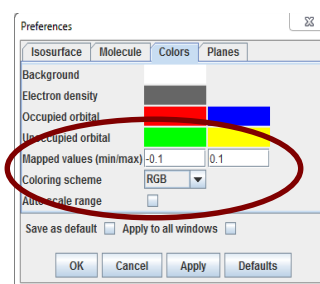
Molecular Orbitals, Natural Atomic Orbitals, Natural Hybrid Orbitals, and Natural Bond Orbitals – The orbitals are printed out in a couple of lists which includes their occupancy and energy. They can be visualized by clicking on the magnifying glass symbol next to them. The default coloration of the lobes of an occupied orbital is **red**/**blue** and an unoccupied orbital is **yellow**/**green**. Like the electrostatic potential maps and other depictions, they can be rendered solid or transparent. In general, the most useful of the orbitals will be the **Molecular Orbitals, Natural Hybrid Orbitals,** and the **Natural Bond Orbitals.**

Natural Hybrid Orbitals – These are the hybridized atomic orbitals that each atom uses to create molecular orbitals. The natural hybrid orbitals may confirm or contradict the hybridizations predicted from the electron geometries of VSEPR theory, but they also use more accurate hybridizations that may or may not have a whole number exponent like sp, sp^2, sp^3, dsp^3, and d^2sp^3. In addition to providing an excellent 3D representation of these orbitals, WebMO displays numerical descriptions of the orbitals in the traditional manner (sp, sp^2, sp^3…) and as percentage character of s, p, and d in the *Description* column. We can ignore any contributions from d-orbitals in CHEM 344.

The table below shows how to translate the NBO orbital descriptions into a more familiar sp^x notation.
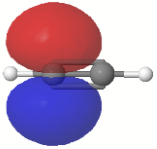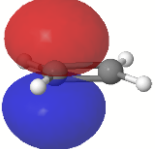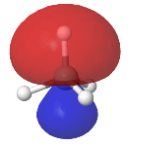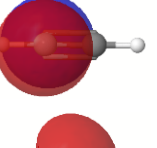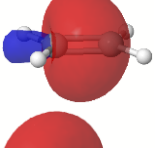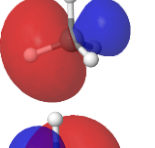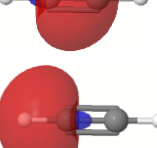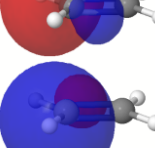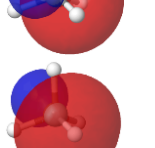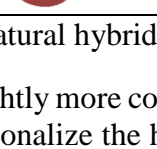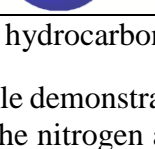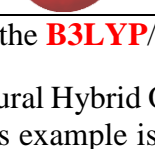
NBO Orbital Description	Common Notation
s(50.00%)**p**1.00(50.00%)**d**0.00(0.00%)	**sp** hybridization, equal parts **s** and **p**
s(33.33%)**p**2.00(66.67%)**d**0.00(0.00%)	**sp²** hybridization, 1part **s** and 2 parts **p**
s(25.00%)**p**3.00(75.00%)**d**0.00(0.00%)	**sp³** hybridization, 1part **s** and 3 parts **p**
† **s**(10.70%)**p**8.33(89.18%)**d**0.01(0.12%)	**sp⁸·³** hybridization, 1part **s** and 8.3 parts **p**
‡ **s**(0.00%)**p**1.00(99.80%)**d**0.00(0.19%)	~ no hybridization, almost pure **p**‡
‡ **s**(53.01%)**p**0.88(46.87%)**d**0.00(0.12%)	**s¹p⁰·⁸⁸** hybridization, 1part **s** and slightly less than 1 part **p**‡

†The hybridization of the nitrogen atom lone pairs in urea from an **MP2**/**6-311+G(2d,p)** calculation. ‡The hybridization of the oxygen atom lone pairs of H_2O from a **CCSD(T)**/**cc-pVTZ** calculation.

It may be useful to review how the hybridized orbitals around an atom combine to create the familiar, idealized, atomic hybridization descriptions of sp, sp^2, and sp^3 shown below from Loudon. An sp^3 hybridized carbon atom has four degenerate sp^3 hybrid orbitals arranged in a tetrahedral geometry. An sp^2 hybridized carbon atom has 3 sp^2 hybrid orbitals arranged in a trigonal planar geometry and a single unhybridized p orbital perpendicular to the plane of the hybridized orbitals. An sp hybridized carbon atom features two linear sp hybrid orbitals and two perpendicular unhybridized p orbitals.

4 sp³ orbitals

3 sp² orbitals and 1 p orbital

2 sp orbitals and 2 p orbitals
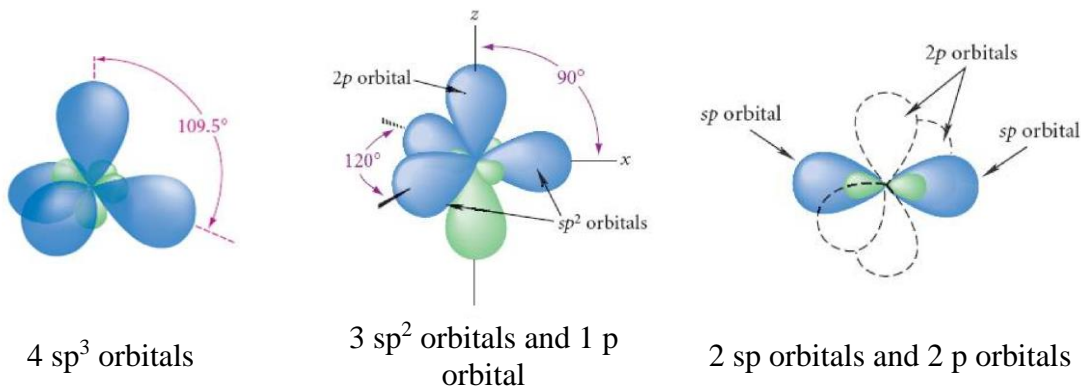
As you will discover, hybridization can be as simple as these idealized descriptions derived from VSEPR predictions of molecular geometry, but it can also be considerably more complicated. Depicted on the next page are 3 classical cases of carbon hybridization in which the NBO hybridization of each carbon orbital is shown. Note that the carbon atoms of acetylene and ethylene are not "perfectly" sp or sp^2 hybridized.

acetylene – sp carbon atom		ethylene – sp² carbon atom		methane – sp³ carbon atom	
	p		p		sp^3
	p		$sp^{1.5}$		sp^3
	$sp^{0.9}$		$sp^{2.3}$		sp^3
	$sp^{1.1}$		$sp^{2.3}$		sp^3

Natural hybrid orbitals for each hydrocarbon are calculated at the **B3LYP**/**6-31G(d)** level.

A slightly more complicated example demonstrates how NBO Natural Hybrid Orbitals can be used to rationalize the hybridization of the nitrogen atoms in urea. This example is discussed in detail in WebMO lecture 2. An optimized structure of urea was obtained at the **MP2**/**6-311+G(2d,p)** level. The lone pairs associated with the nitrogen and oxygen atoms are listed as Natural Hybrid Orbitals 21 – 24 and are shown below. It is apparent that, despite the prediction of VSEPR that the nitrogen atoms would have a trigonal pyramidal molecular geometry arising from a tetrahedral electron geometry and a common assumption of sp^3 hybridization, the lone pairs (orbitals #21 and #22) are approximately 11 % s and 89 % p character ($sp^{8.3}$). This indicates that the nitrogen atoms in urea are **not** sp^3 hybridized (if they were, the lone pair would be found in an sp^3 hybridized orbital). Likewise, if the nitrogen atom were perfectly sp^2 hybridized then the lone pair would be in a 100% p orbital.

