

Introduction

The tutorials that follow provide a brief introduction to both the user interface and the calculation capabilities of *Spartan Student*. The intent is to provide hands-on experience with use of the user interface and in doing so, illustrate the set up, submission, and interpretation of molecular mechanics and quantum chemical calculations. Tutorials are not intended to illustrate the full range of capabilities available in *Spartan Student*, but focus on use of the program to calculate equilibrium and transition-state geometries, to search conformation space, to align molecules, to evaluate reaction thermochemistry and activation energetics and to obtain NMR and infrared spectra.

Operating Spartan (Chapter 2 in the *Spartan Student* overview) outlines the basic workings of *Spartan's* graphical user interface. It should be reviewed before starting the tutorials and referred to as needed. The first and second tutorials (**Basic Operations** and **Acrylonitrile: Building an Organic Molecule**) cover a number of important general features of the program and should be completed first and in that order. The next twelve tutorials cover more specialized topics and may be completed in any order. The last five tutorials point to an entirely different mode of using *Spartan Student* by drawing on the large amount of information from the Spartan Spectra and Properties Database (SSPD).

The **Basic Operations** tutorial requires a file of previously calculated results. In addition, other tutorials need access to experimental spectra in the event that the computer is not online or that specific spectra are not available online. For Windows, these files are located in the tutorials directory accessible from *ProgramFiles(x86)/Wavefunction/Spartan Student v5*, but for security reasons should be copied to a separate location. For Macintosh, this is located in the *SpartanStudent v5* disc image (CD-ROM and/or .dmg file).


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1

Basic Operations

*This tutorial introduces a number of basic operations in **Spartan Student** required for molecule manipulation, property query and spectra and graphics display. Specifically it shows how to: i) open molecules, ii) view different model styles and manipulate molecules on screen, iii) measure bond distances, angles and dihedral angles, iv) display energies, dipole moments, atomic charges and infrared and NMR spectra, and v) display graphical surfaces and property maps. Spreadsheet operations are not illustrated, no molecules are built and no quantum chemical calculations are performed.*

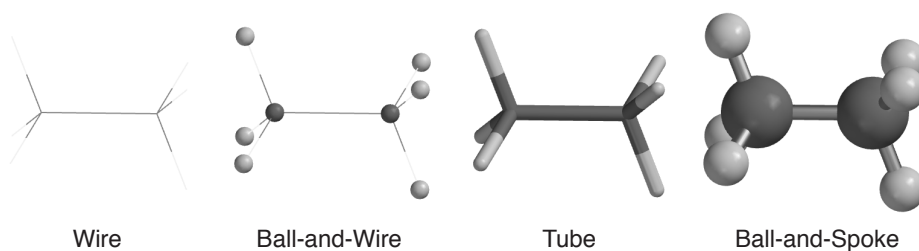
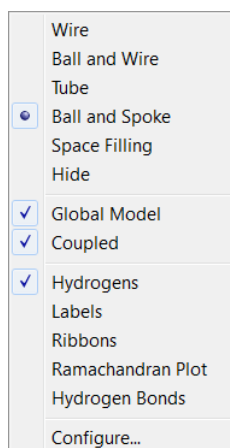
1. Start **Spartan**. Click (left mouse button) on **File** from the menu bar that appears at the top of **Spartan Student's** main window.* Click on **Open...** from the **File** menu that appears. Alternatively, click on the  icon at the top of the screen. A file browser appears.

Move to the *tutorials*** directory, click on **basic operations** and click on **Open** (or double click on **basic operations**). A single file containing *ethane*, *acetic acid dimer*, *propene*, *ammonia*, *hydrogen peroxide*, *acetic acid*, *water*, *cyclohexanone*, *camphor*, *ethylene*, *benzene*, *aniline* and *cyclohexenone* will be opened. A ball-and-spoke model for the first molecule (*ethane*) will be displayed, and its name appears at the bottom right of the screen.

2. Practice rotating (*move* the mouse while holding down the left button) and translating (*move* the mouse while holding down the right button). Click on **Model** from the menu bar.

* The right and left buttons on a touchpad may be used in place of the right and left mouse buttons.

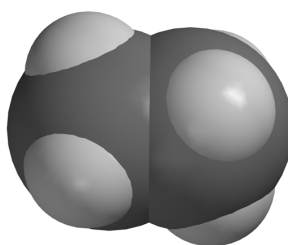
** For Windows, these files are located in the tutorials directory in *ProgramFiles(x86)/Wavefunction/Spartan Student v5* but for security reasons should be copied to a separate location. For Macintosh, this is located at the top level on the installation CD-ROM.



One after another, select **Wire**, **Ball and Wire**, **Tube** and finally **Ball and Spoke** from the **Model** menu. All four model styles for *ethane* show roughly the same information. The wire model looks the most like a conventional line formula. It uses color to distinguish different atoms, and one, two and three lines between atoms to indicate single, double and triple bonds, respectively.




The ball-and-wire model is identical to the wire model, except that atom positions are represented by small spheres, making it easy to identify atom locations. The tube model is similar to the wire model, except that bonds are represented by solid cylinders. The tube model is better than the wire model in conveying three-dimensional shape. The ball-and-spoke model is a variation on the tube model; atom positions are represented by colored spheres, making it easier to see atom locations.

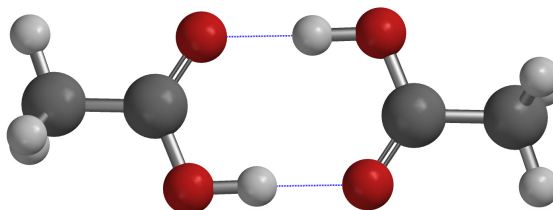
Select **Space Filling** from the **Model** menu.



Space-Filling

The space-filling model is different from the other models in that bonds are not shown. Rather, each atom is displayed as a colored sphere that represents its approximate size. Thus, the space-filling model for a molecule provides a measure of its size. While lines between atoms are not drawn, the existence (or absence) of bonds can be inferred from the extent to which spheres on neighboring atoms overlap. If two spheres substantially overlap, then the atoms are almost certainly bonded, and conversely, if two spheres barely overlap, then the atoms are not bonded. Intermediate overlaps suggest weak bonding, for example, hydrogen bonding.

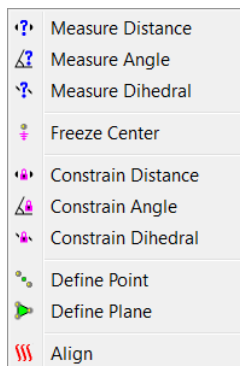
3. Click once on the right arrow key  at the bottom left of the screen. This will move to the next molecule in the document, ***acetic acid dimer***. Its name will appear at the bottom of the screen. If you make a mistake, use the backward  or forward  step keys to locate ***acetic acid dimer*** in the document. Switch to a space-filling model and look for overlap between the (OH) hydrogen on one acetic acid molecule and the (carbonyl) oxygen on the other. Return to a ball-and-spoke model and select **Hydrogen Bonds** from the **Model** menu.






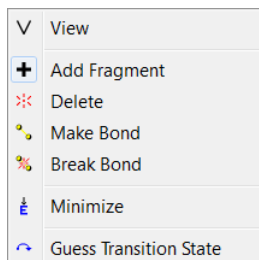
Ball-and-Spoke model for acetic acid dimer with hydrogen bonds displayed



The two hydrogen bonds, that are responsible for holding the acetic acid molecules together, will be drawn.


4. Distances, angles, and dihedral angles can easily be measured using **Measure Distance**, **Measure Angle**, and **Measure Dihedral**, respectively, from the **Geometry** menu.






- a) **Measure Distance**: This measures the distance between two atoms. *Click* once on  to move to the next molecule, *propene*, and then select **Measure Distance** from the **Geometry** menu (or *click* on the  icon at the top of the screen). *Click* on a bond or on two atoms (the atoms do not need to be bonded). The distance (in Ångstroms) will be displayed at the bottom of the screen. Repeat the process for several atoms. When you are finished, select **View** from the **Build** menu (or *click* on the  icon at the top of the screen).

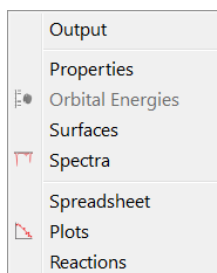



- b) **Measure Angle**: This measures the angle around a central atom. *Click* once on  to move to the next molecule, *ammonia*, and then select **Measure Angle** from the **Geometry** menu (or *click* on the  icon at the top of the screen). *Click* first on H, then on N, then on another H. Alternatively, *click* on two NH bonds. The HNH angle (in

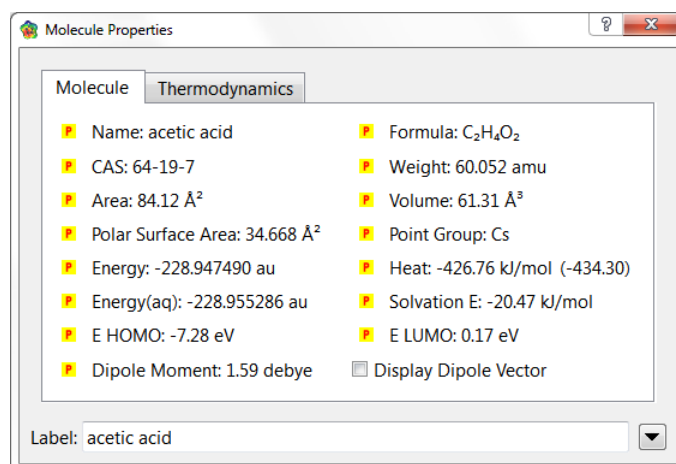
degrees) will be displayed at the bottom of the screen. *Click* on  when you are finished.

c) **Measure Dihedral**: This measures the angle formed by two intersecting planes, one containing the first three atoms selected and the other containing the last three atoms selected. *Click* once on  to move to the next molecule, **hydrogen peroxide**, then select **Measure Dihedral** from the **Geometry** menu (or *click* on the  icon at the top of the screen) and then *click* in turn on the four atoms (HOOH) that make up hydrogen peroxide. The HOOH dihedral angle will be displayed at the bottom of the screen. *Click* on  when you are finished.

5. Energies, dipole moments and atomic charges among other calculated properties, are available from **Properties** under the **Display** menu.

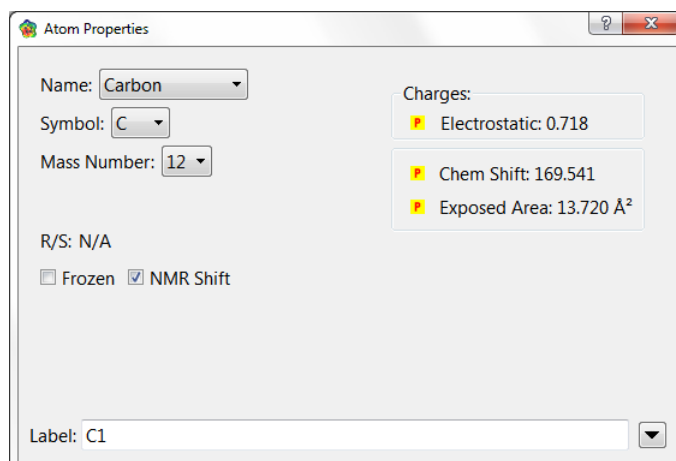



a) **Energy**: *Click* once on  to move to the next molecule, **acetic acid**, and then select **Properties** from the **Display** menu. The **Molecule Properties** dialog appears. It is divided into two parts designated by tabs. **Molecule** provides the energy and other information relating to the isolated molecule, **Thermodynamics** provides the enthalpy, entropy, heat capacity, Gibbs energy and zero-point energy. Make certain that the **Molecule** tab is selected.




This provides the energy for acetic acid in atomic units (**Energy** in au). Also provided is an estimate of the energy in water (**Energy(aq)** in au) and the difference between the two (**Solvation E** kJ/mol).

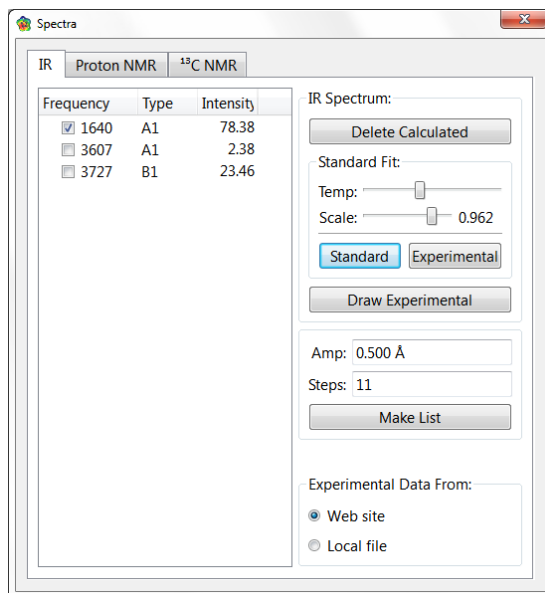
- b) **Dipole Moment:** The magnitude of the dipole moment (**Dipole Moment** in debyes) is also provided in the **Molecule Properties** dialog. A large dipole moment indicates large separation of charge. You can attach the dipole moment vector, $\text{+} \rightarrow$ where the + side refers to the positive end of the dipole, to the model on the screen, by *checking* the box to the left of **Display Dipole Vector** near the bottom of the dialog.
- c) **Atomic Charges:** To display the charge on an atom, *click* on it with the **Molecule Properties** dialog on the screen. The **Atom Properties** dialog replaces the **Molecule Properties** dialog.



Electrostatic atomic charges are given in units of electrons. A positive charge indicates a deficiency of electrons on an atom and a negative charge, an excess of electrons. Repeat for other atoms. Confirm that the positively-charged atom(s) lie at the positive end of the dipole moment vector. When you are finished, close the dialog by *clicking* on .


- d) **Infrared Spectra:** Molecules vibrate (stretch, bend, twist) even if they are cooled to absolute zero. This is the basis of infrared spectroscopy, where absorption of energy occurs when the frequency of a particular molecular motion matches the frequency of the light. Infrared spectroscopy is important for identifying molecules as different functional groups vibrate at noticeably different and characteristic frequencies.

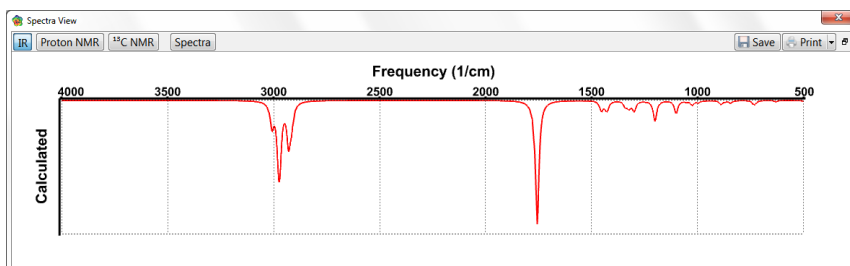
Click once on  to move to the next molecule in the document, **water**. To animate a vibration, select **Spectra** from the **Display** menu and *click* on the **IR** tab. This leads to the **IR Spectra** dialog.



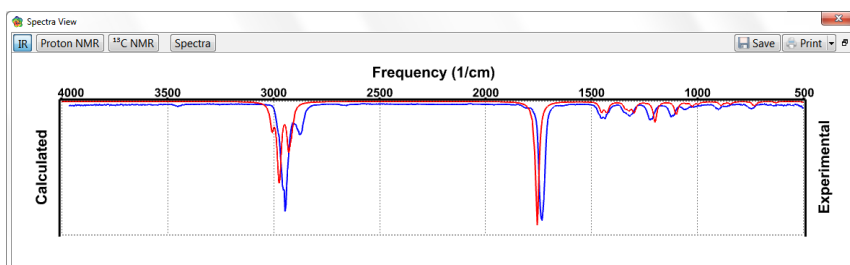
This displays the three vibrational frequencies for the water molecule, corresponding to bending and symmetric and asymmetric stretching motions. One after the other, *click* in the box to the left of each frequency and examine the motion.

(To vary the animation speed, select **Preferences** from the **Options** menu, *click* on the **Settings** tab and move the slider bar below **Animation Speed**.) Turn off the animation by *clicking* in the box of the selected frequency when you are finished.

Click once on  to move to *cyclohexanone*, the next molecule in the list. The **Spectra** dialog now lists 45 frequencies corresponding to the 45 vibrational motions of this molecule with 17 atoms. Examine each in turn (*click* on the entry in the dialog) until you locate the frequency corresponding to the carbonyl stretch. Next, *click* on **Draw Calculated** at the top of the dialog. The infrared spectrum of cyclohexanone appears at the bottom of the screen. Note that the line corresponding to the carbonyl stretch is isolated and that it is very intense, making it easy to find.

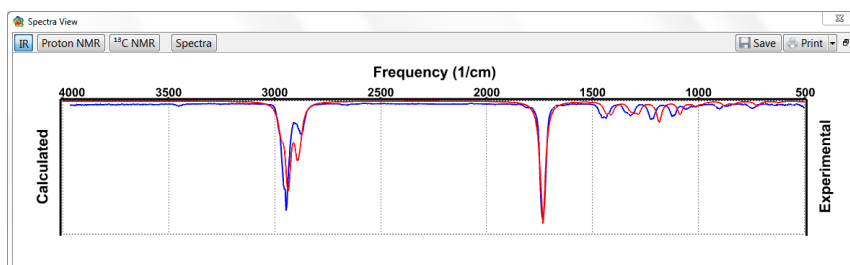


If your computer is connected to the internet, you can draw the experimental IR spectrum for cyclohexanone on top of the calculated spectrum. Select **Web Site** under **Experimental Data From:** at the bottom of the **Spectra** dialog. *Click* on **Draw Experimental**.




