Spartan Student Tutorial and User's Guide

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Table of Contents

Section I
Overview and Operations

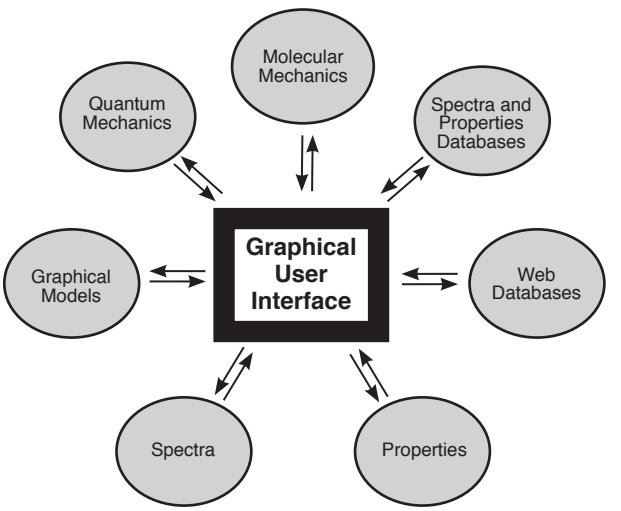
This section includes a total of three chapters. The first two are intended to provide an overview of the components that control access to ***Spartan Student's*** graphical user interface (GUI). The third (**Walking Through Spartan Student**) provides a "guided tour" of the interface, with examples provided (from pre-calculated molecules) demonstrating many rudimentary operations and emphasis on commonly used features. Description of the full range of ***Spartan Student's*** capabilities (and detailed tour through all menu items and interface options) is deferred to Section 3 (**User's Guide**), which is intended to serve as a reference to the current version 9 feature set.

Chapter 1

Spartan Student

This chapter describes the architecture of ***Spartan Student****, focusing on the connectivity of computational, graphical and database components to the user interface. Available molecular mechanics and quantum chemical methods are enumerated and their utility and applicability assessed.*

Spartan Student comprises a series of independent molecular mechanics and quantum chemical calculation modules tightly connected via a graphical user interface that is highly functional, yet simple and uncluttered. It has been designed not only to greatly reduce the number of steps and possibility for human error associated with the preparation of input for calculations, but also to guide the interpretation of output from calculations. The interface may be viewed as an interactive and intuitive analytical device accessing molecular mechanics and quantum chemical techniques.



Included in the interface are 3D builders for organic, inorganic and organometallic molecules, polypeptides and polynucleotides, and a procedure for building transition states. 2D sketch capability for organic and organometallic molecules has been refined with this

version of ***Spartan Student***. Additionally, use of ChemDraw[1] is enabled without having to exit the interface. A ≈6,000 molecule subset of the Spartan Spectra and Properties Database (SSPD) contains structures, infrared and NMR spectra as well as a wide variety of molecular properties obtained from the EDF2/6-31G* density functional model. The wavefunction is included, allowing quick access to a variety of graphical surfaces and property maps. On-line access to the Protein Data Bank (PDB)[2], a collection of >190,000 biological macromolecular structures, is available. Experimental infrared spectra for ≈2,000 molecules are available from the NIST website[3] and experimental NMR spectra for >44,000 molecules are available from NMRShiftDB website.[4]

Spartan Student's interface provides the gateway to a range of modern computational methods[5]. The simplest of these is the MMFF molecular mechanics model, available to determine equilibrium geometries and equilibrium conformers of molecules comprising upwards of several thousand atoms.

Quantum chemical models are required to account for the geometries of transition states as well as for reaction and activation energies.[7] The simplest of these are semi-empirical molecular orbital models. The PM3 model, supported in ***Spartan Student***, has proven successful for determining equilibrium geometries including the geometries of transition-metal compounds, but it is not reliable for the calculation of the reaction or activation energies.

Hartree-Fock molecular orbital models are a mainstay of quantum chemical techniques, in particular, for determining equilibrium and transition-state geometries and reaction energies, and are supported in ***Spartan Student*** with the STO-3G, 3-21G, 6-31G* and 6-311+G** basis sets. Hartree-Fock models generally provide suitable descriptions of many types of reactions, but are ***not adequate*** for thermochemical comparisons where bonds are broken or formed. In addition, they do not provide a proper account of the geometries of molecules incorporating transition metals. Supported in ***Spartan Student*** are the B3LYP, EDF2, and ωB97X-D density functional models (DFT) and the MP2 Møller-Plesset model. All properly account for the energies

of reactions that involve bond making and breaking and both density functional models (but not the MP2 model) properly account for the geometries of molecules incorporating transition metals. DFT and MP2 models are supported with the 6-31G* and 6-311+G** basis sets. The T1[6] thermochemical recipe, providing high accuracy heats of formation for uncharged, closed-shell systems containing H, C, N, O, F, Si, P, S, Cl and Br, is also provided.

Spartan Student provides access to infrared spectra (MMFF, PM3, Hartree-Fock, B3LYP, EDF2, ωB97X-D and MP2 models) and NMR spectra[7] (Hartree-Fock, B3LYP, EDF2, ωB97X-D models only). These are available both as numerical data (vibrational frequencies, chemical shifts) as well as spectral plots. ***Spartan Student*** provides internet access to experimental IR and NMR databases[3,4], allowing direct comparison with calculated spectra. Infrared spectra from density functional models has been corrected using both a multiplicative scale of calculated frequencies and peak width at half height as parameters. Proton and ^{13}C chemical shifts obtained from B3LYP/6-31G* and ωB97X-D/6-31G* as well as proton, ^{13}C and ^{19}F chemical shifts obtained from the EDF2/6-31G* density functional model have been empirically corrected to account for local environment.

Also available are energy, equilibrium and transition state geometry, and frequency calculations using the C-PCM solvation model in conjunction with Hartree-Fock and density functional models only. The model depends only on the dielectric constant of the solvent and preset values are available for typical non-polar and polar solvents as well as water.

New in ***Spartan Student 9*** is calculation of UV/vis spectra (density functional only) based on ground state geometry, with excited state calculation from TDDFT. In general, calculated UV/vis spectra results are not sufficient to identify or confirm color, but are sufficient to indicate if substitutions will shift color toward red or blue.

Spartan Student provides a variety of graphical tools to assist in interpreting the results of calculations. These include molecular orbitals, electron and spin densities, local ionization potentials and electrostatic potentials that can be displayed as surfaces, slices and

property maps. ***Spartan Student*** provides the ability to distinguish accessible and inaccessible regions on a density surface and on property maps based on this surface. Animations can be created and used to depict conformational changes or the progress of chemical reactions.

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1. ChemDraw is not included with ***Spartan Student***, but may be obtained from PerkinElmer (www.perkinelmerinformatics.com). Seamless access to ChemDraw is not available in the Macintosh version although both Windows and Macintosh versions are able to read ChemDraw files.
2. PDB web reference: https://www.rcsb.org.
3. NIST web reference: https://book.nist.gov.
4. NMRShiftDB web reference: https://nmrshiftdb.nmr.uni-koeln.de
5. Full discussion and assessment of the specific molecular mechanics and quantum chemical models available in ***Spartan Student*** is provided in: W.J. Hehre, ***A Guide to Molecular Mechanics and Quantum Chemical Calculations***, Wavefunction, Irvine, 2003. This is available as a PDF on Wavefunction's website (www.wavefun.com). See also: W.J. Hehre, L. Radom, P.v.R. Schleyer and J.A. Pople, ***Ab Initio Molecular Orbital Theory***, Wiley, New York, 1986; Y. Shao, Z. Gan, E. Epifanovsky, A. T. B. Gilbert, M. Wormit, J. Kussmann, A. W. Lange, A. Behn, J. Deng, X. Feng, D. Ghosh, M. Goldey P. R. Horn, L. D. Jacobson, I. Kaliman, R. Z. Khaliullin, T. Kús, A. Landau, J. Liu, E. I. Proynov, Y. M. Rhee, R. M. Richard, M. A. Rohrdanz, R. P. Steele, E. J. Sundstrom, H. L. Woodcock III, P. M. Zimmerman, D. Zuev, B. Albrecht, E. Alguire, B. Austin, G. J. O. Beran, Y. A. Bernard, E. Berquist, K. Brandhorst, K. B. Bravaya, S. T. Brown, D. Casanova, C.-M. Chang, Y. Chen, S. H. Chien, K. D. Closser, D. L. Crittenden, M. Diedenhofen, R. A. DiStasio Jr., H. Dop, A. D. Dutoi, R. G. Edgar, S. Fatehi, L. Fusti-Molnar, A. Ghysels, A. Golubeva-Zadorozhnaya, J. Gomes, M. W. D. Hanson-Heine, P. H. P. Harbach, A. W. Hauser, E. G. Hohenstein, Z. C. Holden, T.-C. Jagau, H. Ji, B. Kaduk, K. Khistyaev, J. Kim, J. Kim, R. A. King, P. Klunzinger, D. Kosenkov, T. Kowalczyk, C. M. Krauter, K. U. Lao, A. Laurent, K. V. Lawler, S. V. Levchenko, C. Y. Lin, F. Liu, E. Livshits, R. C. Lochan, A. Luenser, P. Manohar, S. F. Manzer, S.-P. Mao, N. Mardirossian, A. V. Marenich, S. A. Maurer, N. J. Mayhall, C. M. Oana, R. Olivares-Amaya, D. P. O'Neill, J. A. Parkhill, T. M. Perrine, R. Peverati, P. A. Pieniazek, A. Prociuk, D. R. Rehn, E. Rosta, N. J. Russ, N. Sergueev, S. M. Sharada, S. Sharmaa, D. W. Small, A. Sodt, T. Stein, D. Stück, Y.-C. Su, A. J. W. Thom, T. Tsuchimochi, L. Vogt, O. Vydrov, T. Wang, M. A. Watson, J. Wenzel, A. White, C. F. Williams, V. Vanovschi, S. Yeganeh, S. R. Yost, Z.-Q. You, I. Y. Zhang, X. Zhang, Y. Zhou, B. R. Brooks, G. K. L. Chan, D. M. Chipman, C. J. Cramer, W. A. Goddard III, M. S. Gordon, W. J. Hehre, A. Klamt, H. F. Schaefer III, M. W. Schmidt, C. D. Sherrill, D. G. Truhlar, A. Warshel, X. Xua, A. Aspuru-Guzik, R. Baer, A. T. Bell, N. A. Besley, J.-D. Chai, A. Dreuw, B. D. Dunietz, T. R. Furlani, S. R. Gwaltney, C.-P. Hsu, Y. Jung, J. Kong, D. S. Lambrecht, W. Liang, C. Ochsenfeld, V. A. Rassolov, L. V. Slipchenko, J. E. Subotnik, T. Van Voorhis, J. M. Herbert, A. I. Krylov, P. M. W. Gill, and M. Head-Gordon. Advances in molecular quantum chemistry contained in the Q-Chem 4 program package. [Mol. Phys. 113, 184–215 (2015)].
6. W.S. Ohlinger, P.E. Klunzinger, B.J. Deppmeier, W.J. Hehre, ***J. Phys. Chem. A***, **103**, 10, 2165 (2009).
7. Chemical shifts only. HH coupling constants and splitting patterns are evaluated empirically.

Chapter 2
Operating *Spartan Student*

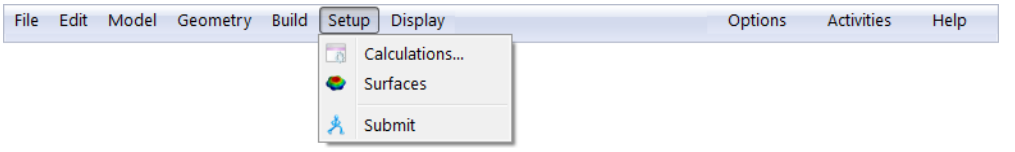
This chapter describes the general operating features of ***Spartan Student****.*

Opening and Exiting/Quitting *Spartan Student*

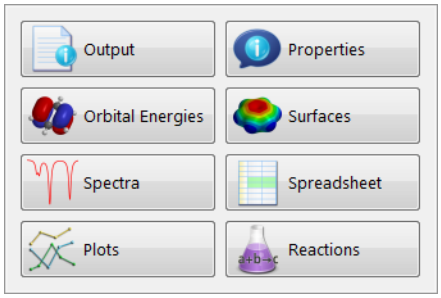
To open from Windows, *click* the Search field next to the Windows icon and type: Spartan Student. *Click* on the ***Spartan Student v.9*** app to open (or *double click* on the ***Spartan Student*** shortcut icon on your desktop). To open from Macintosh, *double click* on the ***Spartan Student*** icon in the Applications Folder. To exit, select **Exit** from the **File** menu (select **Quit Spartan Student** from the **Spartan Student** menu for Mac), or *click* the **Close** button ( ) at the top right (top left for Mac) of the ***Spartan Student*** interface.

Menus and Icons

Program functions may be accessed either from the menu bar or from icons in the toolbar which is directly underneath the menu bar. The menu bar may either be accessed as pull-down menus (**Drop Down**), for example, the **Setup** menu:



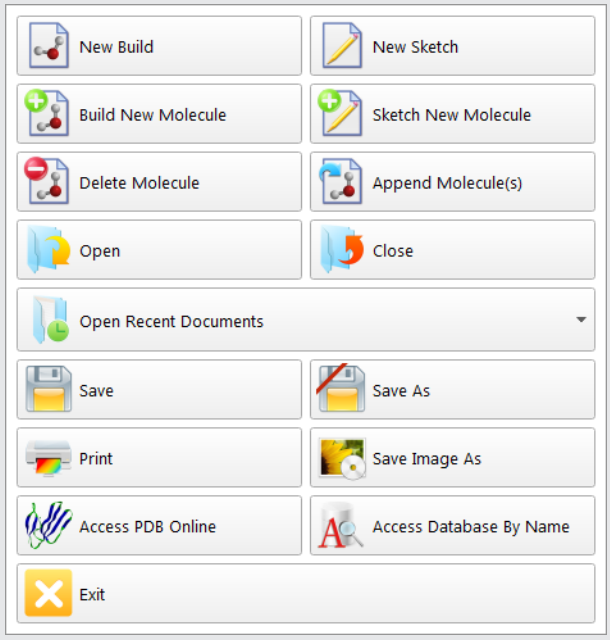
or under Windows (only) from a list of icons presented in a palette (**Button Pad**), for example, the **Display** menu:



Selection is made in the **Settings Preferences** dialog (**Preferences...** under the **Options** menu; **Chapter 10**).

Icons for all menu functions (as shown alongside text in both **Drop Down** and **Button Pad** styles) are available. Display choice (beyond the default initially supplied with ***Spartan Student***) is made in the **Icons** tab (**Preferences...** under the **Options** menu; **Chapter 10**). Icon size is selected from the **Settings** tab (**Preferences...** under the **Options** menu; **Chapter 10**).

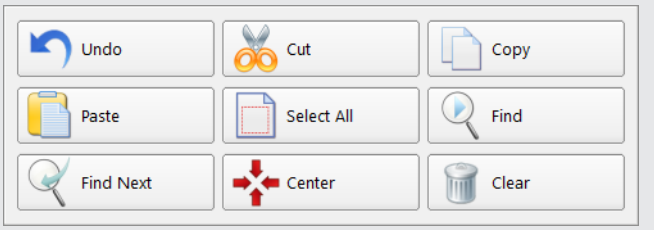
File



Allows you to build or sketch a new molecule or read in a molecule that you have previously saved, to retrieve the structure, properties and IR and NMR spectra from a molecule in ***Spartan Student***'s database from

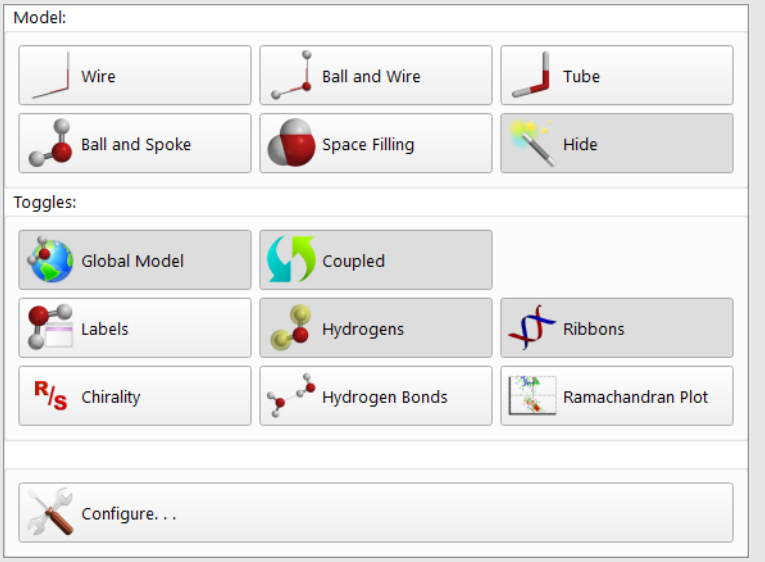
its name, to retrieve a protein structure from the Protein Data Bank, to print what is on screen or save it as an image file, and to make QuickTime movies (Macintosh only). Open, Close, and program Exit functions are also accessible.

Edit



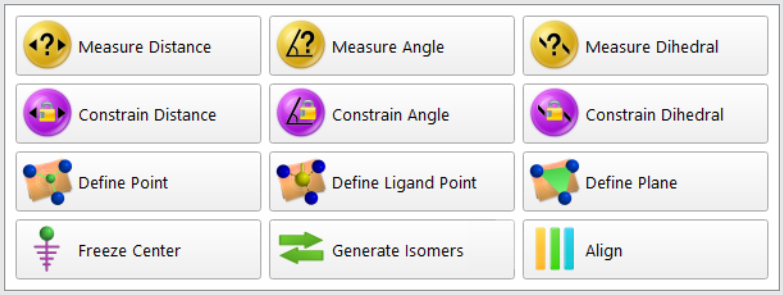
Allows you to transfer information to and from the clipboard, to undo operations, to find text strings and molecule fragments, to center molecules on screen, and to clear the active molecule by deleting it.

Model



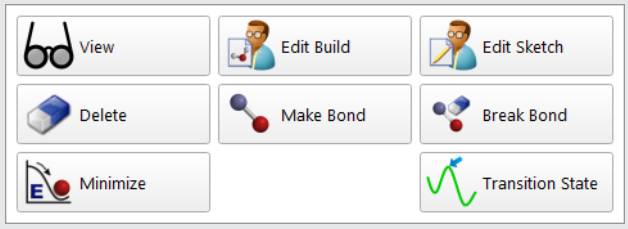
Allows you to control the style of your model, to display hydrogen bonds and to couple or decouple molecules in a multi-molecule document. Enables display of a Ramachandran plot for a protein structure brought in from PDB, toggles on/off display of hydrogen bonds and labels R/S chiral centers.

