

# Spartan Student Tutorials

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# Getting Started

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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 the user interface and in doing so, illustrate the setup, 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 building and sketching a variety of molecules and 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.

*Walking Through Spartan Student (Tutorial 1)* provides a “guided tour” introducing rudimentary program operations. No molecules are sketched (2D) or built (3D) and no calculations are performed. Rather, molecular structures, properties and spectra resulting from previous calculations are examined, as are graphical models for the description of charge distribution and chemical reactivity.

*Sketching Organic Molecules (Tutorial 2) and Building Organic Molecules (Tutorial 3)* present alternative ways to specify molecular structure, the first step in performing a molecular mechanics or quantum chemical calculation. The advantage of 2D sketching over 3D building becomes more and more evident as molecular size and complexity increase, and with the rapidly growing popularity of touch-screen tablets and Windows PC's. The 3D building paradigm is quite general and *Spartan Student* provides tools not only for building organic molecules (described in **Tutorial 3**) but also for inorganic and organometallic molecules and for polypeptides and polynucleotides. The tutorials in these chapters are limited to building/sketching and do not involve either calculations or examining the results of calculations.

The tutorials in *Spectra, Properties, and Graphical Models of Organic Molecules from the Database (Tutorial 4)* and *Spectra, Properties*

*and Graphical Models from Quantum Chemical Calculations (Tutorial 5)* make use of the same molecules sketched or built in the previous chapters, but with focus on obtaining and interpreting the results of calculations.

The tutorials in *Groups of Organic Molecules (Tutorial 6)* introduce multi-molecule documents and associated spreadsheet, plotting and analysis tools available in *Spartan Student*. In order to save time, no quantum chemical calculations are required with all results being drawn from the database (Spartan Spectra Properties Database).

The tutorials in *Spectra of Organic Molecules (Tutorial 7)* further illustrate the use of *Spartan Student* to interpret infrared spectra and to assist in the assignment of NMR spectra.

All of the molecules considered up to this point are either rigid or have been assumed to exist in a single conformer. In reality, most molecules can adopt more than one conformation. The tutorials in *Flexible Molecules (Tutorial 8)* illustrate how to examine the conformational profile of a molecule with only a single rotatable bond, how to assign the lowest-energy conformer of a molecule with multiple degrees of freedom and how to interpret the NMR spectrum of a flexible molecule.

*Organic Reactions (Tutorial 9)* illustrates two approaches available in *Spartan Student* for finding the transition state for an organic reaction. The first starts from a guess based on the structure of the reactant together with a set of “reaction arrows”, while the second moves a geometric variable through the transition state.

Applications to proteins and nucleotides are provided in *Biomolecules (Tutorial 10)*. Access to the PDB is illustrated.

Finally, *Inorganic and Organometallic Molecules (Tutorial 11)* illustrates the inorganic model kit available in *Spartan Student*. An example of a transition state for an organometallic reaction is also provided.

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# Tutorial 1

## Walking Through *Spartan Student*

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*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 models 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, molecules are not sketched or built and no calculations are performed.*

1. Start **Spartan Student**. 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 that appears at the top of the screen. A file browser appears.

 Tap on  at the top of the screen. If the icon is not available, tap on **File** in the menu bar to bring up a palette of icons and then tap on .

Move to the **Tutorials** directory\*, click on **Walking Through Spartan Student** and click on **Open**.

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\* For **Windows**, the **Tutorials** directory is found in **Program Files/Wavefunction/Spartan Student**. It needs to be copied and saved to another location to access. For **Macintosh**, the **Tutorials** directory is on the **Spartan Student** disc image. It needs to be copied to another location available to the user (we recommend Documents or Desktop).



Tap on ***Walking Through Spartan Student*** and tap on **Open**. Note that *click* (left mouse button) and *tap* (one finger) are equivalent as are *double click* and *double tap*. We shall only indicate *click/double click* throughout the text that follows.

A single document 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; its name will appear at the bottom right of the screen. The appearance of the name means that the molecule is included in the  $\approx 6,000$  molecule subset of the Spartan Spectra and Properties Database (SSPD) installed with ***Spartan Student***.

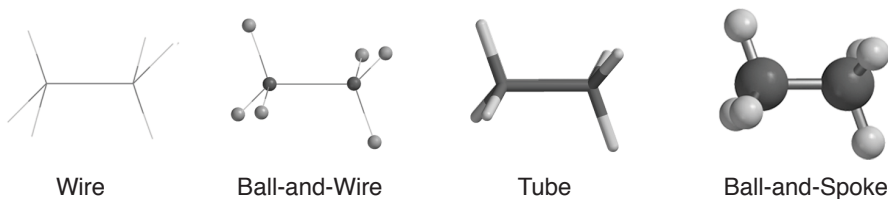
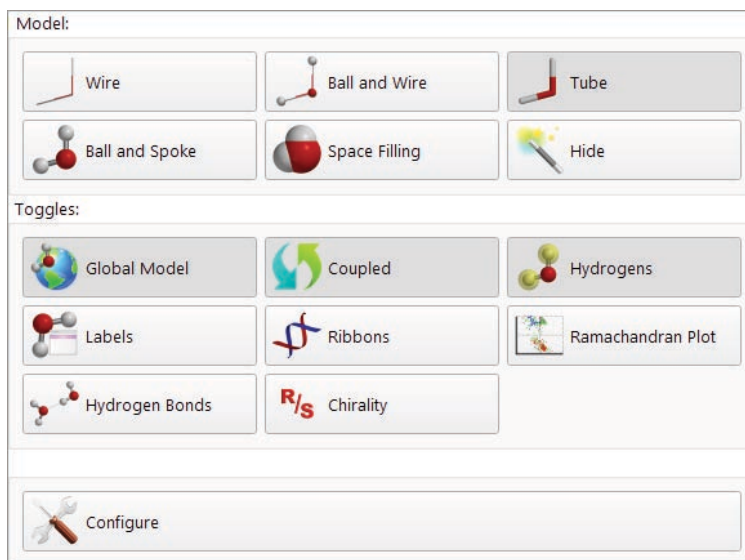
2. Practice rotating (*move* the mouse while holding down the left button), rotating in the plane of the screen (move the mouse while holding down both the left button and the **Shift** key), and translating (*move* the mouse while holding down the right button). Use the scroll wheel to zoom in and out, or alternately move the mouse up or down while holding down both the right mouse button and the **Shift** key.



To rotate, move one finger across the screen. To rotate in the plane of the screen, twist two fingers. To translate, move two fingers across the screen. To zoom in, pinch two fingers together. To zoom out, move two fingers apart.

Click on **Model** from the menu bar.

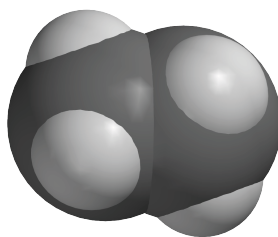




One after another, select **Wire**, **Ball and Wire**, **Tube** and finally **Ball and Spoke** from the palette of icons that results from selection of the **Model** menu. All four models for *ethane* show roughly the same information. The wire model looks the most like a conventional line formula. It 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 colored spheres, making it easy to identify atom locations. The tube model is identical 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 easy to see atom locations.

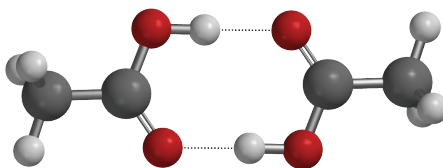
Select **Space Filling** from the palette of icons that results from the selection of **Model** menu.



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 provides a measure of molecular 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 interface. 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 access *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. Click on the **Model** menu and select **Hydrogen Bonds**.



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

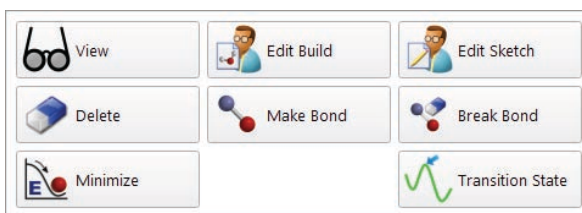
The two hydrogen bonds responsible for holding the acetic acid molecules together will be drawn.

Use the **3** key to toggle between stereo 3D and standard display. To view in 3D you will need to wear red/blue glasses.


- Distances, angles, and dihedral angles can easily be measured with *Spartan Student* using **Measure Distance**, **Measure Angle**, and **Measure Dihedral** (respectively), from the **Geometry** menu.






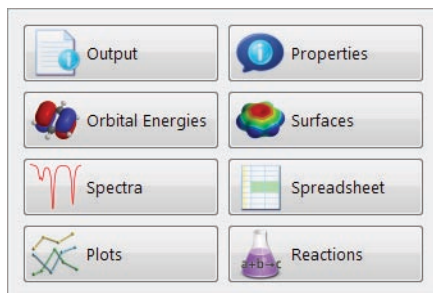
- Measure Distance:** This measures the distance between two atoms. *Click* once on to move to the next molecule, *propene*. *Click* on the **Geometry** menu and select **Measure Distance** (or *click* on the icon if it appears at the top of the screen). *Click* on a bond or on two atoms (the atoms do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





- Measure Angle:** This measures the angle around a central atom. *Click* once on to move to the next molecule, *ammonia*. *Click* on the **Geometry** menu and select **Measure Angle** (or *click* on the icon if it appears at the top of the screen). *Click* first on H, then on N, then on another H.

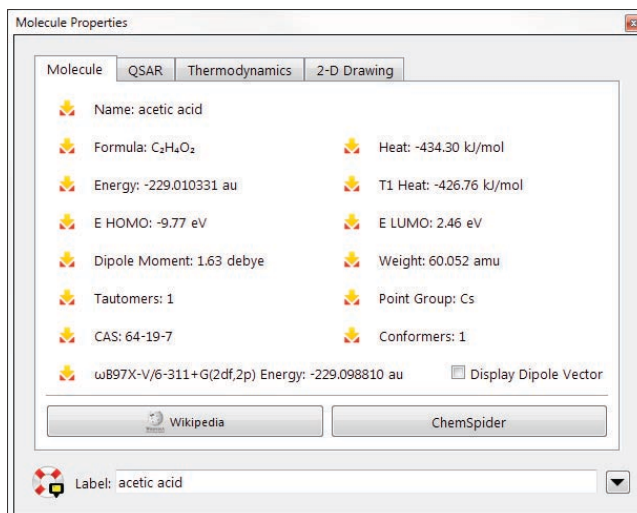
Alternatively, *click* on two NH bonds. The HNH angle (in degrees) will be displayed at the bottom right of the screen. *Click* on  when you are finished.

- 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**. *Click* on the **Geometry** menu and select **Measure Dihedral** (or *click* on the  icon if it appears 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 right of the screen. *Click* on  when you are finished.
5. Energies, dipole moments, atomic charges, thermodynamic and QSAR properties (among other calculated data) are available from **Properties** under the **Display** menu.



### Molecule Properties:

- a) **Molecule:** *Click* once on  to move to the next molecule, **acetic acid**. *Click* on the **Display** menu and select **Properties** (or *click* on  icon if it appears at the top of the screen). The **Molecule Properties** dialog appears. It provides the energy and a host of other information relating to the isolated molecule.

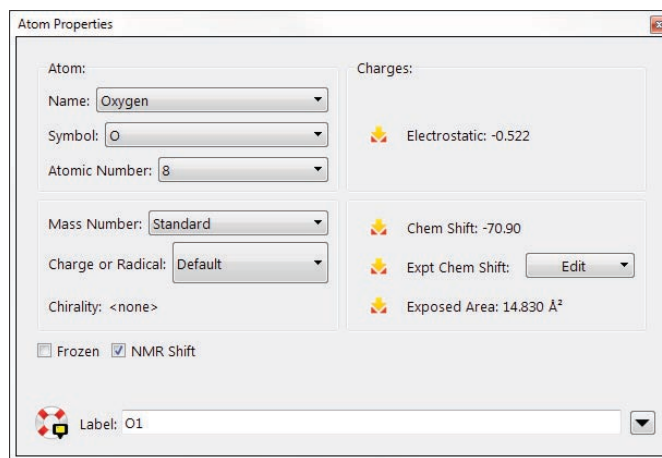



The energy for acetic acid is given in atomic units (**Energy** in au). The magnitude of the dipole moment (**Dipole Moment** in debye) is also provided in the **Molecule** tab. A large dipole moment indicates large separation of charge. You can display the dipole moment vector,  $\text{+} \rightarrow$  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.

The vector will not be displayed if the dipole moment is zero. The dipole moment will not be reported if the molecule is charged because in this case it depends on the location and orientation of the molecule in space.



- b) **QSAR:** Quantitative structure - activity relationship properties including area, volume and polar surface area (and many others) may be accessed from the QSAR tab.
- c) **Thermodynamics:** Thermodynamic properties including zero-point energy, entropy, enthalpy, Gibbs free energy, and heat capacity are available from the Thermodynamics tab.
- d) **2-D Drawing:** Spartan Student Edition will generate a 2-D drawing for anything constructed in 2D or 3D (with a maximum limit of 100 atoms).

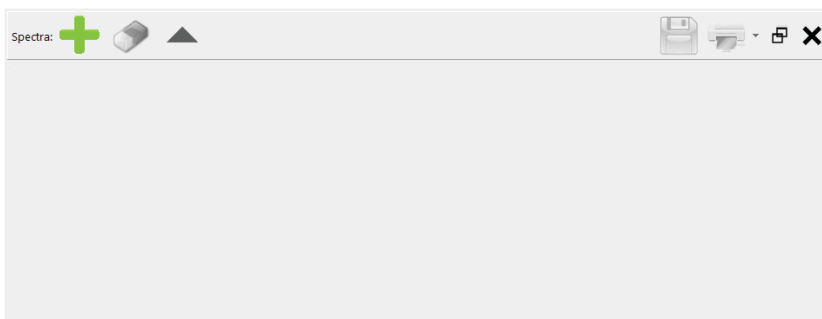
- e) **Atomic Charges:** To display the charge on an atom, *click* on it when the **Molecule Properties** dialog is on screen. The **Atom Properties** dialog replaces the **Molecule Properties** dialog.





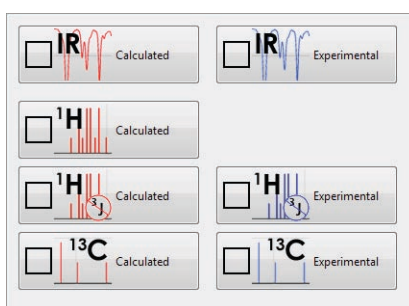
Atomic charges based on the electrostatic potential are given in units of electrons. A positive charge indicates a deficiency of electrons and a negative charge indicates an excess of electrons. Repeat for other atoms. Confirm that the positively-charged atom(s) lie at the positive end of the dipole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

- f) **Infrared Spectra:** Molecules vibrate (stretch, bend, twist) even at absolute zero. The infrared spectrum of a molecule arises due to transitions between ground and excited-state vibrational energy levels, that is, correspondence of the frequency of the light and the energy of vibrational excitation. Infrared spectroscopy is important for identifying molecules as different functional groups vibrate at noticeably different and characteristic frequencies.

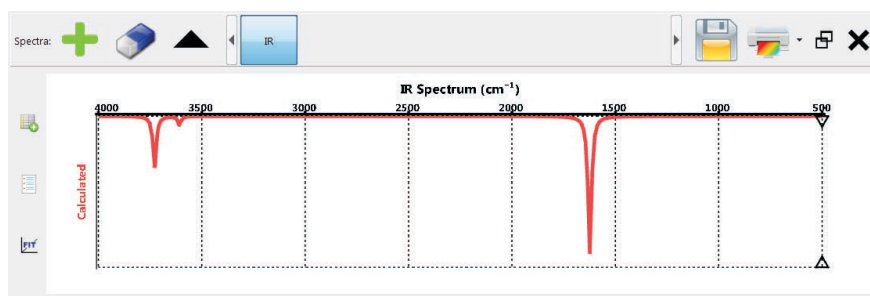
*Click* once on  to move to the next molecule in the document, *water*. To animate a vibration, select **Spectra** from the **Display** menu (or *click* on  if it appears at the top of the screen). This leads to an empty spectra pane at the bottom of the screen.



Click on  at the top left of the pane and select  from the available spectra.




The calculated IR spectrum of water from 4000 - 500  $\text{cm}^{-1}$  appears in the pane.




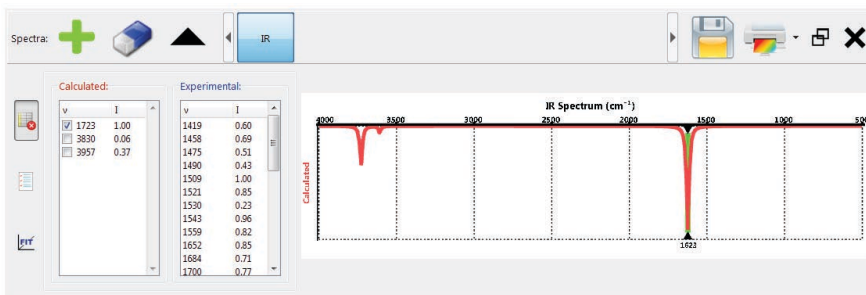
There are three lines, one of moderate intensity around 3728  $\text{cm}^{-1}$ , one very weak around 3608  $\text{cm}^{-1}$  and one very strong around 1623  $\text{cm}^{-1}$ . In turn, move the cursor on the spectrum (move the mouse while holding down the left mouse button over each of these lines). In response, the molecular model will vibrate. The line of moderate intensity corresponds to an asymmetric OH stretching motion, the very weak line





corresponds to a symmetric OH stretching motion and the strong line corresponds to the HOH bend.

To translate the plot inside the pane, position the cursor over the spectrum and move the mouse left or right while holding down the right button. To expand or contract the scale of the IR plot from its default range, position the cursor over the spectrum and use the scroll wheel on your mouse (or alternatively move the mouse while holding down both the right button and **Shift** key). To reset the spectra plot to the original values, *click* on  in the bar at the top of the spectra pane.



To see a complete listing of frequencies and intensities, *click* on  at the left of the spectra pane.



*Click* on each entry in the table to highlight the frequency in the spectrum and animate the vibration. *Click* on  again to dismiss the table and *click* on  to remove the spectrum.

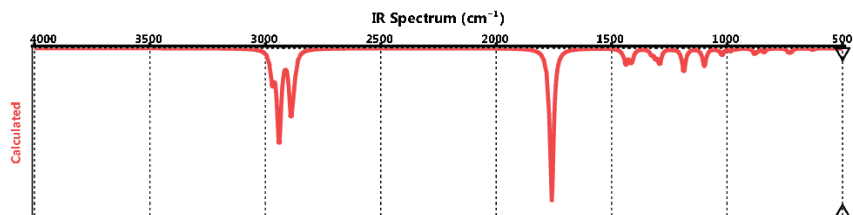


Changing the size of the spectra pane as well as translating and rescaling a spectrum is quite simple with touch screen operations. To resize the spectrum, position one finger inside the menu bar at the top of the spectra pane and move up or down. To translate the spectrum, move two fingers over the spectrum. To alter the scale, pinch two fingers over the spectrum.


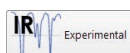
*Click* once on  to move to *cyclohexanone*, the next molecule in the list. The spectra pane is still on screen but should be empty. (If it is not on screen, select **Spectra** from the **Display** menu or *click* on  if it appears at the top of

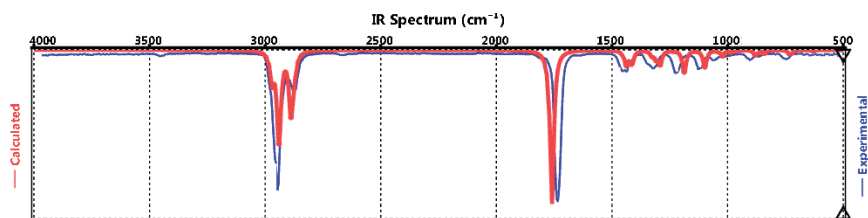


the screen to restore.) Click on  in the bar at the top of the spectra pane and select . The calculated infrared spectrum of cyclohexanone appears.



The spectrum obtained from quantum chemical calculations has been broadened (to account for finite temperature) and scaled (to account for the fact that the underlying energy function is assumed to be quadratic). The same broadening and scaling parameters are used for all molecules. The strongest line appears at  $1759\text{ cm}^{-1}$  and corresponds to a CO stretch. The fact that the line is both intense and isolated from other features in the spectrum makes it a very useful indicator of carbonyl functionality. Move the cursor over this line and examine the “vibrating” model for cyclohexanone on screen above the spectrum.