If you are not online or have trouble downloading the experimental spectrum, select **Local File** under **Experimental Data From:** and find *cyclohexanoneIR.dx* in the *tutorials* directory.

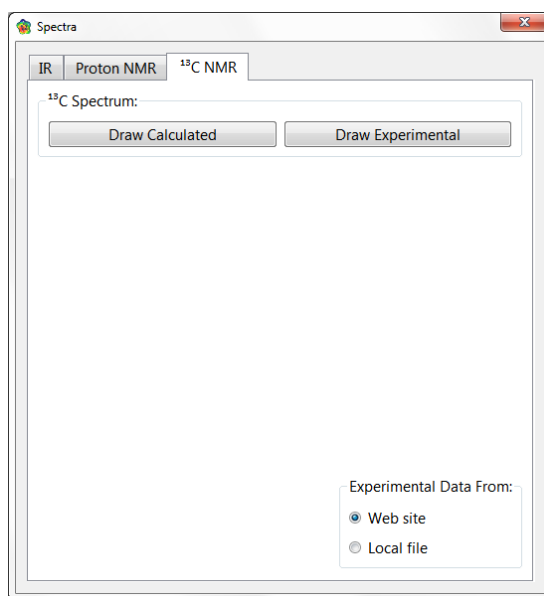
The two spectra are broadly similar. To bring the calculated spectrum into even closer agreement with the experimental spectrum, *click* on the **Experimental** button under **Standard Fit** at the center of the **IR Spectra** dialog.



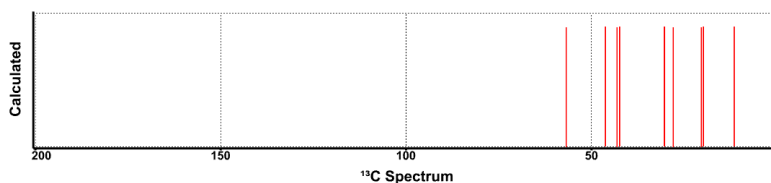
You can remove the plot by *clicking* on both **Delete Calculated** and **Delete Experimental** in the **Spectra** dialog. (These buttons have replaced **Draw Calculated** and **Draw Experimental**, respectively.)

- e) **NMR Spectra:** Along with mass spectrometry, NMR spectroscopy is the most powerful tool available with which to assign molecular structure. Many nuclei exhibit NMR spectra, but proton and ^{13}C are by far the most important.

Click once on  to move to the next molecule in the document, *camphor*. With the **Spectra** dialog on screen, *click* on the ^{13}C NMR tab to bring up the ^{13}C NMR Spectra dialog.

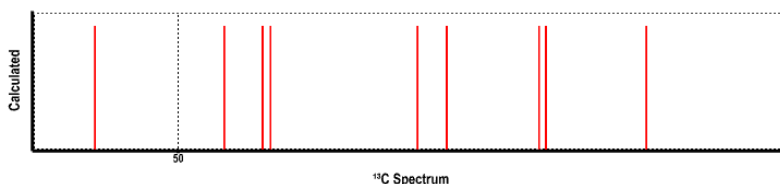


Click on **Draw Calculated** under ^{13}C Spectrum to show the calculated ^{13}C spectrum.

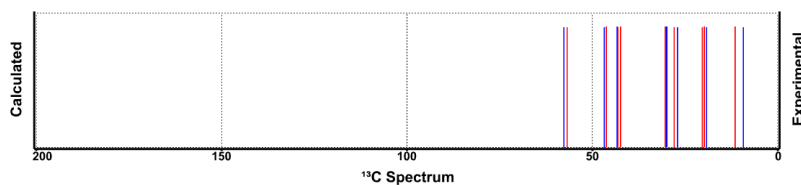


There are nine lines, in the range of 200 to 0 ppm (the tenth line corresponding to the carbonyl carbon is at 218 ppm).

To magnify a region of the spectra, position the cursor at one corner of the region, *drag* the mouse to the opposite corner while holding down the left button, then release the button. Magnifying in the region from 0 to 60 ppm yields the plot.





Select **Local File** under **Experimental Data From:** at the bottom right of the dialog and find *camphor.NMR.dx* in the *tutorials* directory and click on **Draw Experimental** to draw the experimental spectrum.



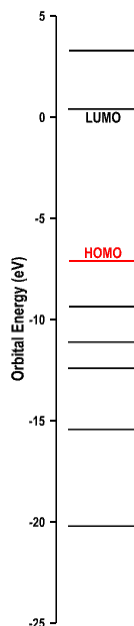
Remove the spectra by *clicking* on **Delete Calculated** and **Delete Experimental** in the ^{13}C NMR Spectra dialog. (These buttons have replaced **Draw Calculated** and **Draw Experimental**, respectively.)

To obtain numerical values for the individual chemical shifts, select **Properties** from the **Display** menu (to bring up the **Atom Properties** dialog) and *click* on the atom of interest. Note that proton shifts in addition to ^{13}C shifts are available.

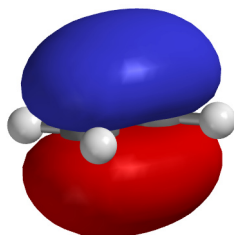
6. *Spartan Student* permits display, manipulation and query of a number of important graphical quantities resulting from quantum chemical calculations. Most important are the **electron density** (that reveals how much space a molecule actually takes up), the **bond density** (that reveals chemical bonds), and key **molecular orbitals** (that provide insight into both bonding and chemical reactivity). In addition, the **electrostatic potential map**, an overlay of the electrostatic potential (the attraction or repulsion of a positive charge for a molecule) on the electron density, is valuable for describing overall molecular charge distribution as well as anticipating sites of electrophilic addition. Another indicator of electrophilic addition is provided by the **local ionization potential map**, an overlay of the energy of electron removal (ionization) on the electron density. Finally, an indicator of nucleophilic addition is provided by the **|LUMO| map**, an overlay of the absolute value of the lowest-unoccupied molecular orbital (the LUMO) on the electron density.

Click once on  to move to the next molecule in the list, **ethylene**. Select **Orbital Energies** from the **Display** menu (or *click* on ). An orbital energy diagram for ethylene will appear at the left of the screen. This provides the energies of all

six occupied valence molecular orbitals and two lowest-energy unoccupied molecular orbitals.

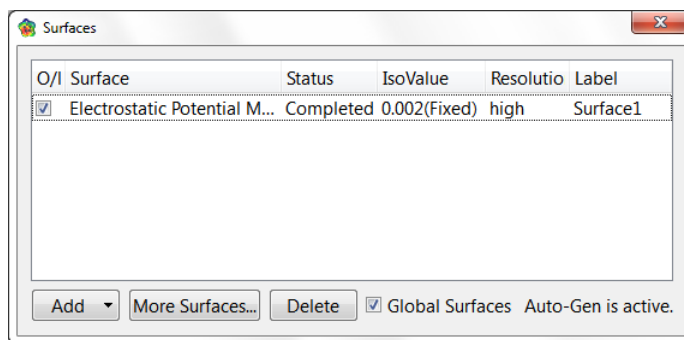


Click on the energy level in the diagram labelled **HOMO**. In a second, the familiar π bond in ethylene will appear.

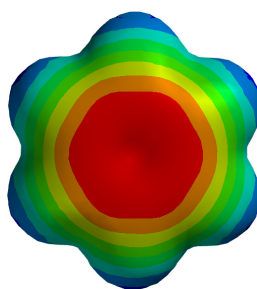


Note that the graphic is made up of separate blue and red surfaces. These correspond to positive and negative values of the orbital (the absolute sign is arbitrary). Examine the other occupied orbitals (by *clicking* on their respective energy levels in the diagram) as well as the lowest-unoccupied molecular orbital (the **LUMO**).

Click once on  to move to the next molecule in the list, **benzene**. Select **Surfaces** from the **Display** menu. The **Surfaces** dialog appears.



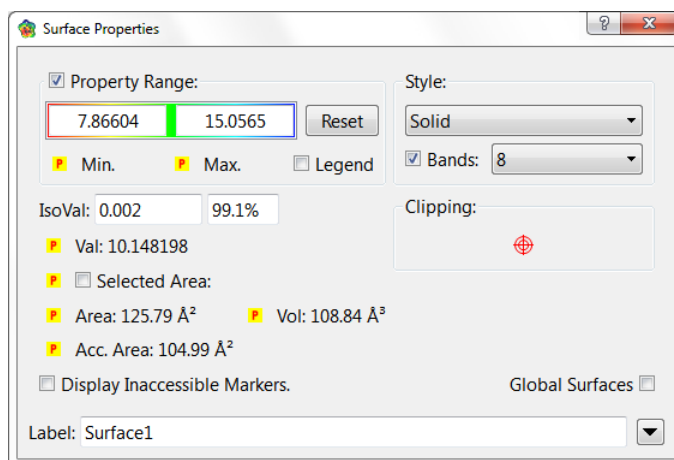
Select ***Electrostatic Potential Map*** inside the **Surfaces** dialog (*click* inside the box to the left of the name). An electrostatic potential map for benzene will appear.*




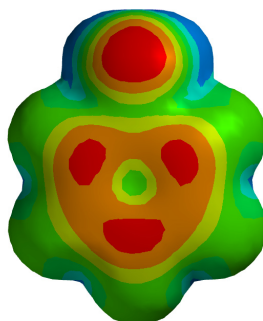
Click on the map. The **Style** menu will appear at the bottom right of the screen. Select **Transparent** from this menu. This makes the map transparent and allows you to see the molecular skeleton underneath. Go back to a **Solid** display (**Style** menu) in order to clearly see color differences. The surface is colored red in the π system (by convention, indicating negative potential and the fact that this region is attracted to a positive charge), and blue in the σ system (by convention, indicating positive potential and the fact that this region is repelled by a positive charge). Bring up the **Properties** dialog (**Display** menu) and *click* on the map. Remove the checkmark from the box to the left of **Bands** in the **Surface Properties** dialog to replace the series of color bands (discrete display) by a continuous display.**


* The graphics shown in this document have been obtained at high resolution. In order to reduce its size, the file associated with this tutorial provides medium-resolution images.

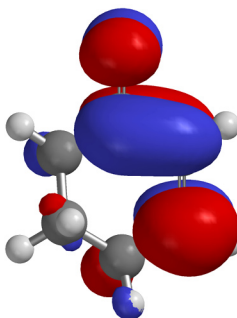
** Discrete displays are the default in *Spartan Student*. You can change the default to continuous displays from the **Molecule Preferences** dialog (**Preferences** under the **Options** menu; **Chapter 10**).



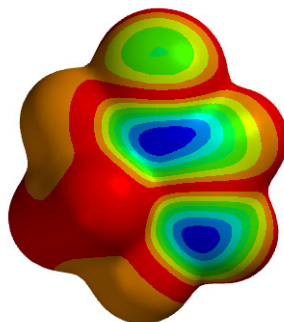
Click once on  to move to the next molecule in the list, ***aniline***, and select ***Local Ionization Potential Map*** inside the **Surfaces** dialog. By convention, red regions on a local ionization potential map indicate areas from which electron removal (ionization) is relatively easy, meaning that they are subject to electrophilic attack. These are easily distinguished from regions where ionization is relatively difficult (by convention, colored blue). Note that the *ortho* and *para* ring carbons are more red than the *meta* carbons, consistent with the known directing ability of the amino substituent.



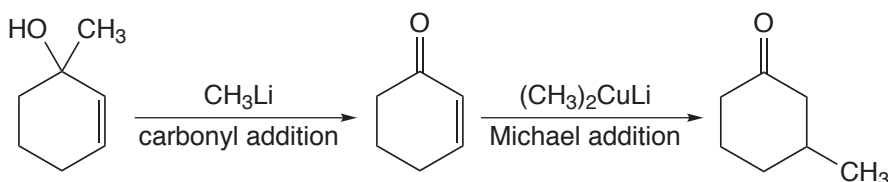
Click once on  to move to the next molecule in the list, ***cyclohexenone***, and select ***LUMO*** inside the **Surfaces** dialog. The resulting graphic portrays the lowest-energy empty molecular orbital (the LUMO) of cyclohexenone. This orbital is delocalized onto several atoms and it is difficult to tell where exactly a pair of electrons (a nucleophile) will attack the molecule.




A clearer portrayal is provided by a LUMO map, that displays the (absolute) value of the LUMO on the electron density surface. By convention, the color blue is used to represent maximum value of the LUMO and the color red, minimum value. First, remove the LUMO from your structure (select **LUMO** in the **Surfaces** dialog) and then turn on the LUMO map (select **|LUMO|Map** in the dialog).



Note that there are two blue regions, one directly over the carbonyl carbon and the other over the β carbon. This is entirely consistent with known chemistry. Enones may either undergo carbonyl addition or conjugate (Michael) addition.



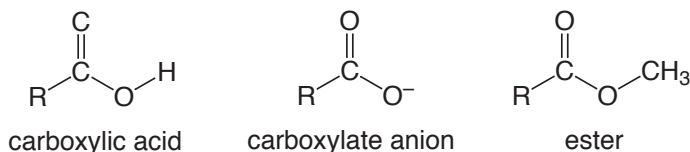
- When you are finished, close the document by selecting **Close** from the **File** menu or alternatively by *clicking* on the  icon at the top of the screen.

2

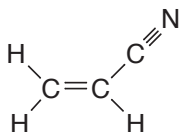
Acrylonitrile: Building an Organic Molecule


This tutorial illustrates use of the organic model kit, as well as the steps involved in examining and querying different molecular model styles and in carrying out a quantum chemical calculation.

The simplest building blocks incorporated into **Spartan Student's** organic model kit are atomic fragments. These constitute specification of atom type, for example, carbon, and local environment, for example, tetrahedral. However, much of organic chemistry is organized around functional groups, collections of atoms, the structure and properties of which are roughly the same in every molecule. The organic model kit also incorporates a small library of functional groups that can easily be extended or modified. For example, the carboxylic acid group may be modified to build a carboxylate anion (by deleting a free valence from oxygen), or an ester (by adding tetrahedral carbon to the free valence at oxygen).

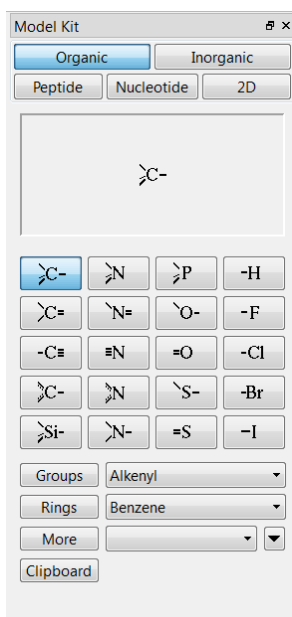


Acrylonitrile provides a good opportunity to illustrate the basics of molecule building in **Spartan Student**, as well as the steps involved in carrying out and analyzing a quantum chemical calculation.



1. Click on **File** from the menu bar. Then click on **New** from the menu that appears (or click on the  icon at the top of the

screen). The organic model kit appears.



At the center of the kit is a library of atomic fragments. *Click* on trigonal planar sp^2 hybridized carbon >C- from the fragment library. A model of the fragment appears at the top of the model kit. Bring the cursor anywhere on screen and *click*. Rotate the carbon fragment (*drag* the mouse while holding down the left button) so that you can clearly see both the double free valence (=) and the two single free valences (-).

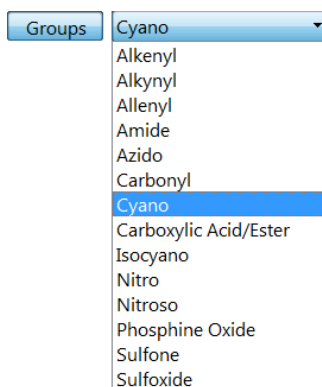
Spartan Student's model kits connect atomic fragments (as well as groups, rings and ligands) through free valences. Any free valences that remain upon exiting a model kit are automatically converted to hydrogen atoms.

2. sp^2 carbon is still selected. *Click* on the double free valence. The two fragments are connected by a double bond, leaving you with ethylene. The name **ethylene** will appear at the bottom right of the screen.* If you make a mistake and *click* instead on the single free valence, select **Undo** from the **Edit** menu. You can also start over by selecting **Clear** from the **Edit** menu.



* This means that ethylene is in the subset of the SSPD database included with *Spartan Student*.



Spartan Student's organic model kit allows only the same type of free valences to be connected, for example, single to single, double to double, etc.

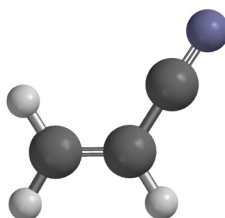
3. Click on **Groups** in the model kit, and select **Cyano** from the functional groups available from the menu.



Click on any of the four single free valences on ethylene (they are equivalent). This bonds the cyano group to ethylene, leaving you with acrylonitrile.* Its name will now appear at the bottom right of the screen.

4. Select **Minimize** from the **Build** menu (or click on the  icon at the top of the screen). The final molecular mechanics energy (36.2 kJ/mol) and symmetry point group (C_s) are provided at the bottom right of the screen.
5. Select **View** from the **Build** menu (or click on the  icon at the top of the screen). The model kit disappears, leaving only a ball-and-spoke model of acrylonitrile on screen.