Geometry



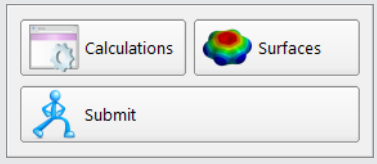
Allows you to measure and constrain bond lengths, angles and dihedrals, define points and planes, specify atoms to be "frozen", elaborate isomers and align molecules.

Build



Allows you to build or sketch and edit molecules, and to build/estimate a transition state geometry based on a library of reactions (using arrow pushing markers).

Setup



Allows you to specify the task to be performed and the theoretical model to be employed for this task, and specify graphical surfaces and property maps and to submit jobs for calculation.*

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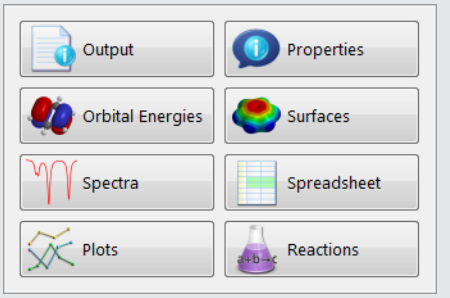
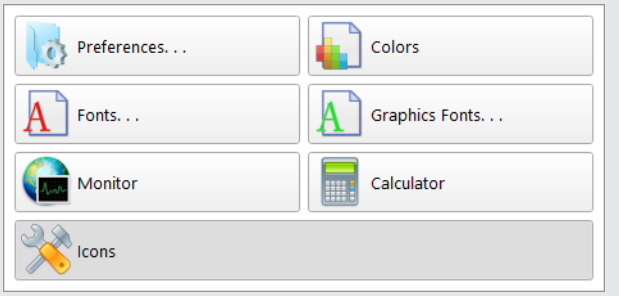
* If a quantum chemical calculation has previously been performed, or if the molecule has been retrieved from the SSPD, surfaces are generated "on-the-fly" from the ***Spartan Student*** graphical interface, and do *not* require submission to generate graphical models.

Display



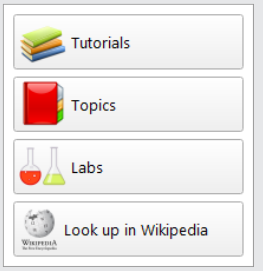
Allows you to display text output, molecular and atomic properties, orbital energy diagrams, surfaces and property maps and infrared and NMR spectra, as well as to access experimental IR and NMR over the internet. Allows you to present data in a spreadsheet and make plots from and perform regression analysis on these data, and to compute reaction energies based either on user data or from entries in the database associated with ***Spartan Student***.

Options



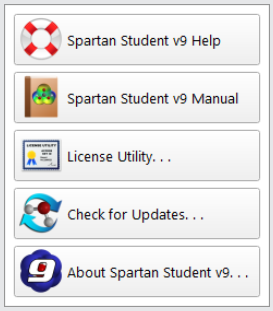
Allows you to set display standards, specify the location of the database, monitor executing jobs and customize colors, icons and other aspects of the graphical user interface.

Activities



Allows you to display tutorials, topics, and lab activities inside of ***Spartan Student*** and to search Wikipedia.

Help



Provides access to information on ***Spartan Student's*** general operation and a number of computational FAQ's, the ***Spartan Student*** **Manual**, and license information. Allows users to check for version updates.

A complete listing of menu functions is provided in **Appendix B**.

Additional Icons

A variety of other icons appear in ***Spartan Student***, both in individual dialogs and in the information bar at the bottom of the screen.

 Post to Spreadsheet

 Search Transition State

 Lock/Unlock Constraints

 Move Up/Down Dialog

 Play

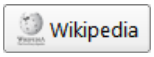
 Pause

 Step

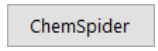
 Extend to Fullscreen

 Revert to Actual Size

 Stop



Look Up in Wikipedia



Look Up in ChemSpider

Tabs

Spartan Student assigns a tab to each open document. When more than a single document is open, these appear in a single row along the bottom of the screen in the order that the documents were created or read. Backward and forward step keys ( and ) at the far right provide access to tabs outside of those displayed. Documents are selected for display by *clicking* on its tab. To the left of each tab is a check box, if checked, this indicates that the document will be displayed on screen even if it is not the selected document. By default, tabs are not checked. Selecting **Pin New Documents** from the **Settings** tab (**Preferences...** under the **Options** menu; **Chapter 10**) changes the behavior and checks all tabs.

Mouse/Keyboard Operations

The following functions are associated with a standard mouse and keyboard. Note: the the zoom function (translation in the z plane) is managed by the center mouse wheel (or moving the finger over the center of the mouse for the standard Macintosh mouse)

Keyboard	Left	Right
–	X/Y rotation, atom/fragment substitution[a], insertion[a]	X/Y translation
Shift	Range selection, Z rotate	Zoom (Z translate)
Ctrl (view mode)	multiple rotation, X/Y rotation for all visible molecules	X/Y translation for all visible molecules
Ctrl (build mode)	selected fragment, X/Y rotation	selected fragment, X/Y translation
Ctrl (build) **Windows**	chiral center inversion[a]	
Command (build) **Macintosh**	chiral center inversion[a]	
Ctrl + **Shift** (view)	Z rotation for all visible molecules	
Ctrl + **Shift** (build) **Windows**	selected fragment Z rotate, absolute chirality inversion[a]	
Command + **Shift** (build mode) **Macintosh**	selected fragment Z rotate, absolute chirality inversion[a]	
Alt Windows (view) **Option Mac** (view)	group selection[b] group selection[b]	
Alt Windows (build) **Option Mac** (build)	bond rotation bond rotation	bond stretching bond stretching

a) Build mode only, requires *double clicking*.
b) With no keys pressed, holding down the center mouse wheel (or both left and right mouse buttons), dragging enables a selection box for group selection.

These broadly fall into two categories: selection (picking) and manipulation (translation/rotation/zooming).

Selection. *Clicking* (left button) selects objects on screen and/or menu items. Left and right buttons together are used to define a selection box for copying to the clipboard, as well as for multiple model selection. Together with the **Shift** key, the left button allows for selection over a range. Together with the **Ctrl** (**Control**) key, the left button allows for multiple selection. Both range and multiple selection apply not only to text items in lists, but to atoms and bonds in molecules as well. Together with the **Alt** key (**Option** key for

Mac), the left button allows for selection of an entire group (detached molecular fragment).

In **Edit Build** mode (only), *double clicking* (left button) on an atom exchanges it with the atom or atomic fragment selected in the model kit. *Double clicking* on an atom while holding down the **Ctrl** key leads to inversion in chirality of the atom and *double clicking* on a molecule while holding down both the **Ctrl** and **Shift** keys inverts the absolute configuration of the molecule. These operations are not available in the 2D sketcher (**Edit Sketch** mode). Once an initial fragment, group or ring has been specified, *double clicking* on the background will insert it alongside (but not bonded to) whatever currently exists on screen.

Manipulation. The left button is used for rotation and the right button is used for translation and scaling of objects on screen. With no keys depressed, moving the mouse while holding down the left button gives rise to rotation about the X and Y (screen) axes, while moving the mouse while holding down the right button gives rise to translation in the X and Y (screen) directions. Together with the **Shift** key, moving the mouse while holding down the left button gives rise to rotation about the Z direction, while moving the mouse while holding down the right button gives rise to scaling. The center (scroll) wheel on the mouse may also be used for scaling.

The **Ctrl** key in conjunction with the left or right mouse buttons and (optionally) the **Shift** key, signifies a change in focus away from the default for the purpose of rotations and translations. Outside of **Edit Build**/**Edit Sketch** mode, the default is focus on a single molecule (the selected molecule). Use of the **Ctrl** key changes focus to the entire set of molecules on screen, meaning that rotations and translations are carried out globally. In **Edit Build** mode (only), the default is focus on the full set of fragments that make up the molecule being constructed, and rotations and translations refer to this set of fragments as a whole. Use of the **Ctrl** key changes focus to a single fragment (the selected fragment), and rotations and translations now refer only to this fragment (does not apply to **Edit Sketch** mode).

In **Edit Build** mode (only), moving the mouse while holding down the **Alt** key (**Option** key for Mac) together with the left mouse button rotates about the selected bond. With the right mouse button, this changes the length of the selected bond. Bond rotation (only) may also be accomplished by moving the mouse up and down inside the demarked area at the left of the screen while holding down the left mouse button (does not apply to **Edit Sketch** mode).

Additional keys control various ***Spartan Student*** functions.

Page Up, Page Down **Home, End**	Moves up (**Page Up**), down (**Page Down**), to the top (**Home**) and to the bottom (**End**) of the set of open molecules. Also, moves up and down pages in the **Output** dialog.
Insert (**Option** for Mac)	In **Edit Build**/**Edit Sketch** fragment mode only, inserts a new fragment on screen. This is accomplished by selecting the fragment from the model kit, holding down the **Insert** key and *clicking* on screen. Insertion may also be accomplished by *double clicking* on the background following selection of a fragment.
Delete	Deletes a fragment, free valence, reaction arrow or the contents of a selection box. This is accomplished by holding down the **Delete** key and *clicking* on the fragment, etc.
Enter (**Return** for Mac)	Required following text or data entry into spreadsheet or dialogs.

Touch-Screen Operations

Tapping is equivalent to *clicking* and *double tapping* is equivalent to *double clicking*. Touch commands for range and multiple selection have not been implemented. One finger motions on screen are equivalent to left button motions (object and bond rotation). Two finger motions are equivalent to right button motions (object translation). Two finger pinching is equivalent to scroll wheel operations (zooming).

Selecting Molecules

While two or more molecules may be simultaneously displayed in ***Spartan Student***'s window (see **Tabs** earlier in this chapter), only one molecule may be selected. Only the selected molecule has access to all capabilities. Molecule selection occurs by *clicking* on its structure model or on any of its associated graphical surfaces. The previously selected molecule is deselected.

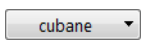
Where the molecule belongs to a document with more than a single molecule, selection from among the different molecules may be made using either the ◀| and |▶ buttons or the scroll bar at the bottom left of the screen. *Clicking* on ▶ at the bottom left of the screen animates the display of molecules in the document, that is, steps through them sequentially. Animation speed is controlled from the **Settings** tab (**Preferences...** under the **Options** menu; **Chapter 10**). *Clicking* on ⏸ (that replaces ▶) stops the animation. If the spreadsheet associated with the document is open (**Spreadsheet** under the **Display** menu; **Chapter 9**), selection can also be made by *clicking* on the molecule label at the left of the spreadsheet.

Two or more molecules from the same document may be displayed at once (although only one may be selected). Molecules are marked for display by *checking* the box immediately to the left of the molecule label in the spreadsheet.

Database

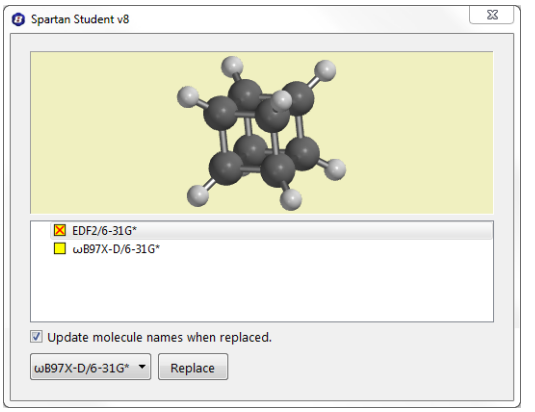
Included with ***Spartan Student*** is a ≈6,000 molecule subset of the Spartan Spectra and Properties Database (SSPD).** This provides infrared and NMR spectra in addition to a variety of molecular properties obtained from the EDF2/6-31G* or ωB97X-D/6-31G* density functional model. The database may be accessed either by molecule name (see **Chapter 3**) or by molecule structure (see below).

The existence of the selected molecule in the database is signaled by its name being displayed at the bottom of the screen.



** The SSPD is a growing collection of >300,000 organic molecules along with associated properties and IR and NMR spectra data. Contact sales@wavefun.com for licensing options.

Details are provided by *clicking* on ▲ to the immediate left of the molecule name (it then changes to ▼). This brings up a dialog that allows a 3D model of the entry in the database to be rotated, translated and scaled using the usual mouse/keyboard commands (you need to position the cursor inside the viewing area). Model style may not be changed.



The selected (on-screen) molecule may be replaced by the selected database entry by *clicking* on **Replace** at the bottom of the dialog. (Replacement can be undone by selecting **Undo** from the **Edit** menu; **Chapter 4**). If ***Update molecule names when replaced*** is checked, the name of the molecule in the database will replace the name previously associated with the molecule.

In the event that the selected (on-screen) molecule belongs to a multi-molecule document, it is possible to replace all molecules in the document for which database entries are available. In this case, *clicking* on **Replace** will give rise to a second dialog. *Clicking* on **All** will replace all the molecules in the document, while *clicking* on **Current** will replace only the selected molecule.

Stereo Displays

Spartan Student supports red-cyan stereo. Red/blue glasses must be worn. To enter stereo-mode, select **Stereo** ON, under the **Stereo** preference (**Options** menu, **Preferences**, **Settings** tab).

Changing Colors and Setting Preferences

Colors and **Preferences...** under the **Options** menu (**Chapter 10**) allow for changing default background and graphical object colors, and for setting (and resetting) program defaults, respectively.

Monitoring and Terminating Jobs

Monitor under the **Options** menu (**Chapter 10**) allows for monitoring of executing jobs as well as for terminating jobs.

Tutorial 1

Walking Through *Spartan Student*

*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, NMR, and UV/vis 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**.

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.

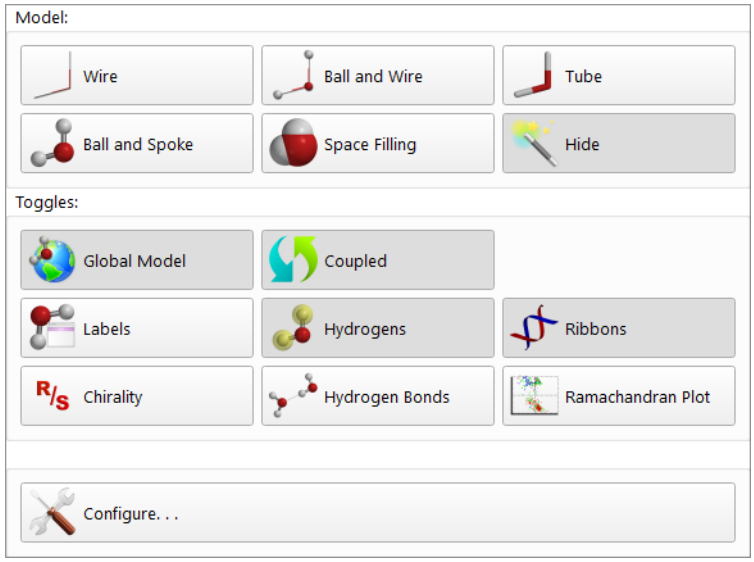
* For **Windows**, the ***Tutorials*** directory is found in ***Program Files/Wavefunction/Spartan Student***. It needs to be copied and saved to another location to access. For **Macintosh**, the ***Tutorials*** directory is on the ***Spartan Student*** disc image. It needs to be copied to another location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

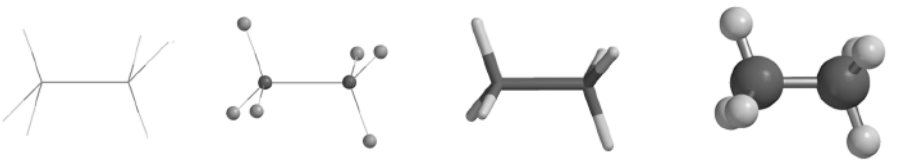
A single document containing ***ethane***, ***acetic acid dimer***, ***propene***, ***ammonia***, ***hydrogen peroxide***, ***acetic acid***, ***water***, ***cyclohexanone***, ***camphor***, ***3-aminobenzophenone***, ***ethylene***, ***benzene***, ***aniline*** and ***cyclohexenone*** will be opened. 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 ≈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.



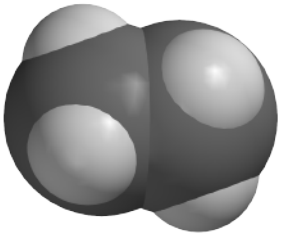


Wire Ball-and-Wire Tube Ball-and-Spoke

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.

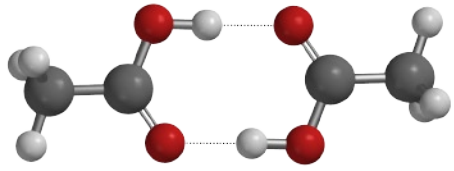


Space-Filling

The space-filling model is different from the others 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.

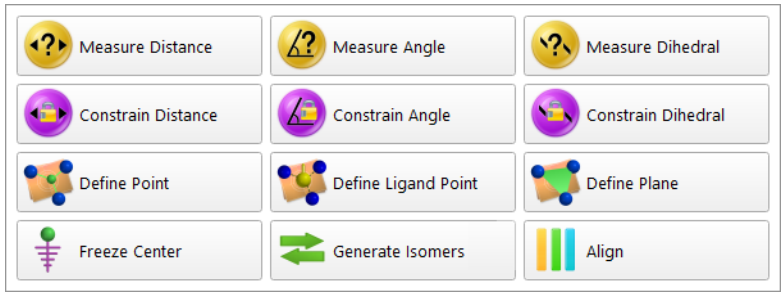
3. *Click* once on the right arrow key at the bottom left of the interface. This will move to the next molecule in the document, ***acetic acid dimer***. Its name will appear at the bottom of the screen. If you make a mistake, use the backward or forward step keys to access ***acetic acid dimer*** in 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**.



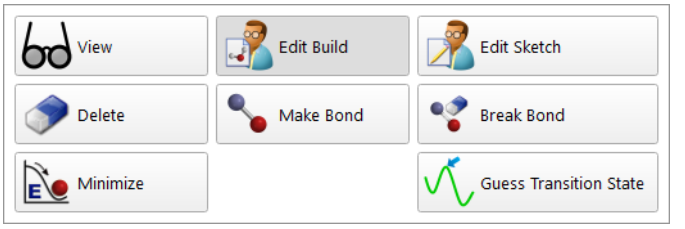
Ball-and-Spoke model for acetic acid dimer
with hydrogen bonds displayed

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

4. 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.



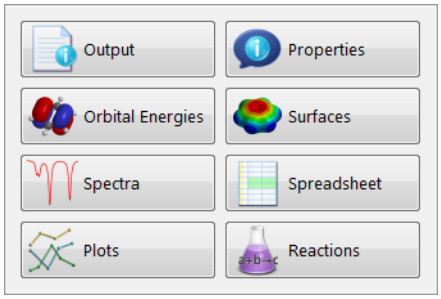
a) **Measure Distance**: This measures the distance between two atoms. *Click* once on ▶| to move to the next molecule, ***propene***. *Click* on the **Geometry** menu and select **Measure Distance** (or *click* on the icon if it appears at the top of the screen). *Click* on a bond or on two atoms (the 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).



b) **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.