Natural Hybrid Orbitals

Display Range				21	- 24	/ 132		

Orbital	Description	Occupancy	Energy	Actions
21	LP(1)N2 s(10.70%)p8.33(89.18%)d0.01(0.12%)	1.873710907	-0.464862402 Hartree	🔍 💾
22	LP(1)N5 s(10.70%)p8.33(89.18%)d0.01(0.12%)	1.873710907	-0.464862402 Hartree	🔍 💾
23	LP(1)O8 s(59.58%)p0.68(40.30%)d0.00(0.12%)	1.979709545	-0.939306801 Hartree	🔍 💾
24	LP(2)O8 s(0.00%)p1.00(99.69%)d0.00(0.31%)	1.890840078	-0.417166066 Hartree	🔍 💾
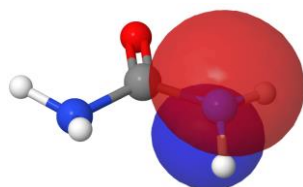
$sp^{8.3}$ N-atom lone pair orbital #21
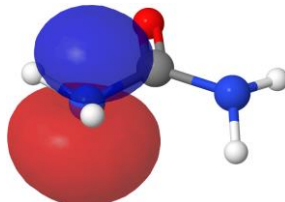
$sp^{8.3}$ N-atom lone pair orbital #22
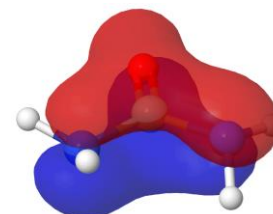
twisted π conjugated MO

The hybridization of the N-atoms in urea is best understood as somewhere between sp^3 (favored by steric repulsion) and sp^2 (favored by π delocalization). The N-atom **lone pair** orbitals (**LP**) can be viewed by clicking on the magnifying glass (LP#23 is shown in the image above). The abbreviations **CR**, **BD**, **LP**, and **RY** indicate **core**, **bonding**, **lone pair**, and high-energy, low-population **Rydberg** orbitals respectively. An ***** is used to designate an empty or low-population orbital. Due to their high-energy, low-occupancy status, the Rydberg orbitals are not important in CHEM 344.

Molecular Orbitals – These calculations provide insight into the molecular orbitals formed when the atomic orbitals are allowed to mix (*i.e.* when bonding occurs). Such orbitals are particularly important when looking at conjugated systems such as benzene (shown below calculated at the **MP2**/**6-31G(d)** level). The molecular orbitals (MOs) shown represent the conjugated π system of benzene. The two MOs shown below depict an occupied orbital showing complete overlap (π_1 or HOMO-4) and an unoccupied orbital showing no overlap (π_6 or LUMO+5). You will be depicting all of the π system orbitals in benzene in one of the subsequent ex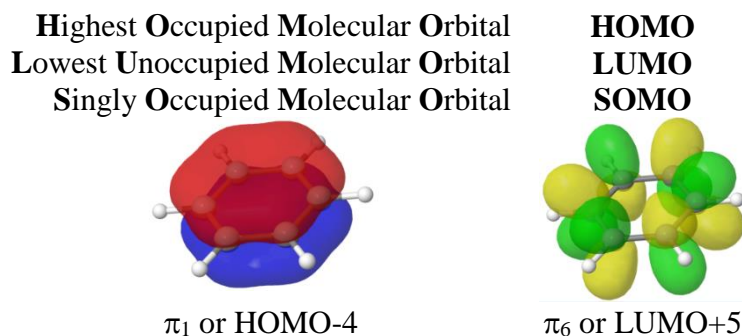ercises. The list below contains some important vocabulary for describing MOs – you need to be familiar with these acronyms.

Highest **O**ccupied **M**olecular **O**rbital	**HOMO**
Lowest **U**noccupied **M**olecular **O**rbital	**LUMO**
Singly **O**ccupied **M**olecular **O**rbital	**SOMO**

π_1 or HOMO-4 π_6 or LUMO+5

NMR – This type of calculation provides an estimate of the ^{1}H and ^{13}C NMR spectra for an input molecule. It is important to note that these spectra do not simulate coupling between nuclei, and so splitting will not be shown. Additionally, because the optimized or equilibrium geometry does not take into account the rotations that occur between conformers in a normal temperature NMR experiment, *equivalent* atoms will not always have equivalent chemical shifts in a calculation output. The output of an NMR calculation can be seen in the ^{1}H-NMR spectrum of 4-chloroanisole (4-methoxychlorobenzene, C_7H_7ClO) shown below calculated at **B3LYP**/**6-31G(d)**. We would predict that this molecule would have three equivalent ^{1}H environments and thus would show three signals in the ^{1}H-NMR spectrum. The output of the NMR calculation shows seven separate H-atom environments and there is no coupling information. This type of calculation can be helpful in differentiating the chemical shift of protons, but additional interpretation will be required to estimate coupling and equivalence. Reducing the peak width to 0.01 ppm will yield a more reasonable spectrum. This value can be adjusted at the bottom of the Absolute NMR Shifts table (see page *4-25)*. **The chemical shift values of interest in output are listed as isotropic chemical shifts.**
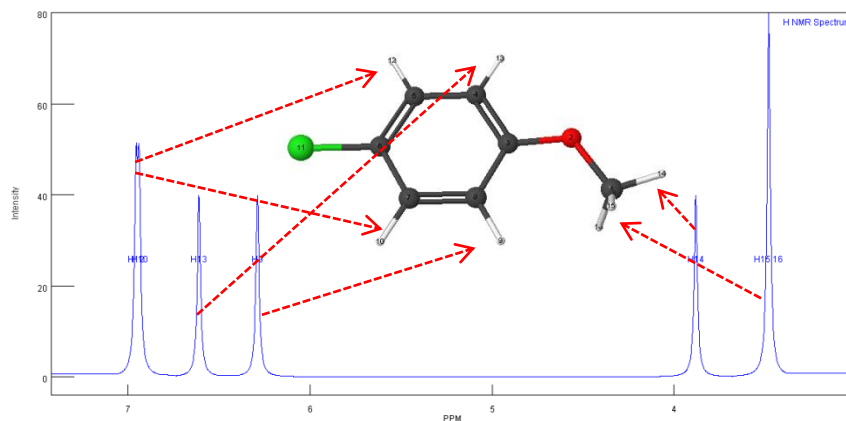
Clearly, a typical ^{1}H-NMR spectrum of 4-chloroanisole would show all of the Me protons (H14-16) as a singlet. Similarly, the aromatic-ring protons *ortho* to the OMe group (H9 & H13) would be equivalent and form a doublet with the typical *ortho* coupling value. The aromatic-ring protons *ortho* to the chloro group (H10 & H12) would also be a doublet with an identical *ortho* coupling value to protons H9 & H13.

4.7 Pre-lab Instructions

To prepare yourself to succeed and to complete this chapter in a reasonable amount of time, **you need to complete the following pre-lab tasks. This replaces the typical pre-lab reagent table, procedure, etc.**

1) **Read sections 4.2 – 4.6 before attending class.** While this lab session does not require the handling of any chemicals or glassware it is still important that you are familiar with the requirements before the lab begins. The more familiar you are with WebMO, the more likely you are to successfully complete the computational experiments in a reasonable amount of time.

2) **Login to WebMO.** Make sure that you are able to access WebMO on the Phoenix cluster before you attend class using the log-in information sent to your wisc.edu email account *approx.* one week prior to your laboratory session. **DO NOT DELETE THIS EMAIL MESSAGE!** As described earlier, you will need a Java-equipped web browser. **If you have difficulty with your current browser, try a different browser and/or update Java.** If you are unable to log-in to WebMO then you will be unable to complete the experiment during class. We may not be able to get you a log-in during class so it is best to do this ahead of time. Contact Dr. Hill and Dr. Esselman (not your TA) by email if you need assistance with a log-in issue.