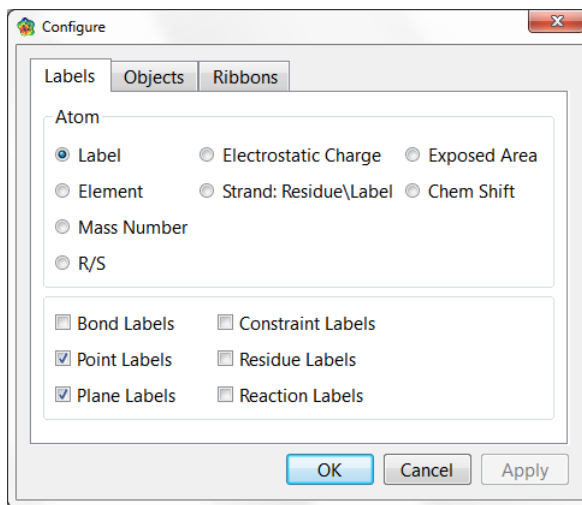
* You could also have built acrylonitrile without using the **Groups** menu. Starting from scratch (**Clear** from the **Edit** menu), first build ethylene as above, then select sp hybridized carbon  from the model kit and then click on one of the free valences on ethylene. Next, select sp hybridized nitrogen  from the model kit and click on the triple free valence on the sp carbon. Alternatively, you could have built the molecule entirely from groups. Starting from scratch, click on **Groups**, select **Alkenyl** from the menu and click anywhere on screen. Then select **Cyano** from the menu of functional groups and click on one of the free valences on ethylene. In general, molecules can be constructed in more than one way.



ball-and-spoke model

This model can be rotated, translated and zoomed by using the mouse in conjunction with keyboard functions. To rotate the model, *drag* the mouse while holding down the left button; to rotate in the plane of the screen also hold down the **Shift** key. To translate the model, *drag* the mouse with the right button depressed. To zoom the model (translation perpendicular to the screen), use the center mouse wheel (scroll wheel) if available, or hold down the **Shift** key in addition to the right button while *dragging* the mouse up (zoom in) or down (zoom out).*

6. Select **Configure...** from the **Model** menu, and *click* to select **Mass Number** under **Atom** in the **Configure** dialog that appears.

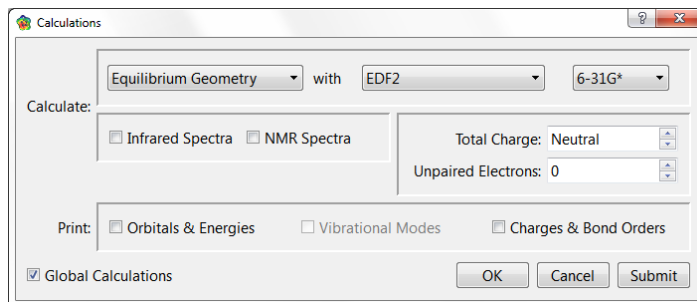


Click on **OK** to remove the dialog. Mass numbers will appear next to the individual atoms. Remove the atom labels by *clicking* to deselect **Labels** from the **Model** menu.**

* For touchpads, the thumb-finger touch/open gesture also zooms in and pinching zooms out.

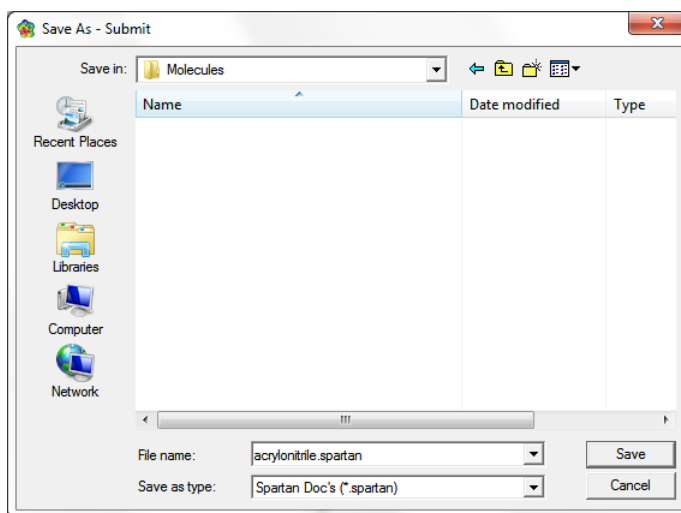
** **Labels** from the **Model** menu is automatically selected (turned on) following a change in the **Configure** dialog by choosing **OK** or **Apply**.

7. Select **Calculations...** from the **Setup** menu, and perform the following operations in the resulting **Calculations** dialog.



Select **Equilibrium Geometry** from the leftmost menu to the right of **Calculate**. This specifies optimization of equilibrium geometry. Select **EDF2** and then **6-31G*** from the middle and right menus to the right of **Calculate**. This specifies an EDF2 density functional calculation using the 6-31G* basis set. This method generally provides a reliable account of geometries. When you finish, *click* on **OK** to remove the dialog.

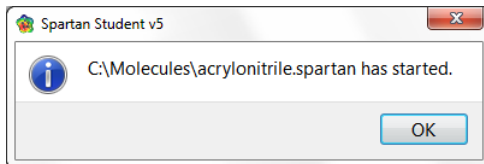
8. Select **Submit** from the **Setup** menu.* A file browser appears.



The name *acrylonitrile* will be presented to you in the box to the right of **File name**. Either use it or type in whatever name

* You could also have *clicked* on **Submit** inside the **Calculations** dialog.

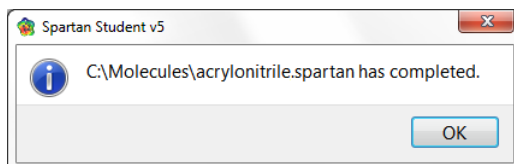
you like and then *click* on **Save**.* You will be notified that the calculation has been submitted.



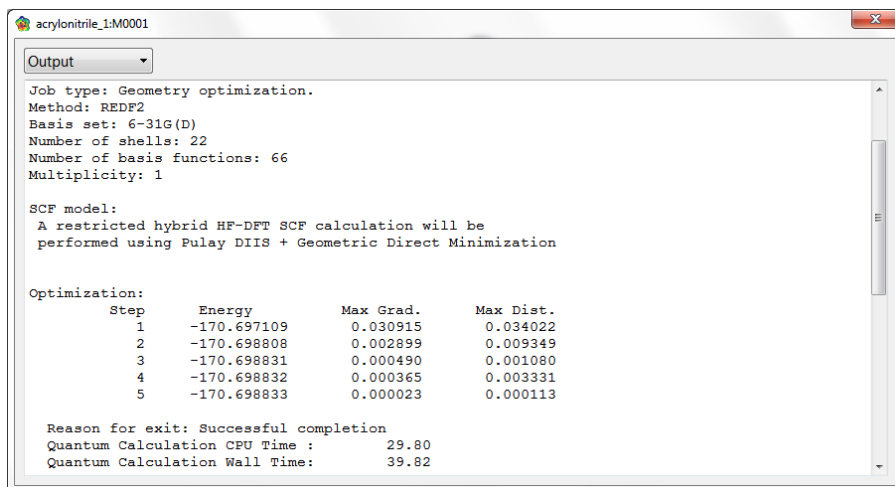
Click on **OK** to remove the message from the screen.

You are not permitted to modify any dialogs or other information associated with a molecule that has been submitted until the calculation has completed.

9. You will be notified when the calculation has completed.




Click on **OK** to remove the message from the screen. Select **Output** from the **Display** menu. A window containing text output for the job appears.



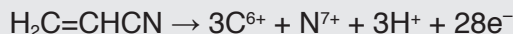
* Proper names will automatically be provided for you to accept, modify or replace whenever the molecule exists in the subset of the SSPD database supplied with *Spartan Student*, and where the document being submitted contains only one molecule. Otherwise the names *spartan1*, *spartan2*, etc., will be provided.

You can scan the output from the calculation by using the scroll bar at the right of the window or by *clicking* (left button) on or inside the output window and using the scroll wheel on your mouse. The information at the top of the dialog includes the task, basis set, number of electrons, charge and multiplicity, as well as further details of the calculation. Below this is the symmetry point group of the molecule that was maintained during the optimization.

Eventually, a series of lines appear, under the heading **Optimization**. These tell the history of the optimization process. Each line (or **Step**) provides results for a particular geometry. Ideally, the energy will monotonically approach a minimum value for an optimized geometry. If the geometry was not optimized satisfactorily an error message, such as: **Optimization has exceeded N steps – Stop**, will be displayed following the last optimization cycle. If this were the case, you would have been notified that the job had failed, rather than seeing the completed message dialog.

Near the end of the output is the final energy (-170.69883 atomic units for acrylonitrile from the EDF2/6-31G* density functional model), and the computation time. Click on  at the top of the output dialog to close it.

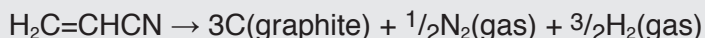
Energy: By convention, Hartree-Fock density functional theory and Møller-Plesset models provide energy results in terms of total energy. This is the energy of a reaction that splits a molecule into isolated nuclei and electrons, for example, for acrylonitrile.



Total energies, as the energies of such reactions are termed, are always negative and may be very large (tens of thousands of kJ/mol). They are most commonly given in atomic units (hartrees).

$$1 \text{ atomic unit} = 2625 \text{ kJ/mol}$$

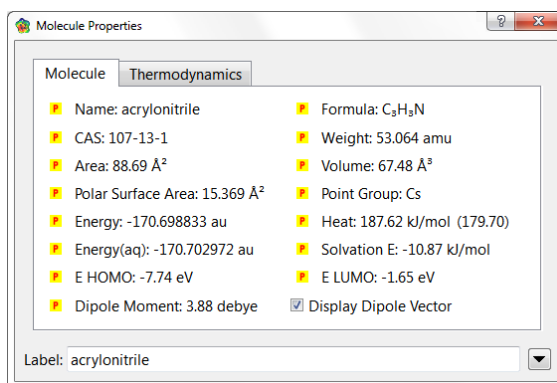
Heat of Formation: Experimental thermochemical data are normally given as heats of formation which corresponds to the enthalpy at 298K of a chemical reaction in which a molecule is converted to a set of standard products. For example, the heat of formation of acrylonitrile is given by reaction,



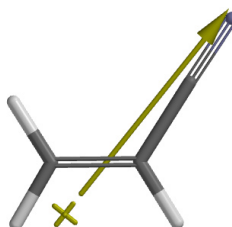
Where graphite, nitrogen molecule and hydrogen molecule are the carbon, nitrogen and hydrogen standards, respectively. Heats of formation may either be positive or negative quantities and generally span a range of only a few hundred kJ/mol.

To summarize, the heat of formation differs from the total energy both with regard to the standard reaction with regard to units. Either provides a suitable basis for thermochemical calculations.

You may examine the total energy and dipole moment among other calculated properties without having to go through the output. Select **Properties** from the **Display** menu to bring up the **Molecule Properties** dialog.

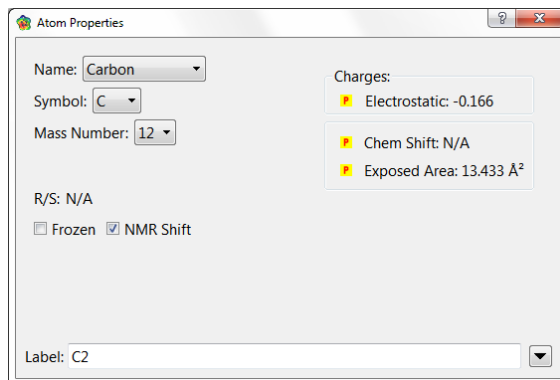



To see the dipole moment vector (indicating the sign and direction of the dipole moment), *check* the box to the right of **Display Dipole Vector**. (wire, ball-and-wire or tube models are best for this display.)




Uncheck the box to remove the dipole moment vector.

Click on an atom. The (**Molecule Properties**) dialog will be replaced by the **Atom Properties** dialog.



Among other things, this provides atomic charges. To obtain the charge on another atom, simply *click* on it. Inspect all the atomic charges on acrylonitrile (by *clicking* on the appropriate atoms). When you are finished, *click* on  at the top of the **Atom Properties** dialog to close it.

10. Select **Surfaces** from either the **Setup** or **Display** menu. *Click* on **Add** (at the bottom of the **Surfaces** dialog that results) and select **Electrostatic Potential Map** from the menu.
11. The graphics calculation will run without needing to submit the job following your request. When it has completed, *check* the box to the left of ***Electrostatic Potential Map*** in the **Surfaces** dialog. The surface itself corresponds to the electron density and provides a measure of the overall size and shape of acrylonitrile. The colors indicate values of the electrostatic potential on this surface; by convention, colors toward red correspond to negative potential (stabilizing interaction between the molecule and a positive charge), while colors toward blue correspond to positive potential. The nitrogen (the most electronegative atom) is red and the hydrogens (the most electropositive atoms) are blue.
12. Select **Close** from the **File** menu (or *click* on ) to remove acrylonitrile from the screen.* Also, close any open dialogs.

* While **Spartan Student** permits as many molecules as desired on screen at a given time, it will be less confusing for first-time users to keep only a single molecule open at a time.

3

Sulfur Tetrafluoride: Building an Inorganic Molecule


This tutorial illustrates the use of the inorganic model kit for molecule building. It also shows how molecular models may be used to quantify concepts from more qualitative treatments.

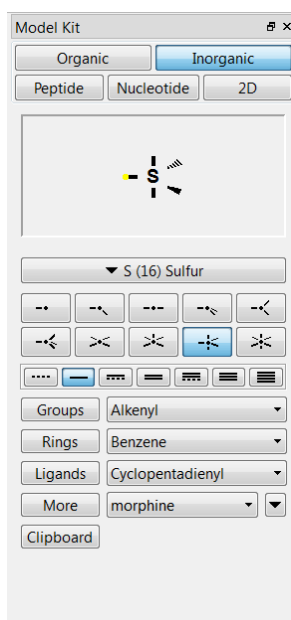
Organic molecules are made up of a relatively few elements and generally obey conventional valence rules. They may be easily built using the organic model kit. However, many molecules incorporate other elements, or do not conform to normal valence rules, or involve ligands. They cannot be constructed using the organic model kit. Sulfur tetrafluoride is a good example.



sulfur tetrafluoride

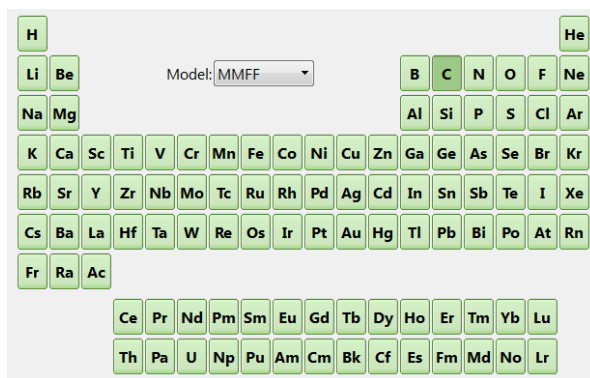
The unusual see-saw geometry observed for the molecule is best thought of as the least crowded way to position five electron pairs (four bonds and a non-bonded electron pair) around sulfur starting from a trigonal bipyramidal arrangement. Because a lone pair is bigger than a bonding electron pair, it occupies an *equatorial* position. Sulfur tetrafluoride provides the opportunity to look at the bonding and charges in a molecule which appears to have an excess of electrons around its central atom (ten instead of eight).

1. Bring up the inorganic model kit by *clicking* on  and then *clicking* on the **Inorganic** tab at the top of the model kit.



The inorganic model kit comprises an atom bar (*clicking* on which bring up the *Periodic Table**) followed by a selection of atomic hybrids, then bond types, and finally **Rings**, **Groups**, **Ligands**, **More** and **Clipboard** menus (all except for **Ligands** are the same as found in the organic model kit).





2. Click on the atom bar to bring up the *Periodic Table*.




Select (*click on*) S in the *Periodic Table* and the five coordinate trigonal bipyramid structure  from the list of atomic hybrids.

* Not all methods are available for all elements. Elements for which a specific method are available will be highlighted following selection of a theoretical model from the **Model** menu that appears in the center of the *Periodic Table*.

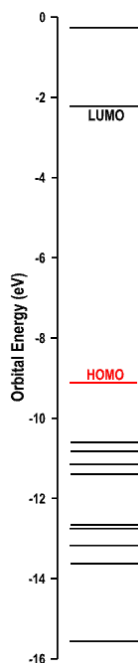
Trigonal bipyramid sulfur will appear at the top of the model kit. *Click* on screen.

3. Again, *click* on the atom bar, select **F** in the *Periodic Table* and the one-coordinate entry  from the list of atomic hybrids. One after the other, *click* on both *axial* free valences of sulfur, and two of the three *equatorial* free valences.
4. It is necessary to delete the remaining free valence (on an *equatorial* position); otherwise it will become a hydrogen. *Click* on  and then *click* on the remaining *equatorial* free valence.
5. *Click* on . *Click* on  to remove the model kit.
6. Select **Calculations...** from the **Setup** menu. Specify calculation of **Equilibrium Geometry*** using the **EDF2 6-31G*** model and *click* on **Submit**. Supply the name *sulfur tetrafluoride see-saw*.
7. After the calculations have completed, select **Properties** from the **Display** menu to bring up the **Molecule Properties** dialog. Next, *click* on sulfur to bring up the **Atom Properties** dialog. Is sulfur neutral or negatively charged, indicating that more than the normal complement of (eight) valence electrons surround this atom, or is it positively charged, indicating ionic bonding?