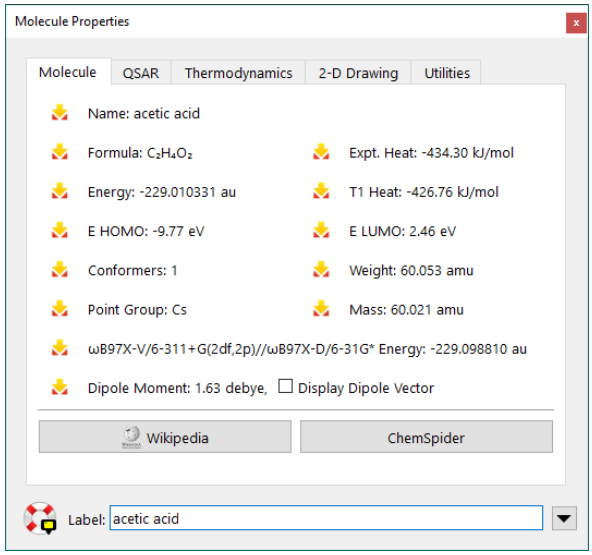
c) **Measure Dihedral**: This measures the angle formed by two intersecting planes, one containing the first three atoms selected and the other containing the last three atoms selected. *Click* once on ▶| to move to the next molecule, ***hydrogen peroxide***. *Click* on the **Geometry** menu and select **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, ⟞→ 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.

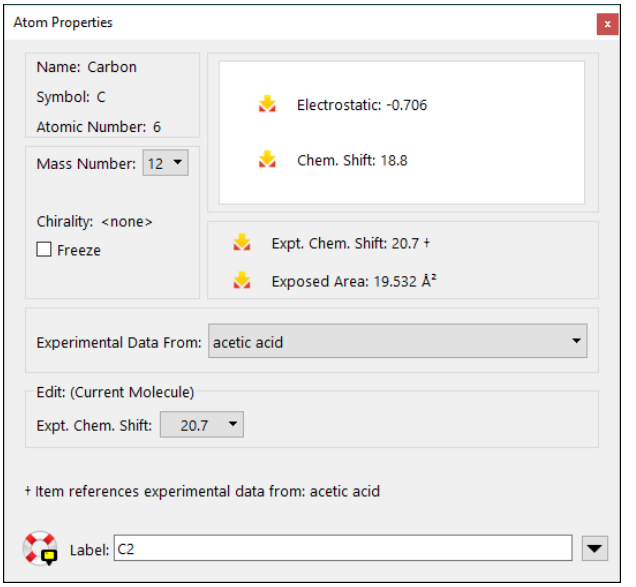
b) **QSAR:** Quantitative structure - activity relationship properties including area, volume and polar surface area (and many others) may be accessed from the QSAR tab.

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) **Utilities:** Access to a number of convenient options related to a molecule's display, color, bonding and absolute configuration are available.

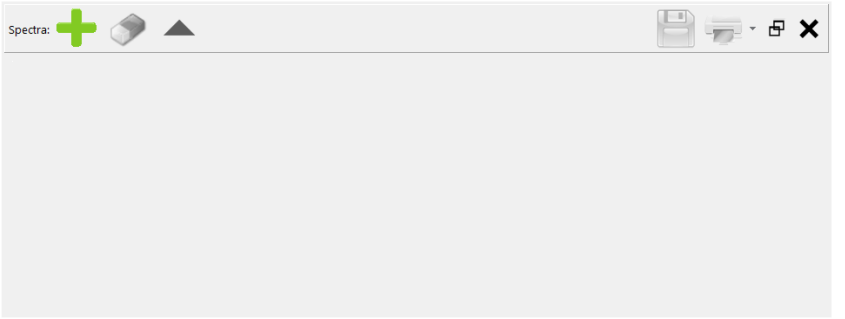
f) **Atomic Charges:** To display the charge on an atom, *click* on it when the **Molecule Properties** dialog is on screen. The **Atom Properties** dialog replaces the **Molecule Properties** dialog.



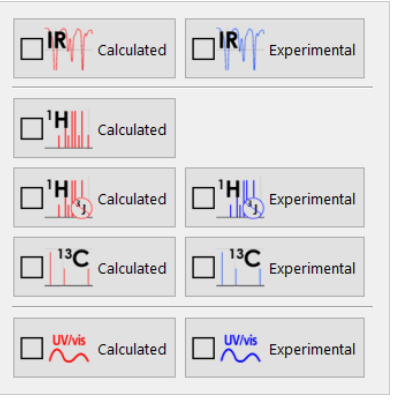
Atomic charges based on the electrostatic potential are given in units of electrons. A positive charge indicates a deficiency of electrons and a negative charge indicates an excess of electrons. Repeat for other atoms. Confirm that the positively-charged atom(s) lie at the positive end of the dipole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

g) **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.

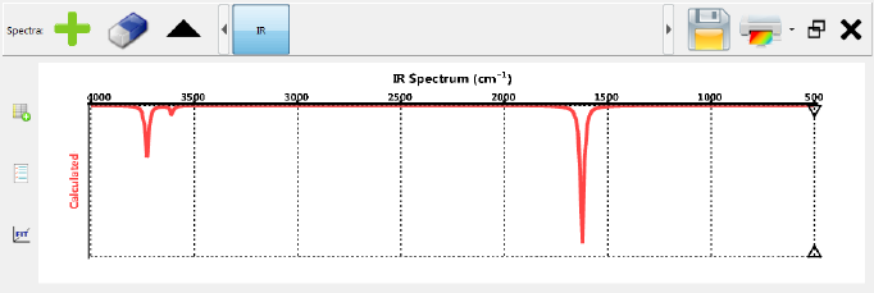
Click once on to move to the next molecule in the document, ***water***. To animate a vibration, select **Spectra** from the **Display** menu (or *click* on if it appears at the top of the screen). This leads to an empty spectra pane at the bottom of the screen.



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



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

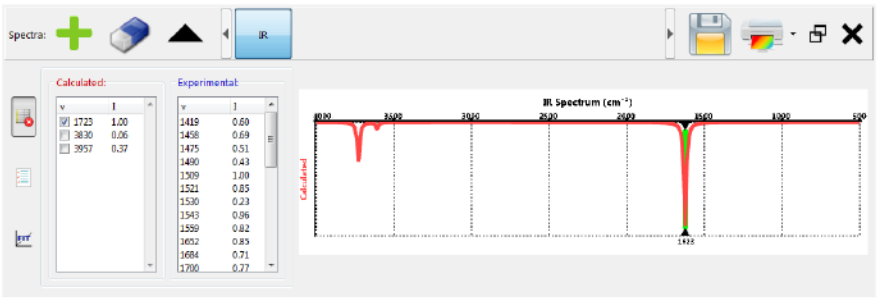


There are three lines, one of moderate intensity around 3728 cm^{-1}, one very weak around 3608 cm^{-1} and one very strong around 1623 cm^{-1}. In turn, move the cursor on the spectrum (move the mouse while holding down the left mouse button over each of these lines). In response, the molecular model 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.

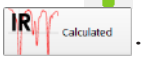
To see a complete listing of frequencies and intensities, *click* on at the left of the spectra pane.



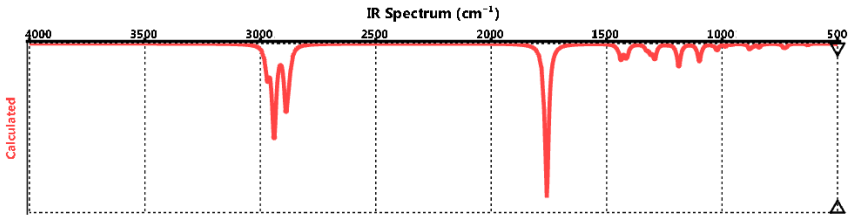
Click on each entry in the table to highlight the frequency in the spectrum and animate the vibration. *Click* on again to dismiss the table and *click* on to remove the spectrum.

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.

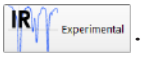
Click once on to move to ***cyclohexanone***, the next molecule in the list. The spectra pane is still on screen but should be empty. (If it is not on screen, select **Spectra** from

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 

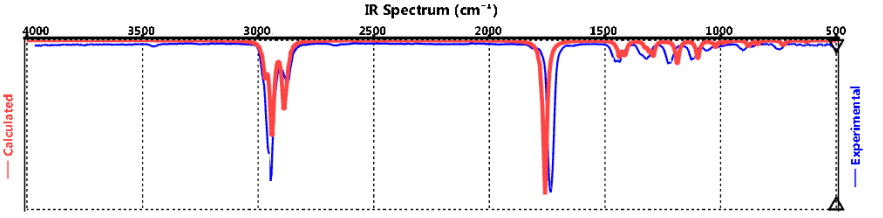
. The calculated infrared spectrum of cyclohexanone appears.



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 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 

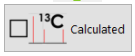
. The experimental IR spectrum (from the public NIST database) is superimposed on top of the calculated spectrum.



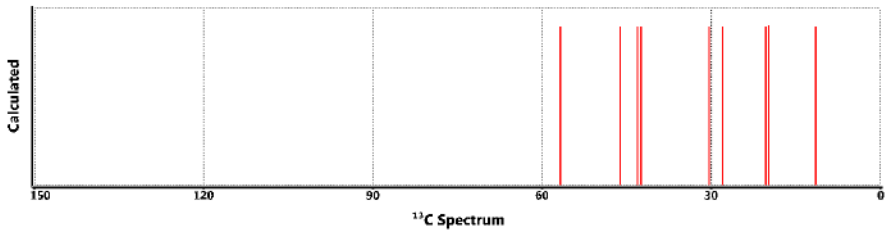
Note that the two spectra are quite similar. This would have not been the case with the raw calculated data, however, calculated frequencies and intensities have been empirically corrected to account for finite temperature and for systematic errors in the theory.

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}C are by far the most important.

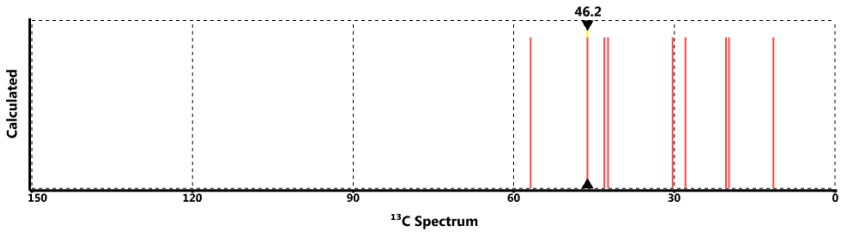
Click once on  to move to the next molecule in the document, ***camphor***. With the spectra pane on screen, *click* on  in the bar at the top of the spectra pane and select 

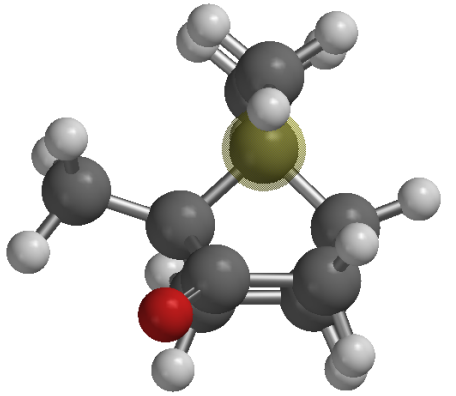
. The calculated ^{13}C NMR spectrum appears.



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.

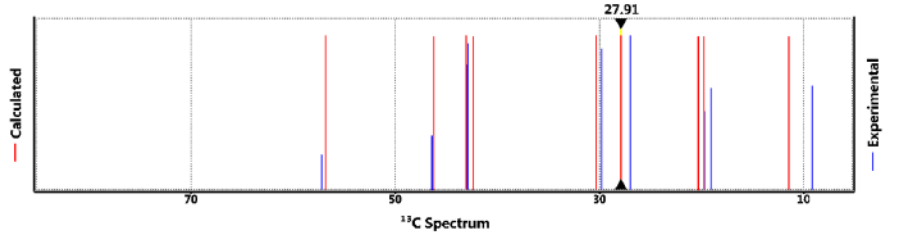
Move the mouse while holding down the left button over the spectrum. When you come to a line, the chemical shift will appear at the top of the spectrum and the atom (or atoms) responsible for this line will be highlighted on the model displayed above the spectrum.



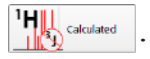


Again, *click* on  in the bar at the top of the spectra pane and select 

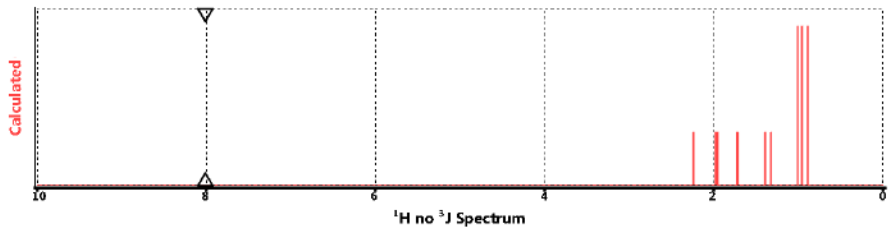
. The experimental ^{13}C spectrum obtained from a public database will be superimposed on top of the calculated spectrum.



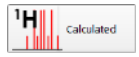
You will see that the overall agreement between calculated and experimental ^{13}C spectra is quite good. As with infrared spectra (see preceding discussion of cyclohexanone), the data resulting from the quantum chemical calculations have been empirically corrected (for density functional calculations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

Click again on  and select 

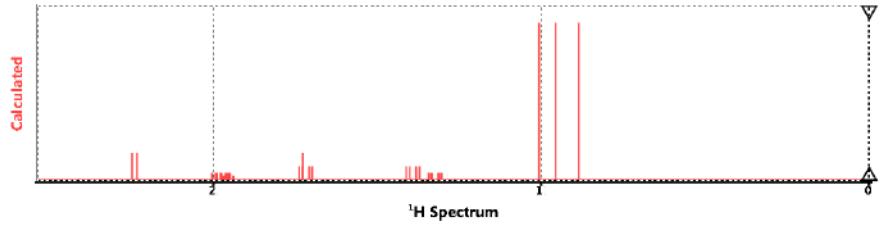
. An "idealized" proton spectrum where three-bond HH coupling constants are set to zero appears.



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}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.



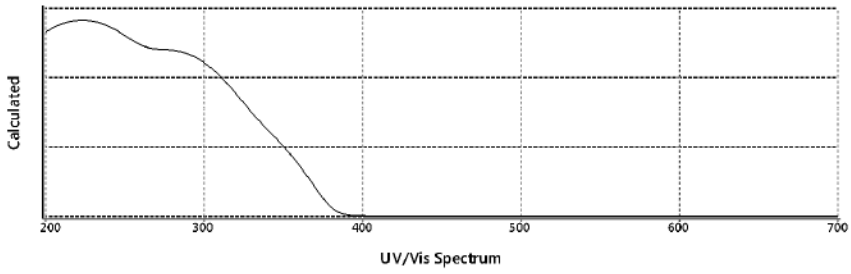
Zoom in on specific lines (scroll wheel) to see the detailed splitting patterns. For example, the two protons at C_3 are both split by the proton at C_4. The doublet at 2.23 ppm shows a much larger splitting than the doublet at 1.99 ppm (you need to zoom way in to see that this is a doublet). This reflects the fact that the proton responsible for the line at 2.23 ppm makes a dihedral angle of 43° with the proton at C_4, whereas the proton responsible for the line at 1.99 ppm makes a dihedral angle of 80°.

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

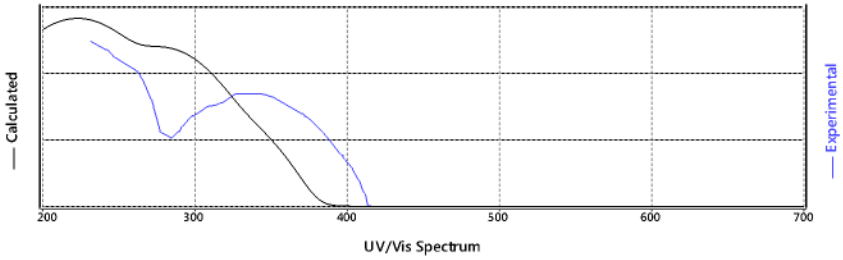
for camphor by *clicking* on the associated button in the bar above the spectra pane. When you are done, remove all three spectra by *clicking*  three times in succession.

f) **UV/visible Spectra:** Absorption of light in the visible or ultraviolet range of the electromagnetic spectrum leads to electronic excitation from the ground-state to excited-states and (in the case of absorption in the visible), is responsible for a molecule's color. UV/visible spectroscopy not only offers a "fingerprint" but is also an important screen to identify molecules that may be damaged by exposure to light.

Click once on  to move to the next molecule, ***3-aminobenzophenone***. The spectra pane should still be on screen. *Click* on  and select  . No empirical corrections have been applied to the calculated spectrum that appears.



Click again on  and select  . The experimental UV/visible spectrum from the freely available NIST database will be drawn on top of the calculated spectrum.

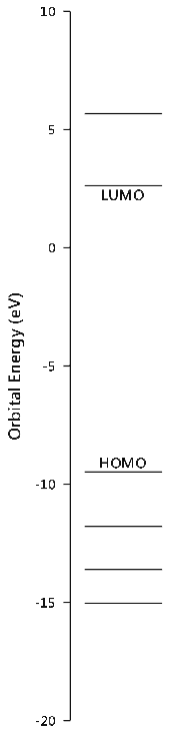


The two spectra are visually similar at least qualitatively. However, calculated and experimental UV/visible spectra are likely to be sufficiently different that the theory will not often be able to account for the "color" of the molecule.

Where the theory is likely to be more successful is in anticipating changes in color resulting from subtle changes in structure. *Click* on  when you are done. Also, remove the spectra pane either by *clicking* on  at the top right or by selecting **Spectra** from the **Display** menu or by *clicking* on  if it appears at the top of the screen.

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.