3) **Draw some molecules and play with the clean up tools.** Become familiar with the WebMO drawing utility and interface before you come to class; you are highly encouraged to play around with the drawing utility and to construct some of the molecules that you will be using in calculations in the experiment such as butane, benzene, aniline, etc.

4) **View the WebMO lectures.** Only by watching the video lectures and reading the prelab material will you understand how computational chemistry is used in the course and be ready to perform the necessary calculations. Specifically you will learn how to use computational chemistry in CHEM 344, and how to use WebMO to run calculations.

5) **Download and install the latest version of MestReNova and JAVA onto your computer of choice.** Links to these required software programs and their installation instructions can be found on the course website.

6) **You will need to note the color of several images during this experiment**. You will be required to print out color images from WebMO depicting orbitals and surfaces. It is easiest to do this using screen captures and printing from a word document. We recommend printing many images per page by use of MS Word or Powerpoint.

4.8   Getting Assistance

It is likely that at some point during this course you will need assistance with performing your calculations or interpreting the results. Please post any questions or issues that you are having to Piazza or see an instructor during office hours.

Include the following information in your posting:

- A description of the exercise, problem, or question that you are attempting to complete. Do not assume that your question responder has a laboratory manual handy.
- A detailed description of the error or problem that you are encountering, including a screen capture of your input molecule. Copy the text of any error messages that the program generates.
- A description of how you have tried to solve the problem. It would not be helpful for us to tell you to do something you've already tried.
- Allow sufficient time for a response - do not assume you'll get an answer at 2:00 am the morning that it is due.

The exercises in this chapter serve as a reference for the calculations that you will perform later in the course. Everything that you need to do for the lab reports is covered in this chapter and it is thus in your own interest to pay attention and ask questions during the 2 hands-on lab sessions.

In addition to familiarizing you with the process of obtaining computational data, the questions in this chapter are designed to give you practice in both the interpretation and written explanation of these data. In a broader sense, the application of computational chemistry to experimental problems is designed to provide you with a deeper understanding of those chemical phenomena.

Treat WebMO usage as a learning experience rather than just a source of points.

4.9   Exercises – Conformations of Butane

Butane exists in several conformations that are energy minima or maxima (transition states) on its potential energy surface. By following the directions below you can prepare a graph of the **HF**/**6-31G(d)** potential energy surface of butane showing these conformational changes.

1.) In the **WebMO Job Manager**, **select New Job** from the job menu. In **Build** mode, draw butane (C_4H_{10}). The simplest way to do this is to press C for carbon (or select carbon from the build menu) and to click the drawing area. This will draw a single carbon atom. In order to add additional carbons connected by single bond, click and drag from the original carbon atom to carbons 2, 3, and 4.
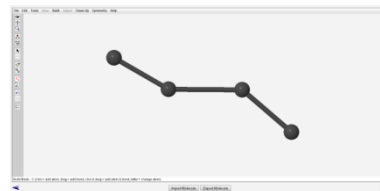
2.) Select **Clean–Up > Comprehensive – Mechanics** in order to add hydrogen atoms to the carbon atoms. Confirm or set the C1-C2-C3-C4 dihedral angle to 180^0 by selecting the **Adjust button** . Click the terminal carbon atom, then hold Shift and click on each of the remaining atoms. Once the atoms are selected, choose **Adjust > Dihedral Angle** from the menu or use the Adjust Dihedral Angle button to set the dihedral angle. **This is how you measure or set dihedral angles in all molecules.**

3.) If built correctly, the Symmetrize button will display the molecular symmetry to be **C₂h***; select this button. The **C₂h*** symbol should now change to a black **C₂h** with no asterisk. Having the correct symmetry will often reduce the computational time; in this case it will also confirm that you've built the correct structure.

4.) While the 4 carbon atoms are still highlighted from step 2, select **Adjust > Scan Coordinate.** Choose to scan the dihedral from 180° to 0° in 18 steps. If done correctly, the three C-C bonds will be highlighted in gold.

5.) Press the continue button in the bottom right to move onto the job-type selections.

6.) Fill out the specifics of the calculation and hit Continue. Always use a Job Name that is descriptive and that you will be able to identify later; the default is the chemical formula but this is not useful. For this calculation select the calculation type of "**Coordinate Scan**" which will perform the scan you set up in step 4. For the **Theory** and **Basis Set** choose **Hartree-Fock** and **Routine: 6-31G(d)**. For the **Charge** and **Multiplicity** select **0** and **Singlet**. At this point, hitting the continue button will submit the job to the phoenix cluster.
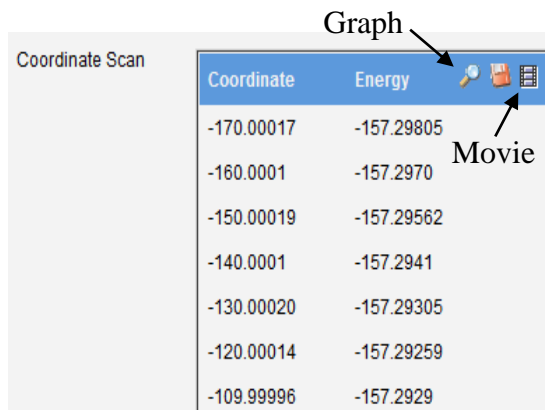
7.) After hitting the continue arrow, your job will enter the queue and eventually begin to run. You should see your job on the list with its name, description, date, status time, etc. When the

status goes from Running to Complete, your job is ready to analyze. When complete you will also see the Name change from plain text to an html link. Click the link and scroll down.

8.) WebMO does a great job of parsing a very long text-only output file from Gaussian and translating it into a format from which you can collect useful information about the molecule. In this case, as we are interested in investigating the dihedral rotation, the section labeled Coordinate Scan will be the most useful. It has a long list of dihedral angles and corresponding energies. Far more fun and exciting is WebMO's ability to show a movie of the molecule going through the dihedral changes and generate a graph for you of the energy *vs*. the dihedral rotation. **1 Hartree/particle = 627.509 kcal/mol**.

Graph

Coordinate Scan

Coordinate	Energy
-170.00017	-157.29805
-160.0001	-157.2970
-150.00019	-157.29562
-140.0001	-157.2941
-130.00020	-157.29305
-120.00014	-157.29259
-109.99996	-157.2929

Movie

9.) Cleverly, the makers of Gaussian09 have supplied a large number of quotes that are appended to the end of a completed calculation as shown below. Find your quote and enjoy it. *It may be extra fun for you and your TA to share your quote in your laboratory notebook, especially if it is a particularly witty one.*

10.) *In your laboratory notebook, draw a potential energy surface in the format shown below for the conformations of butane about the C1-C2-C3-C4 dihedral from 0 to 360°. Label the relative energy values of each local minimum and maximum. Draw a Newman Projection of each conformation under the x-axis. Be aware that the order of conformers may be different in the graph than in WebMO.* (**5 points**)

FOR ALL CALCULATIONS THIS SEMESTER RECORD THE METHOD USED IN YOUR LABORATORY NOTEBOOK, e.g. HF/3-21G, HF/6-31G(d), B3LYP/6-31G(d), etc.