8. Select **Orbital Energies** from the **Display** menu (or *click* on ). An orbital energy diagram for sulfur tetrafluoride will appear at the left of the screen. This will contain the ten highest-energy occupied molecular orbitals and the two lowest-energy unoccupied molecular orbitals.

* It should be noted that were an incorrect geometry specified at the outset, optimization would lead to the correct structure, as long as the starting geometry possessed no symmetry (C_1 point group). Thus, square planar SF_4 in D_{4h} symmetry would remain square planar, while an almost square planar structure (distorted only slightly from D_{4h} symmetry to C_1 symmetry) would collapse to the proper structure.



Click on the energy level in the diagram labelled **HOMO** to display the highest-occupied molecular orbital. Does it point in the expected direction? It is largely localized on sulfur or is there significant concentration on the fluorines? If the latter, is the orbital bonding or antibonding?

9. Build square planar SF_4 as an alternative to the see-saw structure. Bring up the inorganic model kit (), select **S** from the *Periodic Table* and the four-coordinate square-planar structure  from the list of atomic hybrids. Click anywhere on screen. Select **F** in the *Periodic Table* and the one-coordinate entry  from the list of atomic hybrids. Click on all four free valences on sulfur. Click on  and then on .
10. Enter the **Calculations** dialog (**Setup** menu) and specify calculation of equilibrium geometry using the EDF2/6-31G* model (the same level of calculation as you used for the see-saw structure*). Click on **Submit** at the bottom of the dialog, with the name *sulfur tetrafluoride square planar*.
11. After the calculation has completed, bring up the **Molecule**

* You need to use exactly the same theoretical model in order to compare energies or other properties for different molecules.

Properties dialog (**Properties** from the **Display** menu) and note the energy. Is it actually higher (more positive) than that for the see-saw structure?

12. Close both molecules as well as any remaining dialogs.

4

Infrared Spectrum of Acetone







This tutorial illustrates the steps required to calculate and display the infrared spectrum of a molecule. It also illustrates retrieval of the experimental spectrum from an on-line database and fitting the calculated spectrum to the experimental spectrum.

Molecules vibrate in response to their absorbing infrared light. Absorption occurs only at specific wavelengths, which gives rise to the use of infrared spectroscopy as a tool for identifying chemical structures. The vibrational frequency is proportional to the square root of a quantity called a **force constant** divided by a quantity called the **reduced mass**.

$$\text{frequency} \propto \sqrt{\frac{\text{force constant}}{\text{reduced mass}}}$$

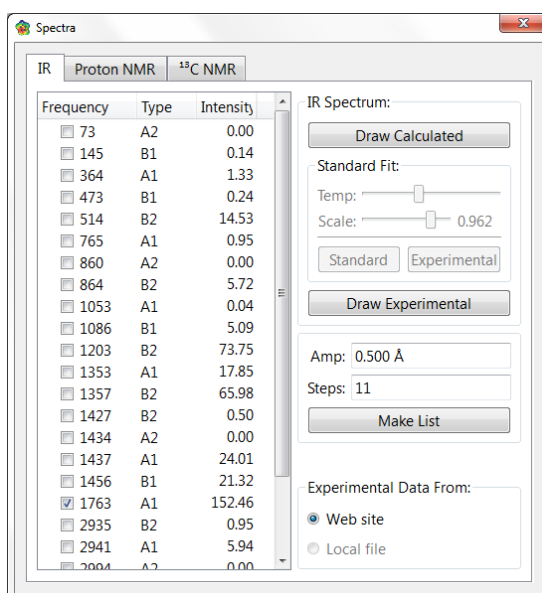
The force constant reflects the flatness or steepness of the energy surface in the vicinity of the energy minimum. The steeper the energy surface, the larger the force constant and the larger the frequency. The reduced mass reflects the masses of the atoms involved in the vibration. The smaller the reduced mass, the larger the frequency.

This tutorial shows you how to calculate and display the infrared spectrum of acetone, and explore relationships between frequency and both force constant and reduced mass. It shows why the carbonyl stretching frequency is of particular value in infrared spectroscopy.

1. Click on  to bring up the organic model kit. Select sp² carbon () and click anywhere on screen. Select sp² oxygen () and click on the double free valence on carbon to make the carbonyl group. Select sp³ carbon () and, one after the other, click on the two single free valences on carbon. Click on  and then on .
2. Enter the **Calculations** dialog (from the **Setup** menu).

Select **Equilibrium Geometry** from the left-hand menu to the right of **Calculate** and **EDF2** and **6-31G*** from the two right-hand menus. *Check Infrared Spectra* in the center of the dialog. You have requested that an infrared spectrum be computed following optimization of geometry. *Click* on **Submit** and accept the name *acetone* supplied to you. This calculation will require several minutes of computer time.

3. Select **Spectra** from the **Display** menu. *Click* on the **IR** tab in the dialog that results to bring up the **IR Spectra** dialog.



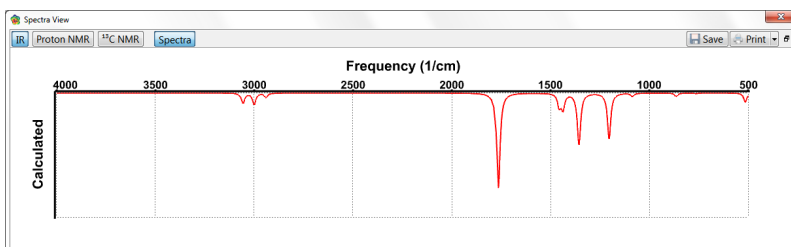
This contains a list of vibrational frequencies for acetone. First *click* on the top entry (the smallest frequency) and, when you are done examining the vibrational motion, *click* on the bottom entry (the largest frequency).

The smallest frequency is associated with torsional motion of the methyl rotors. The largest frequency is associated with stretching motion of CH bonds. Methyl torsion is characterized by a flat potential energy surface (small force constant), while CH stretching is characterized by a steep potential energy surface (large force constant).

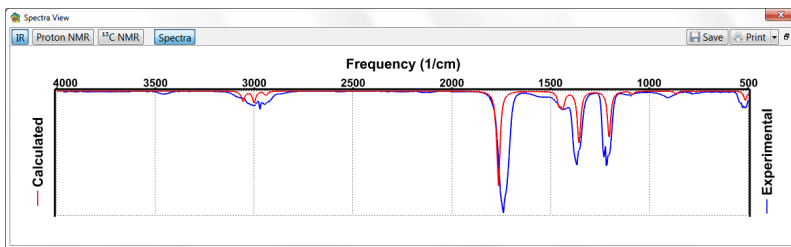
Locate the frequency corresponding to the CO stretch. The experimental frequency is around 1740 cm^{-1} .

The CO stretching frequency is a good chemical identifier because it stands alone in the infrared spectrum and because it is intense.

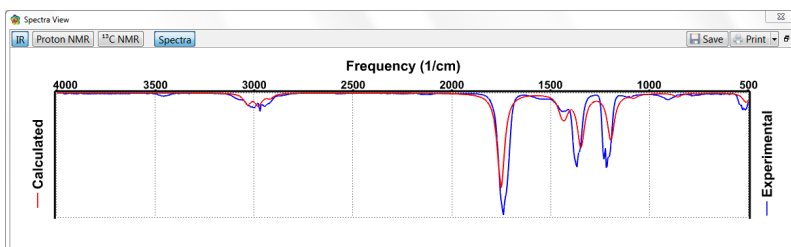
4. Click on **Draw Calculated** to display the calculated infrared spectrum.




If you are on-line, click on **Draw Experimental** to also bring up the experimental spectrum (superimposed on top of the calculated spectrum).



You will note that the two are qualitatively similar, but are shifted relative to each other. To provide a best fit, click on **Experimental** below **Fit** at the top right of the **IR** tab in the **Spectra** dialog.



Note that the calculated spectrum now closely matches the experimental spectrum. When you are done, *click* on **Delete Calculated** (which has replaced **Draw Calculated**) and **Delete Experimental** (which has replaced **Draw Experimental**) inside the **IR Spectra** dialog to remove the two spectra.

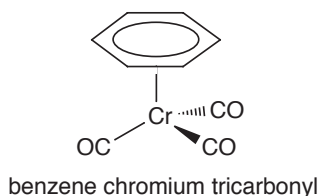
5. Change all the hydrogens in acetone to deuteriums to see the effect which increased mass has on vibrational frequencies. First make a copy of *acetone* (**Save As...** from the **File** menu or *click* on the  icon at the top of the screen). Name the copy *acetone d6* Select **Properties** from the **Display** menu and *click* on one of the hydrogens. Select *2 deuterium* from the **Mass Number** menu. Repeat for the remaining five hydrogens.
6. Submit for calculation. This calculation will require only a few seconds as results for the difficult part (force constants) are already available. When completed, examine the vibrational frequencies. Note that the frequencies of those motions which involve the hydrogens (in particular, the six vibrational motions corresponding to CH stretching) are significantly reduced over those in the non-deuterated system.
7. Close all molecules on screen in addition to any remaining dialogs.



5

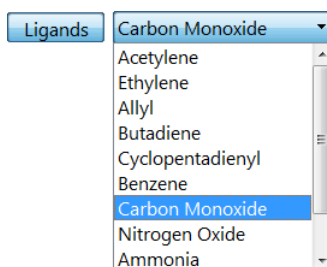
Benzene Chromium Tricarbonyl

This tutorial illustrates calculation of the geometry of a simple organometallic compound. It also shows how an electrostatic potential map may be employed to assess the effect of chromium tricarbonyl on the charge distribution at benzene.

Organic chemists know that an amino group attached to benzene adds electrons to the ring and leads to an increase in electrophilic reactivity, whereas a nitro group has the opposite effect. They probably know less about the effects of complexed substituents, for example, the effect of chromium tricarbonyl complexed to one face of benzene. In this tutorial, you will compare electrostatic potential maps for benzene, aniline, nitrobenzene and benzene chromium tricarbonyl in order to classify the substituent effect of the $\text{Cr}(\text{CO})_3$ group and to rank it alongside of NH_2 and NO_2 groups.

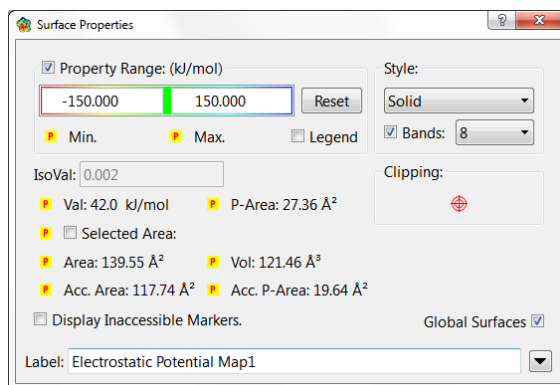


1. Build benzene chromium tricarbonyl. Click on  and bring up the inorganic model kit. Click on the atom bar and select **Cr** from the *Periodic Table*. Select four-coordinate tetrahedral  from the list of atomic hybrids. Click anywhere on screen.
2. Click on **Ligands** in the model kit, select **Benzene** from the menu and click on one of the free valences on chromium.

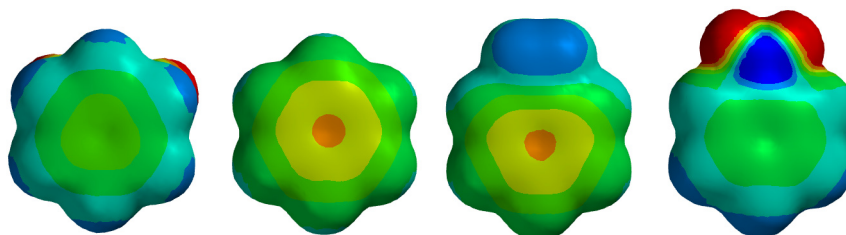


3. Select **Carbon Monoxide** from the **Ligands** menu, and *click* on the remaining (three) free valences on chromium. *Click* on to produce a refined structure.
4. Select **New Molecule** (not **New**) from the **File** menu. The screen will blank. Build benzene (switch to the organic model kit and choose **Benzene** from the **Rings** menu). *Click* on . Again, select **New Molecule** from the **File** menu and build aniline (**Benzene** from the **Rings** menu and from the fragment panel) and *click* on . Select **New Molecule** one last time and build nitrobenzene (**Benzene** from the **Rings** menu and **Nitro** from the **Groups** menu) and *click* on . *Click* on . The document now contains four molecules, benzene chromium tricarbonyl, benzene, aniline and nitrobenzene.
5. Select **Calculations...** (**Setup** menu). Specify calculation of **Equilibrium Geometry** with the **Semi-Empirical PM3** model. Make certain that **Global Calculations** (at the bottom of the dialog) is checked. You want the calculations to apply to all four molecules. *Click* on **OK**.
6. Select **Surfaces** (**Setup** or **Display** menu). *Click* on **Add** and select **Electrostatic Potential Map** from the menu.
7. Submit the job. Name it *benzene chromium tricarbonyl*. When completed bring up the spreadsheet (**Spreadsheet** from the **Display** menu), and *check* the box to the left of the label for all four entries. This allows them to be displayed simultaneously on screen. If **Coupled** (**Model** menu) is *checked*, remove the checkmark by selecting it. The molecules may now be moved independently. Orient each molecule so that you can clearly see the benzene face (exposed face in the case of the organometallic).

8. Select **Electrostatic Potential Map** from the **Surfaces** dialog. In order to better visualize and interpret the electrostatic potential map, select **Properties** from the **Display** menu and *click* on one of the surface maps to display the **Surface Properties** dialog.



Adjust the property range to -150 kJ/mol to 150 kJ/mol, and make sure the **Global Surfaces** box is selected. Compare electrostatic potential maps for both free and complexed benzene, with attention to the exposed benzene face.*




Does the $\text{Cr}(\text{CO})_3$ group donate or withdraw electrons from the ring? Would you expect the aromatic ring in benzene chromium tricarbonyl to be more or less susceptible to electrophilic attack than free benzene? More or less susceptible to nucleophilic attack? If the $\text{Cr}(\text{CO})_3$ is an electron donor, how does it rank relative to an amino group? If it is an electron acceptor, how does it rank relative to a nitro group?

9 optional

9. Repeat the calculations using a more sophisticated theoretical model, specifically the EDF2/6-31G* density functional model.

* Electrostatic potential maps (as well as other maps) for molecules in a group will be put onto the same (color) scale. This allows comparisons to be made among different members.

Make a copy of *benzene chromium tricarbonyl* (); name it *benzene chromium tricarbonyl density functional*. Inside the **Calculations** dialog, specify an **Energy** calculation using the **EDF2** model with the **6-31G*** basis set. You have requested that the PM3 geometries obtained in the previous step be used. Submit. This will require significantly more computer time than the PM3 calculation, although not as much time as would be required were you not to use the PM3 geometries. When completed, examine the electrostatic potential maps. Are they qualitatively similar to those from the PM3 calculations?

10. Remove all molecules and dialogs from the screen.

6

Proton NMR Spectrum of 2-Norbornene

This tutorial illustrates the calculation of the proton NMR spectrum for a simple organic molecule. Chemical shifts are directly evaluated but coupling constants are obtained from an empirical relationship.

Proton NMR spectroscopy was the first tool available to chemists to allow definitive assignment of the molecular structures of complex organic molecules. While it has been supplanted to some extent by ^{13}C NMR spectroscopy and more recently by *routine* X-ray crystallography, it remains indispensable.

NMR is based on the fact that nuclei possess spins that can either align parallel or antiparallel to an applied magnetic field, giving rise to different nuclear spin states. The relative energy of these states (ΔE) depends on the nucleus and on the strength of the applied magnetic field, by way of a simple relationship:

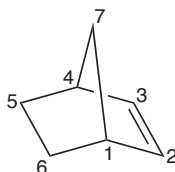
$$\Delta E = \gamma h / 2\pi B_0$$

γ is the gyromagnetic ratio (a constant for a given type of nucleus), $h/2\pi$ is Planck's constant divided by 2π and B_0 is the strength of the magnetic field **at the nucleus**. While the two nuclear spin states are normally in equilibrium, this equilibrium can be upset by applying a second magnetic field. The absorption of energy as a function of field strength (a **resonance**) between the states can then be detected.






The key to the utility of the magnetic resonance experiment is that the energy at which a nucleus resonates depends on its location in the molecule, and is different for each (chemically) distinct nucleus. The reason for this is that the applied magnetic field is weakened by electrons around the nucleus. Nuclei that are well shielded by the electron cloud will feel a lesser magnetic field than those that

are poorly shielded, and will show a smaller energy splitting. The difference, given relative to a standard, is termed a **chemical shift**. By convention, both proton and ^{13}C chemical shifts (treated later in this chapter) are reported relative to tetramethylsilane (TMS) as a standard.