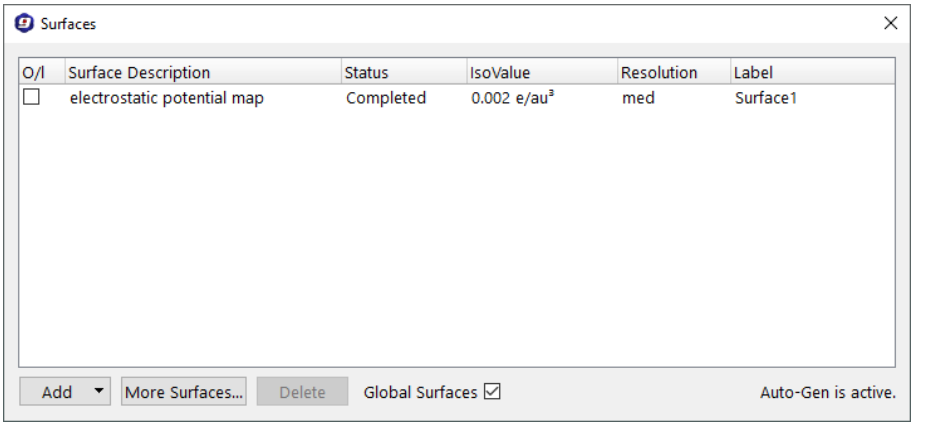
   Click once on  to move to the next molecule in the list, ***ethylene***. *Click* on the **Display** menu and select **Orbital Energies** (or *click*  if it appears at the top of the screen). An orbital energy diagram for ethylene will appear at the left of the screen. This provides the energies of all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

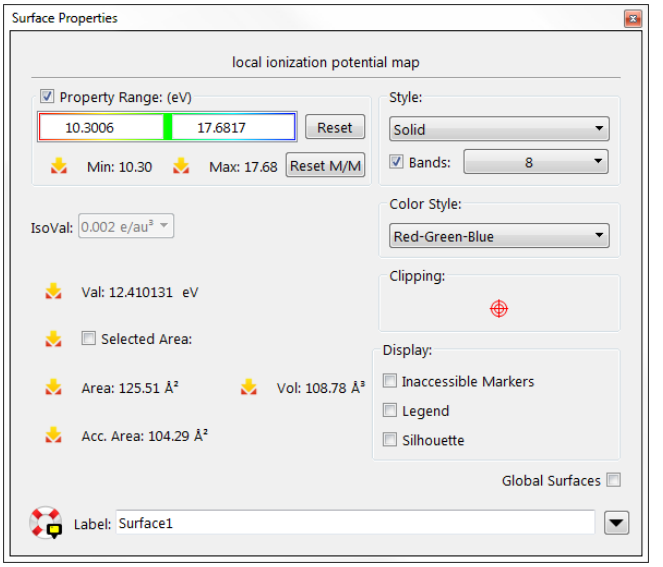
"Swipe" one finger up or down over the orbital energy diagram to move to the next higher or lower energy level.

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 π system (by convention, indicating negative potential and the fact that this region is attracted to a positive charge), and blue in the σ system (by convention, indicating positive potential and the fact that this region is repelled by a positive charge). *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.*

* 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**).

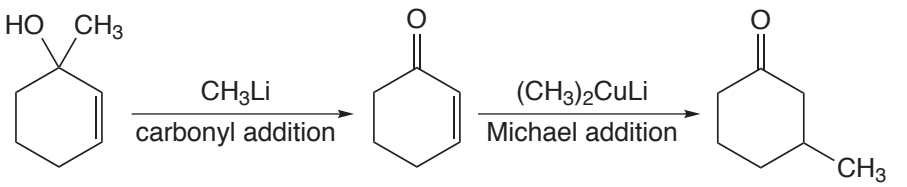


Click once on ▶| to move to the next molecule in the list, ***aniline***, and select ***local ionization potential map*** inside the **Surfaces** dialog. By convention, red regions on a local ionization potential map indicate areas from which electron removal (ionization) is relatively easy, meaning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

Section II

Tutorials

This section includes a brief description (**Getting Started**) of a collection of tutorials organized of 10 Chapters covering a good portion of available features in the ***Spartan Student's*** graphical user interface (GUI). Where appropriate estimates are given for the approximate amount of computational time (these are based on a modestly configures (quad core) laptop.

Completing the full set of tutorials in this section will take a few hours of your time. This will not make you an "expert", but will leave you comfortable enough to navigate throughout ***Spartan Student***. Later tutorials build upon skills introduced in earlier tutorials and will expose you to a wider range of the program's features and capabilities.

Finally, a selection of 42 Labs, organized into the following broad categories:

General Chemistry, **Organic Chemistry**, **Physical Chemistry**, **Organometallic Chemistry**, and **Biochemistry** are available from within the program, accessible from the **Activities** menu.

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Getting Started

The tutorials that follow provide an 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, infrared spectra and UV/vis spectra.

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, to assist in the assignment of NMR spectra, and to introduce the UV/visible spectra calculation.

All of the molecules considered up to this point have either been 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.

Tutorial 2
Sketching Organic Molecules

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

Not only are 2D sketches (or "drawings") more familiar to most chemists (and chemistry students) 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.

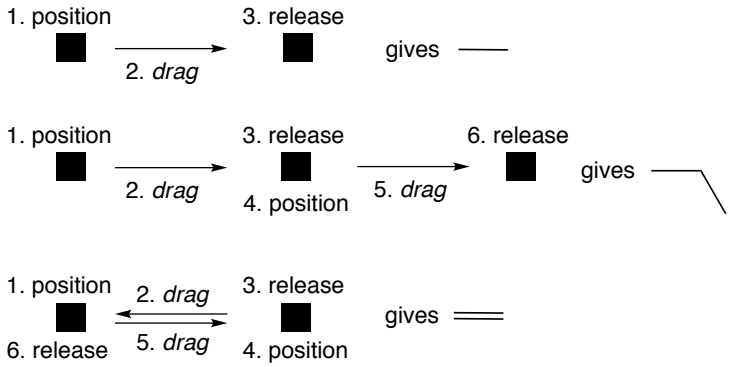
Sketch Palette

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 icons) allows for entering additional elements, functional groups and ligands. 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.



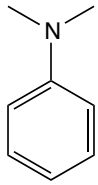
To make a bond touch the screen where you want it to start, move one finger to where you want it to end and lift. Replace position by touch, drag by move and release by lift in the diagram above.

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.

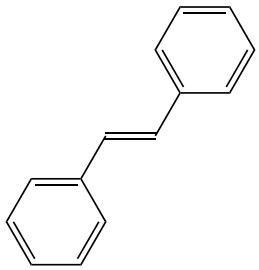
To translate the sketch, move two fingers over the screen. To rotate the sketch in the plane of the screen, "twist" two fingers on the screen. To resize the sketch, pinch (or spread) two fingers on the screen.

N,N-Dimethylaniline



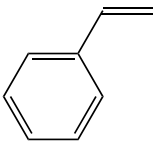
1. Select **New Sketch** from the **File** menu (or *click* on if it appears at the top of the screen) to bring up the sketch pad. *Click* on in the palette and *double click* on screen.
2. *Click* on N in the palette. Position the cursor over the "top" carbon on the benzene ring, *drag* it up and release. You have drawn aniline.
3. *Click* on C in the palette. Position the cursor over the nitrogen, *drag* it up and to the left and release. C 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 C 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.

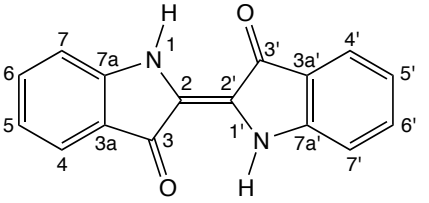


3. is still selected. Position the cursor over the right end of the double bond, *drag* it up and to the right and release.

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.

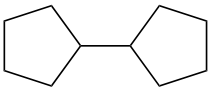
5. Close ***trans-stilbene***.

Indigo

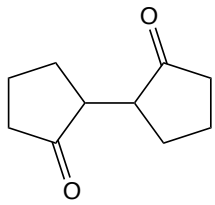


1. Select **New Sketch** from the **File** menu ( ). *Click* on and *double click* on screen.

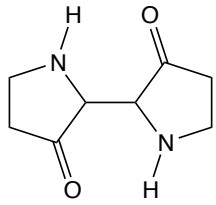
2. is still selected. Position the cursor over C_2 (see numbering in diagram above), *drag* it to the right and release. Your sketch should appear as below.



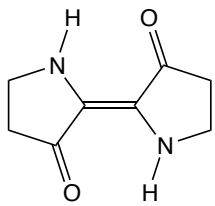
3. Select from the palette. Position the cursor above C_3, *drag* it away from the ring and release. Again position the cursor above C_3, drag it along the CO bond to the oxygen and release. Repeat for C_3'. You are left with a drawing.



4. Select N from the palette and one after another *double click* on C_1 and C_1'.



5. Select C from the palette. Position the cursor above C_2, *drag* it to C_2' and release.

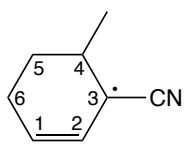


6. Select from the palette and *double click* on the bond connecting C_{3a} and C_{7a}. Repeat for $C_{3a'}$ and $C_{7a'}$.

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_4 (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_1, *drag* to C_2 and release. You have drawn 4-methylcyclohexene.

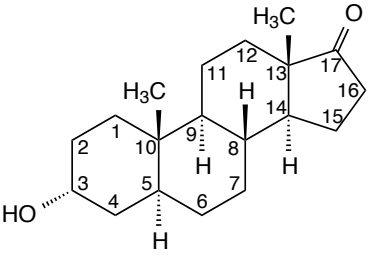
4. *Double-click* on the **More** icon that is located immediately below H and B in the palette, and then *click* on the **Groups** tab. *Click* on **–CN** in the upper right corner. **CN** now appears as the selected icon. Position the cursor over C_3, and *drag* it away from the ring and release. You have drawn 3-cyano-4-methylcyclohexene.

5. One of these icons () will appear in the palette directly below S. If it is not  , *click* on the icon until the icon is  . *Double click* on C_3. A "dot" (radical marker) will appear next to C_3.

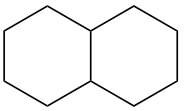
6. *Click* on  to clean up your drawing and *click* on  to make a 3D structure. The name will not appear at the bottom of the screen as this radical is not in the database.

7. Close ***3-cyano-4-methylcyclohexenyl radical***.

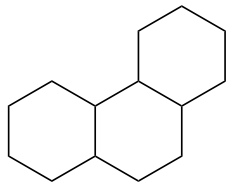
Androsterone



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_{10}, *drag* up and release. Repeat for C_{13}.

5. *Click* on  . Position the cursor over C_3, *drag* down and to the left and release. Position the cursor over C_{17}, *drag* up and to the right and release. Convert the single (CO) bond at C_{17} to a double bond. *Double click* on the C-OH bond to convert this to a carbonyl bond.

6. It is necessary to explicitly specify hydrogens at C_5, C_8, C_9 and C_{14} in order to incorporate the necessary stereochemical cues (up and down "wedges") in your drawing. *Click* on  , position the cursor over C_5, *drag* away from the ring and release. Repeat for C_8, C_9 and C_{14}.

7*. *Click* on  . Position the cursor over C_{10}, *drag* along the bond to the methyl group that you drew in step 4 and release. Repeat for C_{13}. Position the cursor over C_8, *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_3, *drag* along the CO bond that you made in step 5 and release. Position the cursor over C_5, *drag* along the CH bond that you made in step 6 and release. Repeat for the CH bonds at C_9 and C_{14}. 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

* Beginning in ***Spartan Student v.9***, you can sketch with stereochemical markers. This removes the need to first create a bond and *then* modify its stereochemistry.

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.

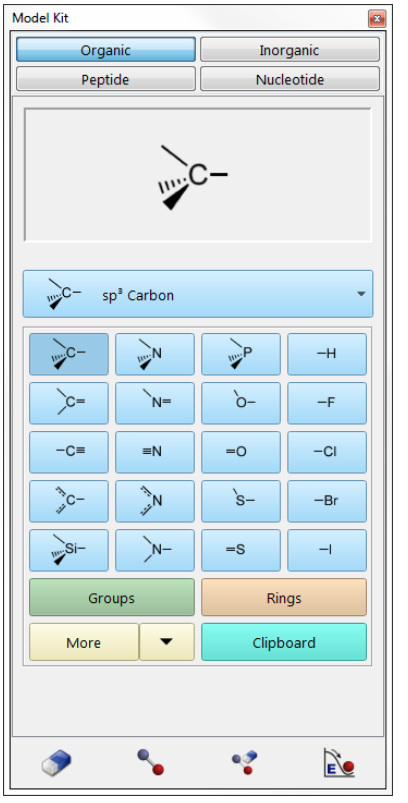
11. Close ***androsterone***.

Tutorial 3
Building Organic Molecules

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.

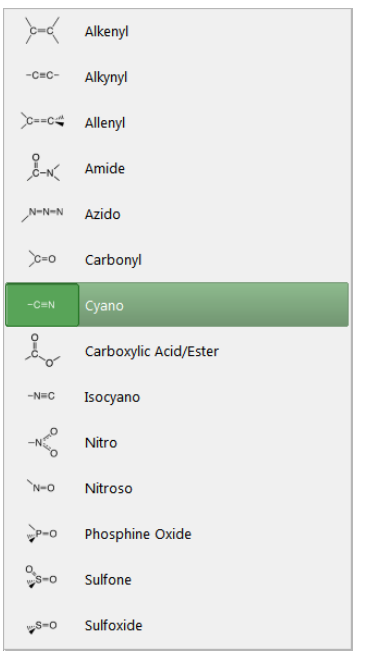


Different hybridization states are included for some elements (C, N, O, and S) from top to bottom.

$C(sp^3)$	$N(sp^3)$	$P(sp^3)$	H
$C(sp^2)$	$N(sp^2)$	$O(sp^3)$	F
C(sp)	N(sp)	$O(sp^2)$	Cl
C(aromatic)	N(aromatic)	$S(sp^3)$	Br
$Si(sp^3)$	N(planar)	$S(sp^2)$	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^2 carbon, depends on the nature of the free valence selected.

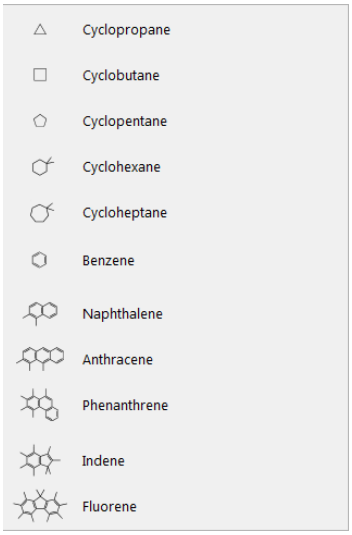
Clicking on the **Groups** button near the bottom of the model kit changes the focus from fragments to groups, one of which will be shown in the box at the top of the model kit and named directly underneath. *Clicking* on the name brings up a menu of available groups.



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.

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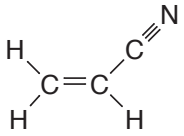
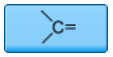
* Additional heterocycles are available from the More button, which accesses a library of additional molecules including nitrogen, oxygen, and sulfur heterocycles.

Acrylonitrile



1. *Click* (left button) on the **File** menu and select (*click* on) **New Build**. Alternatively, *click* on  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 the double free valence (=) and the two single free valences (–).

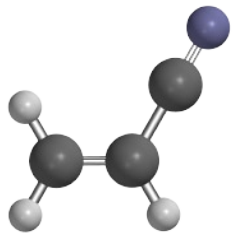
2. sp^2 carbon is still selected. *Click* on the double free valence. The two fragments are connected by a double bond, leaving you with ethylene. The name ***ethylene*** will appear at the bottom right of the screen. If you make a mistake and *click* instead on the single free valence, select **Undo**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

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. As noted, the name appears at the bottom of the screen, indicating as acrylonitrile is in the database.



ball-and-spoke model

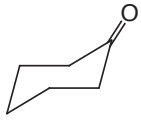
This model can be rotated, translated and zoomed by using the mouse in conjunction with keyboard functions. To rotate the model, *drag* the mouse while holding down the left button; to rotate in the plane of the screen also hold down the **Shift** key. To translate the model, *drag* the mouse with the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

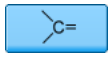
6. Select **Close** from the **File** menu or *click* on at the top of the screen.

* Described is standard 3-button (center wheel) mouse behavior, both Windows and Macintosh allow for user customization of mouse behavior.

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 in the selection bar and select **Cyclohexane** from the list of rings. *Double click* anywhere on screen.

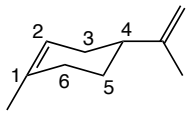
2. Select sp^2 carbon  from the model kit. *Double click* on any carbon (***not a free valence***). The sp^3 hybridized carbon will be replaced by an sp^2 hybridized carbon.

> 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***.

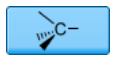
Limonene



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 list of rings. *Double click* anywhere on screen.

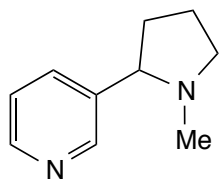
2. *Click* on the **Groups** button near the bottom of the model kit, *click* on the name of whatever group is shown and select **Alkenyl**. *Click* on the *equatorial* free valence on C_4 (see figure above for numbering). You have made vinylcyclohexane.

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_1 and then the *axial* free valence on C_2. You have made 4-vinyl-1-cyclohexene.

4. Select sp^3 carbon  from the model kit and one after another *click* on the free valence on C_1 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**. *Double click* anywhere on screen.

2. *Click* on the name **Benzene** (the currently selected ring) in the model kit and select **Cyclopentane** from the list of rings. *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^2 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 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. Note, if you have built the **R** enantiomer, ***Spartan*** will name this 3-[(2R)-1-methylpyrrolidin-2-yl]pyridine. *Click* on  to access the **Molecule Properties** dialog, *click* on the **Utilities** tab. Finally, *click* on the **Change Absolute Configuration** button. The name (r,s)-nornicotine will appear at the bottom of the interface.

5. *Click* on 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***.

* Bond rotation may also be accomplished by *left clicking* to select the bond, then holding down the **Alt** (Windows) or **Option** (Macintosh) key and with the left mouse button depressed, moving the mouse up or down.

Tutorial 4

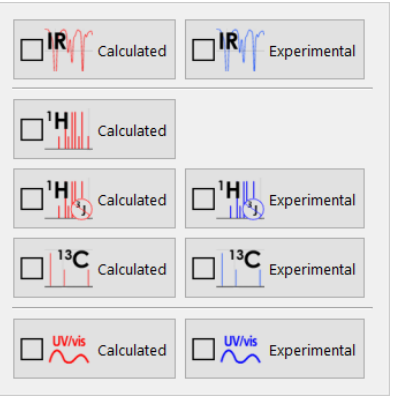
Spectra, Properties and Graphical Models of Organic Molecules from the Database

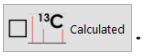
The tutorials in this and the section that follows will utilize the molecules that you built and sketched in the preceding two tutorials. The emphasis shifts from providing input, to analyzing the results of quantum chemical calculations (this tutorial) and to submitting calculations (the following tutorial).