Conveniently, you may wish to export the coordinate scan dihedral angles and hartree energy values to MS Excel for analysis. To do this, choose **Download > Spreadsheet** in the WebMO Job Manager.
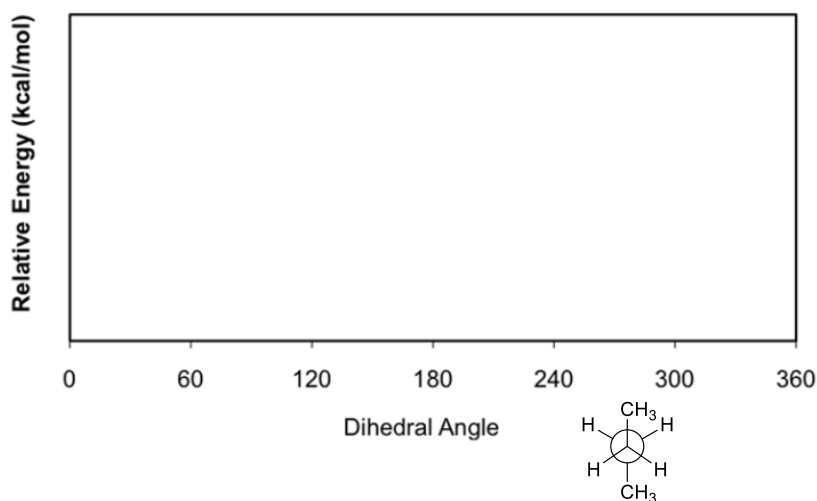
In general, molecules corresponding to local maxima cannot be isolated as they are short-lived transition states, whereas local minima represent potentially isolable molecules (products, reactants, or intermediates). In order to lock butane into a *gauche* or *anti* conformation and prevent it from interconverting it must be stored at temperatures below 20 K (-253 ºC)!

4.10 Exercises – Conformations of Substituted Cyclohexanes

Substituted cyclohexane rings in the chair conformation are often able to undergo a chair flip to place their substituents in either axial or equatorial positions. The exact ratio of *products* to *reactants* is determined by their relative energies, which can be estimated *via* computational modeling. Using the instructions below, model the conformational equilibria of methylcyclohexane and *tert*-butylcyclohexane. (For comparison, empirical A-values for substituted cyclohexanes are in Appendix O)

cyclohexane
R= methyl or *tert*-butyl

2-hydroxytetrahydropyran
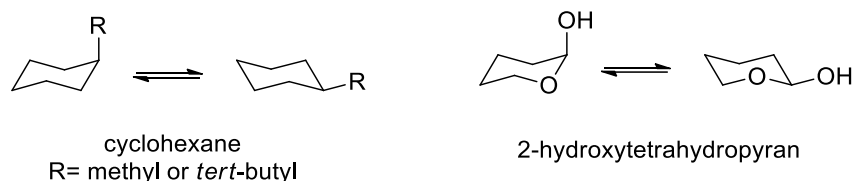
$$K_{eq} = [products]/[reactants] \qquad \Delta E_{reaction} = E_{products} - E_{reactants}$$

1.) Calculate the optimized geometry of each individual molecule with the R substituent in both the axial and equatorial conformations (one molecule = one job, 6 total). Just as with the previous exercise, create a new job file for each molecule and draw the desired structure (or choose the pre-built cyclohexane-chair conformation rings). Select **Build > Fragment.** In the Choose Fragment window, choose the category of **Rings** and fragment **Cyclohexane – Chair**.
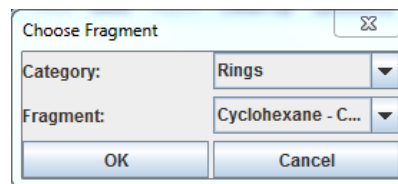
2.) As with the previous exercise, choose **Clean–Up > Comprehensive – Mechanics**. If you have constructed methylcyclohexane and *tert*-butylcyclohexane correctly, WebMO will identify a symmetry point group of C_s for methylcyclohexane. (C_1 is also okay, it will just take longer to run. C1 symmetry is appropriate for *tert*-butylcylcohexane.) Run a separate **HF**/**3-21G** **Optimize + Vib Freq** calculation on each molecule. When finished, confirm that each species is an energy minimum by viewing the vibrational frequencies table.
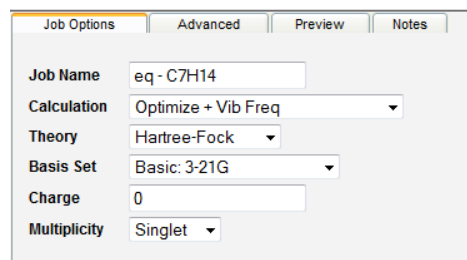
3.) For each of the 6 structures, place a screenshot of the optimized geometry in your laboratory notebook. Obtain the **HF**/**3-21G** energy, **RHF Energy**, from each output file and place it into a table similar to that shown on the subsequent page. For each pair of conformers determine the relative energy difference, ΔE_{rxn}, which is a good measure of the relative stability of each conformer. You will need to convert the energy from Hartrees/particle to kcal/mol using the conversion factor **1 Hartree/particle = 627.509 kcal/mol.**

4.) The relative energy difference, ΔE_{rxn}, between isomers is a useful value that can provide insight into the relative abundance of each species in equilibrium. **As an estimate, a 1.4 kcal/mol difference in relative energy between two molecules will correspond to a factor of 10 in the equilibrium constant, K_{eq}.** In your laboratory notebook, reproduce and complete the table shown below. Energies of the lowest energy conformations of 2-hydroxytetrahydropyran are provided for you. Estimate the K_{eq} value for the equilibria shown below (pay attention to the sign of each ΔE_{rxn}). Display all energy values to the nearest 0.1 kcal/mol.

cyclohexane
R= methyl or *tert*-butyl

2-hydroxytetrahydropyran
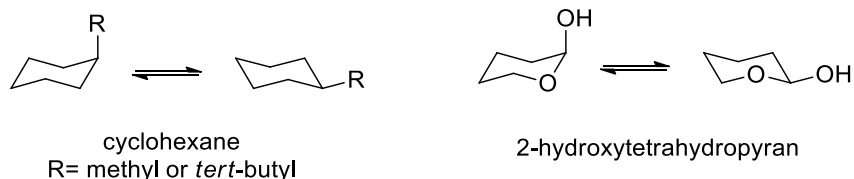
$$\Delta E_{rxn} = E_{products} - E_{reactants}$$

Example: If ΔE_{rxn} of -4.2 kcal/mol, then K_{eq} is roughly 10^3.

$$K_{eq} = 10^{-\Delta E/1.4} = 10^{4.2/1.4} \cong 10^3$$

Molecule Name	Structural Sketch	Energy HF/3-21G (kcal/mol)	ΔE_{rxn} HF/3-21G (kcal/mol)	K_{eq}
axial methylcyclohexane				
equatorial methylcyclohexane				
axial tert-butylcyclohexane				
equatorial tert-butylcyclohexane				
axial 2-hydroxytetrahydropyran		-215222.4972		
equatorial 2-hydroxytetrahydropyran		-215219.0748		

For additional information on the issues involved in the above equilibria, see Loudon p. 277-281 and 1181 or (http://en.wikipedia.org/wiki/Methylcyclohexane or http://en.wikipedia.org/wiki/Anomeric_effect).

4.11   Exercises – Electron-Donating and Electron-Withdrawing Aromatic Substituents

The electron-withdrawing and electron-donating effects of substituent groups on aromatic systems have a great effect upon both the ^{1}H-NMR spectra of these molecules as well as the reactivity of the molecule in electrophilic aromatic substitution (EAS) reactions. These electronic properties can be investigated by comparing the geometries, orbitals, and properties of the three aromatic molecules below.

benzene   aniline   nitrobenzene
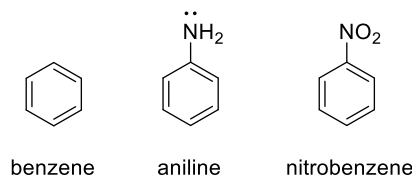
1.) Optimize each of the molecules using a **B3LYP**/**6-31G(d)** **Optimize** + **Vib Freq** calculation. Make sure to clean-up each molecule using the **Comprehensive – Mechanics** tool and check that each has the correct symmetry (benzene – D_{6h}, aniline – C_s, nitrobenzene – C_{2v}). Confirm that all of the vibrational frequencies are positive values and, thus, that the output is a correct minimized structure rather than a transition state. You will need to start over if you have modeled a transition state.