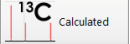
Click again on  and this time select . The experimental IR spectrum (from the public NIST database) is superimposed on top of the calculated spectrum.

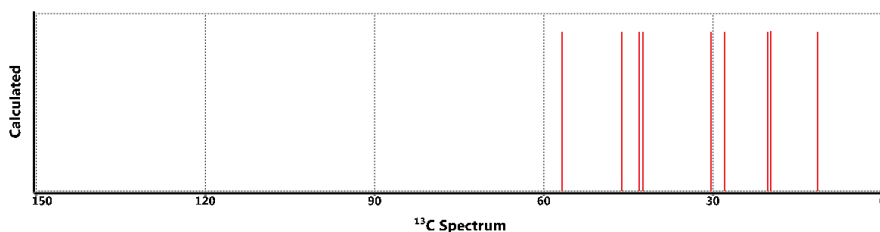


Note that the two spectra are quite similar. This would have not been the case with the raw calculated data, however, calculated frequencies and intensities have been empirically corrected to account for finite temperature and for systematic errors in the theory.

When you are done, select  from the bar at the top of the spectra pane.

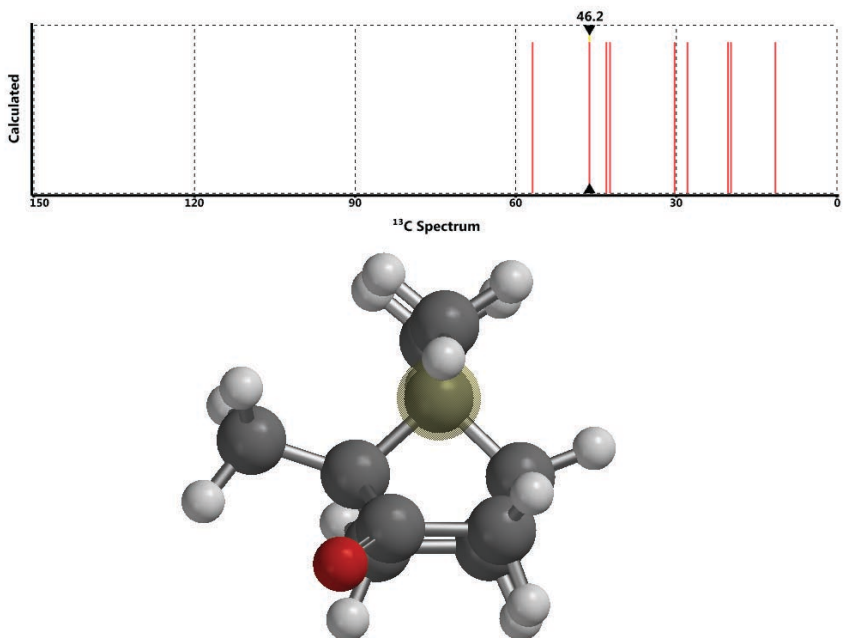
e) **NMR Spectra:** Along with mass spectrometry, NMR spectroscopy is the most powerful tool available with which to assign molecular structure. Among the nuclei that exhibit NMR spectra, proton and  $^{13}\text{C}$  are by far the most important.



Click once on  to move to the next molecule in the document, *camphor*. With the spectra pane on screen, click on  in the bar at the top of the spectra pane and select . The calculated  $^{13}\text{C}$  NMR spectrum appears.

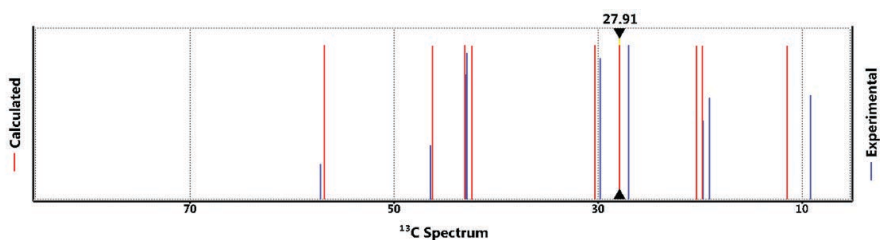


This comprises nine lines, in the range of 150 to 0 ppm (there is a tenth line corresponding to the carbonyl carbon at 217 ppm). You can zoom out to see this line by using the scroll wheel on your mouse. More instructive is to zoom in on the range from 60 to 0 ppm to get a better look at the other lines.


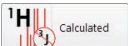
Move the mouse while holding down the left button over the spectrum. When you come to a line, the chemical shift will appear at the top of the spectrum and the atom (or atoms) responsible for this line will be highlighted on the model displayed above the spectrum.

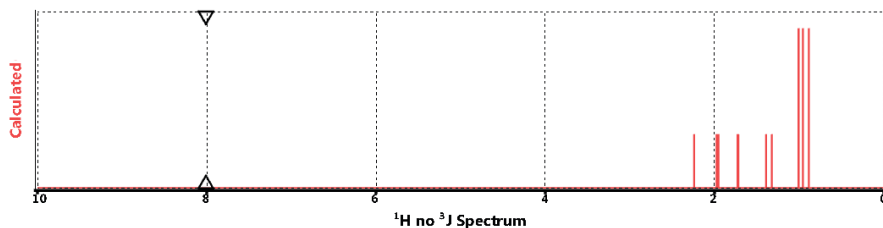


Again, *click* on  in the bar at the top of the spectra pane and select . The experimental  $^{13}\text{C}$  spectrum obtained from a public database will be superimposed on top of the calculated spectrum.


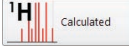


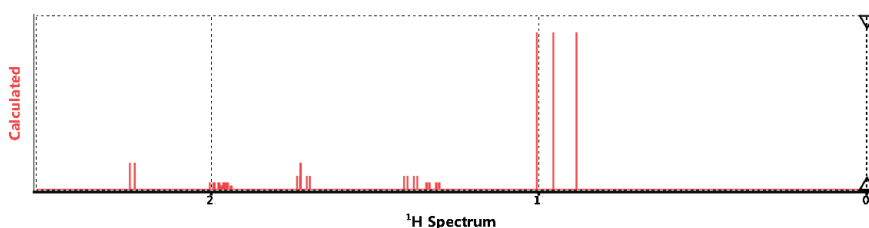
You will see that the overall agreement between calculated and experimental  $^{13}\text{C}$  spectra is quite good. As with infrared spectra (see preceding discussion of cyclohexanone), the data resulting from the quantum chemical calculations have been empirically corrected (for density functional calculations only).

*Click* again on  and select . An “idealized” proton spectrum where three-bond HH coupling constants are set to zero appears.




The manipulations are as before and the hydrogens responsible for selected lines are highlighted in the model. No experimental spectrum is available, but the quality of the match would be expected to be similar to that previously observed with comparison of  $^{13}\text{C}$  spectra.

Click again on  and select  from the palette. The resulting spectrum which takes account of three-bond HH coupling is more complicated and much closer to what would be observed experimentally. Coupling constants and splitting patterns have not actually been calculated from quantum mechanics, but rather have been estimated based on local environment.





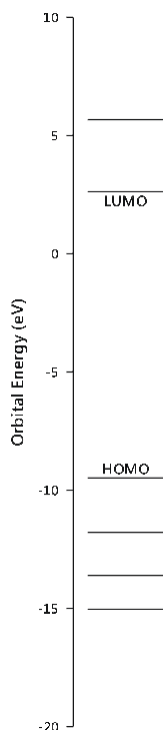
Zoom in on specific lines (scroll wheel) to see the detailed splitting patterns. For example, the two protons at  $\text{C}_3$  are both split by the proton at  $\text{C}_4$ . The doublet at 2.23 ppm shows a much larger splitting than the doublet at 1.99 ppm (you need to zoom way in to see that this is a doublet). This reflects the fact that the proton responsible for the line at 2.23 ppm makes a dihedral angle of  $43^\circ$  with the proton at  $\text{C}_4$ , whereas the proton responsible for the line at 1.99 ppm makes a dihedral angle of  $80^\circ$ .

Finally, note that you can switch among the three calculated NMR spectra (as well as the experimental  $^{13}\text{C}$  spectrum)

for camphor by *clicking* on the associated button in the bar above the spectra pane. When you are done, remove all three spectra by *clicking*  three times in succession.

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**. Click on the **Display** menu and select **Orbital Energies** (or click  if it appears at the top of the screen). 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 unoccupied molecular orbitals.

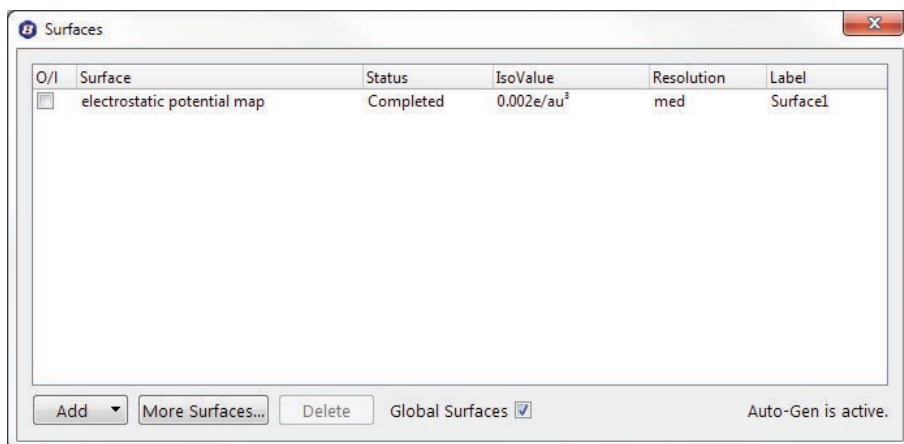



*Click* on the energy level in the diagram labeled **HOMO**. In a second, the familiar  $\pi$  bond in ethylene will appear. Note that the graphic has “blue” and “red” regions. These correspond to positive and negative values of the orbital (the absolute sign is arbitrary). Examine the other occupied orbitals (by *clicking* on their respective energy levels in the diagram) as well as the lowest-unoccupied molecular orbital (the **LUMO**). Note that you can move from one level to the next by moving the mouse up or down while holding down and then releasing the left button.



“Swipe” one finger up or down over the orbital energy diagram to move to the next higher or lower energy level.

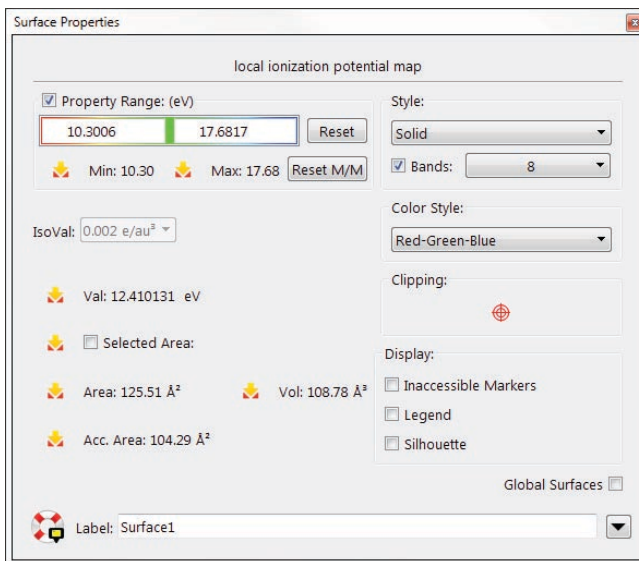
*Click* once on  to move to the next molecule in the list, **benzene**. *Click* on the **Display** menu and select **Surfaces** from the palette (or *click* on  if it appears at the top of the screen). The **Surfaces** dialog appears.





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  $\pi$  system (by convention, indicating negative potential and the fact that this region is attracted to a positive charge), and blue in the  $\sigma$  system (by convention, indicating positive potential and the fact that this region is repelled by a positive charge). *Click* on the **Display** menu and select **Properties** (or *click* on  if it appears at the top of the screen) and *click* on the surface. 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.\*

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



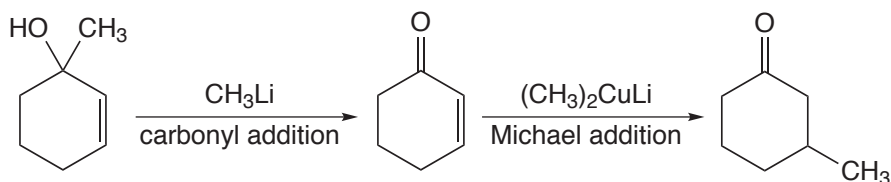
Click once on  to move to the next molecule in the list, ***aniline***, and select ***local ionization potential map*** inside the **Surfaces** dialog. By convention, red regions on a local ionization potential map indicate areas from which electron removal (ionization) is relatively easy, meaning that 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 last 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. 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). By convention, the



color blue is used to represent maximum value of the LUMO and the color red, minimum value. Note that there are two blue regions, one directly over the carbonyl carbon and the other over the  $\beta$  carbon. This is entirely consistent with known chemistry. Enones may either undergo carbonyl addition or conjugate (Michael) addition.



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

# Tutorial 2

## Sketching Organic Molecules

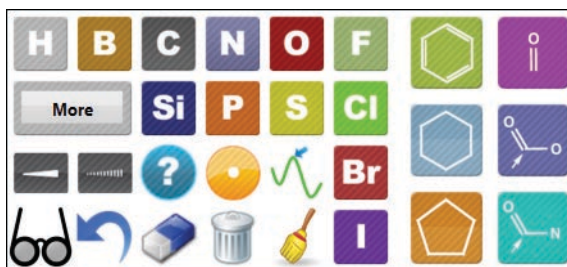
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*The tutorials in this section introduce and illustrate tools to sketch organic molecules in 2D and then to automatically convert them into realistic 3D structures.*

Not only are 2D sketches or drawings more familiar to most chemists than 3D structures, they are often easier to produce especially for complex molecules that may incorporate fused rings or require stereochemistry to be defined. The advent of touch-screen computers makes the argument for sketching as an alternative to building even more compelling. Molecules that require several minutes to build in 3D can be sketched in seconds. The key is automatic and reliable conversion from 2D drawings to 3D structures.

### Sketch Palette

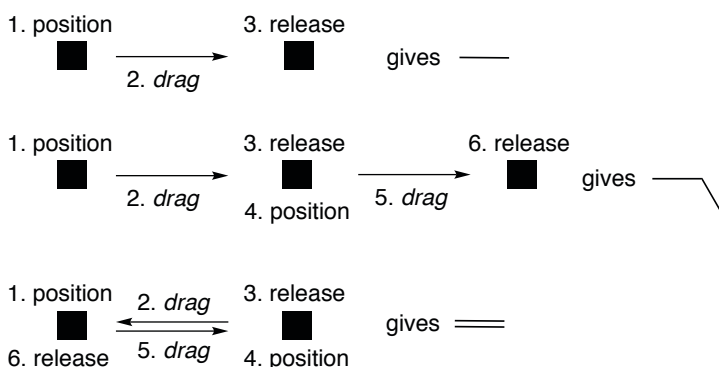
The sketch palette contains tools for making and manipulating 2D drawings, including tools for adding cues to designate stereochemistry.



These include atoms that are most commonly found in organic molecules (H, B, C, N, O, F, Si, P, S, Cl, Br and I), the phenyl, cyclohexyl and cyclopentyl rings and the carbonyl, acid/ester and amide functional groups. A **More** icon (immediately below H and B atoms) allows for entering additional elements and functional groups from a library. The palette also contains stereochemical markers and charge/radical markers.

## Sketching a Molecule

To start a sketch, first select (*click* on) an atom, group, ring or wildcard icon in the palette and then *double click* in the white portion of the screen (the drawing area). To draw a bond, first *click* on an atom, group, or ring icon in the palette to designate what is at the end of the bond, then position the cursor over the atom in the drawing area where you want the bond to start, move the cursor while holding down the left button (“drag” the cursor) to the place in the drawing area where you want the bond to end and release the button. Multiple bonds are made by dragging over existing bonds.



To make a bond touch the screen where you want it to start, move one finger to where you want it to end and lift. Replace position by touch, drag by move and release by lift in the diagram above.

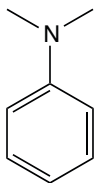
## Manipulating a Sketch








To translate the sketch, move the mouse over the screen while holding down the right button. To rotate the sketch (in the plane of the screen), move the mouse up and down while holding down both the left button and **Shift** key. Use the scroll wheel to resize the sketch.



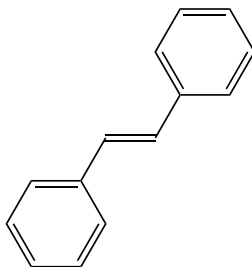
To translate the sketch, move two fingers over the screen. To rotate the sketch in the plane of the screen, “twist” two fingers on the screen. To resize the sketch, pinch (or spread) two fingers on the screen.



## N,N-Dimethylaniline




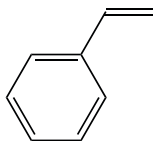
1. Select **New Sketch** from the **File** menu (or *click* on  if it appears at the top of the screen) to bring up the sketch pad. *Click* on  in the palette and *double click* on screen.
2. *Click* on  in the palette. Position the cursor over the “top” carbon on the benzene ring, *drag* it up and release. You have drawn aniline.
3. *Click* on  in the palette. Position the cursor over the nitrogen, *drag* it up and to the left and release.  is still selected. Again position the cursor over the nitrogen, *drag* it up and to the right and release.
4. *Click* on  in the palette to clean up your drawing and *click* on  to produce a 3D structure. The name *N,N-dimethylaniline* will appear at the bottom of the screen as the molecule is in the database.
5. Close *N,N-dimethylaniline*.




## trans-Stilbene



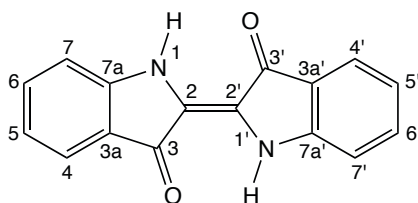
1. Select **New Sketch** from the **File** menu () to bring up the sketch pad. *Click* on  in the palette. Position the cursor on the screen, *drag* it to the right and release. Position the cursor on one end of the line (CC bond) that you have just drawn, *drag* it to the other end and release. You have drawn ethylene.




2. Click on . Position the cursor over the left end of the double bond, *drag* it down and to the left and release. You have drawn styrene.

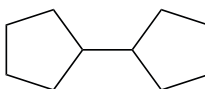



3.  is still selected. Position the cursor over the right end of the double bond, *drag* it up and to the right and release.
4. Click on  to clean up your drawing. Click on  to convert it to a 3D structure. The name ***trans-stilbene*** will appear at the bottom of the screen as the molecule is in the database.
5. Close ***trans-stilbene***.

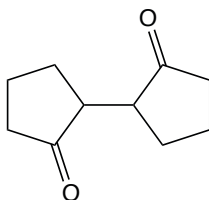
## Indigo



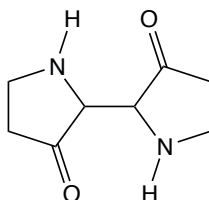
1. Select **New Sketch** from the **File** menu (). Click on  and *double click* on screen.
2.  is still selected. Position the cursor over C<sub>2</sub> (see numbering in diagram above), *drag* it to the right and release. Your sketch should appear as below.



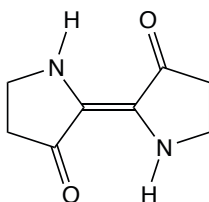
3. Select  from the palette. Position the cursor above C<sub>3</sub>, *drag* it away from the ring and release. Again position the cursor above C<sub>3</sub>, *drag* it along the CO bond to the oxygen and release. Repeat for C<sub>3</sub>'. You are left with a drawing.






4. Select **N** from the palette and one after another *double click* on C<sub>1</sub> and C<sub>1</sub>'.

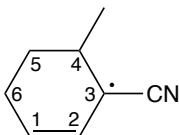


5. Select **C** from the palette. Position the cursor above C<sub>2</sub>, *drag* it to C<sub>2</sub>' and release.



6. Select  from the palette and *double click* on the bond connecting C<sub>3a</sub> and C<sub>7a</sub>. Repeat for C<sub>3a</sub>' and C<sub>7a</sub>'.
7. Click on  to clean up your drawing and click on  to turn it into a 3D structure. The name **indigo** will appear at the bottom of the screen as the molecule is in the database.
8. Close **indigo**.