The database supplied with ***Spartan Student*** provides atomic and molecular properties as well as IR and NMR spectra that have previously been calculated using the ωB97X-D/6-31G* density functional model. 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}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}C spectrum, corresponding to the ten unique carbons in limonene.

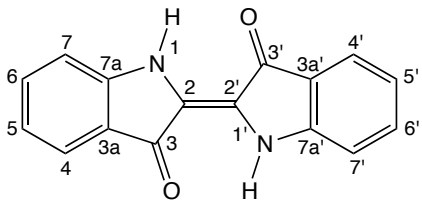
4. Again, *click* on  at the top of the spectra pane, but this time, select 

. The experimental ^{13}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}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.

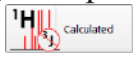
5. Close ***limonene***.

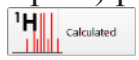
Indigo



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 ωB97X-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 

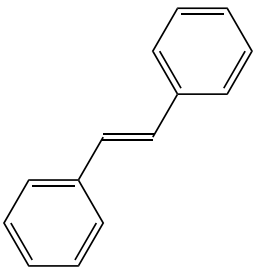
. The same four lines appear, but all are split (as in a real proton spectrum). The lines at ≈ 6.72 and 7.88 ppm are doublets due to C_7 and C_4, respectively (and split by C_6 and C_5, respectively). The lines centering at ≈ 6.9 and 7.48 are quartets (doublet of doublets), due to C_5 and C_6, respectively (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}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



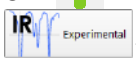
1. Build *trans*-stilbene ( ), minimize ( ) and exit the builder ( ). Alternatively, sketch *trans*-stilbene ( ) and exit the sketcher ( ).

2. *Click* on the name ***trans-stilbene*** at the bottom of the screen, make sure ωB97X-D/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 IR 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 green 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^{-1} (at 1446, 1494 and 1609 cm^{-1}). 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.

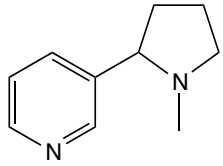
Move one finger over the spectrum to select a line. Move two fingers over the spectrum to shift the range of the scale and pinch two fingers to zoom in and out.

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 ().

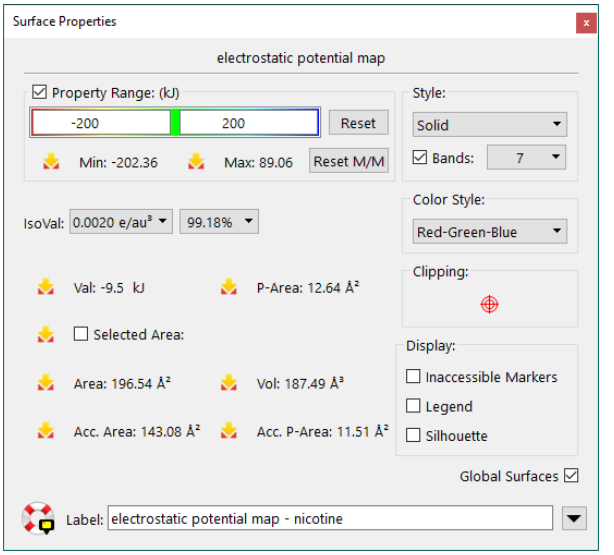
2. *Click* on the name ***nicotine*** at the bottom of the screen, and *click* on **Replace** in the dialog that results. Your structure will be replaced by that in the database making the wave function available.

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 (orange to 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.

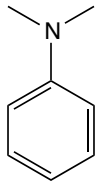


Check the box to the left of **Legend** to display the property range on screen. (*Uncheck* the box to remove the legend.) To translate the legend, *click* on the legend to select, then hold down the right mouse button and move the mouse. The legend is useful when making qualitative comparisons of property 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 relatively 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

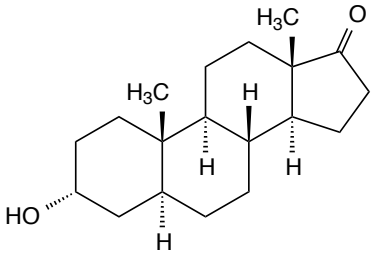


1. Build N,N-dimethylaniline ( ), minimize ( ) and exit the builder ( ). Alternatively, sketch N,N-dimethylaniline ( ) and exit the sketcher ( ).
2. *Click* on ***N,N-dimethylaniline*** at the bottom of the screen and *click* on **Replace** in the dialog that results. Your structure will be replaced 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, easiest atoms to remove an electron from) 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 π* 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 by visualizing the **|LUMO| map** and rotating the molecule, 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.

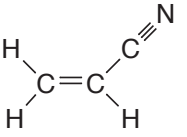
Tutorial 5

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****.*

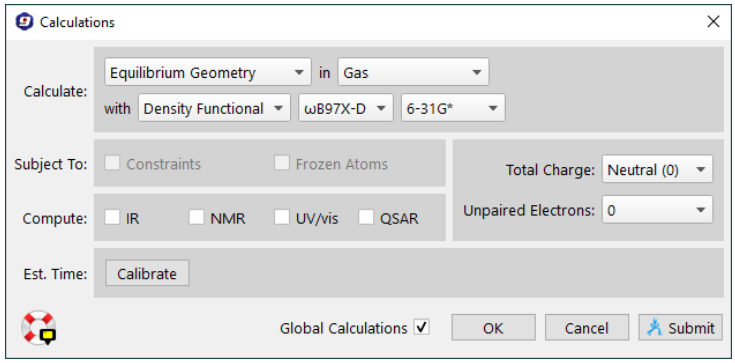
2 min

Acrylonitrile



1. Build acrylonitrile (), minimize () and exit the builder (). Alternatively, sketch acrylonitrile () and exit the sketcher ().

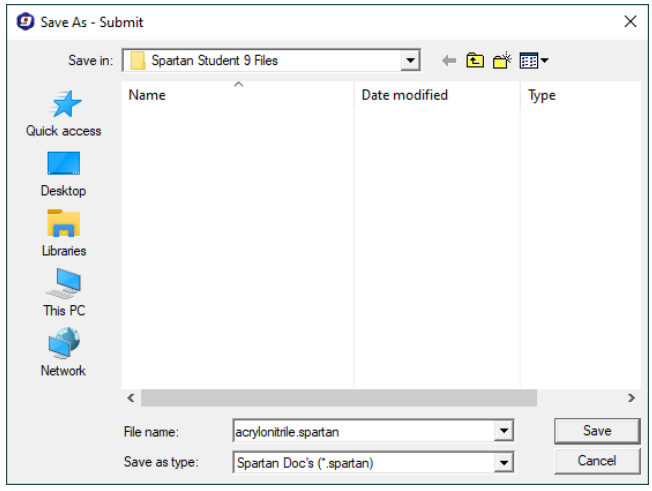
2. Select **Calculations...** from the **Setup** menu or *click* on and perform the following operations in the **Calculations** dialog which appears.



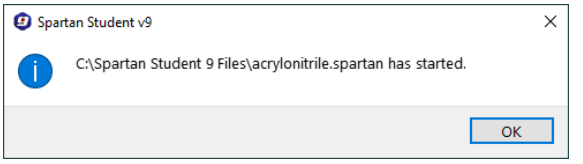
a. Select **Equilibrium Geometry** from the leftmost menu to the right of **Calculate**. This specifies optimization of equilibrium geometry.

b. 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).

c. *Click* on **Submit** at the bottom of the dialog. A file browser appears.



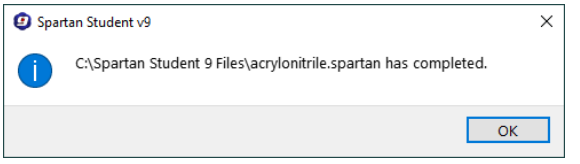
Because the model is in the database (even though we will not use the data), the name ***acrylonitrile*** will be presented to you in the box to the right of **File name:**. Either use it or type in whatever name you like and then *click* on **Save**. You will be notified that the calculation has been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



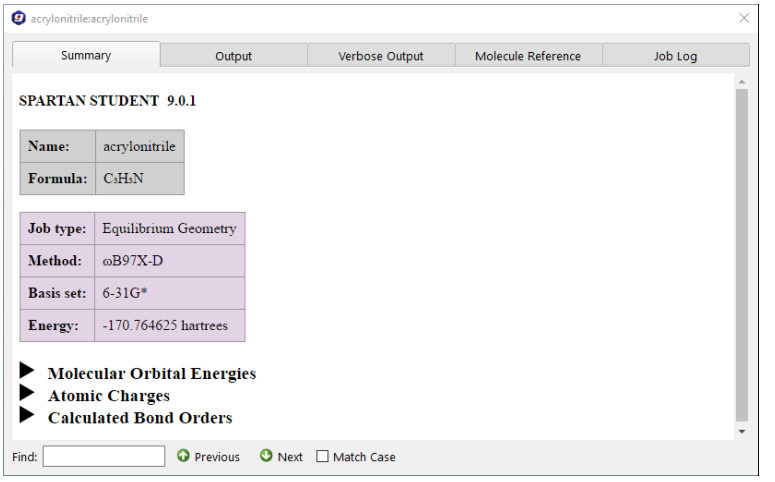
The message will close automatically (after ≈5 seconds); you can also *click* on **OK** to remove the message from the screen.

> 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.



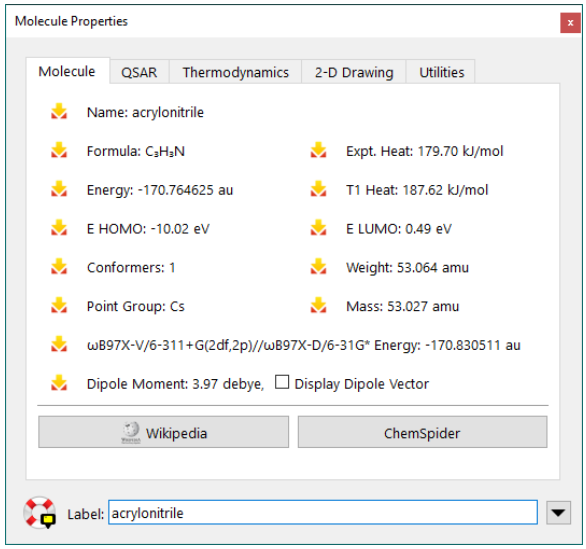
Depending on calculation details, a number of data tables are available (explore by *clicking* on the ▶ indicator to the left of

the title). 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.

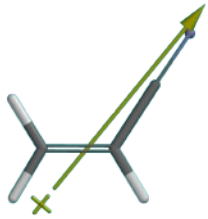
The lines under the heading ***Optimization*** tell the history of the optimization. If the geometry was not optimized satisfactorily an error message, such as: ***Optimization has exceeded N steps – Stop***, will be displayed following the last optimization step and you would be notified that the job had failed.

Near the end of the output is the final total energy (≈-170.764625 atomic units for acrylonitrile with the ωB97X-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.

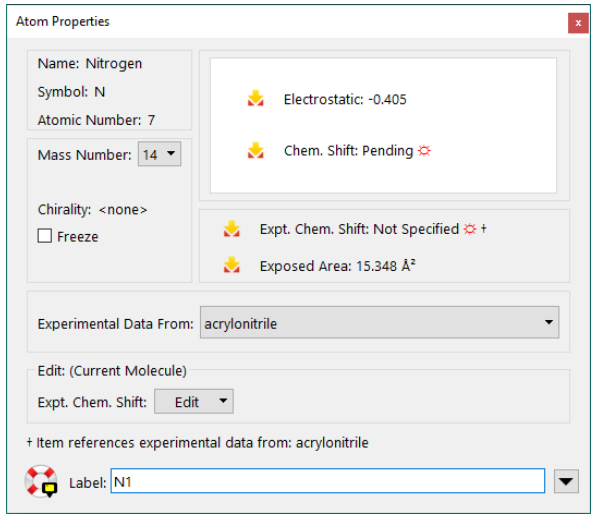


To see the dipole moment vector (indicating the sign and direction of the dipole moment), *check* the box to the right of **Display Dipole Vector**. Wire, ball-and-wire or tube models are best for this display.



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.

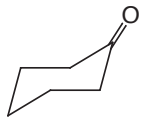
4. Select **Surfaces** from either the **Setup** or **Display** menu ( ). *Click* on **Add** at the bottom of the **Surfaces** dialog that results, and select **electrostatic potential map** from the menu. This requests an electrostatic potential map (an electron density surface onto which the value 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**, **ωB97X-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.

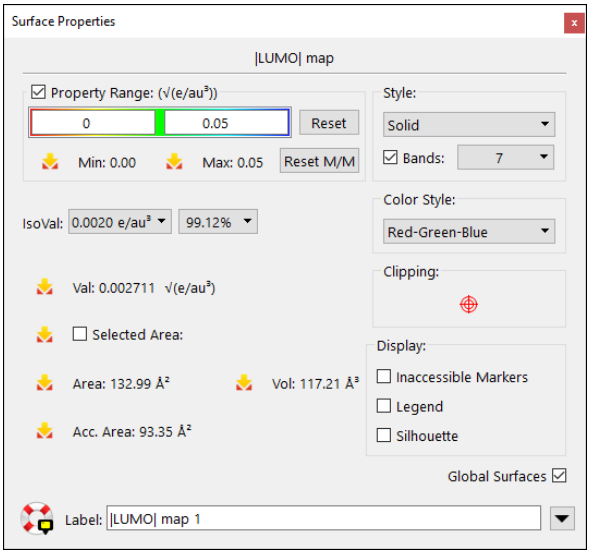
3. Cyclohexanone undergoes nucleophilic attack at the carbonyl carbon, and it is reasonable to expect that the molecule's lowest-unoccupied molecular orbital (the LUMO) will be localized here. To visualize the LUMO, bring up the **Surfaces** dialog (**Surfaces** from the **Setup** or **Display** menu 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 π* 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 "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.

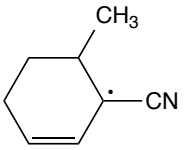


Check the box to the left of **Legend** to display the property range on screen. (Remove the checkmark to remove the legend.) To translate the legend, *click* on the legend to select, then hold down the right mouse button and move the mouse. The legend is useful when making qualitative comparisons of 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



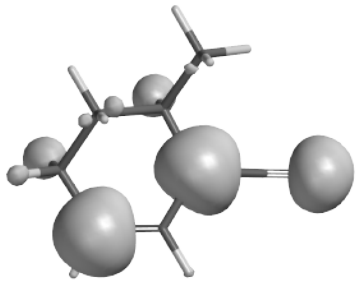
1. Build 3-cyano-4-methylcyclohexenyl radical ( ), minimize ( ) and exit the builder ( ). Alternatively, sketch the radical ( ) and exit the sketcher ( ).

2. Select **Calculations...** from the **Setup** menu ( ). Specify **Equilibrium Geometry**, **Density Functional-Fock**, **ωB97X-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 α 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.



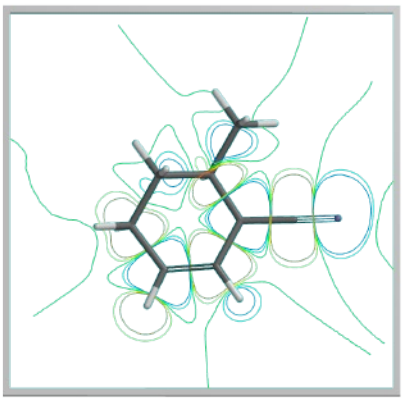
5. Remove the spin density surface (*uncheck* the box to the left of ***spin density*** in the **Surfaces** dialog) and then *check* the box to the left of ***spin density map*** to display a surface on which the spin density is mapped onto the electron density. Note that the areas of maximum spin (colored 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

* 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.

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.

Tutorial 6
Groups of Organic Molecules

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.

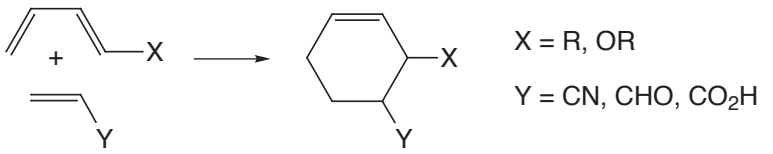
Computational investigations typically involve series of related molecules. Here, it may be of interest to compare geometries, energies or other calculated properties, or to compare trends in calculated and measured properties. ***Spartan Student*** allows molecules to be grouped into a single document, 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 may be 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.

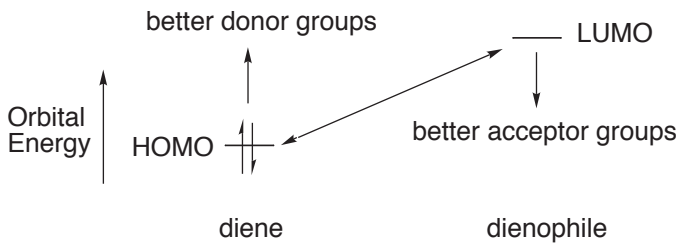
The tutorials in this section introduce and illustrate a number of basic group operations available in ***Spartan Student***, building and manipulating multi-molecule documents, and fitting an experimental observable to one or more calculated properties by way of linear regression. The use of the **Reactions** dialog is illustrated. None of the examples in this tutorial actually require performing quantum chemical calculation as all molecules involved are available from the included 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 π-donor ability of the diene substituent, and with increasing π–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, H_2C=C(H)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 ( ).

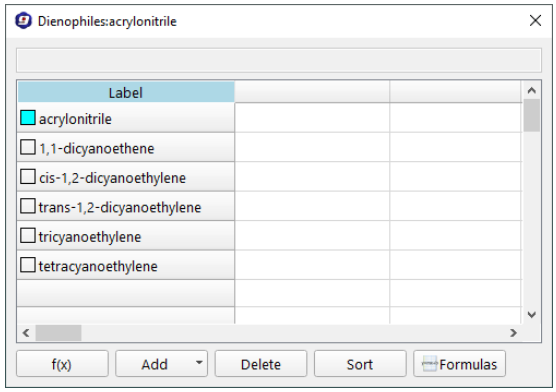
2. Select **Build New Molecule** (not **New Build**) from the **File** menu ( ). This specifies that a new molecule is appended to the end of the current document. The screen will be cleared. *Click* on **Clipboard** at the bottom of the model

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 .

3. 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.

4. *Click* on the name of whatever molecule from the document appears at the bottom of the screen make sure that 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 six are available).

5. 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.