2.) Perform a Natural Bond Orbitals calculation at the same level of theory on the optimized geometry of each molecule using the **New Job Using This Geometry** button. This will generate the MOs that define the π-system orbitals and the hybridization of the nitrogen atom in aniline, and an electrostatic potential map for each species. See pages *4-9* through *4-12* for a more detailed explanation for interpreting these types of calculations.

   For each of the three aromatic species, print a color image of the electrostatic potential map in your laboratory notebook. The electrostatic potential map can be found by clicking on the magnifying glass next to "Electrostatic potential." Make sure that you change the coloration to a standard set of values (-0.05 to 0.05) for each of the three molecules so that they use a consistent color scheme (p. *4-9*). Additionally, label each ring atom with its NPA charge (located in a table in the output file or available by clicking on the magnifying glass which will place them on the structure).

3.) Explain why specific carbon atoms in aniline and nitrobenzene have significantly different electron density than the carbon atoms of benzene. Include resonance structures in your answer. **(5 points)**

4.) For each of the 3 aromatic species, find the MOs that correspond to the π system and depict them in your laboratory notebook. In the case of benzene, there are 6 atoms involved in the π system which results in 6 MOs of π-symmetry – these are #17 (π_1 or HOMO-4), #20 (π_2 or HOMO-1), #21 (π_3 or HOMO), #22 (π_4 or LUMO), #23 (π_5 or LUMO+1), and #27 (π_6 or LUMO+5). Note the alternating colors (symmetries) of the orbitals representing their changing signs and the locations of the nodes. Remember the color scheme of **red**/**blue** and **yellow**/**green** for the occupied and unoccupied molecular orbitals respectively.
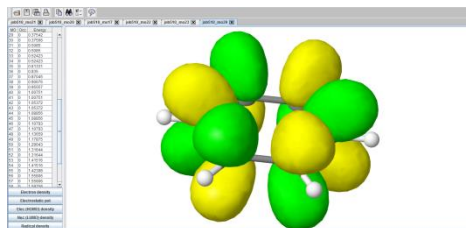
π_6 or
LUMO+5

Due to the electron-withdrawing and electron-donating effects of the NO_2 and NH_2 groups respectively, it is useful to adjust the isovalue (the value that determines the size of the orbital drawn) so that the orbital densities will look more like you expect. Click the **Edit MOviewer** preferences button (⬚) and set the isovalues for aniline to 0.04 and nitrobenzene to 0.004. Doing so will make it easier to tell which atoms are involved in the delocalized π system.
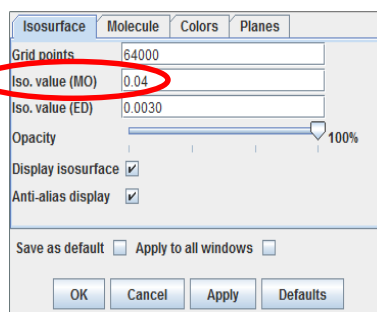
5.) Using the NBO and geometry optimization calculations of aniline, assess the hybridization of the nitrogen atom by answering the following questions.

a. Does the C-N-H bond angle value closely match the standard sp^3 109.5°, sp^2 120°, or sp 180° bond angles or is it somewhere between these values?

b. Where are the amine hydrogen atoms located relative to the aromatic ring? Measure and report the C-C-N-H dihedral angle.

c. It is apparent from the MOs that you looked at in Q5 that aniline has a conjugated π system. Using the Natural Hybrid Orbitals list, express the hybridization of the nitrogen atom lone pair in the standard sp^x notation (see p. **4-10** for details). The nitrogen lone pair is designated LP(1) N.

6.) VSEPR theory predicts that an atom with 1 lone pair and 3 bonding pairs (such as the nitrogen atom in aniline) will have a tetrahedral electron geometry (sp^3 hybridized) and have a trigonal pyramidal geometry due to steric repulsions between H-atoms and the N-atom lone pair. However, in Q5 you observed that the N-atom in aniline is not perfectly sp^3 hybridized (i.e. the hybridization is different from that predicted from a tetrahedral electron geometry). Briefly describe the factors that contribute to this deviation from the predicted sp^3 hybridization and tetrahedral electron geometry. **(5 points)**

4.12 Exercises – NMR Chemical Shift Prediction

The ^{1}H-NMR and ^{13}C-NMR chemical shifts can be estimated relative to TMS using WebMO/Gaussian09 with an appropriate level of theory and basis set. In this exercise, you will compare the experimentally observed chemical shifts of 4'-hydroxyacetophenone with those predicted using empirical parameters and an NMR calculation. In order to make an effective comparison between experimental and theoretical data, you will need to acquire the NMR data for this compound from the course website and process it in MestReNova using the instructions below. The purpose of this exercise is to become familiar with the software packages that will be used throughout the course to analyze and predict NMR spectra.
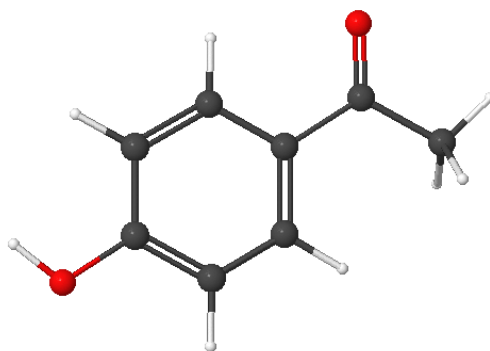
4'-hydroxyacetophenone

Empirically predicted NMR Chemical Shifts:

1) Use the empirical parameters found on the course website or on appendix pages H – J at the end of the laboratory manual. These values have been determined from a range of molecules and can be applied to new molecules to predict likely chemical shifts for their nuclei. The more parameters that are used, the larger the inherent uncertainty in the predicted value. (https://www.chem.wisc.edu/content/chemistry-344-spectroscopy-and-spectrometry)

   Show all shift calculations in your laboratory notebook for later comparison to experimental chemical shifts.

Computationally predicted NMR Chemical Shifts:

2) Create a **New Job** in WebMO and build 4'-hydroxyacetophenone in the conformation depicted above. When symmetrized properly the molecule will have a C_s symmetry point group. Obtain an optimized geometry by performing an **Optimize + Vib Freq** calculation on the molecule using **B3LYP**/**6-31G(d)**. Confirm that your optimized geometry has all positive vibrational frequencies and is not a transition state (See *4-7* through *4-8*).

3) Using the optimized structure, perform an NMR calculation using the same level of theory and basis set. Do not alter the optimized geometry in any fashion before running the NMR calculation.

4) The desired values are the Isotropic chemical shifts listed in the Absolute NMR shift table as shown to the right. It is important to note that the chemical shifts will not be the same for ^{1}H- or ^{13}C-nuclei that are often assumed to be NMR equivalent. A computational prediction cannot take into account which atoms are conformationally equivalent on the NMR timescale. For example, in the molecule under investigation, the two ^{1}H-nuclei *ortho* to the carbonyl are locked into different environments even though they appear as a singlet in an experimental ^{1}H-NMR spectrum.

5) WebMO can display predicted ^{1}H-NMR spectra and ^{13}C-NMR spectra. These are often not particularly helpful because they lack any coupling or splitting of signals and lack equivalency of NMR equivalent atoms. Most often the predicted isotropic chemical shift values are sufficient.

6) On separate WebMO generated images of the optimized structure, write the ^{1}H-NMR and ^{13}C-NMR shift values on the molecule for later comparison with experimental chemical shifts.