While each *unique* proton in a molecule gives rise to a single line (resonance) in the spectrum, the spins on nearby nuclei add and subtract to the external magnetic field. This leads to a splitting of lines, the splitting pattern depending on the number of neighboring protons and their geometry. Discounting splitting, the intensity of the lines is approximately proportional to the number of equivalent protons that contribute. For example, the proton NMR spectrum of 2-norbornene shows six lines, two with unit intensity corresponding to the two different protons on the methylene bridge (C_7), and four with twice the intensity corresponding to protons at C_1 (C_4), C_2 (C_3) and the two different protons on C_5 (C_6).




In this tutorial, you will calculate the proton NMR spectrum of 2-norbornene and compare it with that contained in the Spectral Database of Organic Compounds (SDBS), freely-accessible on the web from the National Institute of Advanced Industrial Science and Technology (AIST) in Japan.*

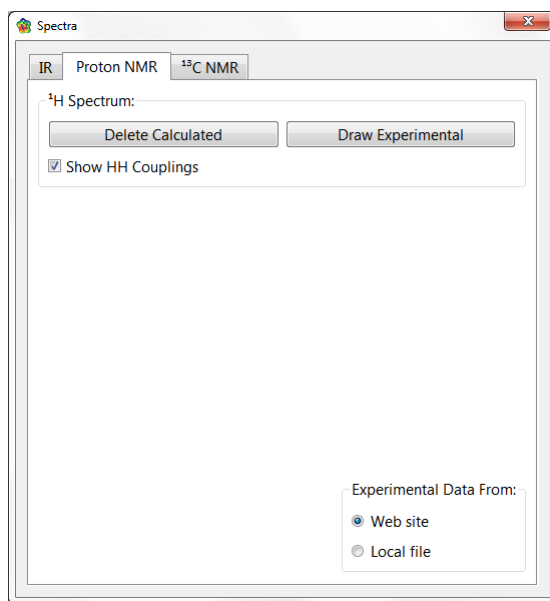
1. Build 2-norbornene. Start from cyclohexane (**Rings** menu), add an sp^3 carbon () to an *axial* ring position and bond to () to a free valence on the opposite side of the ring. Make a double bond between the appropriate ring carbons (). Minimize () and *click* on () .
2. Enter the **Calculations** dialog (**Calculations** from the **Setup** menu), and specify an **Energy** calculation using the **EDF2** model with the **6-31G*** basis set. **Check NMR Spectra** to the right of **Compute**. *Click* on **Submit**. Accept the name **2-norbornene**.

* Web address: http://riodb11.ibase.aist.go.jp/sbds/cgi-bin/cre_index.cgi.

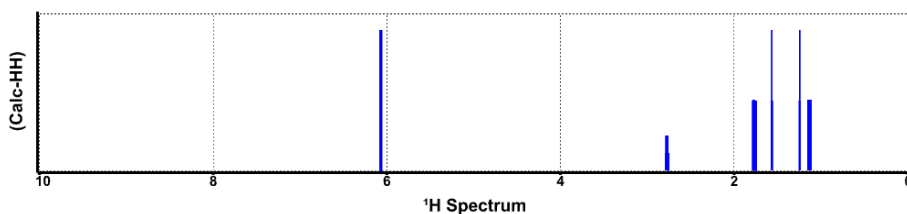
Calculation will require a few minutes.

You can, if you wish, avoid doing any calculations as results are already available in the database. In this case, *click* on  to the left of the molecule name at the bottom of the screen and *click* on **Replace**.

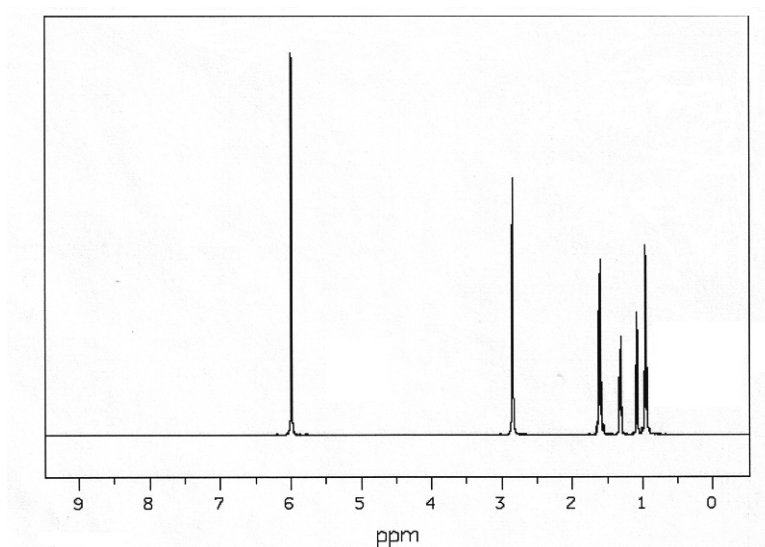
- When it has completed, or after you have retrieved results from the database, proton shifts can be found in the **Atom Properties** dialog. Select **Properties** from the **Display** menu and one after the other *click* on the hydrogens. Propose assignments for the six resonances observed in the experimental spectrum: 5.99, 2.84, 1.61, 1.31, 1.08 and 0.95 ppm.
- Select **Spectra** from the **Display** menu and click on the **Proton NMR** tab. The **NMR Spectra** dialog appears.



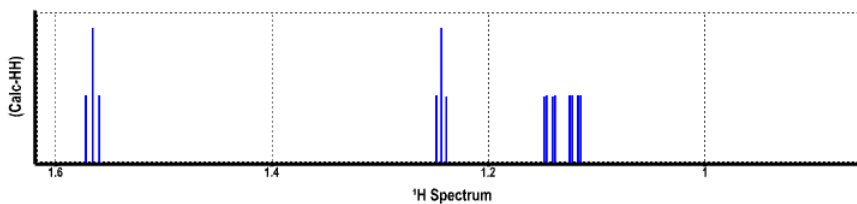
Make certain that **Show HH Couplings** is checked and *click* on **Draw Calculated**. The following proton spectrum appears.



Compare the calculated proton spectrum with that in SDBS (see below or examine it on-line).



5. You may have a difficult time seeing that the lines are split (in both calculated and observed spectra). This is because the splittings are very small relative to differences in the magnitudes of the chemical shifts themselves. *Spartan Student* provides a magnifier tool to assist. To magnify a region in the spectrum, position the cursor at the top left of this region (in the example above, roughly 1.6 ppm), *drag* the mouse to the lower right of the region (in this example, to the axis at 0 ppm) while holding down the left button and then release the button.



Note that you can continue to magnify the “magnified spectra”. To get back to the original, *click* on .

6. Close *2-norbornene* and any remaining dialogs when you are finished.

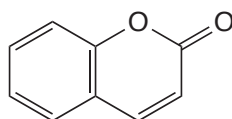
7



^{13}C NMR Spectrum of Coumarin

This tutorial illustrates calculation of a ^{13}C NMR spectrum, matching it to the corresponding experimental spectrum accessed via an on-line database. It illustrates correction of the calculated spectrum for the effect of the local environment.

There are several reasons why NMR spectroscopy, in particular ^{13}C NMR, is one of the most important analytical techniques for characterizing organic molecules. The experiment is straightforward and can be carried out rapidly. It requires relatively small samples and is non-destructive. The resulting (proton decoupled) spectrum is simple, comprising a single line (resonance) for each and every unique carbon. However, assigning ^{13}C spectra can be problematic and prone to error, in particular, where several carbons in a molecule may be in similar environments.

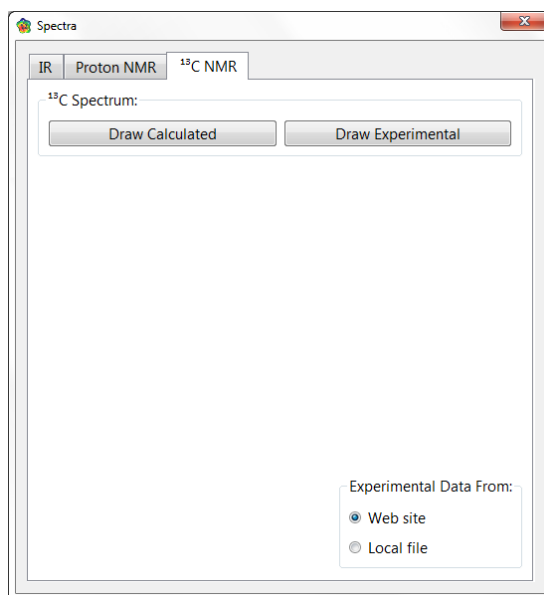
Directly calculated ^{13}C chemical shifts from practical models are not likely to be sufficiently accurate to enable definitive assignments to be made. **Spartan Student** enables calculated ^{13}C chemical shifts from both B3LYP/6-31G* and EDF2/6-31G* density functional models to be corrected for the effects of local chemical environment. In this tutorial, you will compare measured ^{13}C chemical shifts for coumarin with those obtained from corrected EDF2/6-31G* calculations. Coumarin is a good example both because it is simple enough for the experimental assignments to be unambiguous, and because several of the ^{13}C shifts are close and therefore difficult to assign.



1. Build and minimize coumarin, then *click* on . The structure and ^{13}C spectrum is available in the database attached to **Spartan Student** and no calculations are needed. All you need to do is *click* on  to the left of the name (***coumarin***) at the bottom of the screen and then *click* on **Replace** in the dialog which results.

You can, if you like, perform the required calculations. This will give you an idea of how much computer time is actually needed to obtain the structure and ^{13}C spectrum for a small molecule. In this event, do not replace the structure you built with the one in the database. Instead, bring up the **Calculations** dialog (**Setup** menu) and select **Energy** from the left-most menu to the right of **Calculate** and **EDF2** and **6-31G*** from the two right-most menus. **Check NMR Spectra** to the right of **Compute**. *Click* on **Submit** and accept the name ***coumarin***. The calculation will require several minutes to complete.

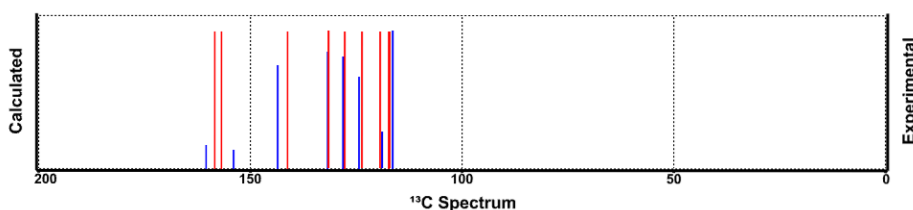
2. Following retrieval from the database (or completion of the calculation), select **Spectra** from the **Display** menu and *click* on the ^{13}C NMR tab. The **NMR Spectra** dialog results.



The experimental ^{13}C spectrum is available online.* Make certain that **Web site** under **Experimental Data From** at the bottom

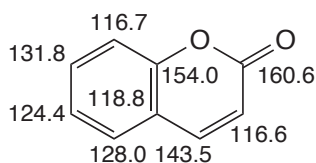
* Skip this and the next two steps if you are not connected to the internet.

right of the dialog is checked, and *click* on **Draw Experimental** under **^{13}C Spectrum** at the right near the top of the dialog. In a few seconds, the experimental spectrum will appear. Then, *click* on **Draw Calculated** at the top right of the dialog. A second spectrum in a different color will be superimposed onto the experimental spectrum.



Click on **Delete Calculated** and **Delete Experimental** to delete both calculated and experimental spectra when you are done. Remove the **NMR Spectra** dialog.

3. Select **Configure** from the **Model** menu to bring up the **Configure Labels** dialog. (If the **Labels** tab is not selected, *click* on it.) Select **Chem Shift** and *click* on **OK**. Calculated chemical shifts are now attached to your model. Simplify the display by removing hydrogens (and chemical shifts attached to them). Select **Hydrogens** from the **Model** menu. (To revert to the original model with hydrogens, simply select **Hydrogens** again.) Associate each of the calculated shifts with the corresponding experimental shifts (shown below) and compute a signed error.



4. Close *coumarin* when you are done.

8

Weak vs. Strong Acids




*This tutorial shows how to use electrostatic potential maps to distinguish between weak and strong acids, and quantify subtle differences in the strengths of closely-related acids. It also illustrates retrieval of information from **Spartan Student's** database.*






Nitric and sulfuric acids are strong acids, acetic acid is a weak acid, and ethanol is a very weak acid. What these compounds have in common is their ability to undergo heterolytic bond fracture, leading to a stable anion and a proton. What distinguishes a strong acid from a weak acid is the stability of the anion. NO_3^- and HOSO_3^- are very stable anions, CH_3CO_2^- is somewhat less stable and $\text{CH}_3\text{CH}_2\text{O}^-$ is even less so.

One way to reveal differences in acidity is to calculate the energy of deprotonation for different acids, for example, for nitric acid.



This involves calculations on both the neutral acid and on the resulting anion (the energy of a proton is zero). Note, however, that the calculations refer to the gas phase, whereas acidity measurements generally are made in a solvent, typically water. An alternative approach, illustrated in this tutorial, involves comparison of electrostatic potential maps for different acids, with particular focus on the potential in the vicinity of the acidic hydrogen. The more positive the potential, the more likely dissociation will occur, and the stronger the acid. Because electrostatic potential maps are obtained for the neutral acids and not for the anions, the gas phase data from the calculations are more likely to relate to aqueous phase measurements, at least in a qualitative sense.

1. Build nitric acid. Click on  to bring up the organic model kit. Select **Nitro** from the **Groups** menu and click anywhere on screen. Add sp^3 oxygen  to the free valence on nitrogen. Click on . Build sulfuric acid. Select **New Molecule** (not


New) from the **File** menu. Select **Sulfone** from the **Groups** menu and *click* anywhere on screen. Add sp^3 oxygen to both free valences on sulfur. *Click* on . Build acetic acid. Again select **New Molecule**. Select **Carboxylic Acid** from the **Groups** menu and *click* anywhere on screen. Add sp^3 carbon  to the free valence at carbon. *Click* on . Finally, build ethanol. Select **New Molecule** and construct from two sp^3 carbons and an sp^3 oxygen. *Click* on , and then on .

2. Bring up the **Calculations** dialog and specify calculation of equilibrium geometry using the EDF2/6-31G* model. *Click* on **OK**. Bring up the **Surfaces** dialog, *click* on **Add** (at the bottom of the dialog) and select **Electrostatic Potential Map** from the menu. Leave the **Surfaces** dialog on screen. Submit for calculation with the name *acids*.
3. When completed, bring up the spreadsheet and *check* the box immediately to the left of the molecule label for all four entries. The four molecules will now be displayed simultaneously on screen. Select (*uncheck*) **Coupled** from the **Model** menu so that they may be independently manipulated, and arrange on screen such that the acidic hydrogens are visible.


Mouse operations normally refer only to the selected molecule. To rotate/translate molecules together, hold down the **Ctrl (Control)** key in addition to the left/right buttons, while moving the mouse.

4. *Click* on **Electrostatic Potential Map** inside the **Surfaces** dialog. Electrostatic potential maps for all four acids will be displayed. Examine the potential in the vicinity of the acidic hydrogen (one of the two equivalent acidic hydrogens for sulfuric acid). Change the scale (color) to highlight differences in this region. Select **Properties (Display menu)** and *click* on one of the maps. Type **0** and **300** inside the boxes underneath **Property Range** in the **Surface Properties** dialog. *Press* the **Enter** key (**return** key for Mac) following each data entry. Regions on the map that are colored blue correspond to acidic sites, the more blue the

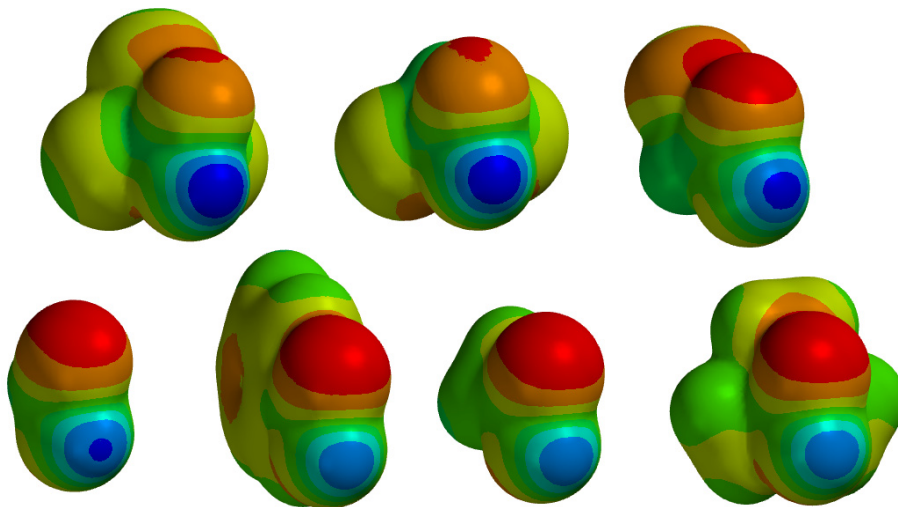
greater the acidity. On this basis, rank the acid strength of the four compounds.

- Remove **acids** and any open dialogs from the screen.
- One after another, build trichloroacetic, dichloroacetic, chloroacetic, formic, benzoic, acetic and pivalic acids. Put all into the same document (**New Molecule** instead of **New** following the first molecule). Click on  when you are finished.