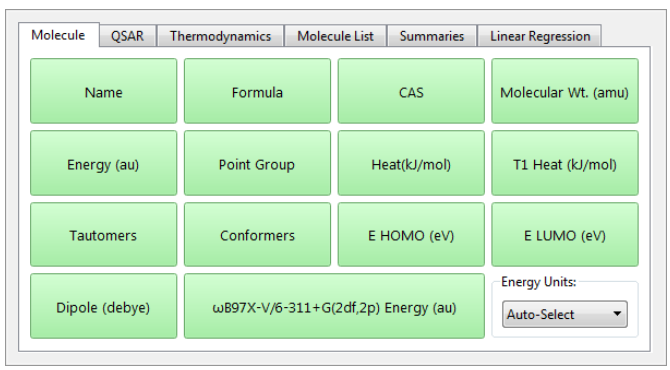
6. Enter experimental relative rates into the spreadsheet.

dienophile	$\log_{10}$ (relative rate)
acrylonitrile	0
1,1-dicyanoethylene	4.64
cis-1,2-dicyanoethylene	1.94
trans-1,2-dicyanoethylene	1.89
tricyanoethylene	5.66
tetracyanoethylene	7.61

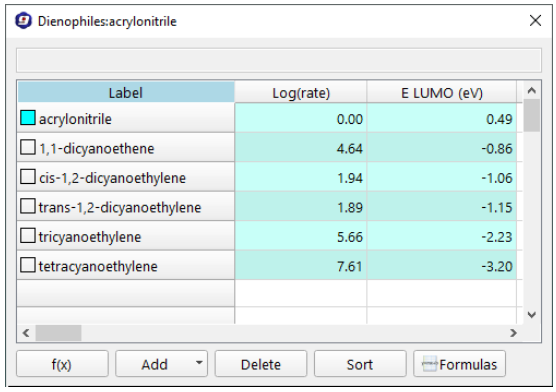
Experimental data from: J. Sauer, H. Weist and A. Mielert, *Chem. Ber.*, **97**, 3183 (1964).

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.

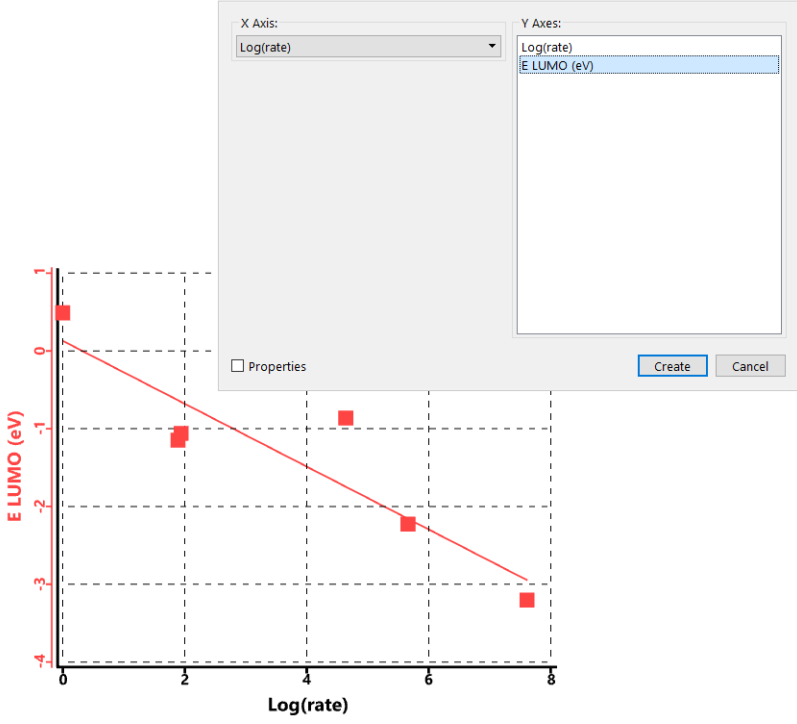


The spreadsheet, which now contains both the calculated LUMO energies and experimental relative rates, has served its purpose. Remove it from the screen by *clicking* on ▬ at the top.



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**.

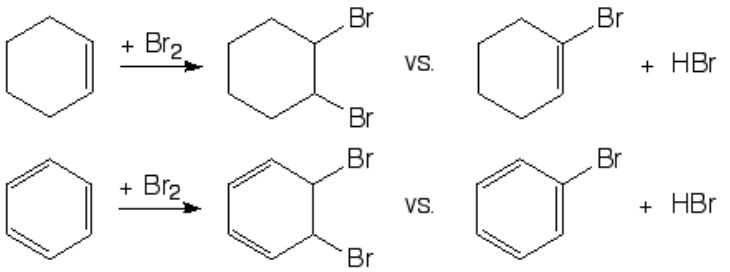


   Click on the **Edit** icon (), and then *click* to choose **Least Squares Fit**. *Click* **Done** when finished. A least-squares line will be drawn through the six data points.

9. Close the document and any open dialogs.

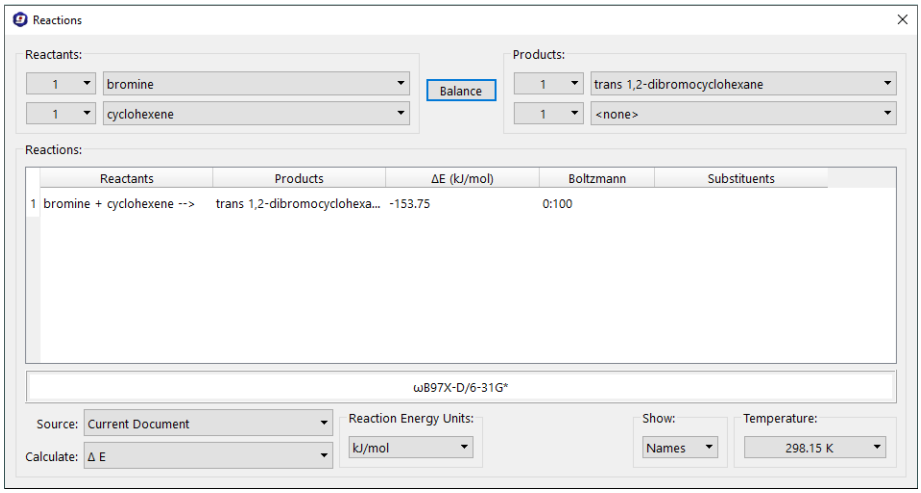
Addition vs. Substitution

Alkenes normally undergo addition reactions whereas aromatic compounds normally undergo substitution reactions. For example, bromine reacts with cyclohexane 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_2) 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.



Compute the energy for Br_2 addition to cyclohexene: select ***bromine*** and ***cyclohexene*** as **Reactants** and ***trans-1,2-dibromocyclohexane*** (and ***<none>***) as **Products**. Note the reaction energy. 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

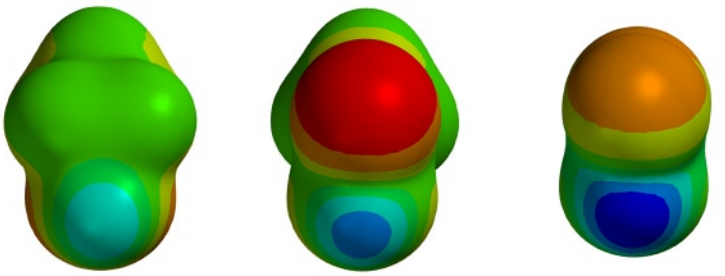
Acid strength is among the most important molecular properties. It is readily available from calculation, either in terms of absolute deprotonation energy,

$$AH \longrightarrow A^- + H^+$$

or, more commonly, as the deprotonation energy relative to that of a standard acid (A°H).

$$AH + A^{\circ -} \longrightarrow A^- + A^\circ H$$

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.



nitric acid acetic acid 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.

2. 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.

3. 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* **pKa** and *press* the **Enter** key (**return** key on Mac). Enter the experimental pK_a'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_a
trichloroacetic (Cl_3CCO_2H)	0.7
dichloroacetic (Cl_2CHCO_2H)	1.48
chloroacetic ($ClCH_2CO_2H$)	2.85
formic (HCO_2H)	3.75
benzoic ($C_6H_5CO_2H$)	4.19
acetic (CH_3CO_2H)	4.75
pivalic ($(CH_3)_3CCO_2H$)	5.03

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

4. 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.

5. 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 left 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 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 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

This collection illustrates applications involving the calculation of IR, proton and ^{13}C NMR spectra, and UV/vis 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 next three tutorials deal with NMR spectroscopy: detailing the steps involved in calculating and displaying the proton spectrum for 1-methylindole and the ^{13}C spectrum of cytisine, and examining the dependence of carbon chemical shifts on stereochemistry. The final tutorial presents the new procedure for calculating and plotting a UV/visible spectra, specifically the organic dye indigo is utilized to demonstrate both steps and performance of the underlying approach.

6 mins

Infrared Spectrum of Methyl Formate

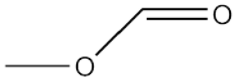
In the harmonic approximation, the frequency at which a diatomic molecule vibrates is proportional to the square root of the ratio of the force constant (the second derivative of the energy with respect to change in bond length) and the reduced mass (the product of the masses of the two atoms divided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

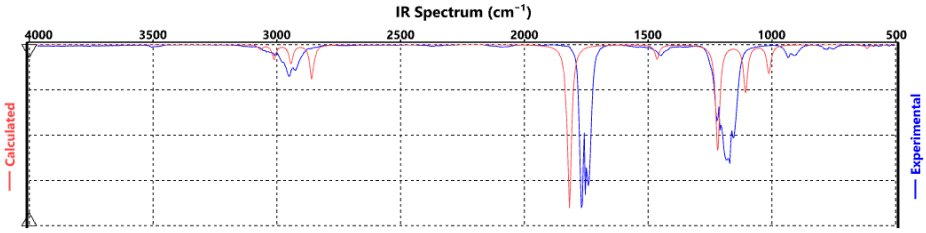
The intensity of absorption for a diatomic molecule is proportional to the change in the dipole moment with change in bond length. The fact that there is no change in the dipole moment of a homonuclear diatomic molecule with change in bond length, means that molecules such as N_2 and O_2, which make 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 impact 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**.

2. 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.



3. 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 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 cm^{-1} and describe its motion.

4. 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.

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

6 mins

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}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 Δ Energy of these states (ΔE) depends on the nucleus and on the strength of the applied magnetic field, by way of a simple relationship.

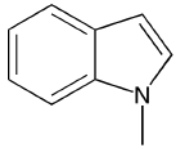
$$\Delta E = \gamma \hbar B_0$$

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

The key to the utility of the magnetic resonance experiment is that the energy at which a nucleus resonates depends on its location in the molecule, and is different for each (chemically) distinct nucleus. The reason is that the applied magnetic field is weakened by electrons around the nucleus. Nuclei that are well shielded by the electron cloud will feel a lesser magnetic field than those that are poorly shielded, and will show a smaller energy splitting. The difference, given relative to a standard, is termed a ***chemical shift***. By convention, both proton and ^{13}C chemical shifts (treated later in this tutorial)

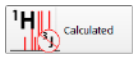
are reported relative to tetramethylsilane (TMS) as a standard.

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.



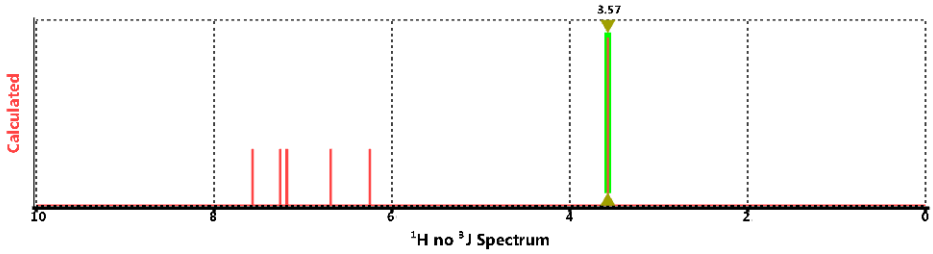
The objective of this tutorial is to calculate the proton NMR spectrum of 1-methylindole and compare it with the experimental proton spectrum in the absence of three-bond HH coupling.

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 ωB97X-D/6-31G* density functional model. *Check* **NMR** and *click* on **Submit**. Accept the name ***1-methylindole***. The calculation will require a few 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 

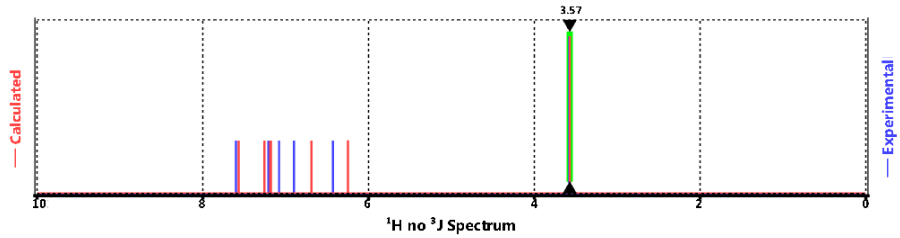
(proton NMR spectrum in which there is no HH coupling).

* 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.

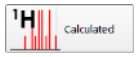


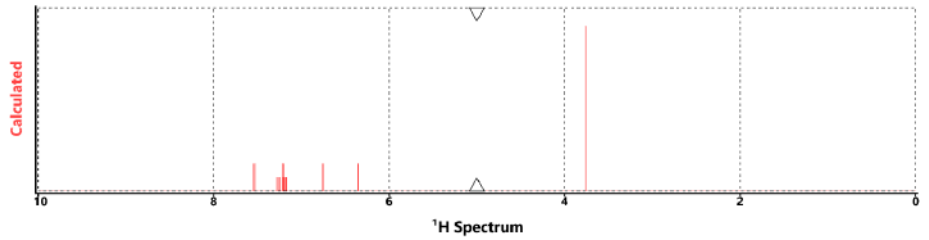
Move the mouse while holding down the left button over the spectrum. When you intersect a line, a numerical value for the proton shift appears at the top of the spectrum.

3. *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.

4. *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 C_2, C_3, C_4 and C_7 are doublets, while those due to protons at C_5 and C_6 are quartets (doublet of doublets).

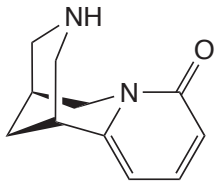
5. Close ***1-methylindole*** and any remaining dialogs.

20 mins

^{13}C Spectrum of Cytisine

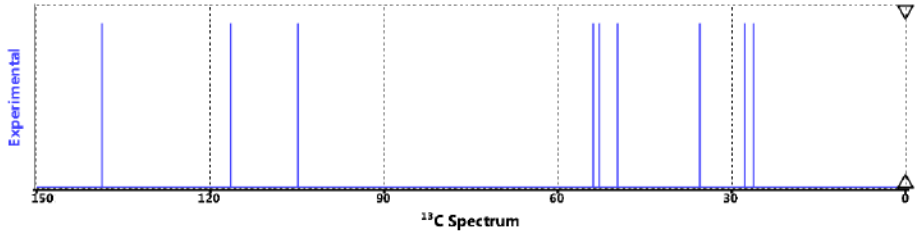
There are several reasons why NMR spectroscopy, in particular, ^{13}C NMR, is one of the most important routine analytical techniques available for characterizing organic molecules. The experiment, which is straightforward and can be carried out rapidly, requires relatively small samples and is non-destructive. The resulting (proton decoupled) spectrum is quite simple, comprising but a single line for each and every unique carbon. However, assigning ^{13}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 ^{13}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*.

2. 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 ^{13}C Experimental (^{13}C experimental spectrum). The experimental ^{13}C spectrum is drawn.



3. Use the calculated spectrum to associate the individual lines in the experimental ^{13}C spectrum with specific carbons in the structure of cytisine. *Click* on and this time select ^{13}C Calculated (^{13}C calculated 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.

---

* Cytisine 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.

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.

4. Close ***cytisine*** and any open dialogs.

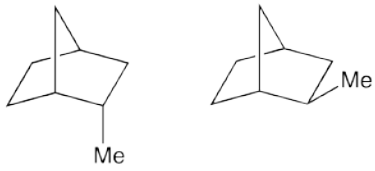
no calculations

Stereochemical Assignments from ^{13}C Spectra

NMR spectroscopy, in particular ^{13}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}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.

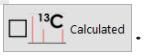


endo *exo*

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.

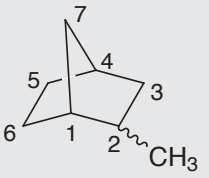
2. Both stereoisomers are available in the database so there is no need to perform any calculations. *Click* on the name of whichever molecule is selected at the bottom of the screen. Confirm that

ωB97X-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}C chemical shifts with experimental values, paying particular attention to differences between *endo* and *exo* stereoisomers.

Experimental ^{13}C NMR Data



	endo	*exo*	Δ
C_1	43.5	42.2	-1.3
C_2	36.8	34.6	-2.2
C_3	40.2	40.7	0.5
C_4	37.3	38.2	0.9
C_5	30.3	30.6	0.3
C_6	29.0	22.4	-6.6
C_7	35.0	38.9	3.9
CH_3	22.3	17.4	-4.9

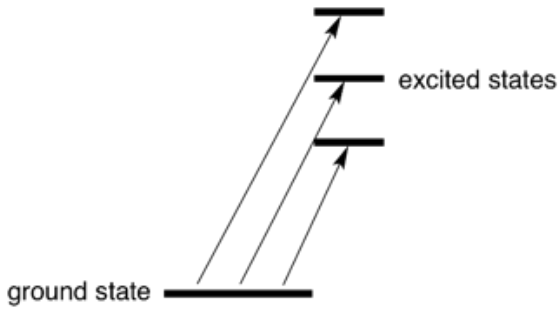
Can the calculations be used to distinguish between the two isomers? Are the differences due to stereochemisty in the experimental shifts reproducible in the calculated shifts?

4. Close the document and any open dialogs.

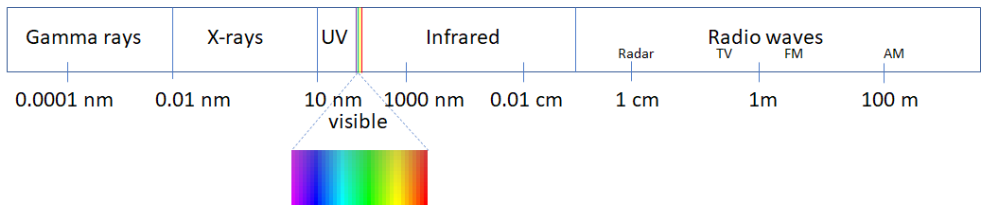
30 mins

UV/visible Spectrum of Indigo

Absorption of light in the ultraviolet (UV) or visible (vis) range of the electromagnetic spectrum leads to electronic excitation (from ground state to excited states). In the case of absorption in the visible range, this determines a molecule's color.



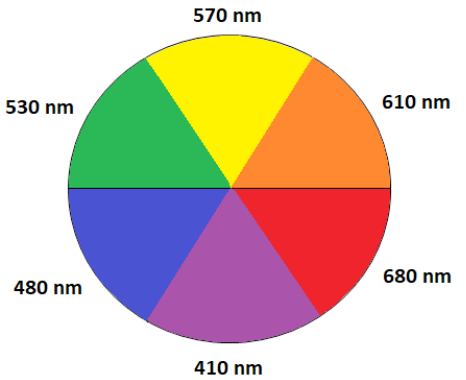
Note the visible band is tiny (≈ 400 – 700 nm).