Absolute NMR Shifts

Atom	Symbol	Isotropic	Anisotropy
1	C*		
2	C*		
3	C*		
4	C*		
5	C*		
6	C*		
7	C*		
8	C*		
9	H*		
10	H*		
11	O		
12	H*		
13	H*		
14	H*		
15	O		
16	H*		
17	H*		
18	H*		

*Denotes shift relative to TMS

TMS shielding (C)	189.7846
TMS shielding (H)	32.1836
^{1}H NMR Spectrum	
^{13}C NMR Spectrum	
Peak Width (ppm)	0.1

Obtaining and processing the experimental NMR spectrum:

7) Obtain the data for the ^{1}H-NMR and ^{13}C-NMR experimental spectra from the course website. The 5 files for the ^{1}H-NMR data (*5101.fid*) and 5 files for the ^{13}C-NMR data (*5102.fid*) are provided for you in a a compressed file, *auto_21.05.14.zip*. Download and extract the data onto your computer.

https://www.chem.wisc.edu/deptfiles/OrgLab/WebMO/4%27-hydroxyacetophenone.zip

Videos of the processing and analysis described below is available via the course website to assist you.

https://www.chem.wisc.edu/content/experiment-4-computational-molecular-modeling-webmo#NMR

8) To process the ^{1}H-NMR data, open the *fid* data file in the *5101.fid* folder in MestReNova (See the course website for information on acquiring the software).
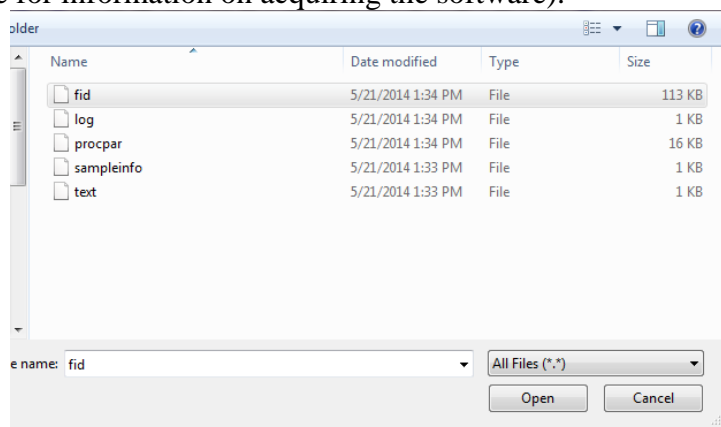
9) To clean-up the spectrum and provide more accurate integrals the phasing of the spectrum may need to be corrected. When opening any fid, immediately pressing **Automatic Phase Correction** ( ), **Baseline Correction** ( ), and **Fit to Highest Intensity** ( ) on the toolbar will generally clean up the spectrum effectively. Do this for all spectra. Occasionally, the spectrum may need a manual phase adjustment (*Shift+P*).

10) Use the manual integral tool (**i**) to select the area to integrate for each signal. To get a more accurate placement of the integral it may be necessary to zoom (**z**) in on each signal. Be sure not to integrate the signal for TMS ($\delta = 0$) and CHCl$_3$ ($\delta = 7.26$).

11) It is possible to set the integration values to convenient values that match the number of hydrogen atoms responsible for that signal. To do so, select the integral value and choose edit integral. In the Integral manage pop-up window, change the normalized value to the desired value. In the spectrum of 4'-hydroxyacetophenone, set the most downfield signal to an integral value of 2.00.
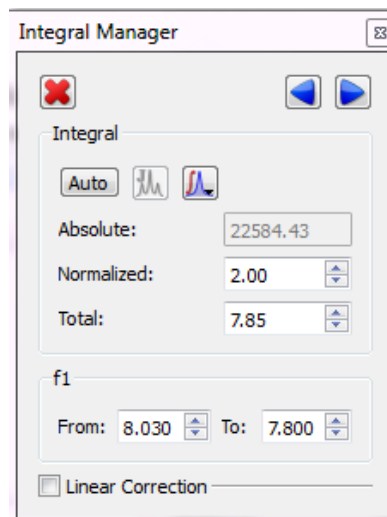
12) Use the expansion button (**e**) to create a zoomed-in inset plot of an interesting region of the spectrum. In this case, an inset plot of the region from about $\delta = 6.7$ to 8.1 ppm may be useful in assigning each ^{1}H-nucleus to its corresponding signal.

13) Peak pick the signals in the spectrum to obtain the approximate J-coupling constants in Hz. First, double click on the expansion plot. Select peaks on the left panel and set the units to Hz using the right panel. Apply the changes. Then press (*Ctrl+K*) in order to peak pick each selected signal. Place the cursor over each signal desired and press the left mouse button. The peak value will be displayed.

14) Before printing make sure the spectrum is zoomed appropriately and aesthetically pleasing. Following any adjustments, the spectrum is ready to save and print. It is advisable to save both the .mnova file as well as a .pdf file and print the pdf.

15) Complete a similar procedure for the ^{13}C-NMR spectrum (*0502.fid*). Remember that in decoupled ^{13}C-NMR the signal integrals are not meaningful. Simply peak pick the important signals in ppm and the spectrum is ready for saving/printing.

16) As in all experiments in CHEM 344, include a copy of each spectrum in your handed-in lab report.

17) For each of the ^{1}H- and ^{13}C-nuclei in the molecule, assign the nucleus to its signal on the experimental NMR spectrum. Compare the estimated chemical shifts for each ^{1}H- and ^{13}C-nucleus by both theoretical methods (empirical parameters & **B3LYP**/**6-31G(d)**) to the experimental values. Explain to what degree the predictions match the experimental spectrum. **(10 pts)**

4.13 Exercises – Relative Basicity of the Nitrogen Atoms of 4-Aminopyridine
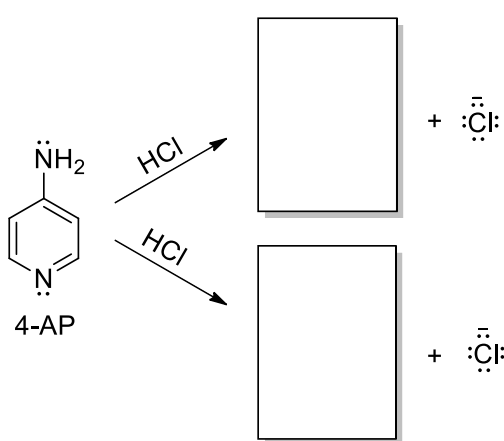
The aromatic heterocycle 4-aminopyridine (4-AP) readily reacts with HCl to produce the protonated species [H-4-AP]$^+$. As shown on the left, 4-AP contains two nitrogen atoms that could potentially be protonated (i.e. react as bases); however, only one product is obtained from this reaction. Clearly, the lone pair on one N-atom is much more basic than the other. *Draw the product of each reaction pathway in your lab notebook.*

Basicity is a thermodynamic property and so we can assess the likelihood of each protonation by analyzing ΔE_{rxn} for each process. In this case, we can simply compare the relative energy difference of the two isomers of [H-4-AP]$^+$ because all the other species are the same in both reactions.

1) Calculate the optimized geometries and relative energies (**B3LYP**/**6-31G(d)**) in kcal/mol of the products (**Optimize + Vib Freq**) for each of the pathways and use these data to fill in the reaction coordinate diagram (right) in your laboratory notebook. Confirm that all of the vibrational frequencies are positive values and that the output is an energy minimum. Label the diagram with the energy difference (kcal/mol) between the protonated species. Use **Clean–up Mechanics** to ensure that all of the species in this exercise have C$_s$ or C$_{2v}$ symmetry.

2) Perform an NBO calculation on the optimized structure of 4-AP in order to view the lone pair hybrid orbitals on the nitrogen atoms. Note their hybridization and draw a 3D image of them superimposed over the molecule in your notebook clearly and correctly indicating their orientation.