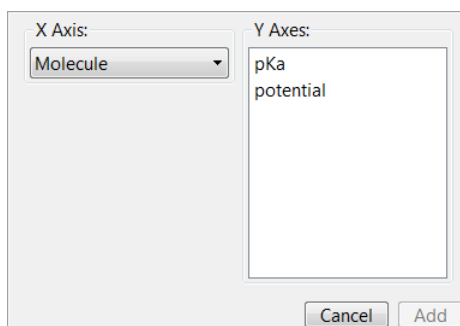
acid	pK _a	acid	pK _a
trichloroacetic (Cl ₃ CCO ₂ H)	0.7	benzoic (C ₆ H ₅ CO ₂ H)	4.19
dichloroacetic (Cl ₂ CHCO ₂ H)	1.48	acetic (CH ₃ CO ₂ H)	4.75
chloroacetic (ClCH ₂ CO ₂ H)	2.85	pivalic ((CH ₃) ₃ CCO ₂ H)	5.03
formic (HCO ₂ H)	3.75		

- Note that the name of the presently selected molecule in the document appears at the bottom of the screen. This indicates that a calculated structure is available in **Spartan Student's** database. Click on  to the left of the name and then click on **Replace All** in the dialog which results. Structures obtained from EDF2/6-31G* calculations (the same model used earlier in this tutorial) will replace those you have built.
- Select **Surfaces** from the **Setup** menu. Click on **Add** at the bottom of the **Surfaces** dialog and select **Electrostatic Potential Map** from the resulting menu. The graphic calculation will proceed without further intervention, but may require a few tens of seconds to complete. Leave the **Surfaces** dialog on screen.
- Bring up the spreadsheet. Expand it so that you can see all seven molecules. First, *left click* to select, then *right click* inside the header cell of the leftmost column and select **Rename Selected using SSPD** from the menu. The name of each molecule will appear. Next, *double click* inside the header cell of an available data column, type **pK_a** and press the **Enter** key (return key for Mac). Enter the experimental pK_a's. Press the **Enter** key (return key for Mac) following each entry.

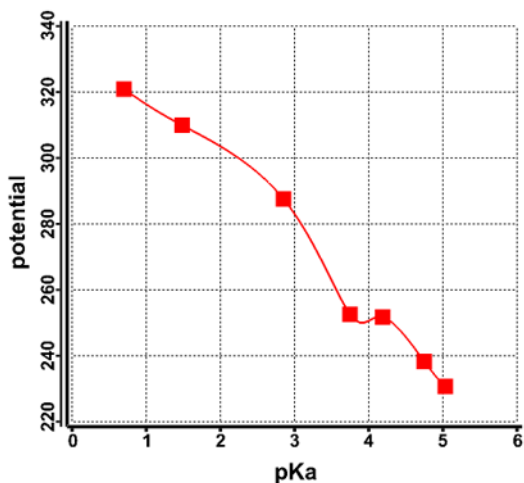
10. Arrange the molecules on screen such that the acidic hydrogen is visible. To display them all at once you need to *check* the box to the left of the **Label** column in the spreadsheet for each entry. To move the molecules independently, you need to select (*uncheck*) **Coupled** from the **Model** menu.
11. Click on **Electrostatic Potential Map** inside the **Surfaces** dialog to turn on the electrostatic potential map for each molecule.



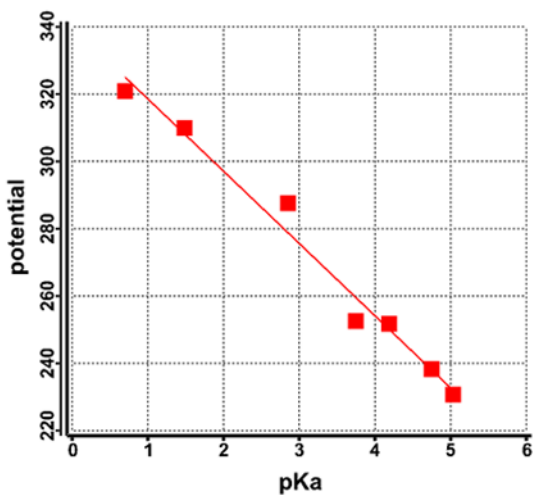
12. Bring up the **Surface Properties** dialog; select **Properties** from the **Display** menu and *click* on one of the electrostatic potential maps. Click on the **P** button next to **Max.** under the property range to post the maximum value for electrostatic potential in each molecule into the spreadsheet. *Double click* the resulting header cell in the spreadsheet and replace the contents with the word *potential*.
13. Select **Plots** from the **Display** menu, then *click* on **Add**.



Select **pKa** under the **X Axis** menu and **potential** from the **Y Axes** list, and *click* on **Add**. The data points are connected by a smooth curve.



Click on **Edit** at the top of the plot and select **Least Squares** from the choices to the right of **Curve** and *click* **Done**. Does the property of maximum electrostatic potential appear to correlate with pKa?



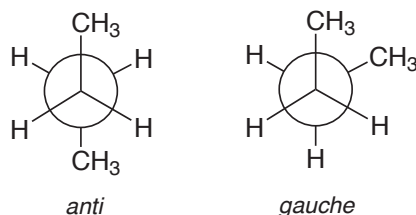
14. Close *carboxylic acids* and any dialogs from the screen.

9







Internal Rotation in *n*-Butane

This tutorial illustrates the steps required to calculate the energy of a molecule as a function of the torsion angle about one of its bonds, and to produce a conformational energy diagram.



Rotation by 180° about the central carbon-carbon bond in *n*-butane gives rise to distinct *anti* and *gauche* staggered structures. Both of these should be energy minima (conformers), and the correct description of the properties of *n*-butane is in terms of a Boltzmann average of the properties of both conformers.






This tutorial shows you how to calculate the change in energy as a function of the torsion angle in *n*-butane, place your data in a spreadsheet and make a conformational energy diagram.

1. Click on  to bring up the organic model kit. Build and minimize. Click on  to dismiss the model kit.
2. Set the CCCC dihedral angle to 0° (*syn* conformer). Click on . Click on the four carbon atoms in sequence. Type **0** (0°) into the box to the right of **dihedral...** at the bottom right of the screen and press the **Enter** key (**return** key on Mac).
3. Select **Constrain Dihedral** from the **Geometry** menu (or click on the  icon at the top of the screen). Select the CCCC torsion, and then click on  at the bottom right of the screen. The icon will change to  indicating that a dihedral constraint is to be applied.

Check the box to the left of **Profile** at the bottom right of the screen. This will result in three additional text boxes.

Constraint(Con1) =   0.00 ° to 0.00 ° Steps: 10 ☒ Profile

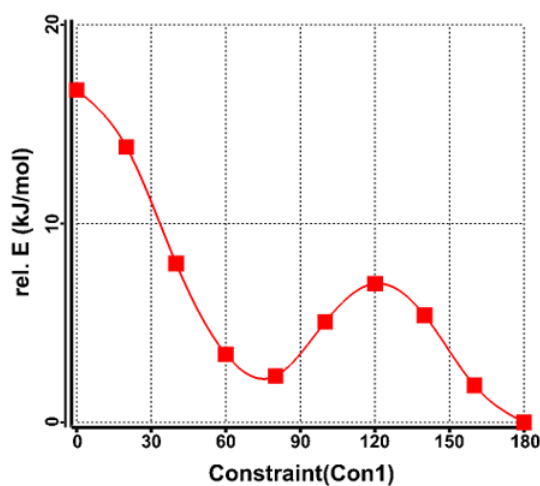
Leave **0** (0°) in the leftmost box, but change the contents of the middle box from **0** to **180** (180°). You need to *press* the **Enter** (**return**) key after you type in the value. **Steps** should be **10**. If it is not, *type* **10** and *press* the **Enter** (**return**) key. What you have specified is that the dihedral angle will be constrained first to 0°, then to 20°, etc. and finally to 180°. Click on .

4. Bring up the **Calculations** dialog (**Setup** menu) and select **Energy Profile** from the first menu to the right of **Calculate**, and **Semi-Empirical** from the second menu. Click on **Submit** and accept the name ***n-butane***. A set of 10 PM3 semi-empirical calculations will be performed.
5. When the calculations on all conformers have completed, they will generate a new document named ***n-butane.prof.M0001***. Choose **Yes** when prompted to open the new file. (You might wish to close ***n-butane*** to avoid confusion.) Align the conformers to get a clearer view of the rotation. Select **Align** from the **Geometry** menu and, one after the other, *click* on either the first three carbons or the last three carbons. Then *click* on the **Align** button at the bottom right of the screen, and finally *click* on . Bring up the spreadsheet (**Display** menu), and enter both the energies relative to the 180° or *anti* conformer, and the CCCC dihedral angles. First, *click* on the label (“M0010”) for the bottom entry in the spreadsheet (this should be the *anti* conformer), then *click* on the header cell for the left most blank column, and finally, *click* on **Add...** at the bottom of the spreadsheet. Select **rel. E** from among the selections in the dialog which results, **kJ/mol** from the **Energy** menu and *click* on **OK**. To enter the dihedral angle constraints, select **Constrain Dihedral** from the **Geometry** menu, *click* on the constraint marker and *click* on  at the bottom of the

* The difference between constraint values is given by: (final-initial)/(steps-1).

screen (to the right of the value of the dihedral angle constraint). Finally, *click* on .

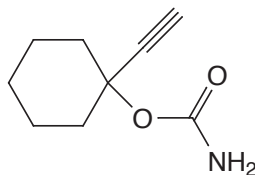
6. Select **Plots...** (**Display** menu), then *click* on **Add**. Select **Constraint (Con1)** from the items in the **X Axis** menu and **rel. E(kJ/mol)** from the **Y Axes** list. *Click* on **Add** to display a plot which, as expected, contains two energy minima (corresponding to the *gauche* and *anti* conformers).





7. Close all files and dialogs.

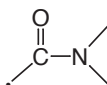
10



Ethinamate




Acrylonitrile, cyclohexanone and camphor are examples of molecules that adopt only a single conformation. Most molecules can adopt more than one conformation, due to rotation about single bonds or puckering of rings. The sedative ethinamate offers both rotation about the ring oxygen bond and the possibility for the carbamate functionality to occupy either the *equatorial* or *axial* position on the ring. This tutorial uses ethinamate to illustrate the procedure needed to find the lowest-energy conformer (global minimum).

1. Bring up the organic model kit (). Click on **Rings**, select **Cyclohexane** from the menu and click anywhere on screen. Click on sp^3 oxygen () in the model kit and add to either an *equatorial* or *axial* free valence on cyclohexane. Click on **Groups** and select **Amide** from the menu. Make certain that free valence on the amide group to be used for bonding is associated with carbon and not with nitrogen. This is indicated by a • on the icon at the top of the model kit.



You can move the bonding position by repeatedly *clicking* on the icon. When you are satisfied, add the amide to oxygen to make the carbamate functionality. Finally, select **Alkynyl** from the **Groups** menu and add to the same carbon on the cyclohexane ring as occupied by the carbamate group (using the remaining *axial* or *equatorial* free valence). Click on  and then on .

2. Bring up the **Calculations** dialog (**Setup** menu). Select **Equilibrium Conformer** from the leftmost menu to the right of **Calculate**. The only model allowed in *Spartan Student* for this task is molecular mechanics (the MMFF model) and this will be selected. All possible conformers will be examined* but only the most stable (according to the MMFF model) will be returned. Click on **Submit** at the bottom of the dialog. Accept the name *ethinamate*.
3. Which group, alkynyl or carbamate, occupies the *equatorial* position?
4. The name *ethinamate* appears at the bottom right of the screen. This indicates that the molecule exists in the subset of the Spartan Spectra and Properties Database (SSPD) included with *Spartan Student*. Click on  immediately to the left of the name, click on **Replace**. The entry in SSPD will replace your model. Is the conformation of ethanimine in the database the same as you have calculated?
5. Close *ethinamate* as well as any open dialogs.

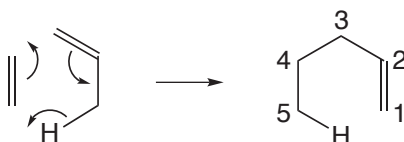
* This system is small, and the possible conformers will be systematically examined. This is not practical for molecules with a large number of degrees of conformational freedom. Here, *Spartan Student* employs Monte-Carlo methods.

11

Ene Reaction



This tutorial illustrates the steps involved in first obtaining an initial guess for, and then obtaining a transition state for a simple chemical reaction. Following this, it demonstrates how to produce a reaction energy diagram.

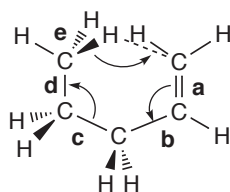
The ene reaction involves transfer of an allylic hydrogen to a double bond. A new carbon-carbon bond is formed, for example, reaction of propene and ethylene leading to 1-pentene.






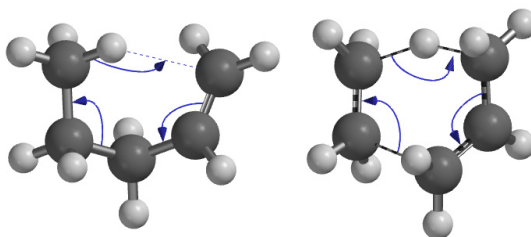
The ene reaction belongs to the class of so-called pericyclic reactions which also includes such important processes as the Diels-Alder reaction and the Cope and Claisen rearrangements.

In this tutorial, you will locate the transition-state for the ene reaction of ethylene and propene and show the detailed motions which the atoms undergo during the course of reaction. It is easier to start from 1-pentene (the product), rather than from the reactants.

1. Bring up the organic model kit and build 1-pentene in a conformation in which one of the terminal hydrogens on the ethyl group is poised to transfer to the terminal methylene group. Click on .
2. Select **Guess Transition States** from the **Build** menu (or click on the  icon at the top of the screen). Click on bond **a** and then click on bond **b** (see figure below). A curved arrow from bond **a** to bond **b** will be drawn.



Next, *click* on bond **c** and then on bond **d**. A second curved arrow from bonds **c** to **d** will be drawn. Finally, *click* on bond **e** and, while holding down the **Shift** key, *click* on the (methyl) hydrogen to be transferred and on the terminal (methylene) carbon to receive this hydrogen. A third curved arrow from bond **e** to the center of a dotted line that has been drawn between the hydrogen and oxygen will appear (see below left). If you make a mistake, you can remove an arrow by selecting **Delete** from the **Build** menu (*click* on ) and then *clicking* on the arrow. (You will need to select  to continue.) Alternatively, hold down the **Delete** key as you *click* on an arrow. With all three arrows in place, *click* on  at the bottom right of the screen. Your structure will be replaced by a guess at the ene transition state (see below right). If the resulting structure is unreasonable, then you have probably made an error in the placement of the arrows. In this case, select **Undo** from the **Edit** menu to return to the model with the arrows and modify accordingly.



- Enter the **Calculations** dialog (**Setup** menu), and specify calculation of transition-state geometry using the 3-21G Hartree-Fock model. Select **Transition State Geometry** from the leftmost menu to the right of **Calculate**, and choose **Hartree-Fock** and **3-21G** from the two rightmost menus. Finally, *check* **IR** under **Calculate**. This will allow you to confirm that you have found a transition state, and that it smoothly connects the reactant and the product. *Click* on **Submit**. Save the file as *ene reaction 1-pentene*.




4. When the job completes, animate the motion of atoms along the reaction coordinate. Select **Spectra** from the **Display** menu and *click* on the **IR** tab. *Click* on the top entry in the list in the **IR** dialog that results. It corresponds to an imaginary frequency, and will be designated with an **i** in front of the number.

A vibrational frequency is proportional to the square root of a quantity that reflects the curvature of the potential surface along a particular (normal) coordinate corrected for the masses of atoms involved in motion along that coordinate. At a transition state (the top of a hill), the curvature is negative (it points down). Since mass is positive, the quantity inside the square root is negative and the frequency is an imaginary number.

Is the vibrational motion consistent with an ene reaction of interest and not with some other process?

5. Controls at the bottom of the **IR** dialog allow for changing both the amplitude of vibration (**Amp**) and the number of steps that make up the motion (**Steps**). The latter serves as a speed control. Change the amplitude to 0.3. *Type 0.3* in the box to the right of **Amp** and *press* the **Enter** key (**return** key on Mac). *Click* on **Make List** at the bottom of the dialog. This will give rise to a group of structures that follow the reaction coordinate from the transition state toward both reactant and product. Remove the original transition state: *click* on **ene reaction 1-pentene** (the vibrating molecule) and close it, along with the **IR** dialog.
6. Enter the **Calculations** dialog and specify calculation of **Energy** using the **Hartree-Fock 3-21G** model. Make certain that **Global Calculations** is checked, and *click* **OK**. Next, enter the **Surfaces** dialog and specify evaluation of a density surface and an electrostatic potential map. *Click* on **Add** and select **More Surfaces...** from the menu. The **Add Surfaces** dialog will appear. Select **density (bond)** from the **Surface** menu and **none** from the **Property** menu. Remove the checkmark from **Fixed**. *Click* on **OK**. Repeat the process, this time selecting **density (bond)**

from the **Surface** menu and **potential** from the **Property** menu. Click on **OK**.