UV/visible spectroscopy provides a molecular "fingerprint", that can be used in identification/detection. This technology is also utilized in concentration measurement and, in general, supports production of materials and products that protect from damage caused from exposure to light.

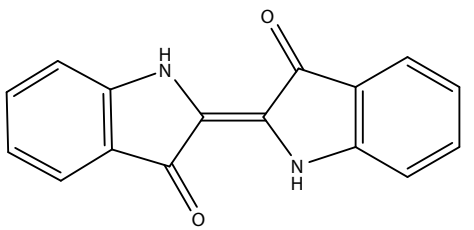
The common presentation is a plot of intensity vs. energy, the latter ranging from the far UV (< 200 nm), through the near UV (200-400 nm) into the visible (400-800 nm). A shorthand is simply to identify the maximum absorption, commonly referred to as λmax. Absorption (in particular maximum absorption) dictates "color" in the sense that it removes a component of the visible spectrum, and what is not removed (absorbed) determines the color that is reflected (seen).

The color wheel (below) affords a convenient way of assessing color. If one "walks across" the color wheel below, and looks at the complementary color convenient . A molecule that absorbs in the green appears red, while one that absorbs in the yellow appears violet.



New in ***Spartan Student Edition v.9***, is the ability calculate and display a UV/visible spectrum, and optionally a corresponding experimental UV/visible spectrum (if available) from NIST (National Institutes of Standards and Technology, https://webbook.nist.gov/chemistry). The student edition can also read in (import) an experimental UV/visible spectrum in the JCAMP (.dx) file format.

Dyes are molecules that absorb in the visible range, and commonly include a network of alternating single and double bonds. Indigo (dye), above, is a dye with a known λ_{max} (maximum absorption) of ≈ 612 nm. Can quantum models be called upon to calculate or confirm color?



1. Build or sketch indigo, explicit instructions for sketching indigo in 2D are provided in the **Sketching Organic Molecules in 2D** section. Indigo is also available from the subset of the **SSPD**

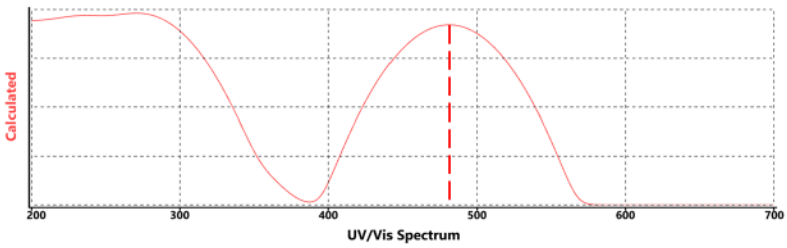
and can be accessed via the **File** menu via the **Access Database by Name**. . . entry. Once you have built, sketched, or retrieved indigo from the database, *click* on  .

2. Select **Calculations…** from the **Setup** menu (), and request an equilibrium geometry using the B3LYP/6-31G* density functional model. *Check* the **UV/vis** button, *click* on the **Submit** button. Accept the provided name. Following the geometry optimization, a ground state and a set of excited state energy calculations will be performed, with resulting data used to generate a calculated UV/vis spectrum.

> When performing UV/vis calculations, ***Spartan Student*** obtains the ground state geometry using the specified DFT model, a subsequent energy calculation for the ground state and the first twenty (20) excited states using the time-dependent density functional theory (TD-DFT) are performed. While additional options exist in the research version, the UV/vis recipe is fixed in the ***Spartan Student*** version, and uses B3LYP/6-31+G* model. For each excited state, ***Spartan Student*** returns a wavelength and intensity (also called the oscillator strength or "strength" in the **Verbose Output**). Wavelength and intensity are used to display the UV/vis spectra plot, where the X axis is the wavelength and the Y axis is the intensity. A fit of the calculated data (wavelength and intensity) to a Gaussian function in which peak width and half height is treated as a parameter (one value for all 20 peaks) which accounts for the line broadening. Additionally, the Y axis uses a logarithmic scale (1.0e-06 to 1.0).

3. Select () from the **Display** menu, and *click* on () and then *click* inside the checkbox for (

). Approximate λ_{max} (maximum absorption) for the calculated spectrum. Note that indigo absorbs both in the visible but also in the near UV range (200 to 400 nm). Use the peak on the right-hand side of the plot to estimate λ_{max}:



With a known experimental λ_{max} of 612 nm, does the calculation provide sufficient results such that they could be used to estimate color based on calculated UV/visible spectra?

While calculated λ_{max} are almost always off by more wavenumbers than allowable to be useful in a computationally predicting color, there are a number of observations that point towards the potential of improved results (and perhaps a new correction scheme). Firstly, including solvent in the calculation has been shown to improve results. Adding to the number of excited states (the procedure in Spartan Student calculates the first twenty) also improves results. In most cases, calculated λ_{max} is lower than experiment (and might be improved by a simple scaling factor).

As is often the case, asking the question in a relative way, is a good strategy for benefiting from cancelation of errors. The UV/visible data does quite well in anticipating the results of a structural substitution (does a change at position X shift).

4. Close ***indigo*** and any open dialogs.

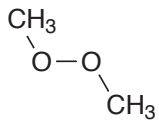
Tutorial 8
Flexible Molecules

This collection demonstrates procedures 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}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°. The most common choice is a truncated Fourier series.

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

Here, ω^{eq} is the ideal dihedral angle and $k^{torsion1}$, $k^{torsion2}$ and $k^{torsion3}$ 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°) 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°) in the original (leftmost) box alone, but change the contents of the box to the right of **to** to **0** (0°). 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°, then to 160°, then to 140°, etc. and finally to 0°*. *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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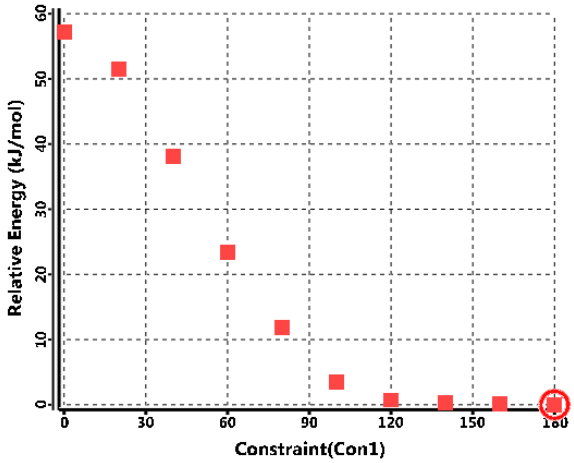
* The difference between constraint values is given by: (final-initial)/(steps-1).

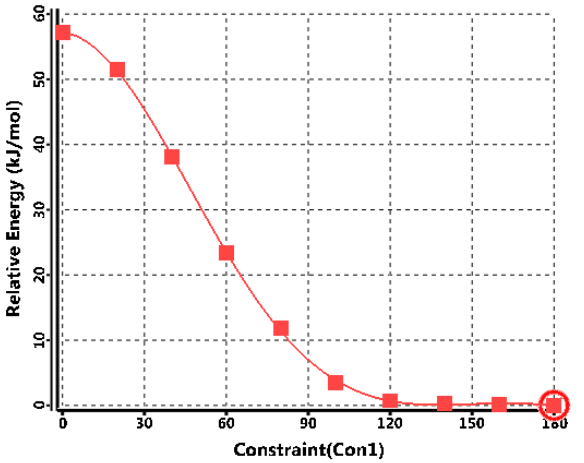
5. When the calculations complete, the results are written to a new document named ***dimethyl peroxide.Prof.spartan***. *Click* on **Yes** following the prompt that will ask you if you want to open this file. Align the conformers. Select **Align** from the **Geometry** menu ( ), one after the other, *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 **Δ Energy** from the quantities under the **Molecule List** tab, **kJ/mol** from the **Δ 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 **Δ 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.



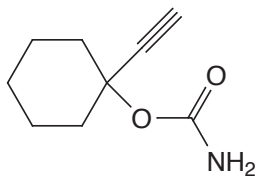
7. Use energies from ωB97X-D/6-31G* density functional calculations, together with the Hartree-Fock geometries to provide a better fitting function. First, make a copy of ***dimethyl peroxide.Prof.spartan***. Name it ***dimethyl peroxide density functional***. Select **Calculations...** from the **Setup** 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.

15 mins

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 **Δ Energy**, **Boltzmann Weights** and **ΔEnergy** from the **Molecule List** tab. 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 utilize 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 will require several minutes (perhaps 10-20 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 do two or more conformers contribute significantly?

5. Close any open documents and dialogs.

15 mins

^{13}C Chemical Shifts Depend on Conformation

At normal temperatures, the time for nuclear spin relaxation is very long relative to the time required for equilibration among conformers. This means that for each of the carbon chemical shifts in the NMR spectrum of a flexible molecule, ^{13}**C**, will be a weighted average of the shifts NMR of the individual conformers, $^{13}C_i$.

$$^{13}\mathbf{C} = \Sigma_i \, \omega_i \, ^{13}C_i$$

The weight, ω_i, is given by the Boltzmann equation, and depends on its energy, ε_i (relative to that of the lowest-energy conformer, ε_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

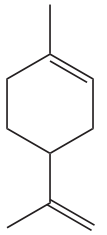
appears in the overall distribution and k is the Boltzmann constant.

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

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 providing 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}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}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 **YES**. Select **Spreadsheet** from the **Display** menu (). *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 **Δ Energy** 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 ωB97X-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 *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}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

This section 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**), another application of coordinate driving 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. 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 is also presented. 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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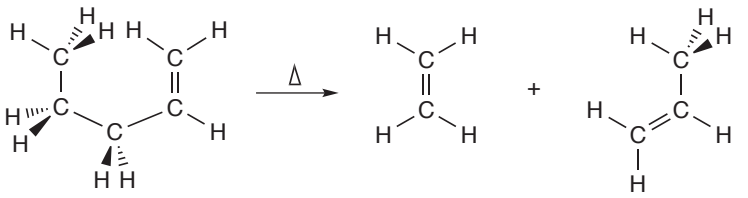
* Where a reaction is unknown to ***Spartan Student***'s transition state library, a fallback technique which averages reactant and product geometries (based on the so-called linear synchronous transit method) is invoked.

10 mins

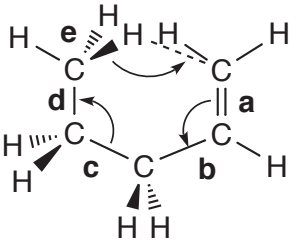
Ene Reaction of 1-Pentene



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 ( ), *click* on in the bar at the top of the spectra pane and *click* on IR Calculated 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 and *click* **OK**. 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...***, 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**.

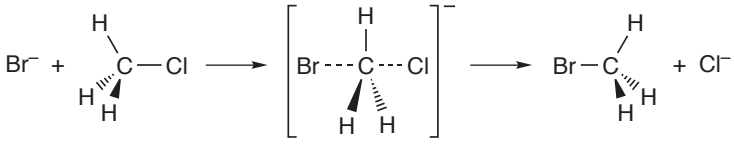
* You need to use **More Surfaces** rather than **Add** as the electrostatic potential is mapped on the bond density surface.

7. Submit for calculation*. Name it ***ene reaction 1-pentene sequence***. Once the job has completed, enter the **Surfaces** dialog and examine the surfaces that you have calculated. For each, step through the sequence of structures (and) keys at the bottom of the screen) or animate the reaction ( ). Note, in particular, the changes in bonding revealed by the bond density surface. Also pay attention to the value of the potential on the migrating atom. This reflects its charge. Is it best described as a proton (blue), hydrogen atom (green) or hydride anion (red)?

8. Close all open documents and dialogs.

10 mins

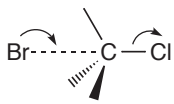
S_N2 Reaction of Bromide and Methyl Chloride



1. The S_N2 reaction passes through a transition state in which carbon is in a trigonal bipyramid geometry and the entering and leaving groups are 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 apply to all fragments, but can be made to apply 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 again. 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. *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.

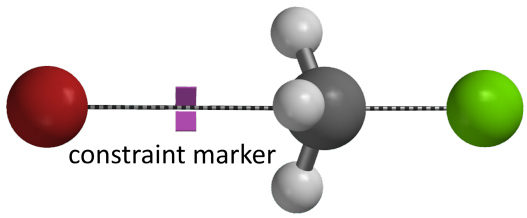
Leave the value **3.8** (3.8Å) in the leftmost box alone, but change the number in the box to the right of **to** to **1.9** (1.9Å) and *press* the **Enter** button. Change the number in the box to the right of **Steps** from **10** (the default) to **20**. 20 Calculations with CBr bond lengths constrained 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**.

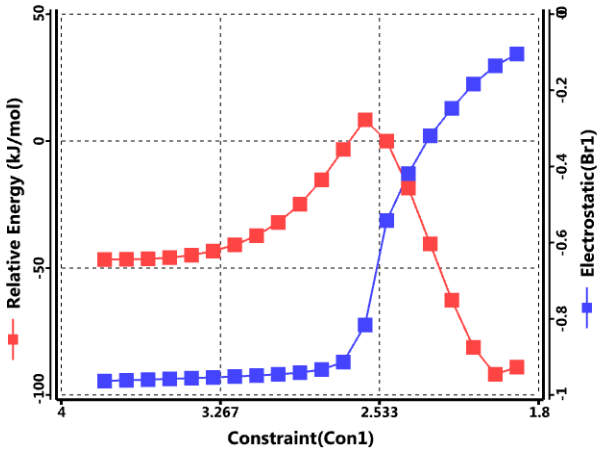
6. Submit the job. Name it ***bromide+methyl chloride***. When completed, it will give rise to a sequence of calculations placed in a new document with the name ***bromide+methyl chloride. Prof.spartan***. Accept the prompt to open this file. Close the first document ***bromide+methyl chloride*** to reduce clutter.

7. Select **Spreadsheet** from the **Display** menu ( ). *Click* on the **Add** button at the bottom of the spreadsheet. Select **ΔEnergy** from the **Energy From Molecule** options under the **Molecules List** tab. 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 **Δ 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 **Δ 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

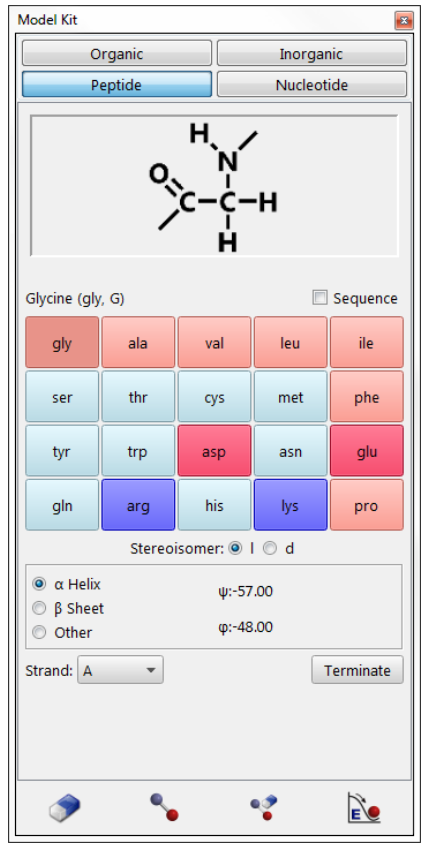
Biomolecules

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 α helix and the β sheet.



α Helix

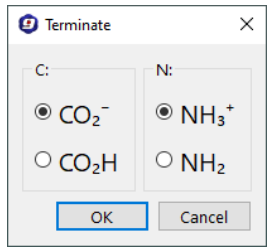
1. Select **New Build** from the **File** menu ( ) and *click* on the **Peptide** builder from the **Model Kit**. This contains a library of the 20 natural amino acids, each identified by a 3-letter code.

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** box checked) and a 2D rendering of non-terminated glycine (**Sequence** box un-checked).

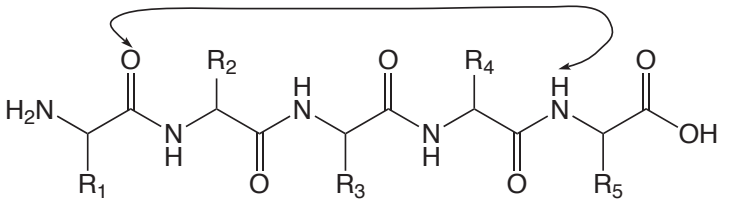
3. Make sure the **Sequence** box is checked, and randomly select an additional 9 amino acid residues. Below the pallet of amino acids are a series of buttons: α **Helix**, β **Sheet** and **Other**. These allow specification of the secondary structure of constructed polypeptide sequences. Select α **Helix** and *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 (CO_2H and NH_2) or as a zwitterionic form (CO_2^- and NH_3^+).



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

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



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

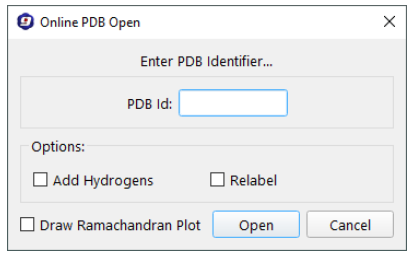
β Pleated Sheet

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 β **Sheet** and *double click* on screen.

8. Again, a model of a 10-residue polypeptide is displayed. This time, the secondary structure is in the β sheet configuration. Terminate the structure in either the uncharged or zwitterionic form.

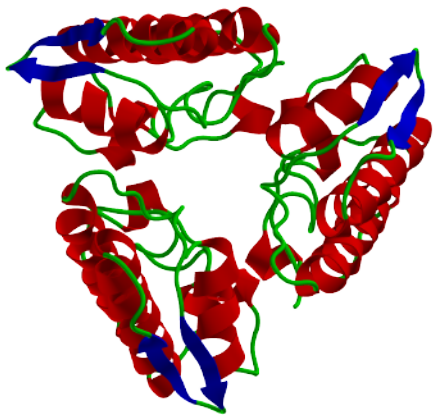
9. *Click* on to remove the model kit. Note that the same 10-residue sequence is significantly longer in the β sheet arrangement. As you did for the α helix, switch to a tube model, and turn on display of hydrogen bonds. The extended β sheet does not contain internal hydrogen bonding so no hydrogen bonds appear. Close the document when you finish examining the β-sheet structure.

10. Hydrogen bonds play a role in connecting β strands to make a β sheet. Select **Access PDB Online...** from the **File** menu.



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

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) remians useful in providing indication of the overall size and shape of the enzyme.