3) Viewing the molecular orbitals will provide additional insight into how they interact with the π system of the aromatic ring. In the output from your Natural Bond Orbitals calculations, search for the resultant π-symmetry Molecular Orbitals, noting which atoms are part of the conjugated system. Place at least one relevant 4-AP molecular orbital in your laboratory notebook.

4) Clearly identify the more basic lone pair in 4-AP and use your data to clearly explain why it is more basic. Include any necessary images of molecules, orbitals, or electrostatic potential maps and a discussion of the key points of the previous question to support your answer. **(5 points)**
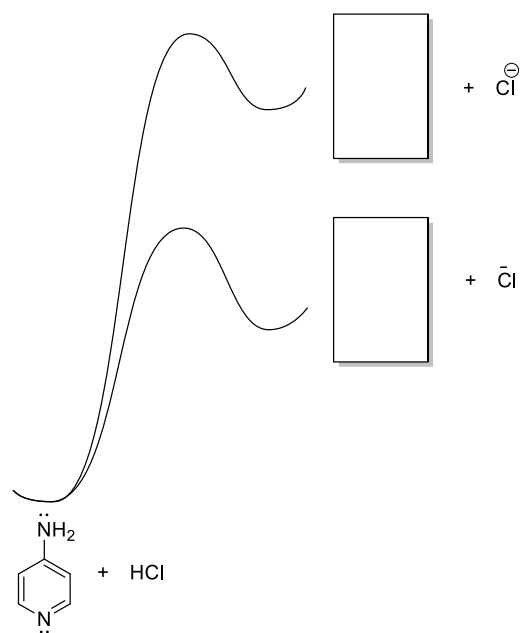
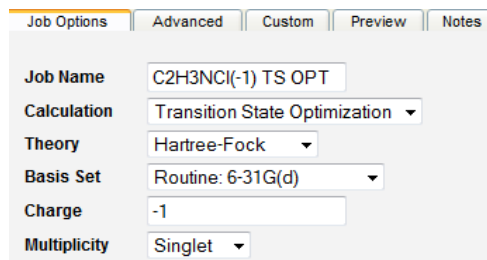## 4.14 Exercises – S$_N$2 Reaction of Chloromethane and Cyanide Anion

Bimolecular nucleophilic substitution (S$_N$2) reactions are of fundamental conceptual importance in organic chemistry. These reactions proceed through a single transition state and follow second order kinetics (first order with respect to each reactant). It is possible to model the transition state of an S$_N$2 reaction and view the molecular motions that correspond to the bond breaking/bond forming process in the transition state. **(5 points for the entire exercise, parts 1 - 6).**

1) Draw in your notebook the electron-pushing mechanism of the S$_N$2 reaction between chloromethane and potassium cyanide as depicted below. Make sure to clearly depict the 3D-geometry of the transition state and label it with a ‡.

$$Rate = k[CH_3Cl][CN^-]$$
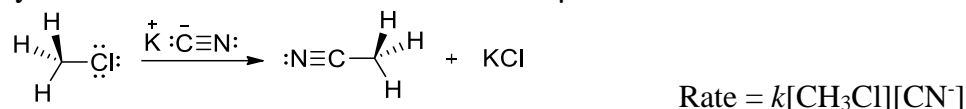
2) The important interactions in an S$_N$2 reaction are between the HOMO of the nucleophile (cyanide anion) and the LUMO of the electrophilic (the carbon atom of chloromethane). Calculate the **HF**/**6-31G(d)** optimized geometries of chloromethane (C$_{3v}$) and cyanide anion (C$_{∞v}$) *via* separate **Opt + Vib Freq** calculations, confirm that each structure is an energy minimum, and use the optimized molecules for an NBO calculation. View the largest lobes of the HOMO of the nucleophile and the LUMO of the electrophile to provide confirmation of the relative orientation and interactions between the nucleophile and electrophile in the reaction. Place these images in your notebook. Use these images and your knowledge of the S$_N$2 reaction to describe the interactions between the nucleophile and electrophile in the reaction and explain how they contribute to the required geometry necessary in this reaction.

3) S$_N$2 reactions are generally not considered to be reversible and so we are not interested in the energies of the reactants and products but, instead, we are interested in the energy of the transition state. In order to build the transition state, care must be taken to build a *trigonal bipyramidal* structure. Follow **exactly** the steps and recommendations listed below to reduce the difficulty of drawing this structure. If done properly, the transition state will be of C$_{3v}$ symmetry; any other symmetry will not necessarily lead to the correct optimized transition state.
   a. Draw a carbon atom with bonds to 5 hydrogen atoms.
   b. Select **Clean-up > Comprehensive - Idealized**.
   c. Set the charge to -1 by right-clicking on the carbon atom or using the adjust tool.
   d. Convert the axial hydrogen atoms to a Cl atom and a CN group (use **Build** tool and avoid using the pre-made cyano group).
   e. Make sure that the bonds are arranged properly and that the carbon atom has a trigonal bipyramidal geometry.
   f. Select **Clean-up > Comprehensive - Idealized**.
   g. Inspect your structure; make any necessary improvements to the geometry.
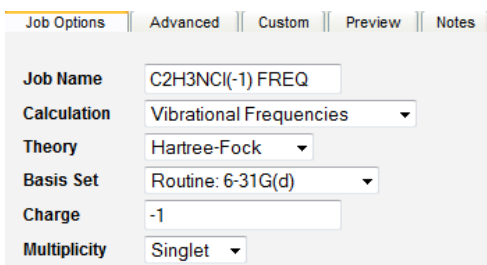
4) Once the molecule is constructed, create a **Transition State Optimization** calculation using **HF**/**6-31G(d)**. Set the Charge to -1 and the multiplicity to singlet. Recall that a transition state is an energy maximum along a pathway between the reactants and products. Gaussian will search to optimize a geometry that has one negative vibrational mode corresponding to that pathway.

Job Options	Advanced	Custom	Preview	Notes
Job Name	C2H3NCl(-1) TS OPT			
Calculation	Transition State Optimization ▾			
Theory	Hartree-Fock ▾			
Basis Set	Routine: 6-31G(d) ▾			
Charge	-1			
Multiplicity	Singlet ▾			

5) If the calculation is correct, the output geometry will represent an energy maximum along the reaction pathway. This can be confirmed by doing a **Vibrational Frequencies** calculation, which will allow you to view the vibrational mode depicting the molecular motion along the reaction pathway at the transition state. In order to use the optimized geometry for this calculation, select "**New Job Using This Geometry.**" If the output of the Transition State Optimization calculation is correct, the Vibrational Frequency calculation will produce an output file with exactly 1 negative vibrational mode.
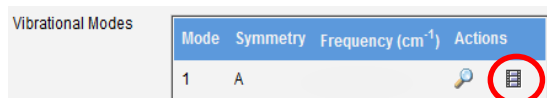
Job Options	Advanced	Custom	Preview	Notes
Job Name	C2H3NCl(-1) FREQ			
Calculation	Vibrational Frequencies ▾			
Theory	Hartree-Fock ▾			
Basis Set	Routine: 6-31G(d) ▾			
Charge	-1			
Multiplicity	Singlet ▾			

Note: We typically do not want to model a conformation that corresponds to an energy maximum on the potential energy surface of a molecule (i.e. a transition state). However, in the case of this S_N2 reaction, we are interested in learning about the transition state and so a negative vibrational frequency is OK.

6) WebMO allows you to visualize the molecular motions that correspond to the calculated vibrational modes. These can be displayed by clicking the movie icon on the Vibrational Modes list in the output file.

| Vibrational Modes	Mode	Symmetry	Frequency (cm^{-1})	Actions
	1	A		🔍 ▤

View this animation to confirm that the negative vibrational mode corresponds to the transition from reactants and products. Copy the value of the negative vibrational frequency into your laboratory notebook and depict the vibrations associated with that value.