### 3-Cyano-4-methylcyclohexenyl Radical





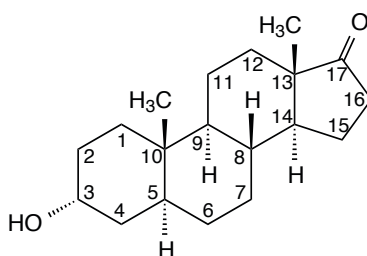

1. Select **New Sketch** from the **File** menu (). Click on  in the palette and *double click* on screen.
2. Click on **C** in the palette. Position the cursor over C<sub>4</sub> (see

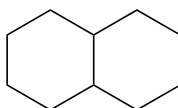
diagram above for numbering), *drag* it away from the ring and release. You have drawn methylcyclohexane.

3. **C** is still selected. Position the cursor over C<sub>1</sub>, *drag* to C<sub>2</sub> and release. You have drawn 4-methylcyclohexene.
4. *Double-click* on the **More** icon that is located immediately below H and B in the palette, and then *click* on the **Groups** tab. *Click* on **-CN** in the upper right corner. **CN** now appears as the selected icon. Position the cursor over C<sub>3</sub>, and *drag* it away from the ring and release. You have drawn 3-cyano-4-methylcyclohexene.
5. One of these icons (🔵, 🔴, 🟡) will appear in the palette directly below **P**. If it is not 🟡, *click* on the icon until the icon is 🟡. *Double click* on C<sub>3</sub>. A “dot” (radical marker) will appear next to C<sub>3</sub>.
6. *Click* on 🧼 to clean up your drawing and *click* on 👓 to make a 3D structure. The name will not appear at the bottom of the screen as this radical is not in the database.
7. Close *3-cyano-4-methylcyclohexenyl radical*.

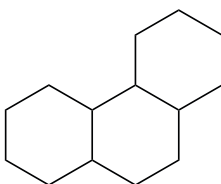
## Androsterone











1. Select **New Sketch** from the **File** menu (📄) to bring up the sketch pad. *Click* on  and *double click* on screen. Cyclohexane is still selected. *Double click* on the 5-10 bond (see diagram above).





2. Cyclohexane is still selected. *Double click* on the 8-9 bond.



3. Click on  and *double click* on the 13-14 bond. You have now drawn the complete steroid skeleton.
4. Click on , position the cursor over C<sub>10</sub>, *drag* up and release. Repeat for C<sub>13</sub>.
5. Click on . Position the cursor over C<sub>3</sub>, *drag* down and to the left and release. Position the cursor over C<sub>17</sub>, *drag* up and to the right and release. Convert the single (CO) bond at C<sub>17</sub> to a double bond. Again position the cursor over C<sub>17</sub>, *drag* along the bond to oxygen and release.
6. It is necessary to explicitly specify hydrogens at C<sub>5</sub>, C<sub>8</sub>, C<sub>9</sub> and C<sub>14</sub> in order to incorporate the necessary stereochemical cues (up and down “wedges”) in your drawing. Click on , position the cursor over C<sub>5</sub>, *drag* away from the ring and release. Repeat for C<sub>8</sub>, C<sub>9</sub> and C<sub>14</sub>.
7. Click on . Position the cursor over C<sub>10</sub>, *drag* along the bond to the methyl group that you drew in step 4 and release. Repeat for C<sub>13</sub>. Position the cursor over C<sub>8</sub>, *drag* along the CH bond that you drew in step 6 and release. Up wedges will appear for all three centers.
8. Click on . Position the cursor over C<sub>3</sub>, *drag* along the CO bond that you made in step 5 and release. Position the cursor over C<sub>5</sub>, *drag* along the CH bond that you made in step 6 and release. Repeat for the CH bonds at C<sub>9</sub> and C<sub>14</sub>. Down wedges will appear for all four centers.
9. Click on  to clean up your drawing. Click on . The name ***androsterone*** should appear at the bottom right of the screen as the molecule is in the database. If it does not, you have made



an error somewhere. Select **Edit Sketch** from the **Build** menu or *click* on  if it appears at the top of the screen to return to the sketch pad.

10. Androsterone incorporates seven chiral centers. To assign them as R or S, select **R/S Chirality** from the **Model** menu or *click* on  if it appears at the top of the screen. R/S labels will appear next to each of the chiral centers.
11. Close *androsterone*.

# Tutorial 3

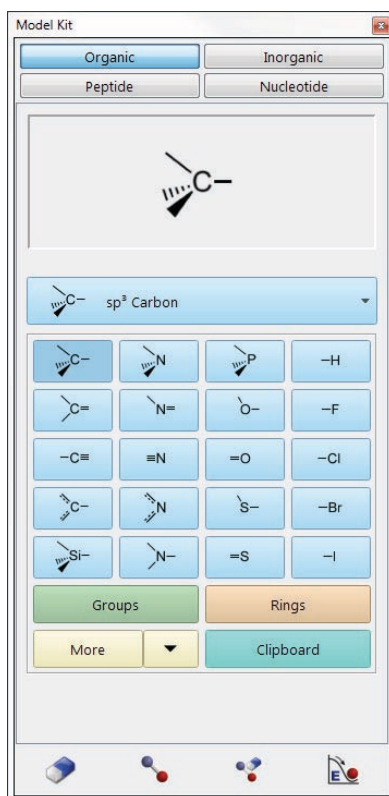
## Building Organic Molecules

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*The tutorials in this section introduce and illustrate tools to build 3D molecular structures. These include atomic fragments, functional groups and rings contained in the organic model kit together with tools for making and breaking bonds, deleting atoms and refining structure.*

### Organic Model Kit

The organic model kit contains a selection of atomic fragments corresponding to elements commonly found in organic molecules.

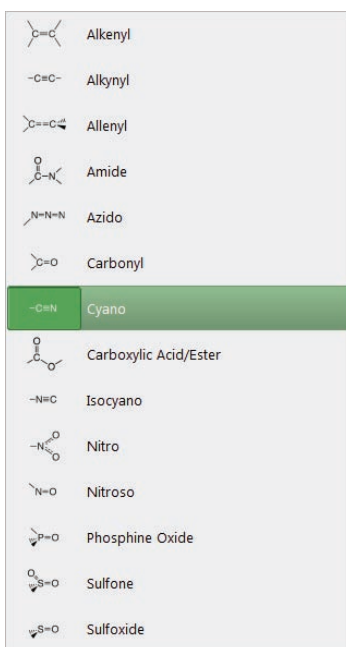


Different hybridization states are included for some elements (C, N, O, and S) from top to bottom.

C(sp <sup>3</sup> )	N(sp <sup>3</sup> )	P(sp <sup>3</sup> )	H
C(sp <sup>2</sup> )	N(sp <sup>2</sup> )	O(sp <sup>3</sup> )	F
C(sp)	N(sp)	O(sp <sup>2</sup> )	Cl
C(aromatic)	N(aromatic)	S(sp <sup>3</sup> )	Br
Si(sp <sup>3</sup> )	N(planar)	S(sp <sup>2</sup> )	I

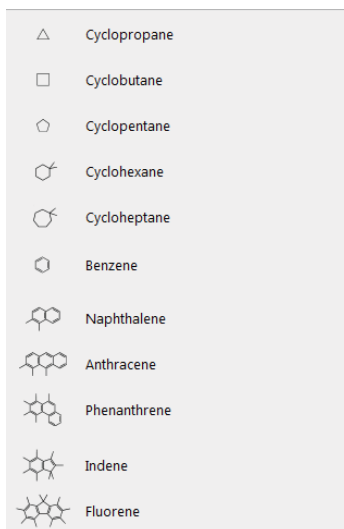
A fragment is chosen by *clicking* on its icon, which is then displayed in a box at the top of the model kit. Once selected, the fragment may be used to initiate building, to add alongside of an existing structure or appended onto an existing structure. To initiate building, *double click* anywhere on screen. To add alongside of an existing structure, *double click* in a blank area on screen. To bond to an existing structure, *click* on a free valence (**not an atom**). Free valences are colored yellow on the selected molecule. Bond type in the case of atomic fragments with multiple bond types, for example, sp<sup>2</sup> carbon, depends on the nature of the free valence selected.

*Clicking* on the **Groups** button near the bottom of the model kit changes the focus from fragments to groups, one of which will be shown in the box at the top of the model kit and named directly underneath. *Clicking* on the name brings up a menu of available groups.



Once selected from the menu, a group may be used to initiate building, to add alongside of an existing structure on screen, or to add to an existing structure.

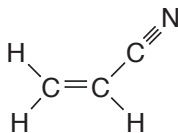
*Clicking* on the **Rings** button near the bottom of the model kit changes the focus to rings, one of which will be shown in the box at the top of the model kit and named immediately underneath. *Clicking* on the name brings up a menu of available rings.


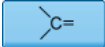







Once selected from the menu, a ring may be used to initiate building, to add alongside of an existing structure on screen, or to add to an existing structure.

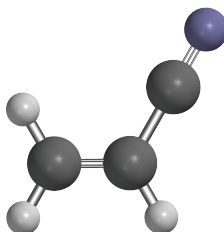
Note that only hydrocarbon rings are available. Heteroatoms may be substituted for carbons, for example, substituting an oxygen for one of the carbons in cyclohexane leading to tetrahydropyran. Note also, that the amide and carboxylic acid/ester groups and the cyclohexane, cycloheptane, naphthalene, phenanthrene, indene and fluorene rings have more than one different free valence. The free valence that is to be used is marked with a gold • (in the icon shown in the box at the top of the model kit). The marked position circulates among the possible positions with repeated *clicking* on the icon. Selection of an *axial* or *equatorial* free valence in cyclohexane and cycloheptane is indicated by the label **ax** or **eq** appearing alongside the icon.

## Acrylonitrile



1. *Click* (left button) on the **File** menu and select (*click* on) **New Build**. Alternatively, *click* on  if it appears at the top of the screen. The organic model kit appears. *Click* on trigonal planar  $sp^2$  hybridized carbon  from the fragment library. A model of the fragment appears at the top of the model kit. Bring the cursor anywhere on screen and *double click* (left button). To maintain compatibility with the sketch builder (see next tutorial), a *double click* is used to add the first fragment. This can be changed to *single click* (as in previous versions of **Spartan Student**) from the **Settings** tab in the **Preferences** dialog (**Preferences** under the **Options** menu). 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 (–).
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 (or *click* on  if it appears at the top of the screen). You can also start over by selecting **Clear** from the **Edit** menu (or *click* on  if it appears at the top of the screen).
3. *Click* on the **Groups** button at the bottom of the model kit, *click* on the name of whatever group is shown in the text box at the top of the model kit, and select **Cyano** from the 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. Click on  at the bottom of the model kit. (You can also select **Minimize** from the **Build** menu or click on  if the icon appears at the top of the screen.) The 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. The name appears at the bottom of the screen as acrylonitrile is in the database.




ball-and-spoke model

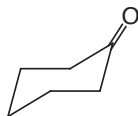
This model can be rotated, translated and zoomed by using the mouse in conjunction with keyboard functions. To rotate the model, *drag* the mouse while holding down the left button; to rotate in the plane of the screen also hold down the **Shift** key. To translate the model, *drag* the mouse with the 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).


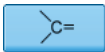


Rotate the molecule by moving one finger over the screen.  
Rotate in the plane of the screen by twisting two fingers.  
Translate by moving two fingers. Zoom by pinching two fingers.

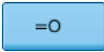


6. Select **Close** from the **File** menu or click on  at the top of the screen.

## Cyclohexanone

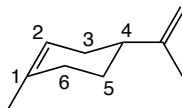



1. Click on the **File** menu and select **New Build** from the palette or click on  at the top of the screen. Click on the **Rings** button near the bottom of the model kit, click on the name of whatever ring is shown and select **Cyclohexane** from the menu. Double click anywhere on screen.
2. Select  $sp^2$  carbon  from the model kit. Double click on any carbon (*not free valence*). The  $sp^3$  hybridized carbon will be replaced by an  $sp^2$  hybridized carbon.


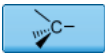


In the Organic Model Kit, fragment replacement is subject both to the usual valence rules and to the availability of free valences. For example, replacement of an  $sp^3$  carbon by an  $sp^2$  carbon requires that at least two free valences are available.

3. Select  $sp^2$  oxygen  from the model kit. Click on the double free valence on the  $sp^2$  carbon. You have made cyclohexanone. Click on  at the bottom of the model kit to produce a structure with  $C_s$  symmetry. Click on  to remove the model kit. The name **cyclohexanone** appears at the bottom of the screen as the molecule is in the database.
4. Close **cyclohexanone**.

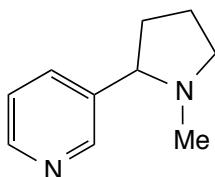
## Limonene


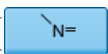


1. Select **New Build** from the **File** menu (or click on the  icon at the top of the screen) to bring up the organic model kit. Click on the **Rings** button near the bottom of the model kit, click on the name of whatever ring is shown and select **Cyclohexane** from the menu. Double click anywhere on screen.

2. Click on the **Groups** button near the bottom of the model kit, click on the name of whatever group is shown and select **Alkenyl** from the menu. Click on the *equatorial* free valence on C<sub>4</sub> (see figure above for numbering). You have made vinylcyclohexane.
3. Click on the **Make Bond** icon () at the bottom of the model kit. One after another click on the *axial* free valence on C<sub>1</sub> and then the *axial* free valence on C<sub>2</sub>. You have made 4-vinyl-1-cyclohexene.
4. Select sp<sup>3</sup> carbon () from the model kit and one after another click on the free valence on C<sub>1</sub> and on the free valence of the vinylic carbon attached to the ring. You have made limonene. Click on  at the bottom of the model kit to give a refined geometry and finally click on () to remove the model kit. The name will appear at the bottom of the screen as limonene is in the database.
5. Close *limonene*.




## Nicotine



1. Select **New Build** from the **File** menu (). Click on the **Rings** button in the model kit. Click on the name of whatever ring is shown in the window at the top of the model kit and select **Benzene** from the menu. Double click anywhere on screen.
2. Click on the name **Benzene** (the currently selected ring) in the model kit and select **Cyclopentane** from the menu. Click on one of the free valences on benzene on screen. You have made phenylcyclopentane (the name will appear at the bottom of the screen).
3. Click on sp<sup>2</sup> nitrogen in the model kit () and double click on the appropriate (*meta*) carbon (not a free valence) in




the benzene ring for the structure on screen. You have made 3-cyclopentylpyridine.

4. Click on  $\text{sp}^3$  nitrogen in the model kit () and *double click* on the appropriate carbon in the cyclopentyl ring for the structure on screen. You have made nornicotine.
5. Click on  $\text{sp}^3$  carbon in the model kit () and click on the free valence on the nitrogen in the pyrrolidine ring. Click on  at the bottom of the model kit to clean up your structure. The name ***nicotine*** will appear at the bottom of the screen as the molecule is in the database.
6. Click on the bond connecting the pyridine and pyrrolidine rings. A red arrow will encircle the bond and will also appear at the top of a narrow shaded band at the left of the screen. While holding down the left mouse button, move the cursor up or down inside this band to rotate about the bond.



Move one finger up and down on the bond to rotate about the bond.

7. Select **R/S Chirality** from the **Model** menu (). The R/S chirality will be displayed. The S isomer is the naturally occurring isomer of nicotine.
8. Close ***nicotine***.

# Tutorial 4

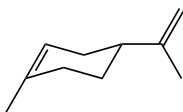
## Spectra, Properties and Graphical Models of Organic Molecules from the Database








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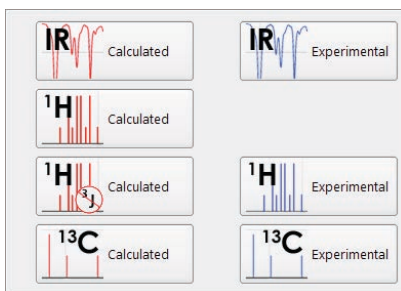
*The tutorials in this and the section that follows will utilize the molecules that you built and sketched in the preceding two tutorials. The emphasis shifts from providing input, to analyzing the results of quantum chemical calculations (this tutorial) and to submitting calculations (the following tutorial).*

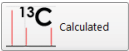
The database supplied with **Spartan Student** provides atomic and molecular properties as well as NMR spectra that have previously been calculated using the  $\omega$ B97X-D/6-31G\* or EDF2/6-31G\* density functional model. Additionally, IR spectra from the EDF2/6-31G\* is also accessible. The wave functions are available, allowing graphical models to be generated and displayed “on-the-fly”.


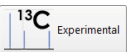

### Limonene



1. Build limonene () , minimize () and exit the builder (). Alternatively, sketch limonene () and exit the sketcher ().
2. Click on the name **limonene** at the bottom of the screen and click on **Replace** in the dialog that results. Properties and spectra for limonene are now available.
3. Select **Spectra** from the **Display** menu, or click on  if it appears at the top of the screen. Click on  at the top of the spectra pane that results to show available calculated spectra (in red) and (possibly) available experimental spectra (in blue).



Select . The calculated  $^{13}\text{C}$  NMR spectrum appears in the spectra pane. Move the cursor horizontally over the spectrum. You will see that when you intersect a line, it will be highlighted in the spectrum and the value of the chemical shift indicated. Also, the carbon (or carbons) in the structure responsible for this line will be highlighted in the structure model (in the top part of the screen). You will see that there are ten lines in the calculated  $^{13}\text{C}$  spectrum, corresponding to the ten unique carbons in limonene.

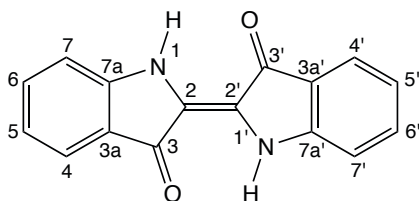
4. Again, *click* on  at the top of the spectra pane, but this time, select . The experimental  $^{13}\text{C}$  spectrum of limonene will be superimposed on top of the calculated spectrum. Visual comparison will give you an idea of what you can expect from  $^{13}\text{C}$  shift calculations. To get an even better idea, alter the range of the scale (initially from 150 to 0 ppm), by moving the cursor over the spectrum while holding down the right button. You can also change the scale (initially from 150 ppm), that is, zoom-in or zoom-out, using the scroll wheel on your mouse. You can return to the original setting by *clicking* on  in the bar at the top of the spectra pane.










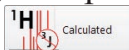

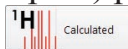



Move one finger over the spectrum to select a line. Move two fingers over the spectrum to shift the range of the scale and pinch two fingers to zoom in and out.

5. Close *limonene*.

## Indigo

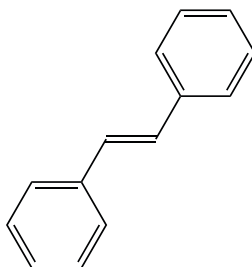











1. Build indigo () , minimize () and exit the builder (). Alternatively, sketch indigo () and exit the sketcher ().
2. Click on the name **indigo** at the bottom of the screen and make sure  $\omega$ B97X-D/6-31G\* is selected and click on **Replace** in the dialog that results. Properties and spectra for indigo are now available. If the name does not appear, then you have made an error. In this case, re-enter either the builder by selecting **Edit Build** from the **Build** menu () , or the sketch pad by selecting **Edit Sketch** from the **Build** menu () and correct your model.
3. The calculated proton NMR spectrum of indigo can be displayed in two ways. The simpler “idealized” presentation assumes that three-bond HH coupling constants are zero. Select **Spectra** from the **Display** menu () to bring up the spectra pane. Click on  in the bar at the top to show available calculated spectra (in red) and possibly available experimental spectra (in blue). Select  from the palette. The spectrum that results shows only lines corresponding to the four unique hydrogens. To see the more familiar (and more complex) proton spectrum, click again on , but this time select . The same four lines appear, but all are split (as in a real proton spectrum). The lines at  $\approx 6.72$  and  $7.88$  ppm are doublets due to  $C_7$  and  $C_4$ , respectively (and split by  $C_6$  and  $C_5$ , respectively). The lines centering at  $\approx 6.9$  and  $7.48$  are quartets (doublet of doublets), due to  $C_5$  and  $C_6$ , respectively (and split by  $C_4$  and  $C_6$  and  $C_5$  and  $C_7$ , respectively).
4. The experimental proton NMR for indigo is not available from the on-line database. However, the experimental  $^{13}\text{C}$  spectrum is available. You can if you wish compare it to the corresponding calculated spectrum. Either is accessed by clicking on  at the

top of the spectra pane followed by selecting the appropriate entry from the resulting palette.