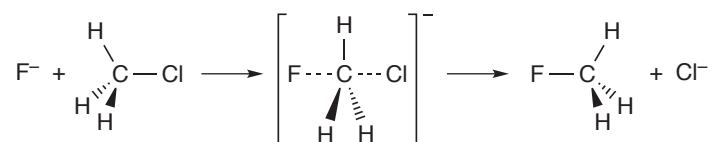
7. Submit for calculation. Name it *ene reaction 1-pentene sequence*. Once the job has completed, enter the **Surfaces** dialog and examine the surfaces that you have calculated (click on **Density** to turn it on). Repeat this procedure for the electrostatic potential map. (Click on **Density** to turn it off and **Electrostatic Potential Map** to turn it on.) For each, step through the sequence of structures ( and ) keys at the bottom of the screen) or animate the reaction (). Note, in particular, the changes in bonding revealed by the bond density surface. Also pay attention to the value of the potential on the migrating atom. This reflects its charge. Is it best described as a proton (blue), hydrogen atom (green) or hydride anion (red)?
8. Close *ene reaction 1-pentene sequence* and any open dialogs.
9. Remove any molecules and dialogs from the screen.




12




S_N2 Reaction of Fluoride and Methyl Chloride

This tutorial illustrates construction of an energy profile for a simple S_N2 reaction. This starts from the reactants, passes through the transition state and ends up with the products.



The S_N2 reaction passes through a transition state in which carbon is in a trigonal bipyramid geometry and the entering and leaving groups are colinear.







1. First, construct methyl chloride. Then select fluorine from the palette of icons in the model kit, *click* on the **Insert** button at the bottom right of the screen or hold down the **Insert** key (option key on Mac) and *click* anywhere on screen. Alternatively, *double click* in a blank area of the screen following selection of fluorine. Two detached fragments, methyl chloride and hydrogen fluoride, appear on screen. *Click* on  and then *click* on the free valence on fluorine. *Click* on . Alternatively, hold down the **Delete** key and *click* on the free valence on fluorine. You are left with methyl chloride and fluorine atom (fluoride). Manipulate the two such that fluoride is poised to attack methyl chloride from the backside (as in the transition state above). (Recall that translations and rotations normally refer to both fragments, but can be made to refer to a single fragment by first *clicking* on the fragment and then holding down on the **Ctrl** key while carrying out the manipulations.)
2. Select **Constrain Distance** from the **Geometry** menu (or *click* on the  icon at the top of the screen). *Click* on F, then on C

and finally *click* on  at the bottom right of the screen. The icon will change to  indicating a constraint is to be applied to this distance. *Type 3.0* (3.0Å) into the box to the right of the icon and *press* the **Enter** key (**return** on Mac). *Click* on . You should get a structure with three-fold symmetry with a CF bond length of 3.0Å.

- Again select **Constrain Distance**. *Click* on the constraint marker between C and F (or *click* on the two atoms in turn). *Check* the box to the left of **Profile** at the bottom right of the screen. This will result in two additional text boxes.

Constraint(Con1) =   3.000 Å to 1.400 Å Steps: 17 ☒ Profile

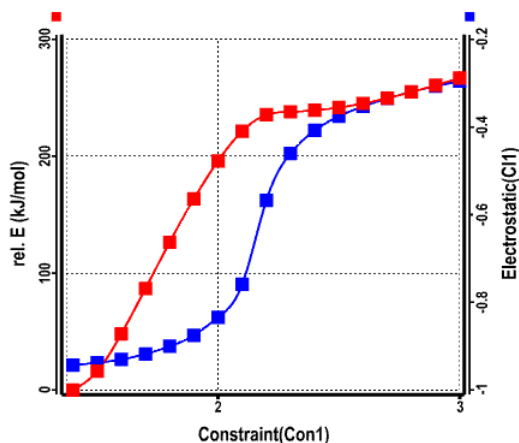
Leave the value **3.000** (3.0Å) in the leftmost box alone, but change the contents of the middle box from **0** to **1.4** (1.4Å). You need to *press* the **Enter** (**return**) key after you type in the value. Set **Steps** to **17** (*type 17* in the box to the right of **Steps** and *press* the **Enter** (**return**) key). What you have specified is that the CF distance will be constrained first to 3.0Å, then to 2.9Å*, etc. and finally to 1.4Å. *Click* on .

- Enter the **Calculations** dialog, and select **Energy Profile**, **Hartree-Fock** and **6-31G*** from the menus to the right of **Calculate**. You need to change **Total Charge** to **Anion**.
- Submit the job. Name it *fluoride+methyl chloride*. When completed, it will give rise to a sequence of calculations placed in *fluoride+methyl chloride.Prof.M0001*. You will be prompted as to whether you want to open this file. *Click* on **Yes**.
- Bring up the **Spreadsheet** (**Spreadsheet** from the **Display** menu). Enter (the constrained) CF distances and chlorine charges in the spreadsheet. Select **Constrain Distance** from the **Geometry** menu, *click* on the constraint marker and *click* on  at the bottom right of the screen. *Click* on . Bring up the **Properties** dialog. *Click* on chlorine and *click* on  to the left of **Electrostatic** under **Charges** in the **Properties** dialog. Select

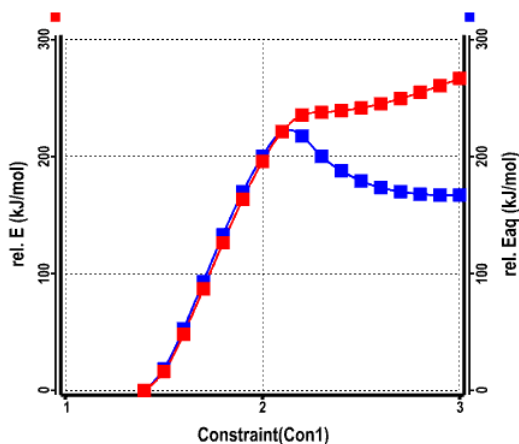
* The difference between constraint values is given by: (final-initial)/(steps-1).

the structure with the shortest CF distance, *click* on **Add...** at the bottom of the spreadsheet and select **rel E** from the menu.




Bring up the **Plots** dialog, *click* on **Add**, and select **Constraint (Con1)** (the distance at which the CF bond has been constrained) from the **X Axis** menu, and both **rel E (kJ/mol)** and **Electrostatic (Cl1)** from the **Y Axes** list. *Click* on **Add**. One plot gives the energy as the reaction proceeds and the other gives charge on chlorine.



7. S_N2 reactions involving charged species normally need to be carried out in highly-polar media, for example, water. Add aqueous phase data (based on the empirical SM5.4 model) to the spreadsheet. *Click* on an empty column header, *click* on **Add...**, select **rel Eaq** from the list of available quantities, and *click* on **OK**. Bring up the **Plots** dialog, *click* on **Add**, and select **Constraint (Con1)** from the **X Axis** and both **relE(kJ/mol)** and **rel Eaq(kJ/mol)** from the **Y Axes** list. *Click* on **Add**.



8 to 10 optional

8. Enter the **Surfaces** dialog. *Click* on **Add** and select **density (bond)** from the **Surface** menu and **none** from the **Property** menu. Remove the checkmark from **Fixed**. *Click* on **OK**. Repeat the process, this time selecting **density (bond)** from the **Surface** menu and **potential** from the **Property** menu. *Click* on **OK**.
9. You don't need to submit the job, but the graphics calculations for all 17 molecules will take 10-20 seconds to complete. When they are done, select *density* inside the **Surfaces** dialog and *click* on  at the bottom left of the screen to animate the display. Note, that bonds are smoothly broken and formed during the course of reaction. *Click* on  to stop the animation.
10. Reenter the **Surfaces** dialog. Turn off display of the density and turn on display of the electrostatic potential map. *Click* on . Relate the migration of negative charge during reaction to the plot of the charge or bromine. Recall that colors near red indicate maximum negative potential.
11. Remove all molecules and any dialogs from the screen.

13

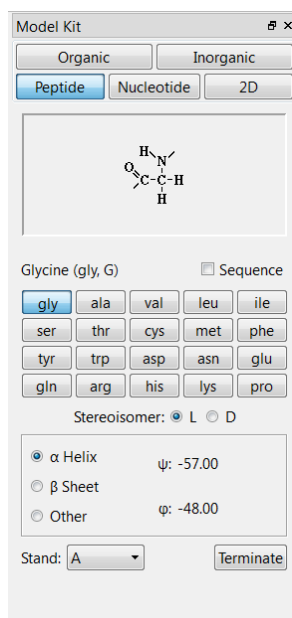
Polypeptides and Polynucleotides

This tutorial illustrates use of the peptide and nucleotide model kits. It shows how hydrogen bonds influence both the secondary structure of polypeptides (proteins) and the double helix of DNA. No quantum chemical calculations are performed.

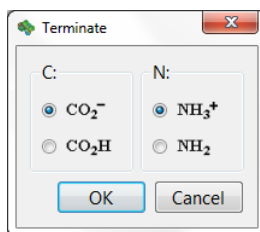
Proteins perform a variety of vital roles in all living organisms: reaction catalysis, transport and storage, structural support, immune protection, and mediation of nerve impulses, to name a few. Despite the variety, all proteins consist of the same basic building blocks (a set of 20 amino acids), and are dominated by two main structural motifs (the α helix and the β pleated sheet).

α Helix

1. Select **New** from the **File** menu and *click* on the **Peptide** builder from the **Model Kit**. This contains a library of the 20 natural amino acids, each identified by a 3-letter code.

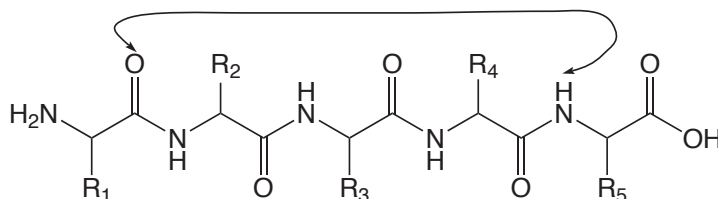


2. Click on **gly-** (glycine). As you toggle the checkbox to the left of **Sequence** on and off, the display window at the top of the model kit will shift between a text field showing **gly** (**Sequence** button checked) and a 2D rendering of non-terminated glycine (**Sequence** button un-checked).
3. Make sure the **Sequence** box is checked, and randomly select an additional 9 amino acid residues. Below the pallet of amino acids are a series of buttons: **α Helix**, **β Sheet** and **Other**. These allow specification of the secondary structure of constructed polypeptide sequences. Select **α Helix** and *click* on screen.
4. A ball-and-spoke model of a 10-residue polypeptide is displayed. There are two open valences (indicated by their yellow color) at either end of this non-terminated polypeptide molecule. From the lower right side of the **Peptide** builder, *click* on the **Terminate** button. The dialog that results lets you terminate the polypeptide either as an uncharged form (CO_2H and NH_2) or as a zwitterionic form (CO_2^- and NH_3^+).



Choose CO_2H and NH_2 (the uncharged form) and *click* on the **OK** button to terminate.

- To simplify the model, display the molecule as a **Tube** model and deselect **Hydrogens** from the **Model** menu. Select **Hydrogen Bonds** from the **Model** menu. Dotted lines depicting hydrogen bonds will appear on screen between the oxygens of carbonyl groups and the nitrogens of amine groups (recall that display of hydrogens has been turned off). In the α helix structure, hydrogen bonds are formed between the $\text{C}=\text{O}$ of one amino acid and NH group of another amino acid, separated by a space of 4 residues. It is this network of internal hydrogen bonding that holds together the α helix.




- To better see the α helix, select **Ribbons** from the **Model** menu. You may also, if you choose, turn off the molecular structure display of the peptide all together, by selecting **Hide** from the **Model** menu. Rotate the model on screen to get an idea of its 3D structure. Note that the hydrogen bonds are still visible. Close the document when you finish examining the α helix structure.

β Pleated Sheet

- Select **New** from the **File** menu and *click* on the **Peptide** builder from the **Model Kit**. The ten-residue sequence you previously constructed will remain in the viewer window at the top of the builder (if not, make sure the **Sequence** box is checked and

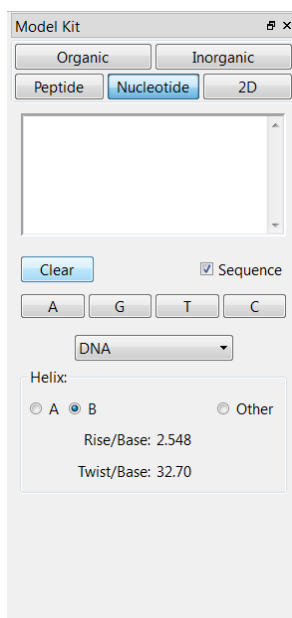
randomly choose another 10 amino acids). Select **β Sheet** and *click* on screen.

8. Again, a model of a 10-residue polypeptide is displayed. This time, the secondary structure is in the β sheet configuration. Terminate the structure in either the uncharged or zwitterionic form.
9. *Click* on  to remove the model kit. Note that the same 10-residue sequence is significantly longer in the β sheet arrangement. As you did for the α helix, switch to a tube model, turn hydrogens off and turn on display of hydrogen bonds. The extended β sheet does not contain internal hydrogen bonding so no hydrogen bonds appear. Close the document when you finish examining the β -sheet structure.
10. Hydrogen bonds play a role in connecting β strands to make a β sheet. Select **Access PDB** from the **File** menu and specify **1JIC***. Turn on hydrogen bonds (**Model** menu). Hydrogen bonds appear *between* different β strands. Note that hydrogen bonds may also exist between residues on the same strand, in this example they form a hairpin turn resulting the same β sheet running adjacent to itself but in the opposite (or anti-parallel) direction. Close **1JIC** when you have finished examining the β -sheet structure.

B-DNA

11. Select **New** from the **File** menu and *click* on the **Nucleotide** model kit.

* PDB designation 1JIC. Torres, A.M., Kini, R.M., Selvanayagam, N., Kuchel, P.W.; *J. Biochem.* **360**: 539-548 (2001).



This model kit includes options for building a variety of nucleic acid sequences (based on nucleotide residues) included both single and double stranded DNA and RNA, as well as hybrid DNA-RNA sequences. Choose **DNA** from the menu in the middle of the **Nucleotide** model kit.

12. Just below the viewer window (inside the model kit) are four buttons designating the nucleotide bases. *Click* on **A** (adenine). Toggle the check-box to the left of **Sequence** on and off. The display window at the top of the model kit will shift between a text field showing **A-** (with the **Sequence** button checked) and a 2D rendering of adenine (with the **Sequence** button unchecked). Note that even though the 2D rendering displays only the nucleotide base, when building, the entire nucleotide, include the organic base (purine or pyrimidine), sugar (ribose), and phosphate group, will be inserted on screen. In the case of double-stranded sequences, the complementary base will also be inserted.
13. *Click* on screen to insert an adenosine nucleotide, and its complementary base thymine nucleotide. Select **Hydrogen Bonds** from the **Model** menu to display hydrogen bonding between the AT base pair. Note that adenosine-thymine pairings

in double stranded DNA will always form two hydrogen bonds, where as guanine-cytosine pairings result in the formation of three hydrogen bonds. When you are finished examining the A-T base pair, select **Clear** from the **Edit** menu.

14. Make sure the **Sequence** box is checked, and randomly select an additional 15-20 nucleotide bases. Below the pallet of nucleotide bases is a series of buttons (marked **A**, **B**, and **Other**) that provide for specification of the nucleotide sequence **Helix**. Select **B** for the helix type and *click* on screen. (DNA exists in three forms, A, B, and Z. Almost all DNA in living organisms is in the B-DNA configuration.)
15. Select **Tube** and **Ribbon** from the **Model** menu. Display of hydrogen bonds has already been specified. If you turned this off, hydrogen bonds can be accessed from the **Model** menu. Also select **Configure** from the **Model** menu and *click* on the **Ribbons** tab. Select **By Strand** from the **Coloring** options and *click* **OK**. The ribbon tracing the backbone of the sequence you constructed from the builder is colored red; the complementary sequence is colored blue.
16. Because the glycosidic bonds of the base pairs (bonds connecting the base pairs to their sugar molecules) are not exactly opposite one another, B-DNA has two clearly visible grooves (called the major groove and the minor groove). The major groove is ~ 12 Å wide and the minor groove is roughly half that size. Select **Space-Filling** from the **Model** menu and locate the major and minor grooves in your B-DNA sequence.
17. Close all open documents.

14

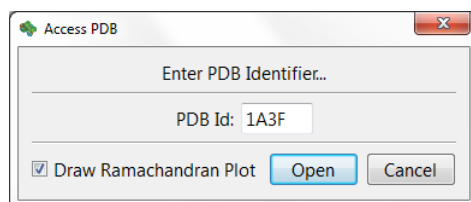
Biomolecules

This tutorial illustrates models appropriate to large biomolecules (proteins and nucleotides), in particular, ribbon displays of secondary structure and display of hydrogen bonds. No calculations are performed.

Treatment of very large molecules, proteins and nucleotides (biopolymers) most important among them, requires models which are simpler than those appropriate for small organic and inorganic molecules. This refers both to structural models for display and manipulation (where a simplified ribbon display of the biomolecule's backbone is used) and to theoretical models used for calculation of structure and properties (where molecular mechanics replaces quantum chemical models).

This tutorial uses an enzyme (phospholipase A2) extracted from the venom of the common cobra (*Naja naja*) to illustrate a variety of models for the display of biomolecules, including ribbon displays to elucidate the backbone and hydrogen-bond displays to disclose some of the forces holding the structure together.

1. From the **File** menu, *click* on **Access PDB...** then *type* **1A3F*** in the PDB Id code: field and *click* on **Open****.



Note that a simple ribbon display, demarking the protein

* PDB designation 1A3F. Segelke, B.W., Nguyen, D., Chee, R., Xuong, N.H., Dennis, E.A.; *J.Mol. Bio.*, **279**, 223-232 (1998).