Note: The movie icon is very useful for occasions when you calculate a transition state by mistake. When this happens, click the movie icon of the negative mode and study the motions of the molecule to understand which bonds are trying to break or twist (i.e. how the molecule is trying to get out of the transition state). Make the changes and resubmit the job.

7) To reveal the reaction pathway of the imaginary vibrational mode, re-optimize the transition state using **B3LYP**/**6-31G(d)** (not **HF**/**6-31G(d)**) and perform an intrinsic reaction coordinate (IRC) calculation. **When correct and complete, this calculation will show changes in the molecular geometry from the transition state to the reactants or products. This process can be viewed by clicking on the geometry sequence movie icon and the energy curve of the reaction is plotted in a graph by WebMO.**

4.15 Exercises – Bond Length and Bond Strength

1) The relative reactivity of carbon-halogen (C-X) bonds is a critical concept for understanding the reactivity of many organic molecules. Such reactivity will be important in two experiments that you will perform during CHEM 344 (Grignard and Suzuki reactions). The reactivity of the C-X bond (or any bond) is itself dependent on the bond strength, with stronger bonds generally being less reactive than weaker bonds. The strength of a bond can be assessed by calculation of the energy required for homolytic cleavage of that bond (i.e. the energy required to form a pair of radicals from the bond). To explore this concept, you will determine the C-X bond dissociation energy (BDE, kcal/mol) for a series of halobenzenes (Ph-X, X = F, Cl, Br) using the equation shown below.

X = F, Cl, Br
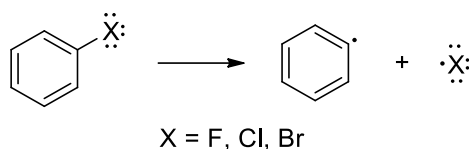
$$BDE = (E_{Ph\ radical} + E_{X\ radical}) - E_{PhX}$$

Optimize each molecule shown above (**Opt + Vib Freq, B3LYP/6-31G(d)**) and confirm that you have modeled an energy minimum. **In order to make a radical species**, you will need to build an atom with an open valence. For the phenyl radical, the simplest method is to delete one hydrogen atom from benzene (do not clean up the structure after deleing the H-atom). For the halogen radicals, simply place a halogen atom in the build window and submit the calculation. **For all radicals**, make sure that the charge is neutral and that the multiplicity is set to doublet in the Job Options window. These calculations may take a bit longer than usual so set the number of processors/node to 2 on the Advanced Job Options tab. Report the energies (kcal/mol) of all species in an organized table.

2) In a separate organized table, display your BDE results and the C – X bond distances of each aryl halide (Ångstrom, Å, 10^{-10} m). Bond distances are measured by clicking the Adjust icon, clicking on an atom in the bond you wish to measure, keeping pressed the Shift key and then clicking the other atom in the bond. The bond distance will appear in **blue** at bottom left corner of the screen.

3) Use your data to explain the relationship between BDE, bond length, and chemical reactivity in this series of halobenzenes **(5 points)**.

4.16 Exercises – {Fun Insights into Molecules}

When learning the basics of molecular structure it is easy to pick up many generalizations and over-simplifications that can lead to suboptimal understanding of structures. The **OPTIONAL** exercises below represent some simple cases where these generalizations and over-simplifications lead to incorrect interpretations of molecular structure. It is recommended that you try to answer the question based upon your previous learning and compare that to the insight that can be gained from computational chemistry.

a) Let's take a look at formal charges. While generally thought of as book-keeping tools, they are often used as real indicators of charge by students. For the molecules shown below, draw a Lewis structure of the molecule and then calculate the NPA charges and an electrostatic potential map of a geometry optimized using **B3LYP**/**6-31G(d)**. What is the calculated charge at each atom of the charged molecules shown below? Do the formal charges accurately represent the actual calculated charge? **The charge distribution and structures of H_2OCl^+, NO_2^+, and CH_3CO^+ are calculations specifically related to experiments in CHEM 344.**
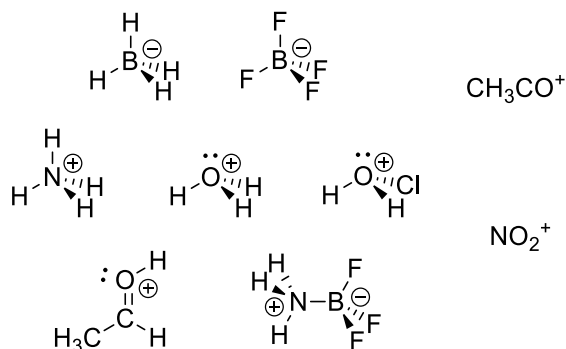
b) Next, lets think about the repulsive size of lone pairs. The VSEPR theory explains the decreasing H-X-H (X = C, N, O) bond angles in CH_4, NH_3, and H_2O by invoking the notion that lone pairs are highly diffuse and repulsive, and exert a large steric effect on neighboring electron pairs. In essence, they "compress" the bond angles in CH_4, NH_3, and H_2O. With this in mind, would you expect the conformational equilibrium of piperidine (shown below) to favor location of the N-atom lone pair at the axial or equatorial position? Complete some **B3LYP**/**6-31G(d)** geometry optimizations of each isomer and calculate the equilibrium constant (K_{eq}). Is this outcome consistent with the predictions of VSEPR theory?
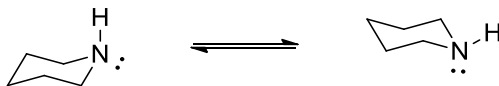
c) Finally, it is very easy to make some incorrect assumptions about molecular geometries using VSEPR and periodic trends. Compute the **B3LYP**/**6-31G(d)** optimized geometries of each of the following oxygen containing molecules and their sulfur and selenium-containing analogs. Measure their bond angles and compare them to each other. Are these values what you would expect from VSEPR? For the peroxide (Me-O-O-Me) and corresponding disulfide and diselenide, you may need to look for more than one conformer. Performing a Natural Bond Orbital calculation will provide a valuable insight into the hybridization of each of the oxygen, sulfur, and selenium lone pairs.

$$H_3C \diagdown \!\!\!{}^{O} \!\!\!\diagup H \qquad H_3C \diagdown \!\!\!{}^{S} \!\!\!\diagup H \qquad H_3C \diagdown \!\!\!{}^{Se} \!\!\!\diagup H$$

$$Me \diagup \!\!\!{}^{O} \!\!\!\diagdown \!\!\!{}_{O} \!\!\!\diagup Me \qquad Me \diagup \!\!\!{}^{S} \!\!\!\diagdown \!\!\!{}_{S} \!\!\!\diagup Me \qquad Me \diagup \!\!\!{}^{Se} \!\!\!\diagdown \!\!\!{}_{Se} \!\!\!\diagup Me$$
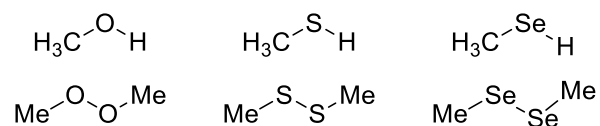
CHEM 344 Computational Molecular Modeling

Name:

Report

Discretionary pts (legibility, organization etc.)   _____/5

4.9   Exercises – Conformations of Butane   _____/5

4.10   Exercises – Conformations of Substituted Cyclohexanes   _____/5

4.11   Exercises – ED and EW Aromatic Substituents   _____/10

4.12   Exercises – NMR Prediction   _____/10

4.13   Exercises – Relative Basicity of the Nitrogen Atoms of 4-Aminopyridine   _____/5

4.14   Exercises – S_N2 Reaction of Chloromethane and Cyanide Anion   _____/5

4.15   Exercises – Bond Length and Bond Strength in Aryl Halides   _____/5

4.16   Exercises – {OPTIONAL} Fun Insights into Molecules   _____/0

                                                           Total   **_____/50**