5. Close *indigo*.


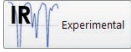
### *trans*-Stilbene



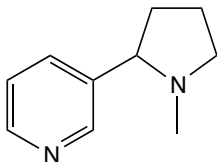
1. Build *trans*-stilbene () , minimize () and exit the builder (). Alternatively, sketch *trans*-stilbene () and exit the sketcher ().
2. Click on the name ***trans-stilbene*** at the bottom of the screen, make sure EDF2/6-31G\* is selected and then click on **Replace** in the dialog that results. Data are now available.
3. Select **Spectra** from the **Display** menu (). Click on  in the bar at the top of the spectra pane and select  Calculated. The calculated IR spectrum of *trans*-stilbene appears in the spectra pane. You may find it valuable to increase the size of the spectrum. Position the cursor inside the bar at the top of the spectra pane and *drag* it up.
4. Move the cursor horizontally over the spectrum. You will see that as you intersect a line in the spectrum, it will turn yellow and the value of the frequency will appear at the bottom. In addition, the molecular model “vibrates” to reflect the motion that the molecule undergoes. Examine the motions of one or more of the lines of moderate intensity in the vicinity of 1500 cm<sup>-1</sup> (at 1446, 1494 and 1609 cm<sup>-1</sup>). You might find it useful to expand the scale (use the scroll wheel) or to shift it (move the mouse horizontally over the spectrum while holding down the right button). You can return to the original settings by clicking on () in the bar at the top of the spectra pane.









Move one finger over the spectrum to select a line. Move two fingers over the spectrum to shift the range of the scale and pinch two fingers to zoom in and out.

5. Click on  from the bar at the top of the spectra pane and select . The experimental IR spectrum of *trans*-stilbene obtained from the public NIST database will be superimposed onto the calculated spectrum. Note that the two spectra are similar although the experimental spectrum exhibits a number of (small) lines not found in the calculated spectrum.
6. Close *trans-stilbene*.

## Nicotine

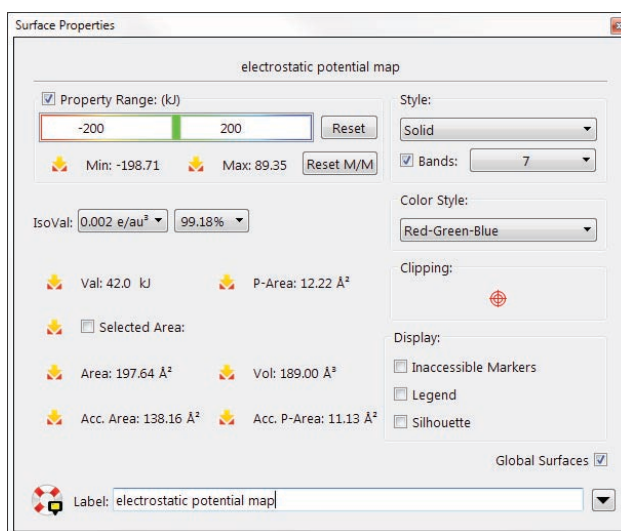


1. Build nicotine () , minimize () and exit the builder (). Alternatively, sketch nicotine () and exit the sketcher ().
2. Click on the name ***nicotine*** at the bottom of the screen, and click on **Replace** in the dialog that results. Your structure will be replaced by that in the database making the wave function available.
3. Select **Surfaces** from either the **Setup** or **Display** menu or click on () if it appears at the top of the screen. Click on **Add** (at the bottom of the **Surfaces** dialog that results) and select **electrostatic potential map** from the menu. This requests an electrostatic potential map (an electron density surface onto which the value of the electrostatic potential is mapped). A line ***electrostatic potential map*** appears at the top of the dialog.

The graphics calculation will run automatically following your request. When it completes in a few seconds, 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 nicotine. 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 two nitrogen atoms show the largest negative potential (red). Which is the more negative, the nitrogen in the pyridine ring or that in the pyrrolidine ring?

4. Quantify your observation. Select **Properties** from the **Display** menu or *click* on (🔍) if it appears at the top of the screen and *click* anywhere on the electrostatic potential map. This will bring up the **Surface Properties** dialog.



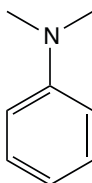
Check the box to the left of **Legend** to display the property range on screen. (Uncheck the box to remove the legend.) To translate the legend, *click* on the legend to select, then hold down the right mouse button and move the mouse. The legend is useful when making qualitative comparisons of property values. Turn the map such that you can clearly see the pyridine nitrogen and *click* on the area that is “most red”. An arrow marks the point on the surface and the value of the potential is shown to the right of the legend. Do the same for the pyrrolidine nitrogen.










Tap on the legend to select. Move two fingers to move it around the screen. Pinch two fingers to make the legend smaller or larger.

5. Nicotine is very small and it is easy to associate regions on the map with the underlying molecular skeleton. This becomes more difficult with increasing molecular size. Change the presentation, from the **Style** menu located both inside the **Surface Properties** dialog and at the bottom right of the screen. Select **Transparent** or **Mesh** from this menu. You now can see through the map to the underlying molecular structure.
6. Close *nicotine* and any open dialogs.

### N,N-Dimethylaniline



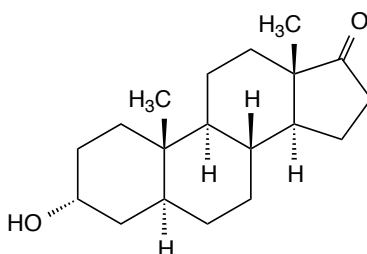
1. Build N,N-dimethylaniline () , minimize () and exit the builder () . Alternatively, sketch N,N-dimethylaniline () and exit the sketcher () .
2. Click on *N,N-dimethylaniline* at the bottom of the screen and click on **Replace** in the dialog that results. Your structure will be replaced by that in the database.
3. Select **Surfaces** from either the **Setup** or **Display** menu () . Click on **Add** at the bottom of the **Surfaces** dialog that results and select **local ionization potential map** from the menu. This requests a map showing the energy required to remove an electron (the ionization potential) as a function of its location on the electron density surface. Calculation is automatic and will only take a few seconds. When completed, check the box to the left of *local ionization potential map* in the **Surfaces** dialog. Select **Properties** from the **Display** menu or click on () . Click on the local ionization potential map surface. Click on the



**Reset M/M** button. This puts the property range on an absolute scale which is useful when examining individual molecules. The color convention is the same as for the electrostatic potential map, although the scale is completely different. Local ionization potentials are always positive. Colors toward red correspond to small ionization potentials (greatest electrophilic reactivity) and colors toward blue correspond to large ionization potentials. Note that the red regions on the map are over the *ortho* and *para* ring positions. This is exactly what is experimentally observed.


4. Close *N,N*-dimethylaniline and any open dialogs.

### Androsterone



1. Build androsterone (🖨️), minimize (🖨️) and exit the builder (👁️). It is much easier to sketch the molecule (🖨️) and exit the sketcher (👁️).
2. Click on the name **androsterone** at the bottom right of the screen and click on **Replace** in the dialog that results. Your structure will be replaced by that in the database. If the (correct) name is not provided, then you have made a mistake. In this case, re-enter the builder by selecting **Edit Sketch** from the **Build** menu (👤).
3. Select **Orbital Energies** from the **Display** menu or click on 🖨️ if it appears at the top of the screen. An orbital energy diagram will appear at the left of the screen. To examine the molecular orbital corresponding to a line in the diagram, click on the line. You will see that the LUMO is a  $\pi^*$  orbital localized on the carbonyl group. It is clearly more concentrated on carbon than on oxygen, but you cannot easily tell which side of the steroid skeleton (toward or away from the two methyl groups) it is concentrated.

For this, a LUMO map is a much better graphical model.

4. Select **Surfaces** from the **Display** menu (). Click on **Add** and select **|LUMO| map** from the menu. The graphics calculation will run automatically and will only require a few seconds. When completed, *check* the box to the left of **|LUMO| map** inside the **Surfaces** dialog. The largest (absolute) values of the LUMO are colored blue. Note that you can easily see that the LUMO is more concentrated on the face away from the methyl groups.
5. Close *androsterone* and any open dialogs.

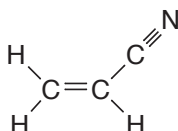
# Tutorial 5







## Spectra, Properties and Graphical Models of Organic Molecules from Quantum Chemical Calculations

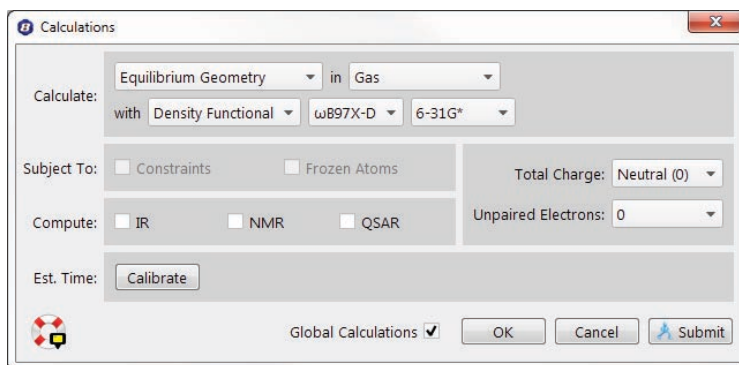
*The tutorials in this section provide the earliest, and some of the simplest examples, of specifying and performing quantum chemical calculations. As in the previous tutorial, they refer back to **Tutorials 2 and 3**.*

2 min

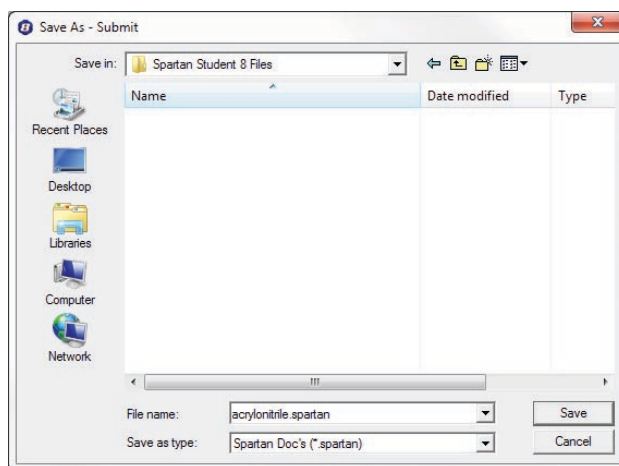
### Acrylonitrile



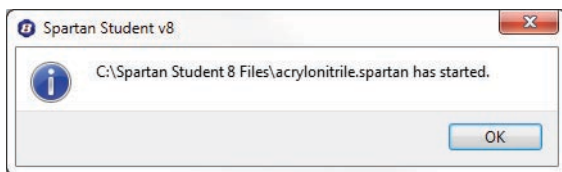
1. Build acrylonitrile () , minimize () and exit the builder (). Alternatively, sketch acrylonitrile () and exit the sketcher ().
2. Select **Calculations...** from the **Setup** menu or *click* on  and perform the following operations in the **Calculations** dialog which appears.



- Select **Equilibrium Geometry** from the leftmost menu to the right of **Calculate**. This specifies optimization of equilibrium geometry.
- Select **ωB97X-D** and **6-31G\*** from the middle and rightmost menus to the right of **Calculate**. This requests that the **ωB97X-D/6-31G\*** density functional model is to be used for this calculation (the same model as that in the database).
- Click on **Submit** at the bottom of the dialog. A file browser appears.



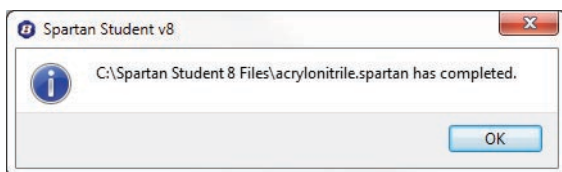
Because the model is in the database (even though we will not use the data), the name *acrylonitrile* will be presented to you in the box to the right of **File name**:. Either use it or type in whatever name you like and then *click* on **Save**. You will be notified that the calculation has been submitted.




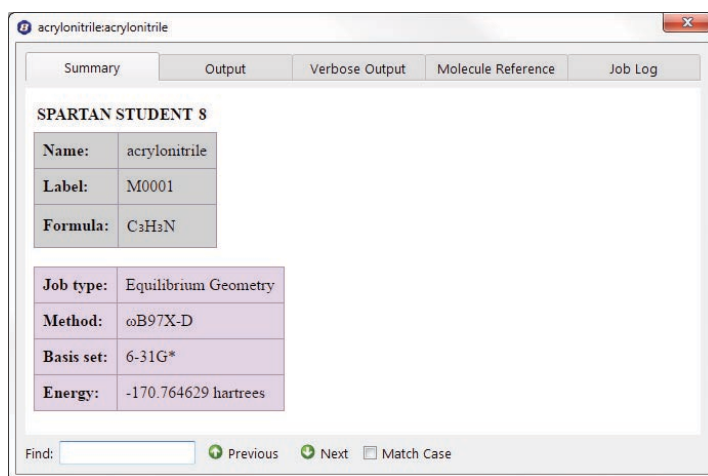
The message will close automatically (after  $\approx 5$  seconds); you can also *click* on **OK** to remove the message from the screen.

After a molecule has been submitted, and until the calculation has completed, you are not permitted to modify any dialogs or other information associated with it.

3. You will be notified when the calculation has completed (less than a minute).




*Click* on **OK** to remove the message from the screen. Select **Output** from the **Display** menu or *click* on  if it appears at the top of the screen. A window containing a summary of the calculation appears.



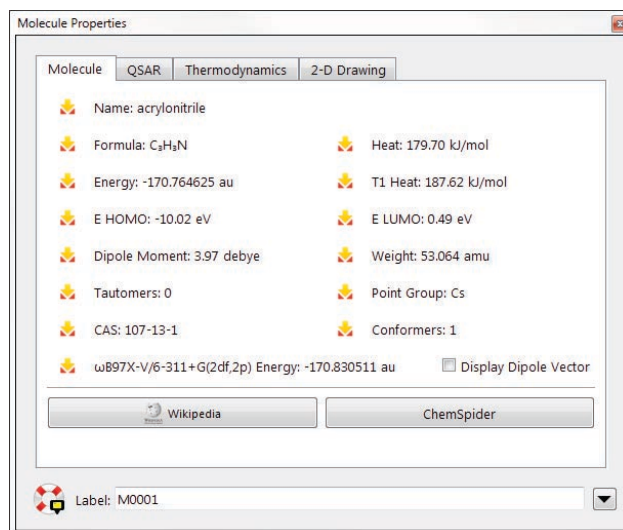
Additional data is accessed by clicking on the **Output** tab. You can scan this by using the scroll bar at the right of the window

or by *clicking* (left button) on or inside the output window and using the scroll wheel on your mouse. Additional information includes the task, basis set, number of electrons, number of unpaired electrons and the charge, as well as further details of the calculation including the number of threads used during the calculation. Below this is the symmetry point group of the molecule that was maintained during the optimization.

The lines under the heading **Optimization** tell the history of the optimization. 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 step and you would be notified that the job had failed.

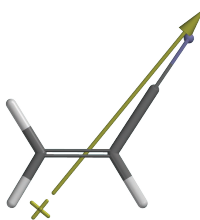
Near the end of the output is the final total energy ( $\approx -170.764625$  atomic units for acrylonitrile with the  $\omega$ B97X-D/6-31G\* model), and the computation time. *Click* on  at the top of the output dialog to close it.

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 based on the electrostatic potential. 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.

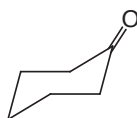
4. Select **Surfaces** from either the **Setup** or **Display** menu (). *Click* on **Add** at the bottom of the **Surfaces** dialog that results, and select **electrostatic potential map** from the menu. This requests an electrostatic potential map (an electron density surface onto which the value of the electrostatic potential is mapped). The graphics calculation will run automatically (without needing to resubmit the job) following your request. When it completes in a few seconds, *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.

5. Close *acrylonitrile* and any open dialogs.


2 min

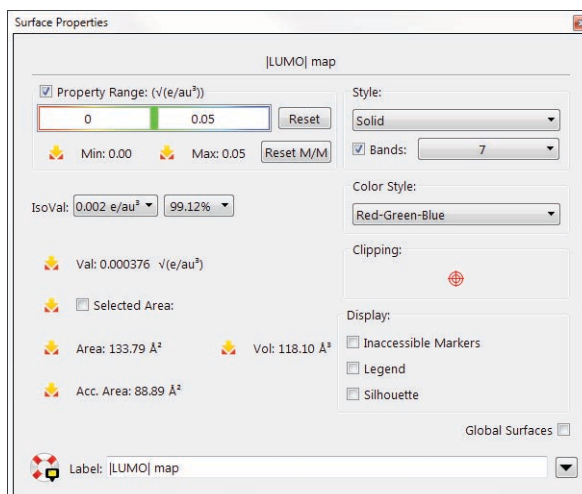
## Cyclohexanone



1. Build cyclohexanone () , minimize () and exit the builder () . Alternatively, sketch cyclohexanone () and exit the sketcher () .
2. Select **Calculations...** from the **Setup** menu or *click* on  . Specify **Equilibrium Geometry**,  $\omega$ **B97X-D** and **6-31G\*** from the three menus to the right of **Calculate**. *Click* on **Submit** and accept the name *cyclohexanone*. Wait until the calculation completes (2-3 minutes) before proceeding to the next step.
3. Cyclohexanone undergoes nucleophilic attack at the carbonyl carbon, and it is reasonable to expect that the molecule's lowest-unoccupied molecular orbital (the LUMO) will be localized here. To visualize the LUMO, bring up the **Surfaces** dialog (**Surfaces** from the **Setup** or **Display** menu or *click* on  ). *Click* on **Add** and select **LUMO** from the menu. Also request an electron density surface onto which the (absolute) value of the LUMO has been mapped in color (a so-called LUMO map). *Click* on **Add** and select **|LUMO| map** from the menu. The two graphics calculations will run automatically and will require only a few seconds.



4. *Check* the box to the left of **LUMO** in the **Surfaces** dialog. You will see that the resulting graphic is a  $\pi^*$  orbital primarily localized on the carbonyl group, consistent with the fact that nucleophiles (electron pairs) add to the carbonyl carbon. See if you can tell on which face of the carbonyl carbon is the LUMO more concentrated.
5. *Uncheck* the box to the left of **LUMO** in the **Surfaces** dialog (to turn off the display of the LUMO, it operates in toggle mode). Then *check* the box to the left of **|LUMO| map** to display the electron density surface onto which the (absolute) value of the LUMO has been mapped. By convention, colors toward red indicate small (absolute) values of the LUMO (near zero), while colors toward blue indicate large (absolute) values of the LUMO. We are looking for a “blue spot”. Note that it is directly over the carbonyl carbon. This corresponds to the maximum value of the LUMO and is where nucleophilic attack will occur.
6. You will see that the blue spot over the *axial* face of the carbonyl carbon is bigger (and more blue) than that over the *equatorial* face. This indicates preferential attack by nucleophiles onto the *axial* face. Quantify the difference by measuring the (absolute) value of the LUMO on these two faces. Select **Properties** from the **Display** menu or *click* on  and *click* anywhere on the graphic to bring up the **Surface Properties** dialog.

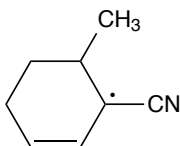








Check the box to the left of **Legend** to display the property range on screen. (Remove the checkmark to remove the legend.) To translate the legend, *click* on the legend to select, then hold down the right mouse button and move the mouse. The legend is useful when making qualitative comparisons of property values. Turn the map such that you can clearly see the *axial* face of the carbonyl carbon, and *click* on the area of maximum blue. The (absolute) value of the LUMO at the surface point you have selected is provided in the dialog to the right of **Val**. Note the value, and then turn the map over such that you can now see the *equatorial* face of the carbonyl carbon, and *click* on the region of maximum blue on this face. Do these values support your qualitative conclusions from viewing the image?


7. Close *cyclohexanone* and any open dialogs.

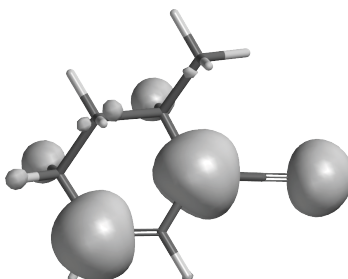
8 mins

### 3-Cyano-4-methylcyclohexenyl Radical



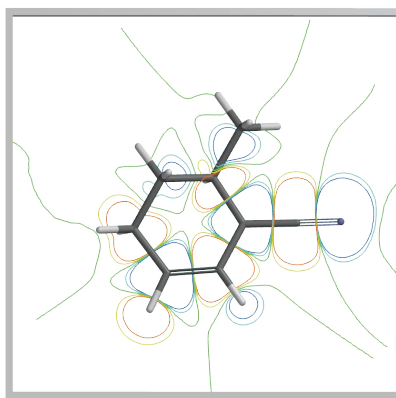
1. Build 3-cyano-4-methylcyclohexenyl radical () , minimize () and exit the builder (). Alternatively, sketch the radical () and exit the sketcher ().
2. Select **Calculations...** from the **Setup** menu (). Specify **Equilibrium Geometry**, **Density Functional-Fock**,  $\omega$ **B97X-D**, and **6-31G\*** from the menus to the right of **Calculate**. This molecule has one unpaired electron. If you sketched it (which requires that you explicitly specify the radical center) the number of unpaired electrons will be correct. However, if you built the molecule, you will need to change **Unpaired Electrons** from **0** to **1**. Click on **Submit** at the bottom of the **Calculations** dialog. Name it *3-cyano-4-methylcyclohexenyl radical*. (A name will not be provided as the radical is not in the database.) Wait for the calculations to complete before proceeding.