** If you do not have an internet connection, the file 1A3F is available from the *tutorials* directory.

backbone (secondary structure) has replaced the usual structural models (ball-and-spoke, tube, etc.).



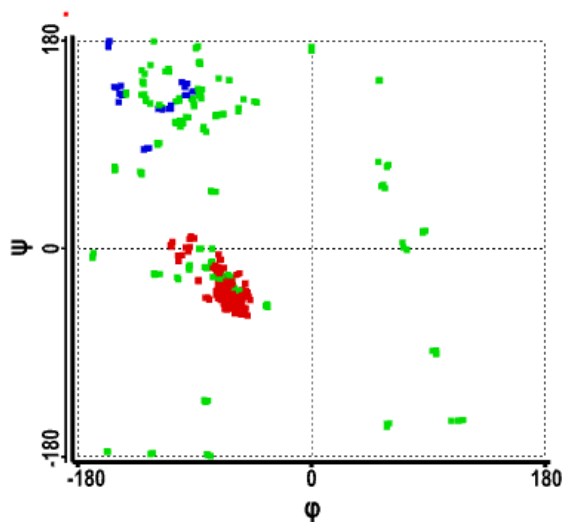
To see why this is preferable, turn on (select) one of these models from the **Model** menu. The model styles that provide detail of the enzyme's primary structure have completely obliterated a significant structural detail (namely that this enzyme is comprised of three identical sub-units). Note, however, that a space-filling model (**Space-Filling** from the **Model** menu) does provide indication of the overall size and shape of the enzyme.

2. To better visualize the three sub-units, turn the selected model style off (choose **Hide** from the **Model** menu) and select **Configure** from the **Model** menu, click on the **Ribbons** tab, and finally select **By Strand**. Note that each oligomer is colored differently. Explore the remaining options for coloring (click **Apply** after each selection). **Monochrome** provides a single colored model useful for tracing the backbone of the biomolecule. **By Secondary Structure** gives information about how the backbone is organized (alpha-helices are colored red, beta-sheets are colored blue, while any remaining segments are colored green). **By Residue** provides a multi-colored display where each unique color represents a specific amino acid residue type. To further explore, *click* on the **OK** button to dismiss the **Configure** dialogue, and then *click* on the individual colored segments of the ribbon. The specific peptide or amino acid residue (in the case of peptide chains, proteins, or enzymes)

or nucleotide base (in the case of nucleotide chains, DNA, or RNA) will be specified in the lower right of the workspace.

Hydrogen bonding is known to be a decisive factor in determining the three-dimensional structures of biopolymers. The base pairs in complementary strands which make up DNA are held together by hydrogen bonds. Helical structures in proteins are also maintained by hydrogen bonds as are neighboring strands in so-called β sheets.

3. Select **Ramachandran Plot** from the **Geometry** menu.





Each point gives the dihedral angles between a pair of amino acids (the so-called ϕ and ψ angles). Note that many points fall into two clusters, one corresponding to helices and the other to β sheets.

4. Close **1A3F**.

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Isomeric C₅H₈ Dienes

In addition to 2-methyl-1,3-butadiene, *cis* and *trans*-1,3-pentadiene (conjugated dienes) and 1,4-pentadiene (a non-conjugated diene), there are three other C₅H₈ dienes: 3-methyl-1,2-butadiene (1,1-dimethylallene) 1,2-pentadiene (ethyl allene) and 2,3-pentadiene (1,3-dimethylallene).

1. Build all seven C₅H₈ dienes (place in a single document) and bring up the spreadsheet (**Spreadsheet** from the **Display** menu). With any of the dienes selected, *click* on the **Replace All** button in the **Preview** dialog (brought up by *clicking* on  to the left of the molecule name at the bottom of the screen). This will substitute entries in SSPD for all seven C₅H₈ dienes. To enter names into the spreadsheet, *click* on the top left header cell (**Label**), hold down the right mouse button and select **Rename Selected Using SSPD** from the menu. Bring up **Molecule Properties** dialog (**Display** menu) and *click* on the  button to the left of **Heat**. This enters the T1 heat of formation (the experimental heat of formation is given in parenthesis where available from the NIST database).
2. Using the spreadsheet and the molecular properties dialog, verify that the T1 model correctly reproduces the ordering of experimental heats. Then use the T1 heats to answer the following questions:

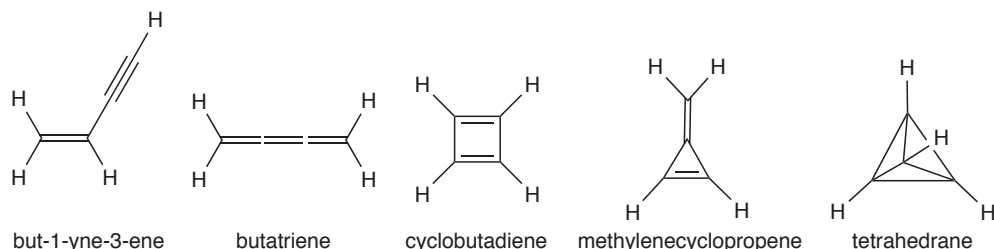
What is the difference in stability (heat) between the best of the three conjugated dienes and 1,4-pentadiene? What is the approximate energy gain due to conjugation? What is the difference in stabilities between the best of the substituted allenes and the best of the conjugated dienes?
3. Close any molecules and dialogs that are open on screen.

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Infrared Spectra of Short-Lived Molecules

While infrared spectroscopy is by no means as formidable a tool as NMR for elucidating the structures of molecules, it does offer significant advantages that make it the method of choice in some instances. It is more sensitive, meaning that it can be used to detect transient species, for example, molecules trapped in an inert matrix at very low temperature. On the practical side, an infrared spectrometer is inherently simpler (more robust) and can be put into a much smaller package than an NMR spectrometer. This means that the spectrometer can be brought to the sample rather than the other way around. Imagine, putting an NMR spectrometer on the Mars rover! The problem is that IR spectroscopy unlike NMR typically does not provide an unambiguous structure. However, a close match to a calculated spectrum may offer convincing evidence for the veracity of a particular structure (or a mismatch convincing evidence that a structure is incorrect).

The infrared spectrum of an unknown C_4H_4 isomer shows noticeable absorptions at 854, 1608, 2994 and 3080 cm^{-1} . Possible structures include but-1-yne-3-ene, butatriene, singlet-1,3-butadiene, methylenecyclopropene and tetrahedrane.



1. Build all five molecules and put into a single document (start with **New Molecule** and not **New** following the first molecule). Replace your structures with those from the database. *Click* on

 to the right of the molecule name at the bottom of the screen to bring up the **Preview** dialog and *click* on **Replace All**.

2. Give proper names to the compounds. Open the spreadsheet (**Spreadsheet** under the **Display** menu), *click* on **Label** (the leftmost header cell), then *right click* and select **Rename Selected Using SSPD** from the menu that appears.
3. Select **Spectra** from the **Display** menu and *click* on the **IR** tab at the top of the resulting dialog. Numerical values of the frequencies and infrared intensities of the selected molecule in the document will appear at the left of the dialog. Note that the frequencies have been scaled to take account of systematic errors in the calculations. To see unscaled frequencies, move the slider bar to the right of **Scale:** from 0.962 (the default) to 1.000. To return to scaled frequencies, *click* on the **Standard** button. Display the infrared spectrum of the selected isomer. *Click* on **Draw Calculated** at the right of the dialog. Move through the list to bring up the spectra for the other isomers.

The calculated infrared spectrum of which C₄H₄ isomer best fits the unknown infrared spectrum?

4. Close any molecules and dialogs that are open on screen.

17

Using ^{13}C NMR Spectra to Distinguish Structural Isomers

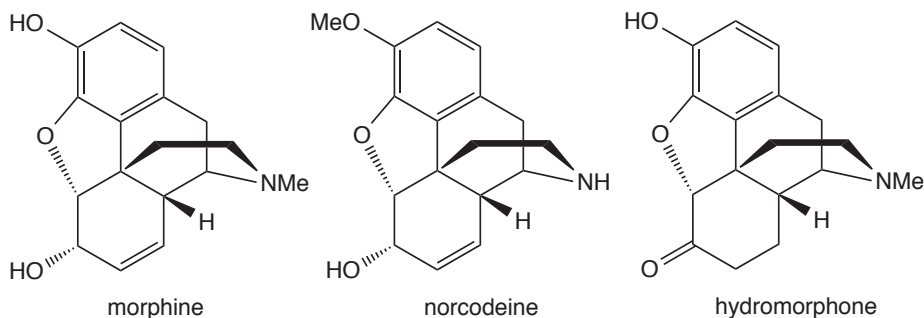
NMR spectroscopy, in particular ^{13}C NMR spectroscopy, is arguably the single most important tool available to an organic chemist to establish molecular structure. Obtaining an NMR spectrum is straightforward and the spectrum itself is very simple, comprising but a single line for each unique carbon in the molecule. Because a mass spectrum is normally also available, the molecular formula will be known, and assignment of the NMR reduces to deciding among possible isomers. Chemical evidence (how the molecule was made) can usually be counted on to eliminate some choices and to strengthen the case for others. Still, pinning an NMR spectrum to a particular molecule can be difficult and fraught with error.

NMR assignment problems can be reduced but not altogether eliminated by requiring that both proton and ^{13}C NMR spectra are consistent with a particular structure. This is routine practice. In principal, all ambiguity can be eliminated by cross-correlating the results of the ^{13}C NMR with those of proton NMR using a variety of so-called 2D spectra. However, 2D NMR experiments are not yet the norm, if for no other reason because they require significant instrument time on a spectrometer that may cost upward of \$1,000,000.

The fact that NMR spectra for reasonable size organic molecules may now be routinely calculated in a few minutes to a few hours on a personal computer costing \$1000 or less raises the possibility for another tool to assist with spectral assignments. Whether this possibility becomes a reality ultimately depends on the ability of the calculations to obtain NMR spectra that are sufficiently accurate to distinguish among the different isomers.

In this tutorial we see which of three structural isomers with molecular formula $C_{17}H_{19}NO_3$ (morphine, norcodeine and hydromorphone) best fit the NMR spectrum of an unknown isomer, or if clear assignment is not possible.

1. Build morphine, norcodeine and hydromorphone and put in the same document. (If the name for each fails to appear at the bottom of the screen, then you have made a mistake.)



Click on the **Replace All** button at the bottom of the **Preview** dialog. This will substitute structures from SSPD for what you have built. To name the three isomers, bring up a spreadsheet (**Spreadsheet** under the **Display** menu), *click* on **Label** (the leftmost header cell), then *right click* and choose **Rename Selected Using SSPD** from the menu.

2. Bring up the ^{13}C **NMR Spectra** dialog (**Spectra** under the **Display** menu) and *click* on the ^{13}C **NMR** tab. *Click* on **Draw Calculated** in the section designated ^{13}C **Spectra**. Next, *check* **Local File** in the section designated **Experimental Data From**, *click* on **Draw Experimental**, move to the *using SSPD* subdirectory under the *tutorials* directory and *click* on *unknown C17H19NO3 carbon NMR*. You will need to repeat this two more times (providing the same experimental spectrum for each of the three candidates). Calculated and experimental ^{13}C spectra now appear on the same plot. Step through the three isomers. Which, if any, of the calculated ^{13}C spectra best fits the experimental spectrum? To associate lines with specific carbons in each of the calculated spectra, bring up the **Atom Properties** dialog. Select **Properties** from the **Display** menu and *click* on an atom. Alternatively, you can attach chemical

shifts as labels on your structures. Select **Configure** from the **Model** menu and *click* on **Chem Shift** under **Atom** in the dialog that results. Simplify your models by changing to a tube model (**Tube** under the **Model** menu) and by removing hydrogens from the model (**Hydrogens** under the **Model** menu).

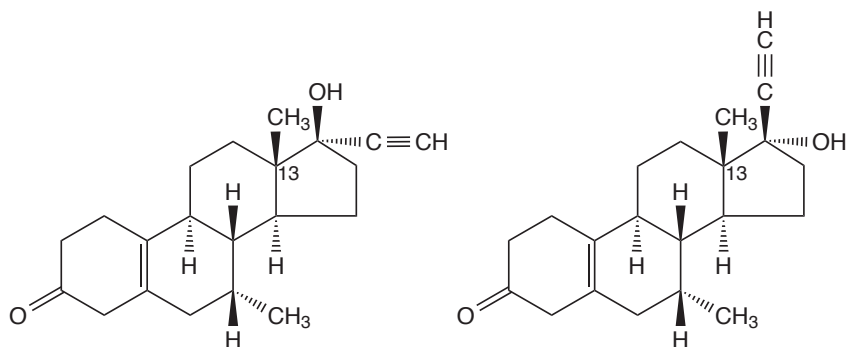
3. Close any molecules and dialogs that are open on screen.

18

Using ^{13}C NMR Spectra to Distinguish Stereoisomers

The combination of 1D and 2D NMR spectra is usually able to provide unambiguous assignment of molecular structure, including assignment of stereochemistry. However, practical considerations (time on an expensive instrument) often make 2D experiments the exception rather than the normal. Distinguishing stereoisomers may be difficult experimentally, simply because the alternatives are likely to be structurally very similar. For the same reason, it is likely to be an ideal case for calculations, because comparisons between molecules with similar structures should benefit from cancellation of errors. Are calculated ^{13}C NMR spectra good enough to be able to clearly be able to distinguish between stereoisomers?

The hydroxyl CO bond in tibolone, shown below on the left, is *gauche* to the methyl group at C_{13} (the alkyne is *anti*), whereas it is *anti* (and the alkyne is *gauche*) in the stereoisomer shown on the right. The experimental ^{13}C spectrum of a molecule that has been assigned as tibolone shows a line at 12.7 ppm attributed to the methyl group at C_{13} and lines at 88.9 and 74.8 ppm attributed to the internal and external alkyne carbons, respectively.



1. Build both stereoisomers and replace your structures with those in SSPD. (If the name for each fails to appear at the bottom of

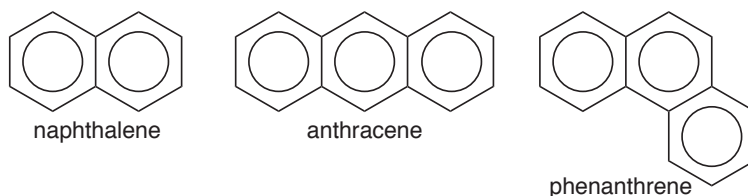
the screen, then you have made a mistake.) Select **Properties** from the **Display** menu and for each stereoisomer, record the calculated ^{13}C shifts for the methyl group carbon and for the two alkyne carbons. Do the calculations support or refute the experimental assignment, or are they ambiguous?

2. Close any molecules and dialogs that are open on screen.

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Electrophilic Reactivity of Polycyclic Aromatics

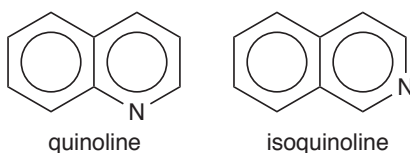
Naphthalene, anthracene and phenanthrene undergo electrophilic substitution similar to benzene. Are they likely to be more or less reactive? Local ionization potential maps should be able to provide an answer. The lower the potential on the aromatic ring, the more likely it is to give up an electron, that is, the more susceptible it will be to electrophilic attack.



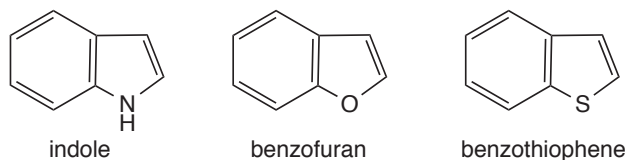
1. Build benzene, naphthalene, anthracene and phenanthrene and put into a single document. With any of the four molecules selected, *click* on **Replace All** from the **Preview** dialog. Give the molecules proper names. Bring up a spreadsheet (**Spreadsheet** under the **Display** menu), *click* on **Label** (leftmost header cell), then *right click* on an empty header cell and choose **Rename Selected Using SSPD** from the menu.
2. Bring up the **Surfaces** dialog from the **Setup** or **Display** menu and make certain that **Global Surfaces** is *checked*. *Click* on **Add** at the bottom of the dialog and select **Local Ionization Potential Map** from the menu. When the graphics calculations have completed (a few tens of seconds), bring up the spreadsheet (**Spreadsheet** under the **Display** menu) and *check* the box to the left of each of the four entries. The four molecules will now be simultaneously displayed, but they will be coupled. To move them independently, select **Coupled** from the **Geometry** menu (this will remove the checkmark to the left). Position the four

molecules on screen such that the π system is visible, and *check Local Ionization Potential Map* inside the **Surfaces** dialog. Which of the four molecules is indicated by its local ionization potential map to be most susceptible to electrophilic attack? Which positions on naphthalene, anthracene and phenanthrene are most susceptible?

3. Compare local ionization potential maps for naphthalene, quinoline and isoquinoline. Focusing on the carbon ring, which of the three is likely to be most susceptible to electrophilic attack? Which is likely to be least susceptible?



4. Compare the local ionization potential map for naphthalene with those of indole, benzofuran and benzothiophene. Focusing on the carbon ring, which of the four compounds is most susceptible to electrophilic attack? Which is the least susceptible?



5. Close any molecules and dialogs that are open on screen.