3. Select **Surfaces** from the **Setup** or **Display** menu or *click* on . *Click* on **Add** and select **spin density** from the menu. *Click* on **Add** and select **spin density map** from the menu. You have requested two different representations of spin distribution. The first presents spin density as a surface of constant value, while the second uses color to map the value of the spin density onto an electron density surface. Finally, request the singly-occupied molecular orbital. *Click* on **Add** one more time and select **aHOMO** (the highest-occupied molecular orbital of  $\alpha$  spin that is, the orbital that contains the unpaired electron) from the menu.
4. The three graphics you requested will run automatically and will require only a few seconds to complete. When they are done, *check* the box to the left of **spin density** in the **Surfaces** dialog to display the spin density surface. Note that the spin density is delocalized over two of the ring carbons and onto the cyano group.



5. Remove the spin density surface (*uncheck* the box to the left of **spin density** in the **Surfaces** dialog) and then *check* the box to the left of **spin density map** to display a surface on which the spin density is mapped onto the electron density. Note that the areas of maximum spin (colored blue) closely match those where the surface is large in the previous image.
6. Remove the spin density map (*uncheck* the box to the left of **spin density map**), and then *check* the box to the left of **aHOMO** (the molecular orbital which holds the unpaired electron). Aside from the colors (different signs of the orbital), note that this graphic is nearly identical to the previously-displayed image of the spin.

7. *Uncheck* the box to the left of **aHOMO**. *Click* on **More Surfaces...** at the bottom of the (**Surfaces**) dialog, and select **Slice** from the **Surface** menu and **spin density** from the **Property** menu. *Click* on **OK**. A new line **Slice, spin** appears in the window at the top of the dialog.\* *Select* it by *checking* the box at the left. A plane (a slice of spin density) surrounded by a frame appears in the middle of the model on screen. *Click* inside the frame to select. The frame will turn gold. Position the cursor outside the frame, then *press* both the **Shift** key and right button and move the mouse up and down (or use the scroll wheel). This will zoom the plane. You can also translate and rotate the plane independently of the molecule using the usual mouse operations. Alternatively, you can move the molecule and plane together by first *clicking* on the molecule (the frame will now turn white) and then using the mouse. For all operations, be certain to keep the cursor positioned outside of the frame. Size and orient the slice as you wish.



Tap on the graphic to select the graphic and on the frame to select the frame. Use one finger to rotate and two fingers to translate the graphic or frame. Pinch two fingers to zoom the graphic or frame.

8. Remove **3-cyano-4-methylcyclohexenyl radical** and any open dialogs.

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\* You can change the display style from **Contours** to **Solid** or **Transparent** using the **Style** menu at the bottom right of the screen. This will appear only when the slice is selected.

# Tutorial 6

## Groups of Organic Molecules

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*The tutorials in this section introduce and illustrate a number of basic operations involved in processing groups of molecules, as well as the associated spreadsheet for organizing and fitting data and facilities for making plots.*

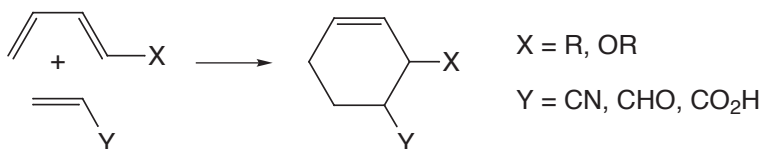
Computational investigations typically involve series of related molecules. Here, it may be of interest to compare geometries, energies or other calculated properties, or to compare trends in calculated and measured properties. **Spartan Student** allows molecules to be grouped into a single document, either manually, or automatically as a result of following a particular vibrational motion, or from a scan of a dihedral angle. Once grouped, molecules may be aligned. Calculations may be performed either on individual molecules or on the complete group of molecules, and the results analyzed individually or altogether to seek out trends.

Associated with a multi-molecule document is a spreadsheet. This allows convenient access to virtually any calculated quantity that can be given a value. Additionally, data may be entered manually into the spreadsheet or pasted from other applications such as Excel. Data in the spreadsheet may be manipulated, linear regression analyses performed and plots displayed. Alternately, the data in a **Spartan Student** spreadsheet may be pasted into Excel (or other applications) for further analysis.

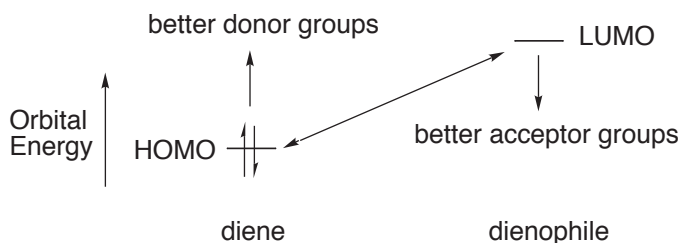
The tutorials in this section introduce and illustrate a number of basic group operations available in **Spartan Student**, building and manipulating multi-molecule documents, and fitting an experimental observable to one or more calculated properties by way of linear regression. The use of the **Reactions** dialog is illustrated. None of the examples in this tutorial actually require performing quantum chemical calculation as all molecules involved are in the database.

## Dienophiles in Diels-Alder Cycloadditions






The most common Diels-Alder reactions involve electron-rich dienes and electron-deficient dienophiles.







The rate of these reactions generally increases with increasing  $\pi$ -donor ability of the diene substituent, and with increasing  $\pi$ -acceptor ability of the dienophile substituent. This can be rationalized by noting that donor groups raise the energy of the highest-occupied molecular orbital (the HOMO) on the diene, while acceptor groups lower the energy of the lowest-unoccupied molecular orbital (the LUMO) on the dienophile. Thus, the HOMO-LUMO gap is reduced, leading to enhanced stabilization.

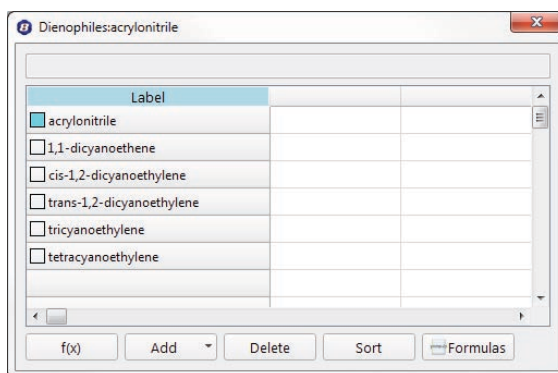




The objective of this tutorial is to correlate experimental relative rates of Diels-Alder cycloadditions involving cyclopentadiene and a variety of cyanoethylenes with dienophile LUMO energies.

1. Build () and minimize () acrylonitrile,  $\text{H}_2\text{C}=\text{C}(\text{H})\text{CN}$ . Select **View** from the **Build** menu (). Copy the structure to the clipboard. Either *right click* on the background and choose **Copy** from the resulting contextual menu, or select **Copy** from the **Edit** menu ()
2. Select **Build New Molecule** (not **New Build**) from the **File** menu (). This requests that a molecule that has yet to be built is to be appended onto the end of a group of molecules in which the currently selected molecule (acrylonitrile) is a member.

The screen will be cleared. *Click* on **Clipboard** at the bottom of the model kit and *double click* on screen. Acrylonitrile will appear. *Click* on **Groups** in the model kit, select **Cyano** and add to the appropriate free valence on acrylonitrile to make 1,1-dicyanoethylene. *Click* on .

- Repeat this procedure (**Build New Molecule**, followed by **Clipboard**, followed by **Groups**, followed by ) four more times to build *cis* and *trans*-1,2-dicyanoethylene, tricyanoethylene and tetracyanoethylene. When you are all done (six molecules in total in a single document), *click* on  to remove the model kit.
- Click* on the name of whatever molecule from the document appears at the bottom of the screen make sure that  $\omega$ B97X-D/6-31G\* is selected and *click* on **Replace** in the dialog that results, and then *click* on **All**. Your structures will be replaced by those from the database (all six are available).
- Select **Spreadsheet** from the **Display** menu ().




You can move among the six molecules either by *clicking* inside the “**Label**” cells at the far left of the spreadsheet, or by using the  and  (step) keys at the bottom left of the screen.

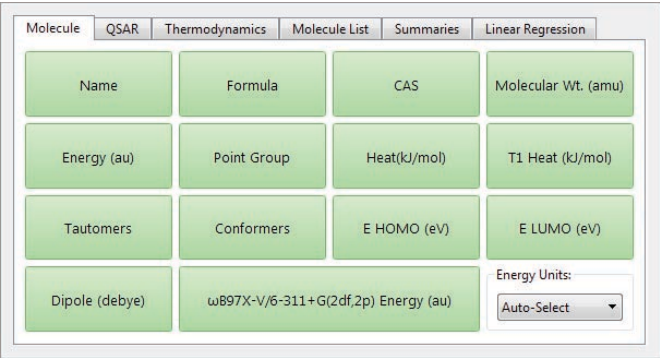
- Enter experimental relative rates into the spreadsheet.




dienophile	$\log_{10}$ (relative rate)	dienophile	$\log_{10}$ (relative rate)
acrylonitrile	0	1,1-dicyanoethylene	4.64
<i>trans</i> -1,2-dicyanoethylene	1.89	tricyanoethylene	5.66
<i>cis</i> -1,2-dicyanoethylene	1.94	tetracyanoethylene	7.61
Experimental data from: J. Sauer, H. Weist and A. Mielert, <i>Chem. Ber.</i> , <b>97</b> , 3183 (1964).			

*Double click* inside the header cell for a blank column in the spreadsheet, type **Log(rate)=** and *press* the **Enter** key (**return** key on Mac). You need to press the **Enter** key (**return** key on Mac) following each entry (or use the  key). Sort by relative rate. *Click* on the column header **Log(rate)**, and then *click* on **Sort** at the bottom of the spreadsheet.

7. *Click* inside a header cell for a blank column and *click* on **Add...** at the bottom of the spreadsheet. Alternatively, *right click* inside the header cell for a blank column in the spreadsheet, and select **Add...** from the contextual menu that results. Select **E LUMO (eV)** from the list in the dialog that results.





The spreadsheet, which now contains both the calculated LUMO energies and experimental relative rates, has served its purpose. Remove it from the screen by *clicking* on  at the top.



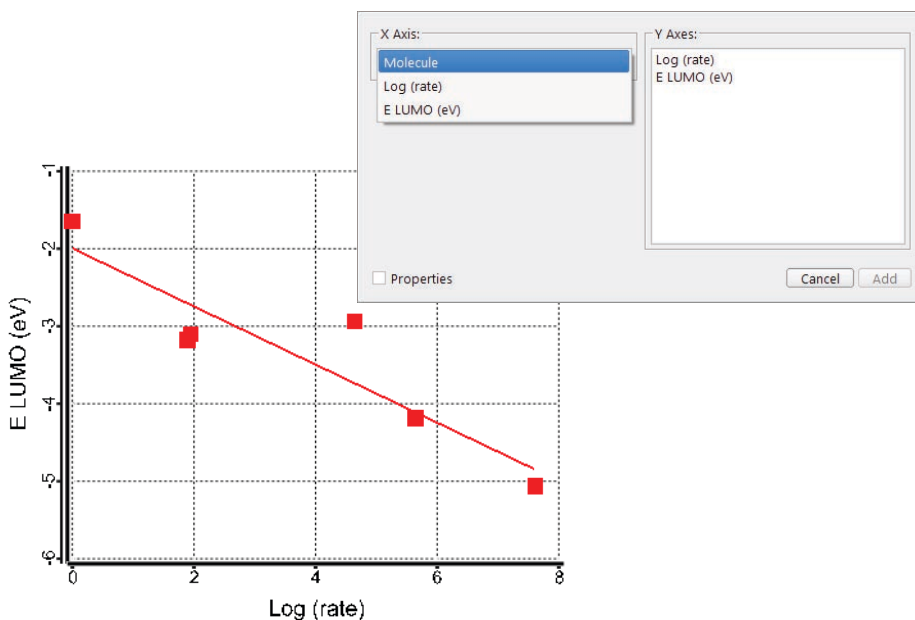
Dienophiles:tricyanoethylene


Label	Log(rate)	E LUMO (eV)
<input type="checkbox"/> acrylonitrile	0.000	0.49
<input type="checkbox"/> 1,1-dicyanoethene	4.64	-0.86
<input type="checkbox"/> cis-1,2-dicyanoethylene	1.94	-1.06
<input type="checkbox"/> trans-1,2-dicyanoethylene	1.89	-1.15
<input checked="" type="checkbox"/> tricyanoethylene	5.66	-2.23
<input type="checkbox"/> tetracyanoethylene	7.61	-3.20

f(x) Add Delete Sort Formulas

8. Select **Plots...** from the **Display** menu or *click* on  if it appears at the top of the screen. This leads to an empty plot pane at the right of the screen. *Click* on  in the bar at the top of the pane.

Select **Log(rate)** from the list of items in the **X Axis** menu and **E LUMO(eV)** from the **Y Axes** list, and *click* on **Create**.

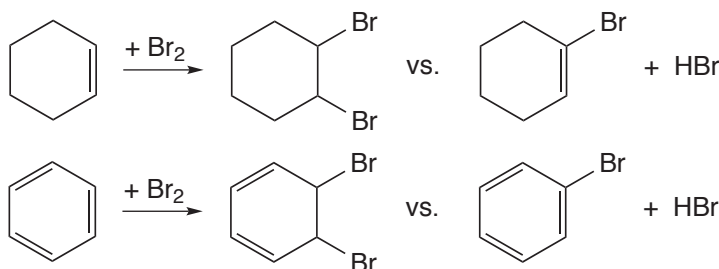


*Click* on the **Edit** icon () , and then *click* to choose **Least Squares Fit**. *Click* **Done** when finished. A least-squares line will be drawn through the six data points.






9. Close the document and any open dialogs.

## Addition vs. Substitution

Alkenes normally undergo addition reactions whereas aromatic compounds normally undergo substitution reactions. For example, bromine reacts with cyclohexene to give *trans*-1,2-dibromocyclohexane (the addition product) not 1-bromocyclohexene, whereas it reacts with benzene to give bromobenzene (the substitution product) not *trans*-5,6-dibromo-1,3-cyclohexadiene.



The objective of this tutorial is to establish the preferred product for each reaction.

1. One after another, build or sketch cyclohexene, *trans*-1,2-dibromocyclohexane, 1-bromocyclohexene, benzene, *trans*-5,6-dibromo-1,3-cyclohexadiene, bromobenzene, bromine (Br<sub>2</sub>) and hydrogen bromide (eight molecules in total). Put all in the same document. Use **New Build** () or **New Sketch** () for the first molecule and **Build New Molecule** () or **Sketch New Molecule** () for each successive molecule.
2. Click on the name of whatever molecule from the document appears at the bottom of the screen, confirm ωB97X-D/6-31G\* is selected and click on **Replace** in the dialog that results and then click on **All**. Your structures will be replaced by those from the database (all eight are available).
3. Select **Reactions** from the **Display** menu or click on  if it appears at the top of the screen.

Reactions

Reactants:

1 bromine

1 cyclohexene

Balance

Products:

1 trans-1,2-dibromocyclohexane

1 <none>

Reactions:

	Reactants	Products	ΔE (kJ/mol)	Boltzmann	Substituents
1	cyclohexene + bromine -->	trans-1,2-dibromocyclohexane	-153.75	0:100	

ωB97X-D/6-31G\*

Source: Current Document

Reaction Energy Units: kJ/mol

Show: Names

Temperature: 298.15 K

Calculate: Δ E

Compute

Choose **Current Document** from the menu to the right of **Use**. Compute the energy for Br<sub>2</sub> addition to cyclohexene: select *cyclohexene* and *bromine* as **Reactants** and *trans-1,2-dibromocyclohexane* (and <none>) as **Products** and *click* on the **Compute** button at the bottom center of the dialog. Repeat for the corresponding substitution energy (same reactants but the products are 1-bromocyclohexene and hydrogen bromide) and for both addition and substitution reactions of benzene (reactants are *benzene* and *bromine* and products are *trans-5,6-dibromomo-1-3-cyclohexadiene* and <none> for addition and *bromobenzene* and *hydrogen bromide* for substitution).

Are all reactions thermodynamically favorable (*exothermic*)? If any of the reactions are not *exothermic*, provide a rationale as to why they are not. Why is there a change in preferred reaction in moving from the alkene to the arene?

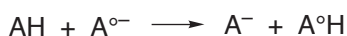
4. Close the document and any open dialogs.

## Acidities of Carboxylic Acids

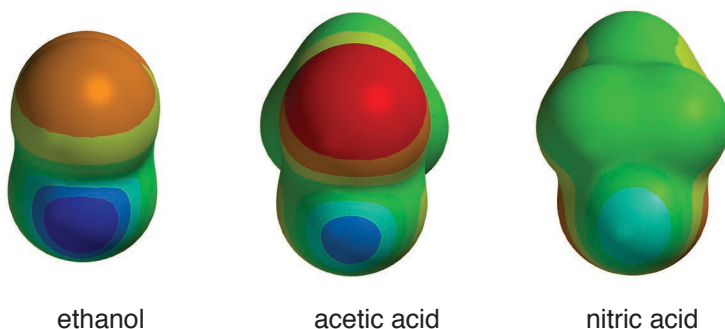
Acid strength is among the most important molecular properties. It is readily available from calculation, either in terms of absolute deprotonation energy,







or, more commonly, as the deprotonation energy relative to that of some standard acid ( $\text{A}^\circ\text{H}$ ).






Electrostatic potential maps may offer an alternative to energy calculations for the description of relative acidities. In particular, the value of the electrostatic potential in the vicinity of the acidic hydrogen in the neutral acid might be expected to reveal gross trends in acidity. For example, the acidic hydrogen in a strong acid, such as nitric acid, is more positive than that in a weak acid, such as acetic acid, which in turn is more positive than that in a very weak acid, such as ethanol.





The objective of this tutorial is to use electrostatic potential maps to quantify changes in acid strength due to subtle variations in structure.



1. One after the other, build or sketch trichloroacetic, dichloroacetic, chloroacetic, formic, benzoic, acetic and pivalic acids. Put all molecules into the same document. Use **New Build** (  ) or **New Sketch** (  ) both from the **File** menu for the first molecule and use **Build New Molecule** (  ) or **Sketch New Molecule** (  )



- ) both from the **File** menu for each successive molecule. *Click* on  when you are done.
- All of the molecules that you have built are available in the database. *Click* on the name of whichever molecule is selected at the bottom of the screen, *click* on **Replace** in the dialog that results and finally on **All**. The wave function is also provided as part of the database entry allowing electrostatic potential maps to be made.
  - Select **Spreadsheet** from the **Display** menu or *click* on . Expand it so that you can see all seven molecules, and that two data columns are available. *Double click* inside the header cell of the next available data column, *type* **pK<sub>a</sub>** and *press* the **Enter** key (**return** key on Mac). Enter the experimental pK<sub>a</sub>'s (given on the next page) into the appropriate cells under this column. You need to *press* the **Enter** (**return**) key following each entry. Alternatively, use the  key to move to the next cell.

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

Experimental data from: E.P. Sargeant and B. Dempsey, *Ionization Constants of Organic Acids in Aqueous Solution*, IUPAC no. 23, Pergamon Press, 1979.

- Arrange the seven molecules on screen such that you can clearly see the acidic hydrogen on each. To display all molecules at once, *check* the box to the left of the molecule name (**Label** column) in the spreadsheet for each entry. To manipulate the molecules independently of one another, *click* to deselect **Coupled** from the **Model** menu or *click* on  if it appears at the top of the screen.
- Select **Surfaces** from either the **Setup** or **Display** menus or *click* on  and then select **electrostatic potential map**. When the electrostatic potential map calculations complete (they will be marked “completed”), *check* the box at the left of **electrostatic potential map** in the **Surfaces** dialog. Select **Properties** from

the **Display** menu or *click* on  and *click* on the electrostatic potential map to display the **Surface Properties** dialog. *Click* on  to the right of **Max** inside the **Surface Properties** dialog. The maximum value of the electrostatic potential (corresponding to the acidic proton) will be pasted to the spreadsheet. Leave the dialog on screen.

6. Plot experimental  $\text{pK}_a$  vs. maximum in the electrostatic potential. Select **Plots** from the **Display** menu or *click* on  and then select **pKa** under the **X Axis** menu and **Property Max (Surface)** from the **Y Axes** list. *Click* on **Create**. *Click* on **Edit** (). Choose **Least Squares Fit** and *click* on **Done**. Does there appear to be a correlation between  $\text{pK}_a$  and the maximum value of the electrostatic potential?
7. Close the document and any remaining dialogs from the screen.

# Tutorial 7

## Spectra of Organic Molecules

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*This tutorial illustrates applications involving the calculation of IR and proton and  $^{13}\text{C}$  NMR spectra.*

In addition to equilibrium geometries, reaction energies and diverse molecular properties, calculations are able to account for molecular spectra. The infrared spectrum arises from the transitions between ground and excited vibrational states, while the NMR spectrum arises from transitions between nuclear spin states. While experimental spectra are used to provide clues to the structure of an unknown molecule, that is, features in the spectrum are taken as evidence for features in the molecular structure, a calculated spectrum starts with a known structure. A high degree of similarity with a measured spectrum may be taken as evidence that the calculated molecule is the same or at least very similar to that for which a spectrum was measured. Lack of similarity suggests that the two molecules are not the same.

The first tutorial in this section deals with the infrared spectrum of methyl formate. It details the steps needed to calculate a spectrum and to relate the spectrum to the underlying molecular structure. The remaining three tutorials deal with NMR spectroscopy: detailing the steps involved in calculating and displaying the proton spectrum for 1-methylindole and the  $^{13}\text{C}$  spectrum of cytosine, and examining the dependence of carbon chemical shifts on stereochemistry.

6 mins

### Infrared Spectrum of Methyl Formate

In the harmonic approximation, the frequency at which a diatomic molecule vibrates is proportional to the square root of the ratio of the force constant (the second derivative of the energy with respect to change in bond length) and the reduced mass (the product of the

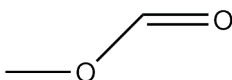
masses of the two atoms divided by their sum). This is in the infrared region of the electromagnetic spectrum. Frequency increases with increasing force constant or stiffness of the bond and decreases with increasing masses of the atoms involved in the bond.



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

The same expression applies for each of the  $3N-6$  vibrations of a polyatomic molecule with  $N$  atoms. Cartesian (or internal) coordinates need to be transformed to normal coordinates, a system that leads to a diagonal matrix of second energy derivatives. For a polyatomic molecule, these will typically involve the motions of several (and perhaps all) of the atoms.

The intensity of absorption for a diatomic molecule is proportional to the change in the dipole moment with change in bond length. The fact that there is no change in the dipole moment of a homonuclear diatomic molecule with change in bond length, means that molecules such as  $\text{N}_2$  and  $\text{O}_2$ , which make up the bulk of the earth's atmosphere, are transparent in the infrared. The intensity of each of the individual lines in an infrared spectrum of a polyatomic molecule follows from the change in dipole moment along the associated normal coordinate. Note that some of the normal coordinates in a polyatomic molecule may not lead to a change in dipole moment, for example, the symmetric stretch in carbon dioxide where both CO bonds are simultaneously moved.



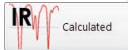


This tutorial illustrates the steps required to calculate and display an infrared spectrum and to compare it with an experimental spectrum. It illustrates how the ease or difficulty of molecular motion and atomic masses affect frequency.

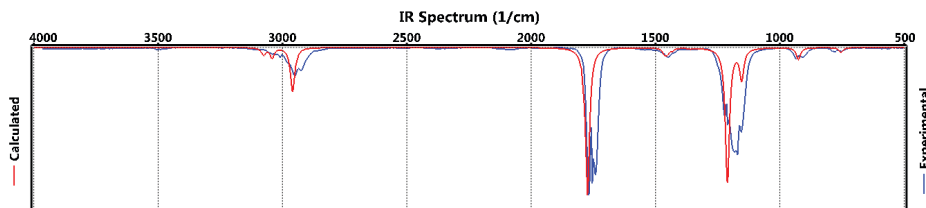





1. Build methyl formate and *click* on . Select **Calculations...** from the **Setup** menu () and request an equilibrium geometry using the EDF2/6-31G\* density functional model. *Check IR* and



click on **Submit**. Accept the name.\*

- After the calculation has completed (several minutes), select **Spectra** from the **Display** menu () . Click on the  in the bar at the top of the spectra pane and select  from the palette of icons. Click on the  again and select  from the icon palette. Calculated (in red) and experimental (in blue) infrared spectra are now superimposed.



- Move the mouse while holding down the right button to shift the cursor across the spectrum. Position it over the intense line in the (calculated) spectrum at  $1817\text{ cm}^{-1}$ . Note that the molecular model (on screen above the spectra pane) vibrates. Describe the motion. Position it over the intense line at  $1211\text{ cm}^{-1}$  and describe its motion.
- Select **Save As** from the **File** menu () to make a copy of methyl formate; name it *methyl formate d3*. Select **Properties** from the **Display** menu or click on  and click on one of the three hydrogen atoms on the methyl group to bring up the **Atom Properties** dialog. Change **Mass Number** from **Standard** to **2 Deuterium**. Repeat for the other two methyl group hydrogen atoms. Resubmit the calculation (it will require only a few seconds) by selecting **Submit** () from the **Setup** menu. Compare the frequencies of the undeuterated and deuterated forms of methyl formate, and identify which change the most and which change the least. Explain your results.
- Close all molecules and dialogs that are open on screen.

\* If you see a different value, you likely have a different conformer of methyl formate. Methyl formate is in the database and you can, if you like, avoid doing any calculations and simply retrieve it. In this case, click on the name at the bottom of the screen and then click on **Replace** in the dialog that results.

## Proton NMR Spectrum of 1-Methylindole

Proton NMR spectroscopy was the first tool available to chemists that allowed definitive assignment of the molecular structures of complex organic molecules. By the 1970's, it had largely replaced infrared spectroscopy and to a large extent chemical proofs of structure.  $^{13}\text{C}$  NMR is now more dominant, but proton NMR remains an essential tool in the chemist's arsenal.

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 ( $\Delta E$ ) depends on the nucleus and on the strength of the applied magnetic field, by way of a simple relationship.

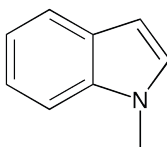
$$\Delta E = \gamma \hbar B_0$$

$\gamma$  is the gyromagnetic ratio (a constant for a given type of nucleus),  $\hbar$  is Planck's constant divided by  $2\pi$  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 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  $^{13}\text{C}$  chemical shifts (treated later in this tutorial) are reported relative to tetramethylsilane (TMS) as a standard.

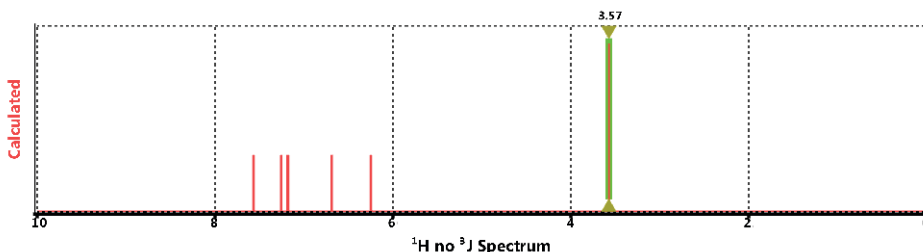
While each *unique* proton in a molecule gives rise to a single line (resonance) in the spectrum, the spins on nearby nuclei add and subtract to the external magnetic field. This leads to a splitting of

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 1-methylindole would be expected to show seven lines, six with unit intensity corresponding to the protons on the indole ring and one line with three times the intensity corresponding to the three equivalent methyl group protons.





The objective of this tutorial is to calculate the proton NMR spectrum of 1-methylindole and compare it with the experimental proton spectrum in the absence of three-bond HH coupling.

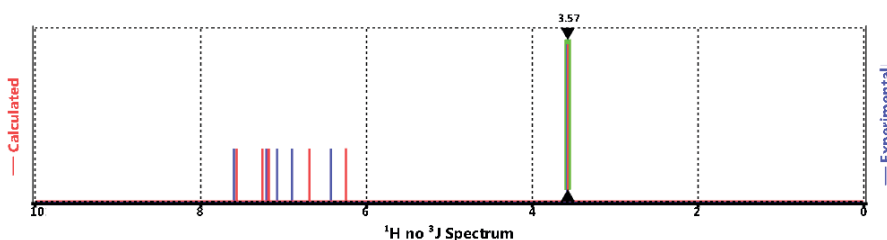
1. Build or sketch 1-methylindole. If you build, *click* on and then on . If you sketch, *click* on . Select **Calculations...** from the **Setup** menu or *click* on . Specify calculation of equilibrium geometry using the  $\omega$ B97X-D/6-31G\* density functional model. *Check* **NMR** and *click* on **Submit**. Accept the name **1-methylindole**. The calculation will require several minutes.\*
2. When the calculation has completed (or after you have retrieved results from the database), select **Spectra** from the **Display** menu or *click* on . *Click* on in the bar at the top of the spectra pane and select (proton NMR spectrum in which there is no HH coupling).




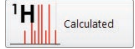
\* 1-methylindole is in the database and you can, if you like, avoid doing any calculations and simply retrieve it. In this case, *click* on the name at the bottom of the screen and then *click* on **Replace** in the dialog that results.

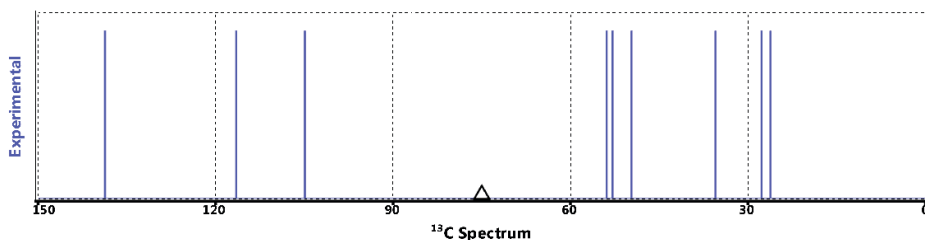
Move the mouse while holding down the left button over the spectrum. When you intersect a line, a numerical value for the proton shift appears at the top of the spectrum.

- Click again on  and this time select  (experimental proton NMR spectrum with HH coupling constants set to 0). The experimental spectrum will be retrieved from the public NMR database and displayed on top of the calculated spectrum. Proton-proton coupling has been eliminated (all coupling constants are assumed to be 0).



The comparison gives you an idea of the level of agreement that can be expected between calculated and experimental proton spectra.

- Click again on  and select  (calculated proton NMR spectrum). The calculated proton spectrum that now appears accounts for three-bond HH coupling. Note that coupling constants not calculated but rather evaluated empirically based on the three-dimensional geometry of the molecule.



You can focus in on details by a combination of zooming the spectrum (scroll wheel) and shifting the displayed range (move the mouse while holding down both the right button and **Shift** key). You will see that lines due to protons at  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$  and  $\text{C}_7$

are doublets, while those due to protons at C<sub>5</sub> and C<sub>6</sub> are quartets (doublet of doublets).

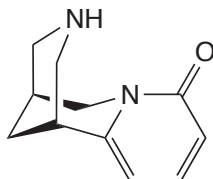
5. Close *1-methylindole* and any remaining dialogs.



20 mins

## <sup>13</sup>C Spectrum of Cytisine




There are several reasons why NMR spectroscopy, in particular, <sup>13</sup>C NMR, is one of the most important routine analytical techniques available for characterizing organic molecules. The experiment, which is straightforward and can be carried out rapidly, requires relatively small samples and is non-destructive. The resulting (proton decoupled) spectrum is quite simple, comprising but a single line for each and every unique carbon. However, assigning <sup>13</sup>C spectra is by no means trivial, even for molecules that might appear to be quite simple. The problem is that the positions of the lines in the spectrum (the chemical shifts) are very sensitive to the environment in which the carbons find themselves. Where two or more carbons in a molecule reside in what appears to be similar environments, it may be very difficult to distinguish them.

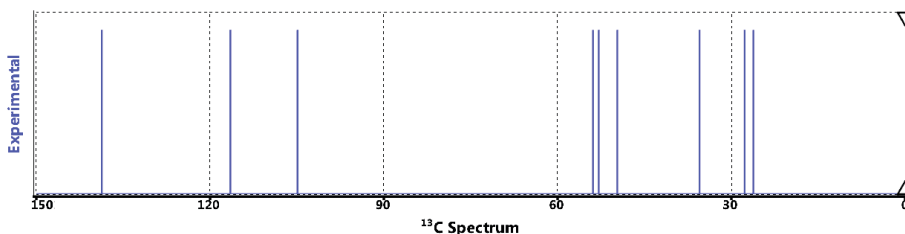
This tutorial uses the alkaloid cytisine to illustrate the use of calculated <sup>13</sup>C spectra to assist in assigning the measured spectrum of the molecule.


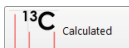


1. Either build and minimize or sketch cytisine and *click* on . Select **Calculations...** from the **Setup** menu or *click* on  and specify calculation of equilibrium geometry with the ωB97X-D/6-31G\* density functional model. *Check NMR*, *click* on **Submit** and accept the name *cytisine*. The job will require

upwards of 15 minutes to complete\*.

- When the calculation is done (or after you have accessed information from the database), select **Spectra** from the **Display** menu or *click* on . *Click* on  in the bar at the top of the spectra pane and select  (experimental  $^{13}\text{C}$  spectrum). The experimental  $^{13}\text{C}$  spectrum is drawn.



- Use the calculated spectrum to associate the individual lines in the experimental  $^{13}\text{C}$  spectrum with specific carbons in the structure of cytosine. *Click* on  and this time select  (calculated  $^{13}\text{C}$  spectrum). The calculated spectrum (in red) will be superimposed on top of the experimental spectrum (in blue). This gives an impression of the performance of the quantum chemical calculations. It also allows you to assign the lines in the (calculated) spectrum to individual carbons and by inference to assign the lines in the experimental spectrum. Move the mouse while holding down the left button over the spectrum. When the cursor overlaps a line in the spectrum, the value of the chemical shift will be shown, and the carbons responsible will be highlighted in the structure model.
- Close *cytosine* and any open dialogs.

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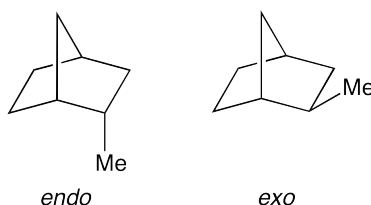
\* Cytosine is available in the database. If you decide to use this instead of doing the calculations, *click* on the name at the bottom of the screen and *click* on **Replace** at the bottom of the dialog that results.



## Stereochemical Assignments from $^{13}\text{C}$ Spectra



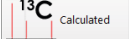


NMR spectroscopy, in particular  $^{13}\text{C}$  spectroscopy, is without doubt the method of choice to establish the three-dimensional structure of organic molecules. Only X-ray diffraction provides more definitive results, although the requirement of a crystalline sample severely limits its application. The availability of a “virtual NMR spectrometer” offers organic chemists an entirely new paradigm for structure determination, that is direct comparison of a measured spectrum with calculated spectra for one or more chemically reasonable candidates.

The objective of this tutorial is to compare calculated  $^{13}\text{C}$  chemical shifts for *endo* and *exo* stereoisomers of 2-methylnorbornane with the corresponding experimental shifts. The question to be answered is whether or not the calculations are able to reproduce differences in chemical shifts as a function of stereochemistry.

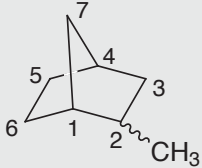
1. Build or sketch *endo* and *exo* stereoisomers of 2-methylnorbornane.



Place both in the same document. Use **Build New Molecule** () or **Sketch New Molecule** () from the **File** menu (instead of **New Build** or **New Sketch**) for the second stereoisomer.

2. Both stereoisomers are available in the database so there is no need to perform any calculations. *Click* on the name of whichever molecule is selected at the bottom of the screen. Confirm that  $\omega\text{B97X-D/6-31G}^*$  is selected and *click* on **Replace** in the dialog that results and then on **All**.
3. Select **Spectra** from the **Display** menu or *click* on , *click* on  in the bar at the top of the spectra pane and select . You can switch between the two stereoisomers using the  and .

► keys at the bottom of the screen. Compare the  $^{13}\text{C}$  chemical shifts with experimental values, paying particular attention to differences between *endo* and *exo* stereoisomers.

Experimental $^{13}\text{C}$ NMR Data		<i>endo</i>	<i>exo</i>	$\Delta$
	C <sub>1</sub>	43.5	42.2	-1.3
	C <sub>2</sub>	36.8	34.6	-2.2
	C <sub>3</sub>	40.2	40.7	0.5
	C <sub>4</sub>	37.3	38.2	0.9
	C <sub>5</sub>	30.3	30.6	0.3
	C <sub>6</sub>	29.0	22.4	-6.6
	C <sub>7</sub>	35.0	38.9	3.9
	CH <sub>3</sub>	22.3	17.4	-4.9

Can the calculations be used to distinguish between the two isomers?

4. Close the document and any open dialogs.



# Tutorial 8

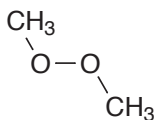
## Flexible Molecules

*This tutorial describes issues associated with calculations on flexible molecules.*

The three tutorials in this section illustrate applications involving molecules with more than one stable conformer, that is, molecules that incorporate rotatable single bonds or flexible rings. The first tutorial deals with a molecule with only one degree of (conformational) freedom. The goal here is not only to identify the “best” conformer, but also to rationalize why it is the best. The second tutorial deals with a molecule with multiple degrees of freedom and multiple conformers. The goal here is to identify the best (lowest energy) conformer. The final tutorial involves a molecule with several degrees of conformational freedom. Its goal is to obtain the lowest energy conformers that contribute to the molecule’s Boltzmann distribution (with molecular mechanics), and then to calculate the NMR spectrum for these conformers and compare the calculated  $^{13}\text{C}$  NMR to a known experimental NMR.

8 mins

### Internal Rotation in Dimethylperoxide







Any function chosen to represent the energy of rotation about a single bond needs to repeat itself in  $360^\circ$ . The most common choice is a truncated Fourier series.

$$E^{\text{torsion}}(\omega) = k^{\text{torsion1}} (1 - \cos(\omega - \omega^{\text{eq}})) + k^{\text{torsion2}} (1 - \cos 2(\omega - \omega^{\text{eq}})) \\ + k^{\text{torsion3}} (1 - \cos 3(\omega - \omega^{\text{eq}}))$$

Here,  $\omega^{\text{eq}}$  is the ideal dihedral angle and  $k^{\text{torsion1}}$ ,  $k^{\text{torsion2}}$  and  $k^{\text{torsion3}}$  are


parameters. The three terms are independent and may be independently interpreted. The first (one-fold) term accounts for the difference in energy between *syn* and *anti* conformers, the second (two-fold) term for the difference in energy between planar and perpendicular conformers, and the third (three-fold) term for the difference in energy between eclipsed and staggered conformers.


The objective of this tutorial is to interpret the potential energy function for rotation about the oxygen-oxygen bond in dimethylperoxide.

1. Build dimethylperoxide. If the molecule is not already in an *anti* conformation, select **Measure Dihedral** from the **Geometry** menu () and set the COOC dihedral angle to **180** ( $180^\circ$ ) by *typing* **180** in the box at the lower right of the screen and *pressing* the **Enter** key (**return** key on Mac). **Do not minimize**.
2. Select **Constrain Dihedral** from the **Geometry** menu (). Select the COOC 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 two additional text boxes.










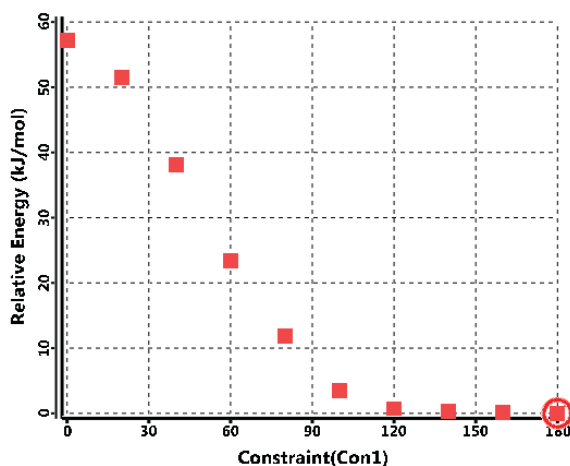
Leave **180** ( $180^\circ$ ) in the original (leftmost) box alone, but change the contents of the box to the right of **to** to **0** ( $0^\circ$ ). You need to *press* the **Enter** (**return**) key after you type in the value. **Steps** should be **10**. If it is not, *type* **10** and *press* the **Enter** (**return**) key. What you have specified is that the dihedral angle will be constrained first to  $180^\circ$ , then to  $160^\circ$ \*, then to  $140^\circ$ , etc. and finally to  $0^\circ$ . *Click* on .


4. Select **Calculations...** from the **Setup** menu () and specify **Energy Profile**, **Hartree-Fock** and **6-31G\*** from the menus to the right of **Calculate**. *Click* on **Submit** and accept the name **dimethyl peroxide**.

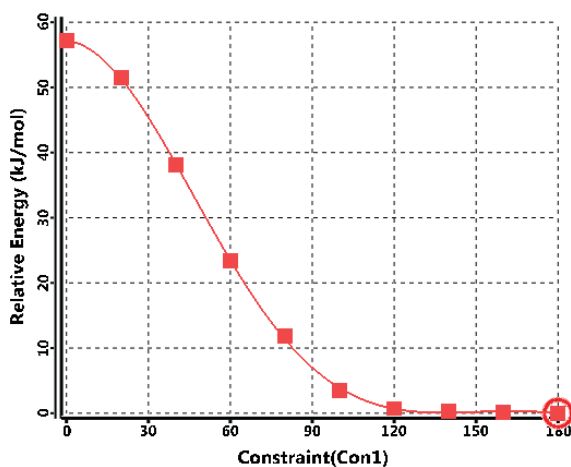
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\* The difference between constraint values is given by: (final-initial)/(steps-1).

5. When the calculations complete, the results are written to a new document named *dimethyl peroxide.Prof.spartan*. Click on **Yes** following the prompt that will ask you if you want to open this file. Align the conformers. Select **Align** from the **Geometry** menu () , one after the other, *click* on both oxygens and on one of the carbons, and finally *click* on the **Align** button at the bottom right of the screen. Select **Spreadsheet** from the **Display** menu () , and enter both the energies relative to the 180° conformer, and the COOC dihedral angles. First *click* on the label (**M0001**) for the top entry in the spreadsheet (the 180° conformer), then *click* on the header cell for the leftmost blank column, and finally, *click* on **Add** at the bottom of the spreadsheet. Select **rel. E** from the quantities under the **Molecule List** tab, **kJ/mol** from the **Relative Energy Units** menu. To enter the dihedral angle constraints, select **Constrain Dihedral** from the **Geometry** menu () , *click* on the constraint marker attached to dimethylperoxide and *click* on  at the bottom of the screen (to the right of the value of the dihedral angle). *Click* on .
6. Select **Plots** from the **Display** menu () . Click on  at the top of the (empty) plot pane and select **Constraint(Con1)** from the **X Axis** menu and **Relative Energy (kJ/mol)** from the **Y Axes** list; *click* on the **Create** button.

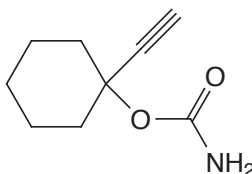


By default, the data points are not connected. To fit the points to a Fourier series, *click* on  at the top of the plot pane and select **Fourier** to the right of **Curve** in the resulting dialog. Check the box to the left of **Curve** and *click* the **Done** button.



7. Use energies from B3LYP/6-31G\* density functional calculations, together with the Hartree-Fock geometries to provide a better fitting function. First, make a copy of *dimethyl peroxide.Prof.spartan*. Name it *dimethyl peroxide density functional*. Select **Calculations...** from the **Setup** menu () and select **Energy**, **ωB97X-D** and **6-31G\*** from the three menus to the right of **Calculate**. Make certain that **Global Calculations** (at the bottom of the dialog) is *checked* to signify that energy calculations are to be performed on all conformers. *Click* on **Submit**.
8. Energy calculations for all ten conformers will require a few minutes to complete. When they are done, examine the plot and compare it to the energy plot produced earlier.
9. Remove all molecules and dialogs from the screen.



## Ethinamate



Ethinamate, a prescription drug previously used for the treatment of insomnia, provides a very simple example of a molecule with multiple conformers. These arise from rotation about the CO single bond connecting the carbamate group and the cyclohexane ring and the “flipping” of the ring. Rotation about the other CO single bond can be ignored as the “cis” conformer drawn above is much lower in energy than the “trans” alternative.

1. Build or sketch ethinamate. Click on . Select **Calculations...** from the **Setup** menu (), and specify **Conformer Distribution** from the menu to the right of **Calculate**. MMFF molecular mechanics is the only model available in *Spartan Student*. Click on **Submit**, and accept the name *ethinamate*.
2. When the job completes (a few seconds), all low-energy conformers will be placed in a new document *ethinamate.Conf.spartan*. Click on **OK** to the request to open this document. Select **Spreadsheet** from the **Display** menu (), and size the spreadsheet such that all rows (corresponding to different conformers) are visible. Click on the top row of the spreadsheet (corresponding to the lowest-energy conformer according to the MMFF model). Click on **Add** at the bottom of the spreadsheet. Select **Relative Energy** and **Boltzmann Weights** from the **Molecule List** tabs, **kJ/mol** from the **Relative Energy Units** menu. Describe the lowest-energy conformer. Does the carbamate group prefer to be *equatorial* or *axial*? Does one conformer dominate the Boltzmann distribution or are two or more conformers needed to account for 90%? Have you found the expected number of conformers? If not, describe any “missing” conformers and suggest why they are missing.

3. See if the results of the molecular mechanics calculations (identity of the lowest-energy conformer and makeup of the Boltzmann distribution) maintain if you move to a better theoretical model.

Make a copy of *ethinamate.Conf.spartan* (Save As from the **File** menu or *click* on ). Name it *ethinamate conformers density functional*. Select **Calculations...** from the **Setup** menu () with this copy and specify calculation of **Equilibrium Geometry** using the **B3LYP/6-31G\*** density functional model. Make certain that **Global Calculations** at the bottom of the dialog is checked. (This applies the calculation model to all the molecules in the document and not just the selected molecule.) *Click* on **Submit**.

4. The calculations may require at least 10-20 minutes or more (depending on your computer). When completed, bring up the spreadsheet and identify the best conformer. Is it the same as that assigned from the MMFF calculations? If not, is the *equatorial* or *axial* preference for the carbamate group the same? Is the Boltzmann distribution similar in the sense that one conformer dominates or two or more conformers contribute significantly.
5. Close any open documents and dialogs.

15 mins

### <sup>13</sup>C Chemical Shifts Depend on Conformation

At normal temperatures, the time for nuclear spin relaxation is very long relative to time required for equilibration among conformers. This means that for each of the carbon chemical shifts in the NMR spectrum of a flexible molecule, <sup>13</sup>C, will be a weighted average of the shifts NMR of the individual conformers, <sup>13</sup>C<sub>i</sub>.

$$^{13}\text{C} = \sum_i \omega_i ^{13}\text{C}_i$$


The weight,  $\omega_i$ , is given by the Boltzmann equation, and depends on its energy,  $\epsilon_i$  (relative to that of the lowest-energy conformer,  $\epsilon_0$ ) and on temperature,  $T$ . Summation is over all conformers (including the

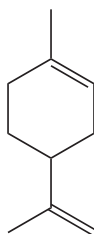
lowest-energy conformer),  $g_i$  is the number of times that conformer  $i$  appears in the overall distribution and  $k$  is the Boltzmann constant.



$$\omega_i = g_i \exp - [\varepsilon_i - \varepsilon_0/kT] / \sum_j \{ \exp - [\varepsilon_j - \varepsilon_0/kT] \}$$








In practice, conformers that are 10 kJ/mol or more above the lowest-energy conformer make a negligible contribution to the total (at room temperature). However, molecular mechanics is not capable of supplying conformer energies within such a tight threshold and looser limits (involving more conformers) are needed for preliminary steps in a calculation of Boltzmann weights.

In this tutorial, you will see how well the  $^{13}\text{C}$  spectrum of the “best” (lowest-energy) conformer of limonene reproduces the experimental room temperature NMR. More generally, you will assess the sensitivity of  $^{13}\text{C}$  chemical shifts to change in conformation.

1. Build or sketch limonene. Click on .



2. Select **Calculations...** from the **Setup** menu () and request a **Conformer Distribution** using the **MMFF** molecular mechanics model. Click on **Submit** and accept the name **limonene**.
3. The job will complete in a few seconds and you will be asked whether or not you wish to open **limonene.Conf.M0001**, the document containing the full list of conformers. Click on **OK**. Select **Spreadsheet** from the **Display** menu () with this list. Click on the top row of the spreadsheet to select the lowest energy conformer. Click on **Add** at the bottom of the spreadsheet, click on the **Molecule List** tab, select both **rel. E** and **Boltzmann Weights** and click anywhere on screen to dismiss the dialog.
4. Delete any conformers that are more than 40 kJ/mol higher in energy than the best conformer, as they will not contribute significantly to the Boltzmann distribution.

5. Select **Calculations...** from the **Setup** menu and specify an **Energy** calculation and **Density Functional** and  $\omega$ **B97X-D** with the **6-31G\*** basis set. We are simplifying the calculations by using MMFF geometries, but several conformers are involved and it will require several minutes. *Check NMR* to the right of **Calculate** and confirm **Current Model** is selected to the right of **NMR**. *Click* on **Submit**.
6. When the calculation completes, select **Spectra** from **Display** menu () , *click* on  in the bar at the top of the spectra pane and select  . *Click* again on  and this time select the experimental  $^{13}\text{C}$  spectrum  for each of the low-energy conformers. You can move from one conformer to another using the “step keys” ( and ) at the bottom left of the screen. While the calculated spectrum changes from one conformer to another, there is only one experimental spectrum. Is there significant variation as you move from one conformer to another? Does the spectrum from the lowest-energy conformer adequately reproduce the experimental spectrum?
4. Close any open documents and dialogs.



# Tutorial 9

## Organic Reactions

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*This tutorial outlines and illustrates strategies for locating and verifying transition states for organic reactions.*

While unique valence structures may generally be written for most molecules and, based on these structures, reasonable guesses at bond lengths and angles may be made, it is often difficult to designate appropriate valence structures for transition states, let alone specify detailed geometries. The reason is the complete absence of experimental data for the structures of transition states. However, calculated transition-state geometries are now commonplace, and ***Spartan Student*** provides both a library of calculated transition-state geometries and a facility for automatically matching an entry in this library with the reaction at hand.\*

***Spartan Student*** also provides a procedure for driving user-defined coordinates. Aside from conformational analysis (see discussion in **Tutorial 8**), the major application of this is to force reactions, thereby permitting identification of transition states.

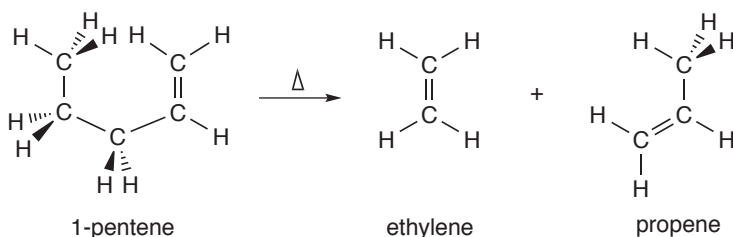
The first tutorial in this section illustrates ***Spartan Student***'s automatic procedure for guessing transition-state geometries, and the use of vibrational analysis to verify that a particular structure corresponds to a transition state and to show the motion connecting it to reactants and products. The second tutorial illustrates how a reaction may be driven through a transition state.

An example of a transition state calculation for an organometallic reaction is provided in **Tutorial 11 *Inorganic and Organometallic Molecules***.




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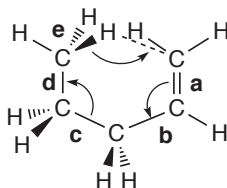
\* Where a reaction is unknown to ***Spartan Student***'s transition state library, a fallback technique which averages reactant and product geometries (similar to the so-called linear synchronous transit method) is invoked.

## Ene Reaction of 1-Pentene







The proposed mechanism of the ene reaction involves simultaneous transfer of a hydrogen atom and CC bond cleavage. The objective of this tutorial is to establish the transition state for the ene reaction of 1-pentene and to examine the reaction coordinate for evidence of concerted motion.






1. 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. To rotate about a (single) bond, first *click* on it to select (it will be marked by a red arrow), and drag the mouse up or down in the area below  at the left of the screen. Alternatively, hold down the left button and **Alt** key (**option** key on Mac) and move the mouse up and down. Minimize and *click* on .
2. Select **Transition State** from the **Build** menu or *click* on  if it appears at the top of the screen. *Click* on bond **a** in the figure on the following page and then *click* on bond **b**. A curved arrow from double bond **a** to single bond **b** will be drawn.

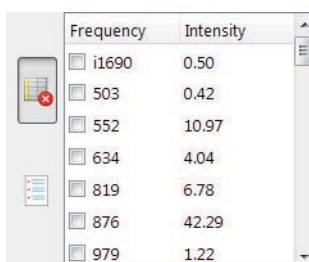


Next, *click* on bond **c** and then on bond **d**. A second curved arrow from bonds **c** to **d** will be drawn. Finally, *click* on bond **e** and then, *click* on the (methyl) hydrogen to be transferred and next on the terminal (methylene) carbon to receive this hydrogen.

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.

If you make a mistake, you can remove an arrow by selecting **Delete** from the **Build** menu () 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  (Search Transition State) at the bottom right of the screen. Your structure will be replaced by a guess at the ene transition state. 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.

3. Select **Calculations...** from the **Setup** menu () and specify calculation of transition-state geometry using the 3-21G Hartree-Fock model. Select **Transition State Geometry**, **Hartree-Fock** and **3-21G** from the three menus to the right of **Calculate**. *Check IR*. This will allow you to confirm that you have found a transition state, and that it smoothly connects reactant and product. *Click* on **Submit** and name it *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  in the bar at the top of the spectra pane and *click* on  in the palette that results. *Click* on  (Tables) at the left of the spectra pane to bring up a list of frequencies and intensities.






Frequency	Intensity
i1690	0.50
503	0.42
552	10.97
634	4.04
819	6.78
876	42.29
979	1.22

*Click* the top entry in the list. It corresponds to an imaginary frequency, and will be designated with an **i** in front of the number.

As detailed in **Tutorial 7** of the *Spartan Student* Manual, vibrational frequency is proportional to the square root of the ratio of the force constant (reflecting the curvature of the potential surface along a particular coordinate) divided by a combination of the masses of atoms involved in motion along that coordinate. At a transition state (a maximum in the reaction coordinate), the curvature is negative. Since the mass term 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?

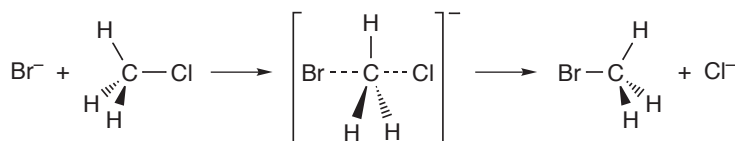
5. Click on  (Make List) at the left of the spectra pane. Controls in the dialog that result allow for changing both the amplitude of vibration (**Amp**) and the number of steps that make up the motion (**Steps**). Leave the number of steps (11) alone but change the amplitude to 0.3. Type **0.3** in the box to the right of **Amplitude:** and press the **Enter** key (**return** key on Mac). Next, click on **Make List** at the bottom of the dialog. This will give rise to a new document containing 11 structures that follow the reaction coordinate down from the transition state both toward reactant and product. You are done with *ene reaction 1-pentene*, so close it.
6. With focus on the new document, select **Calculations...** from the **Setup** menu () and specify **Energy**, **Hartree-Fock** and **3-21G** from the three menus to the right of **Calculate** (the same as used to obtain the transition state and calculate the frequencies). Make certain that **Global Calculations** is checked. Select **Surfaces** from either the **Setup** or **Display** menu () and specify evaluation of two surfaces: a bond density surface and a bond density surface onto which the electrostatic potential has been mapped. Before you do so, make certain that **Global Surfaces** is checked. Click on **More Surfaces...**<sup>\*</sup>, select **density (bond)** for **Surface** and **none** for **Property** and click on **Apply**. Select **density (bond)** for **surface** and **potential** for **Property** and click on **OK**.



\* You need to use **More Surfaces** rather than **Add** as the electrostatic potential is mapped on the bond density surface.

- 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. 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)?
- Close all open documents and dialogs.


10 mins

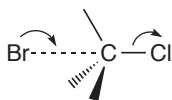
## S<sub>N</sub>2 Reaction of Bromide and Methyl Chloride







- The S<sub>N</sub>2 reaction passes through a transition state in which carbon is in a trigonal bipyramid geometry and the entering and leaving groups are collinear. To build it, first construct methyl chloride. Then select bromine from the palette of icons in the model kit. Hold down the **Insert** key (**option** key on Mac) and *click* on screen opposite chlorine. Alternatively, *double click* on screen. Two detached fragments, methyl chloride and hydrogen bromide, appear on screen. *Click* on  or hold down the **Delete** key and then *click* on the free valence on bromine. You are left with methyl chloride and bromine atom (bromide). Manipulate the two such that bromide is poised to attack methyl chloride from the backside (as in the transition state above). (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.) ***Do not minimize.*** *Click* on .

\* In this example, you have requested graphical surfaces prior to submitting the calculation. You could also have requested them to be done “on-the-fly” following the calculation.


2. Select **Transition State** from the **Build** menu (). Click on bromide and then *click* first on carbon and then on bromide. A dotted line will be drawn from bromine to carbon, together with an arrow from bromine to the center of this line. Next, *click* on the CCl bond and then *click* on the chlorine, and *click* a second time on chlorine. A second arrow from the carbon-chlorine bond to the chlorine will be drawn.













Click on  (Search Transition State) at the bottom right of the screen. Your structure will be replaced by a guess at the transition state.

3. Select **Measure Distance** from the **Geometry** menu or *click* on  if it appears at the top of the screen and then *click* on the CBr bond. Replace the current CBr distance in the box at the bottom right of the screen by **3.8** (3.8Å) and *press* the **Enter** button. You have made a complex representing the reactant.
4. Select **Constrain Distance** from the **Geometry** menu or *click* on  if it appears at the top of the screen. Click on the CBr bond, and then *click* on  at the bottom right of the screen. The icon will change to  indicating a constraint is to be applied to this distance. Check the box to the left of **Profile** at the bottom of right of the screen. This will result in two additional text boxes.

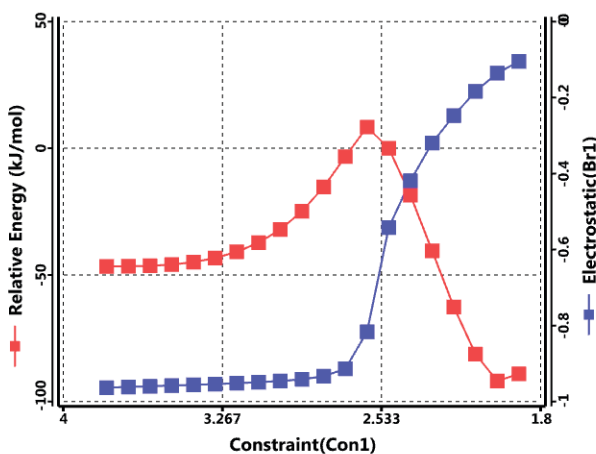






Leave the value **3.8** (3.8Å) in the leftmost box alone, but change the number in the box to the right of **to** to **1.9** (1.9Å) and *press* the **Enter** button. Change the number in the box to the right of **Steps** from **10** (the default) to **20**. 20 Calculations with CBr bond lengths constrained from 3.8Å (the starting point) to 1.9Å (the ending point) will be performed. The transition state should have a CBr distance in between these values. Click on .

5. Select **Calculations...** from the **Setup** menu () and select **Energy Profile** in **Water** and **Hartree-Fock 3-21G** from the menus to the right of **Calculate**. You also need to change **Total Charge** to **Anion**.
6. Submit the job. Name it *bromide+methyl chloride*. When completed, it will give rise to a sequence of calculations placed in a new document with the name *bromide+methyl chloride.Prof.spartan*. Accept the prompt to open this file. Close the first document *bromide+methyl chloride* to reduce clutter.
7. Select **Spreadsheet** from the **Display** menu (). Click on the **Add** button at the bottom of the spreadsheet. Select **Relative Energy** from among the quantities listed under the **Molecules List** tab and **kJ/mol**. Next, enter the (constrained) CBr distances and bromine charges in the spreadsheet. Select **Constrain Distance** from the **Geometry** menu () click on the constraint marker in the model and click on  at the bottom right of the screen. Click on . Select **Properties** from the **Display** menu () to bring up a **Properties** dialog. Click on bromine and click on  to the left of **Electrostatic Charges** in the **Atom Properties** dialog. Close the spreadsheet and select **Plots** from the **Display** menu () to bring up the **Plots** dialog. Click on  in the bar at the top of the dialog and select **Constraint (Con1)** (the distance at which the CBr bond has been constrained) from the **X Axis** menu, and both **Relative Energy (kJ/mol)** and **Electrostatic (Br1)** from the **Y Axes** list in the dialog that results. Click on **Create**. By default, the data points are not connected. Click on  in the bar at the top of the plots plane, select **Point-to-Point** for both **Relative Energy (kJ/mol)** and **Electrostatic(Br1)**. Also set the **X Axis Range** from **4** to **1.8**. and click on **Done**.

One plot gives the energy as the reaction proceeds and the other gives charge on bromine. Are the two related? Explain.





8.  $S_N2$  reactions involving charged species normally need to be carried out in highly-polar media, for example, water. The C-PCM solvent model available with *Spartan Student* allows the effect of solvent to be estimated.
9. Select **Surfaces** from either the **Setup** or **Display** menu (). Click on **More Surfaces....** \* Select **density (bond)** from the **Surface** menu and **none** from the **Property** menu and click on **Apply**. Select **density (bond)** from the **Surface** menu, but this time **potential** from the **Property** menu. Click on **OK**. Do not close the **Surfaces** dialog. The *Spartan Student* interface will perform these graphics calculations *on-the-fly*, however, it will take 30 seconds to a minute to complete the two surfaces for all 20 molecules on the list.
10. When completed, *check* the box to the left of the bond density surface inside the **Surfaces** dialog (the first one you specified) to turn it on. 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  at the bottom of the screen when you are done.
11. Turn display of the bond density off (*uncheck* the box) inside the **Surfaces** dialog, and then turn display of the electrostatic potential mapped onto the bond density on. Click on . Relate

\* You need to use **More Surfaces** rather than **Add** as the electrostatic potential is mapped on the bond density surface.



the migration of negative charge during reaction as indicated by colors in the electrostatic potential map to the plot you constructed in step 8. Recall, that colors near red indicate maximum negative potential.

12. Remove all molecules and any remaining dialogs from the screen.

# Tutorial 10

## Biomolecules


*The two tutorials in this chapter illustrate models appropriate to large biomolecules (proteins and polynucleotides), in particular, ribbon displays of secondary structure and display of hydrogen bonds. No calculations are performed.*

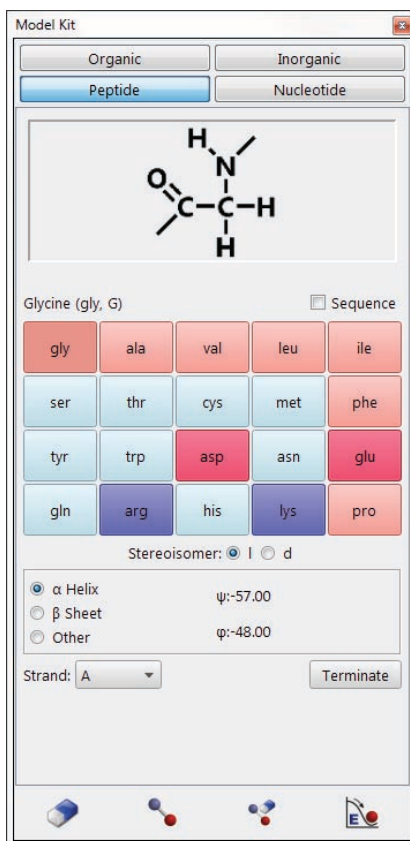
Treatment of very large molecules, proteins and polynucleotides (biopolymers) most important among them, requires models which are simpler than those appropriate for small organic and inorganic molecules. This refers both to structural models for display and manipulation (where a simplified ribbon display 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).

### Structural Motifs in Proteins

Two main themes dominate the 3-dimensional structures of essentially all proteins, the  $\alpha$  helix and the  $\beta$  sheet.

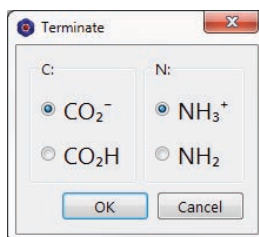
#### $\alpha$ Helix

1. Select **New Build** 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



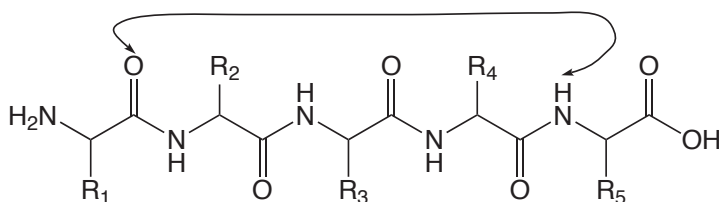
window at the top of the model kit will shift between a text field showing **gly** (**Sequence** button checked) and a 2D rendering of non-terminated glycine (**Sequence** button un-checked).

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:  $\alpha$  **Helix**,  $\beta$  **Sheet** and **Other**. These allow specification of the secondary structure of constructed polypeptide sequences. Select  $\alpha$  **Helix** and *double 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 ( $\text{CO}_2\text{H}$  and  $\text{NH}_2$ ) or as a zwitterionic form ( $\text{CO}_2^-$  and  $\text{NH}_3^+$ ).






Choose  $\text{CO}_2\text{H}$  and  $\text{NH}_2$  (the uncharged form) and *click* on the **OK** button to terminate.

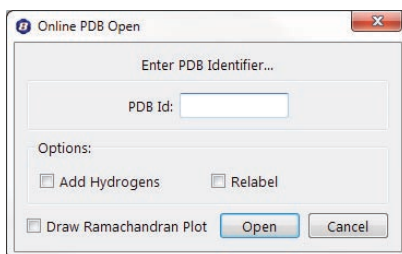
5. To simplify the model, display the molecule as a **Tube** model and deselect **Hydrogens** from the **Model** menu. Select **Hydrogen Bonds** from the **Model** menu. Dotted lines depicting hydrogen bonds will appear on screen between the oxygens of carbonyl groups and the nitrogens of amine groups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





6. To better see the  $\alpha$  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  $\alpha$  helix structure.

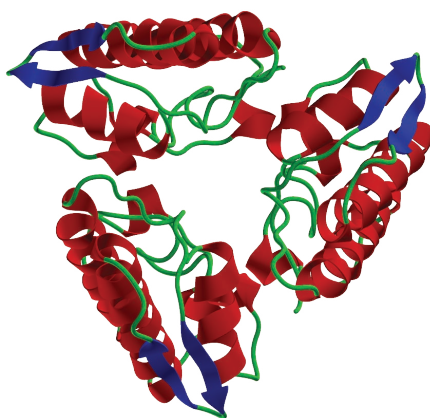
## $\beta$ Pleated Sheet

7. Select **New Build** 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 9 amino acids). Select **Sheet** and *click* on screen.
8. Again, a model of a 10-residue polypeptide is displayed. This time, the secondary structure is in the  $\beta$  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  $\beta$  sheet arrangement. As you did for the  $\alpha$  helix, switch to a tube model, turn hydrogens off and turn on display of hydrogen bonds. The extended  $\beta$  sheet does not contain internal hydrogen bonding so no hydrogen bonds appear. Close the document when you finish examining the  $\beta$ -sheet structure.
10. Hydrogen bonds play a role in connecting  $\beta$  strands to make a  $\beta$  sheet. Select **Access PDB Online...** from the **File** menu or *click* on () if it appears at the top of the screen.



Type **1JIC\*** into the dialog that results and *click* on **Open**. Turn on hydrogen bonds (**Hydrogen Bonds** from the **Model** menu or *click* on  if it appears at the top of the screen). Hydrogen bonds appear *between* different  $\beta$  strands. Note that hydrogen bonds may also exist between residues on the same strand, in this example they form a hairpin turn resulting in the same  $\beta$  sheet running adjacent to itself but in the opposite (or anti-parallel) direction. Close **1JIC** when you have finished examining the  $\beta$ -sheet structure.

11. Select **Access PDB Online...** from the **File** menu () , type **1A3F\*\*** into the resulting dialog and *click* on **Open**. Note that a simple ribbon display, showing the protein backbone (secondary structure) has replaced the usual structural models (ball-and-



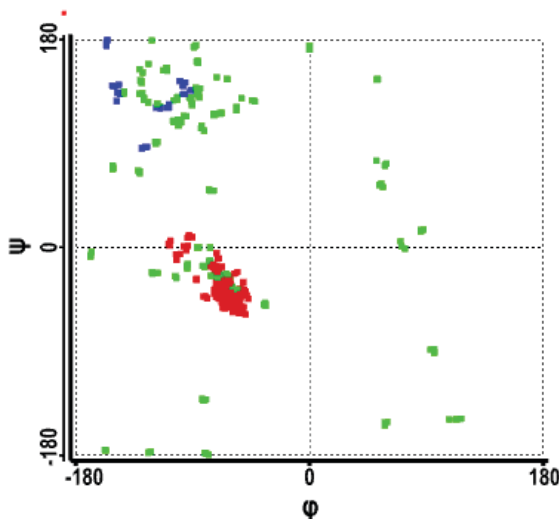
spoke, tube, etc.). To see why this is preferable, turn on (select) one of these models from the **Model** menu. The model styles that provide detail of the enzyme's primary structure completely obscure a significant structural detail (namely that this enzyme is comprised of three identical sub-units). 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.

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

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

12. 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, select **By Strand** for **Coloring** and **Extended Ribbons** for **Style** and *click Apply*. 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.
13. Select **Ramachandran Plot** from the **Geometry** menu.



Each point gives the dihedral angles between a pair of amino acids (the so-called  $\phi$  and  $\psi$  angles). Note that many points fall

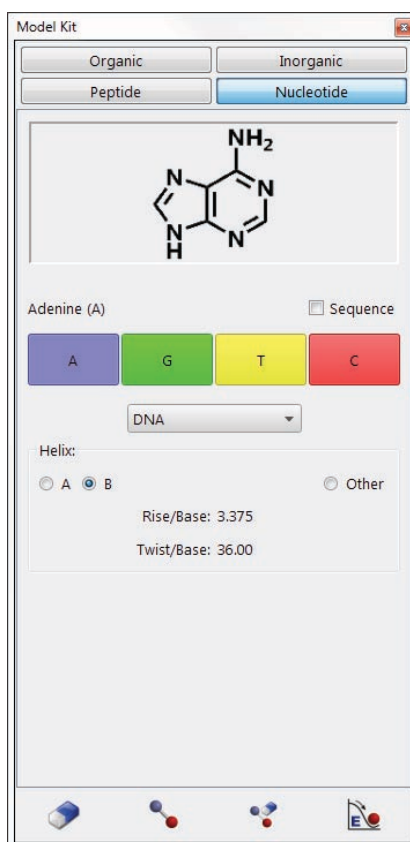
into two clusters, one corresponding to helices and the other to  $\beta$  sheets.

14. Close **1A3F**.


## Structure of DNA

Only a single motif, a helix, defines the elegant structure of DNA.

1. Select **New Build** from the **File** menu () and *click* on the **Nucleotide** model kit.



This model kit includes options for building a variety of nucleic acid sequences (based on nucleotide residues) including 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.

2. 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.
3. *Double 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, whereas 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.
4. 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 *double click* on screen. (DNA exists in three forms, A, B, and Z. Almost all DNA in living organisms is in the B-DNA configuration.)
5. 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 or *click* on  if it appears at the top of the screen 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.



6. 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  $\approx 12$  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.
7. Close all open documents.

# Tutorial 11

## Inorganic and Organometallic Molecules

*This chapter shows how to construct inorganic and organometallic molecules using **Spartan Student's** inorganic model kit.*


Many molecules are made up of a relatively few elements and obey conventional valence rules. They may be easily built using the organic model kit. However, others cannot be assembled with this model kit either because they incorporate other elements, or do not conform to normal valence rules or involve ligands. Important among these are inorganic and organometallic compounds involving transition metals.

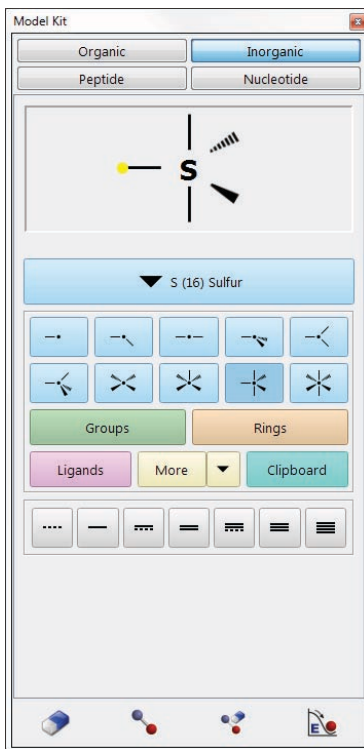
1 min

### Sulfur Tetrafluoride



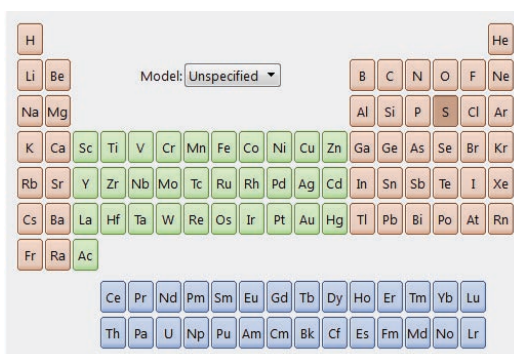
Sulfur tetrafluoride cannot be constructed using **Spartan Student's** organic model kit. This is because sulfur is not in its normal bent dicoordinate geometry, but rather in a trigonal bipyramid geometry with one of the *equatorial* positions vacant. However, the molecule can easily be made using the inorganic model kit.


1. Select **New Build** from the **File** menu (  ) and then select **Inorganic** from the menu at the top of the model kit.









The inorganic model kit comprises a selection bar (initially, *clicking* on the selection bar brings up the *Periodic Table*) followed by a selection of atomic hybrids. Buttons access menus of groups, rings and ligands, additional libraries (**More**) and the clipboard. Finally, a selection of bond types is provided at the bottom of the model kit.

2. *Click* on the selection 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.

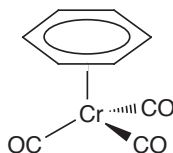
*Click* on screen. A trigonal bipyramid sulfur will appear at the top of the model kit.

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 (). Select **Equilibrium Geometry\***, **Density Functional**, **ωB97X-D**, and **6-31G\*** from the menus to the right of **Calculate** and *click* on **Submit**. Accept the name *sulfur tetrafluoride*.
7. When the job completes, select **Properties** from the **Display** menu () and *click* on an atom, for example, sulfur. The atomic charge based on the electrostatic potential will appear in the (**Atom Properties**) dialog. Are the charges consistent with covalent or ionic bonding?
8. Select **Surfaces** from the **Display** menu, *click* on **Add** and select **HOMO** from the menu that results. The graphics calculation is automatic and will take only a second or two. When completed, *check* the box to the left of **HOMO** inside the **Surfaces** dialog. Is the highest-occupied molecular orbital in sulfur tetrafluoride consistent with the notion that sulfur is surrounded by six electron pairs? Elaborate.
9. Close *sulfur tetrafluoride* and any open dialogs.

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\* 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.

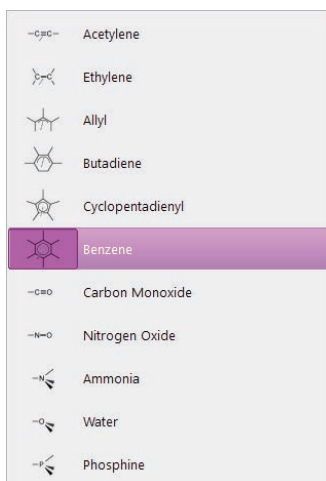
## Benzene Chromium Tricarbonyl



benzene chromium tricarbonyl

Does a chromium tricarbonyl group donate or withdraw electrons from an aromatic ring to which it is coordinated? The objective of this tutorial is to find out by comparing electrostatic potential maps for benzene chromium tricarbonyl and free benzene.







1. Select **New Build** from the **File** menu () and then **Inorganic** from the menu at the top of the model kit. *Click* on the selection bar and select **Cr** from the *Periodic Table*. Select the four-coordinate tetrahedral structure  from the list of atomic hybrids. *Click* anywhere on screen.
2. *Click* on **Ligands** in the model kit, select **Benzene** from the menu of available ligands.



*Click* on one of the free valences on the four-coordinate chromium center.

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.

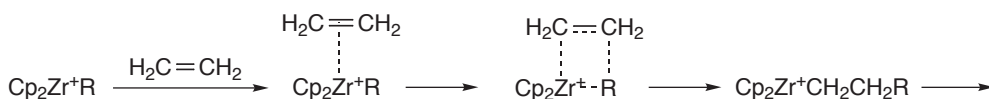
4. Select **Build New Molecule** from the **File** menu (). Click on **Rings**, select **Benzene** and click on the screen. Click on  and then on . The document now contains both benzene chromium tricarbonyl and benzene.
5. Select **Calculations...** from the **Setup** menu (). Specify calculation of **Equilibrium Geometry** and **PM3** from the menus to the right of **Calculate**. Make certain that **Global Calculations** (at the bottom of the dialog) is checked. Click on **OK**.
6. Select **Surfaces** from either the **Setup** or **Display** menu (). Click on **Add** and choose **electrostatic potential map** from the menu. Make certain that **Global Surfaces** is checked. Do not close the **Surfaces** dialog.
7. Submit the job (**Submit** from the **Setup** menu). Name it *benzene chromium tricarbonyl*. When completed select **Spreadsheet** from the **Display** menu () and check the box to the left of the label for both entries. This allows the two molecules to be displayed simultaneously on screen. By default, **Coupled (Model menu)** is checked. Remove the checkmark by selecting it. The two 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. Check *electrostatic potential map* in the **Surfaces** dialog. 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?
9. Close the documents and any open dialogs.

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\* 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.

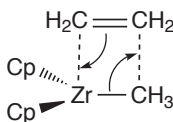
## Ziegler-Natta Polymerization of Ethylene

Ziegler-Natta polymerization involves a metallocene. This complexes an olefin, which then inserts into the metal-alkyl bond.





The object of this tutorial is to obtain a transition state for insertion of ethylene into  $\text{Cp}_2\text{ZrCH}_3^+$ .







1. Select **New Build** from the **File** menu () and then **Inorganic** from the menu at the top of the model kit. Click on the selection bar and select **Zr** from the *Periodic Table*. Select  from the list of hybrids and click on screen. Select **Cyclopentadienyl** from the **Ligands** menu and click on two of the free valences on zirconium.
2. Select **Organic** from the menu at the top of the model kit to move to the organic model kit. Select  $\text{sp}^3$  carbon  and click on the remaining free valence on zirconium. Select **Alkenyl** from the **Groups** menu, hold down the **Insert** key (option key on Mac) and click anywhere on screen or double click in a blank area on screen.
3. Orient the two fragments ( $\text{Cp}_2\text{ZrCH}_3$  and ethylene) as shown below:



(To move the fragments independently, hold down the **Ctrl** key.)

4. Select **Transition State** from the **Build** menu () . Click on the ZrC (methyl) bond, and then one after another, click on the methyl carbon and on one of the ethylene carbons. Next, click on the ethylene double bond and then, one after another, click on the other ethylene carbon and on zirconium. Click on  (Search Transition State) at the bottom right of the screen. In a

few seconds, a guess at the transition state appears.

5. Select **Calculations...** from the **Setup** menu (). Specify **Transition State Geometry** and **PM3** from the menus to the right of **Calculate**. Change **Total Charge** to **Cation** and *check IR*. *Click* on **Submit** and name the job ***Cp2ZrMe cation + ethylene***.
6. When the job has completed, select **Spectra** from the **Display** menu (). *Click* on the  in the bar at the top of the spectra pane and select   (calculated IR Spectrum). The infrared spectrum calculated for the transition state appears. *Click* on  (Tables) at the far left of the spectra pane. This brings up a list of calculated frequencies and infrared intensities. Note that the frequency value at the top of the list is preceded by an “i”. This designates it as imaginary. *Click* on this frequency and examine the vibrational motion. Would you describe the process as concerted or occurring in discrete steps?
7. Close ***Cp2ZrMe cation + ethylene*** and any open documents and dialogs.