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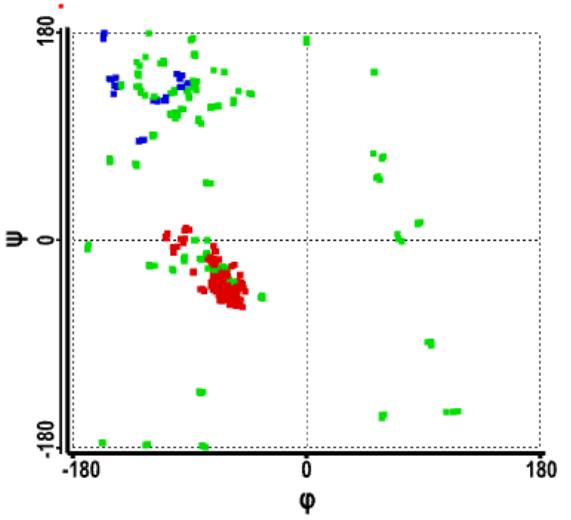
* PDB designation 1JIC. Torres, A.M., Kini, R.M., Selvanayagam, N., Kuchel, P.W.; *J. Biochem*. **360**: 539-548 (2001).

** 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 **Model** menu.



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

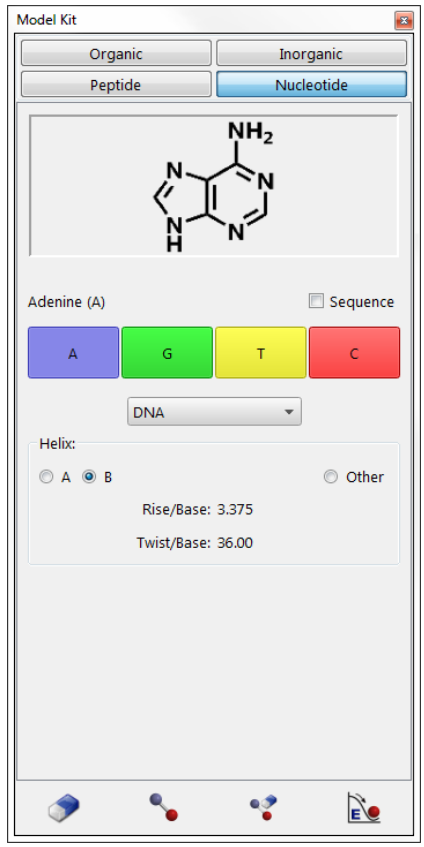
into two clusters, one corresponding to helices and the other to β sheets.

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** box checked) and a 2D rendering of adenine (with the **Sequence** box un-checked). Note that even though the 2D rendering displays only the nucleotide base, when building, the entire nucleotide, including 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 is also 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 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 ≈ 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

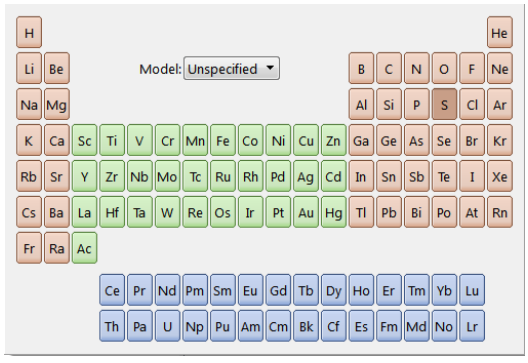
Sulfur Tetrafluoride

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.

Double 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**, ω**B97X-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.

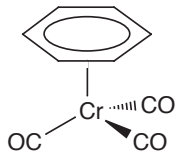
9. Close ***sulfur tetrafluoride*** and any open dialogs.

---

* 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.

10 mins

Benzene Chromium Tricarbonyl

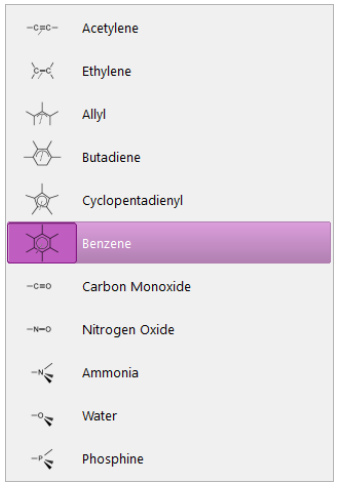


benzene chromium tricarbonyl

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. *Double 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 *double 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 $Cr(CO)_3$ 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.

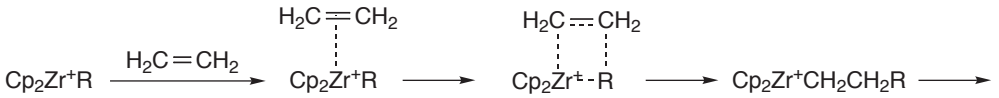
---

* 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.

5 mins

Ziegler-Natta Polymerization of Ethylene

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

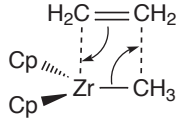


The object of this tutorial is to obtain a transition state for insertion of ethylene into $Cp_2ZrCH_3^+$.

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 *double 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 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 (Cp_2ZrCH_3 and ethylene) as shown below:



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

4. Select **Guess 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.

Section III

User's Guide

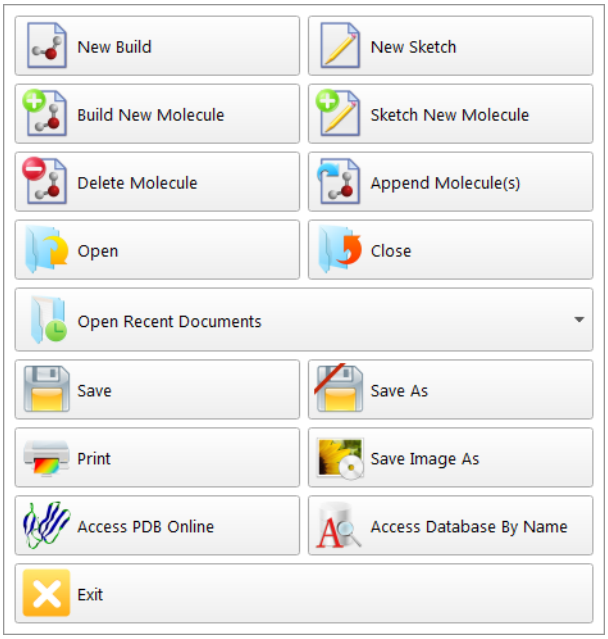
This section describes the functions available under the menus incorporated into ***Spartan Student***, and is intended to serve as a general reference to the program. The coverage follows the order of the menus presented in the user interface: **File**, **Edit**, **Model**, **Geometry**, **Build**, **Setup**, **Display**, **Options**, **Activities** and **Help**. The functions and usage of each of the menu entries is described. Entries under the **File**, **Model**, **Geometry** and **Build** menus deal primarily with the input and construction of both 2D drawings and 3D structures and with their display and query. Entries under the **Setup** menu specify molecular mechanics or quantum chemical models, and designate what properties and spectra are to be obtained, and request one or more graphical models and include the submit function for jobs passed on to computational programs (submitted in the background). Entries under the **Display** menu access calculated quantities including calculated spectra. Entries under the **Options** menu set program defaults and user preferences, designate paths to databases of calculated and experimental information.

The chapters in this section provide only limited commentary about the performance and requirements of different computational methods and the utility of different graphical models. Additional information is provided under ***Topics*** accessed from the ***Activities*** menu, which also accesses PDF files comprising the ***Tutorials*** and ***Labs***. The **Help** menu provides additional technical help under ***Spartan Student v9 Help***, Includes the full program, manual as s PDF file, accesses details **About** the program and contains the **License Utility** (allowing for upgrading the licensing, renewing maintenance, configuring the license type, etc.). New in this release, the **Check for Updates…** entry compares the user's version with the latest available for download, and alerts the user to newer versions. Note, the software will *not* automatically update, this tool only *alerts* users to the availability of newer versions.

Chapter 3

The File Menu*

*The **File** menu accesses a 2D sketch pad, model kits to build, edit and substitute molecules in 3D, the file system to read and write both native and non-native files, print text and on-screen graphics, save on-screen graphics as image files, the database of quantum chemical results by name, the online PDB database of protein and nucleotide structures.*



New Build ( )

Brings up a model kit and clears the screen. Model kits are discussed in **Chapter 7**.

New Sketch ( )

Brings up the 2D sketch pane and clears the screen. The 2D sketch pane is discussed in **Chapter 7**.

* The **File** menu previously contained Screen Recording tools. These are now accessible through the operating system: **Win**+**Alt**+**R** for Windows, **Command**+**Shift**+**5** for Macintosh.

Build New Molecule ()

Brings up a model kit and clears the screen. **Build New Molecule** differs from **New Build**, in that the resulting molecule is appended to the end of the document associated with the molecule (or sketch) that is presently selected.

Sketch New Molecule ()

Brings up the 2D sketch pane and clears the screen. The menu bar is still accessible, but only the **View** () and **Sketch New Molecule** () icons are available. **Sketch New Molecule** differs from **New Sketch** in that the resulting sketch is appended to the end of the document associated with the molecule (or sketch) that is presently selected.

Delete Molecule ()

Deletes the selected molecule(s) from a document. Deleting the last molecule leads to an empty document.

Append Molecule(s)... ()

Appends molecules from one or more documents onto the end of the current document. **Append Molecule(s)...** leads to a file browser from which one or more documents may be selected.*

Open... ()

Opens a file that contains all information associated with a particular

---

* Alternatively, molecules may be appended onto an existing document either by copy/paste operations using the clipboard or by *dragging* from an external window. Both require that the spreadsheet associated with the destination document be open on screen.
To copy a molecule open on screen onto the clipboard, first select (*click* on) it, and then select **Copy** from the **Edit** menu. Alternatively, *click* on its label in its spreadsheet (in the leftmost column), and then select **Copy** from the **Edit** menu. The latter permits several molecules to be selected (and copied) at once using the **Shift** and **Ctrl** keys in the usual manner. Once on the clipboard, the molecule or molecules may be moved to the destination list by *clicking* on an empty row header in the spreadsheet (for the destination document), and then selecting **Paste** from the **Edit** menu.
To copy a document from an external window, *drag* it onto the open spreadsheet (associated with the destination document) inside of ***Spartan Student***. Several documents can be *dragged* at once using the **Shift** and **Ctrl** keys in the usual manner.

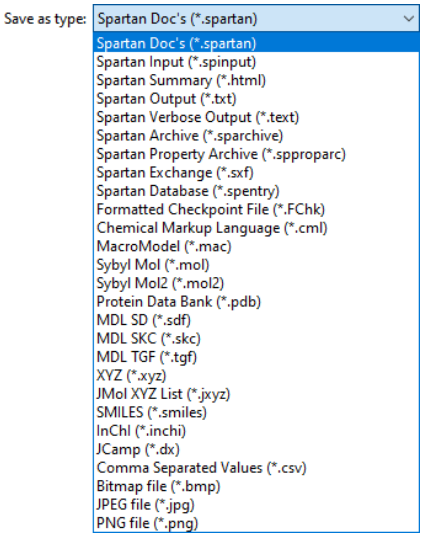
molecule (or list of molecules). In addition to native (.spartan) files (documents) including 2D sketch files, supported are files containing 2D drawings, 3D structures and 1D strings. Also supported are file formats for experimental IR and NMR spectra. Non-native files are normally hidden from view, but may be seen by selecting **All Files** from the **Files of type** menu at the bottom of the dialog.

Open Recent Documents ( )

Brings up a list of (at most) ten recent documents. *Clicking* on one opens the document.

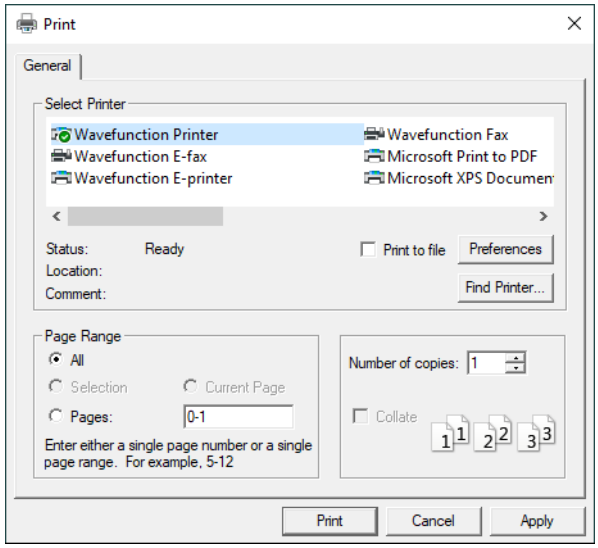
Save ( )
Save As... ( )
Save Image As... ( )

Saves the document containing the selected molecule ***exactly as it appears on screen***. Opening the document will bring it on screen exactly as it was last saved. If the document has not previously been named, **Save** behaves as **Save As...**. Documents may be either be saved in native format or in one of the formats listed under **Save As...**. In addition, Bitmap (.bmp), JPEG (.jpg) and PNG (.png) graphics file formats are supported. Selection is made under the **Save as type** menu in the **Save As** dialog. **Save Image As...** allows for saving molecules as high resolution PNG files.



Print ( )

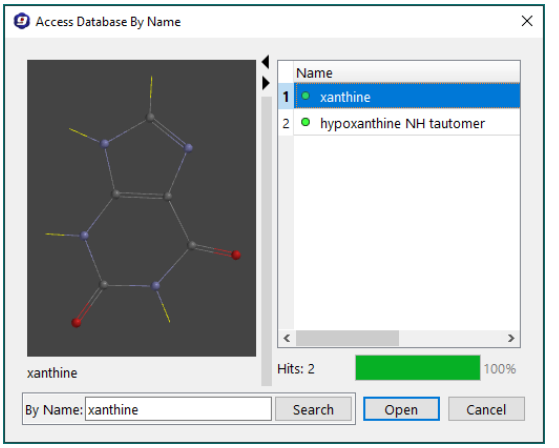
Selection leads to a dialog in order to designate a printer, specify print layout and number of copies. It also allows printing to a file.



The contents of the spreadsheet (**Spreadsheet** under the **Display** menu; **Chapter 9**) may be printed using **Print** from the contextual menu. The results of a reaction energy calculation (**Reactions...** under the **Display** menu; **Chapter 9**), may be printed using **Print** from the contextual menu.

Access Database By Name... ( )

Included with ***Spartan Student*** is a ≈6,000 molecule subset of the Spartan Spectra and Properties Database (SSPD). The individual entries correspond to calculations from the ωB97X-D/6-31G* density functional model and each includes the structure, energy, infrared and NMR spectra, as well as a variety of molecular and atomic properties. The wave function is available allowing graphical surfaces and property maps to be computed on-the-fly. Selection brings up a dialog:

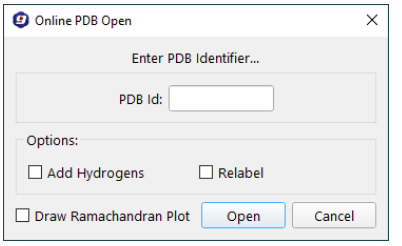


A name search is initiated by entering a name (or partial name) in the box to the right of **By Name:** at the bottom of the **Access Database by Name** dialog. The search will return all entries that include whatever text string is entered into this box. For example, searching xanthine will not only result in xanthine, but also any related molecules.

Following the search, one or more hits may be retrieved by selecting them from the hit list and then *clicking* on **Retrieve**. **Shift** and **Ctrl** keys are used in the usual way to select multiple entries from the hit list.

Access PDB Online... ( )

Provides access to the online **P**rotein **D**ata **B**ank (**PDB**)* comprising more than 190,000 protein and nucleotide structures. Selection results in a dialog.



To access a PDB structure, enter the four character identification code in the box to the right of **PDB ID** and *click* on **Open**. If the PDB entry contains more than one structure and/or the PDB ID yields more than one entry, all structures will be returned in a single document.

* The web address is https://www.rcsb.org.

PDB access will typically require a few seconds. The PDB ID will appear at the right and a ribbon model of the protein or nucleotide will appear on screen. A Ramachandran plot associated with a protein structure may either be drawn upon initial retrieval of the PDB file by *checking* the box to the left of **Draw Ramachandran Plot** or later from **Ramachandran Plot** under the **Model** menu (**Chapter 5**).

Screen Recording

For **Windows** (10 or higher) use the **Win**+**Alt**+**R** keys to start screen recording of the focused window. A menu is presented allowing the "Stop" recording feature. Similarly, for **Macintosh** use the **Command**+**Shift**+**5** keys to access the screenshot toolbar for MacOS Mojave or higher.

Close ( )

Closes the document containing the selected molecule, as well as any document specific dialogs. If the document has not previously been saved, a name is requested. If a previously-saved document has been altered, verification that the changes are to be saved is requested.

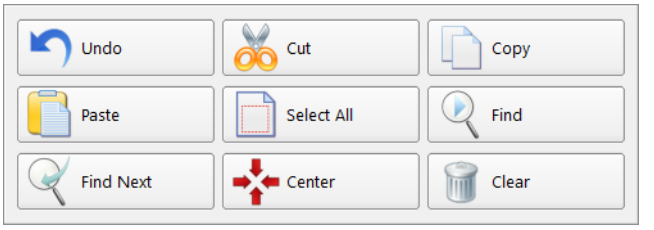
Exit ( )

Exits ***Spartan Student***, that is, clears the screen and closes all open documents. A prompt for a name is provided for each document that has not previously been saved.

Chapter 4

The Edit Menu

*Operations under the **Edit** menu provide for undoing commands, copying items to and from the clipboard, finding text and graphics, centering molecules on screen and clearing the selected molecule.*



Undo ( )

Undoes the last operation from the **Build** and **Edit** menus. Undoes transition-state formation (see **Transition State** in **Chapter 7**).

Cut ( ), Copy ( ), Paste ( )

Cut moves the selected item to the clipboard and removes it from the document. **Copy** copies the item to the clipboard. The item is unaffected. **Paste** transfers the contents of the clipboard to the selected location. The contents of the clipboard are unaffected. Among the important uses of the clipboard are:

(i) Transferring on-screen graphics into other applications such as Microsoft Word® and PowerPoint®.

(ii) Temporary storage of a 3D molecular structure for use in molecule building. Temporary storage of a 2D sketch is accomplished using **Copy/Paste** under a contextual menu (see **Chapter 7**).

(iii) Transferring data between ***Spartan Student*** spreadsheets and between a ***Spartan Student*** spreadsheet and other applications such as Microsoft Excel®.

(iv) Making multi-molecule documents and/or transferring molecules between documents.

Copy operations for (i) and (ii) also refer to the contents of a selection box ***if one has been drawn***, but to the selected molecule if a box has not been drawn. **Copy** operations from a spreadsheet refer to all spreadsheet information associated with a document if selection is made on the header cell of the leftmost column, but only to the selected (text) information if selection is made on any other column. Further discussion relating to use of the clipboard in molecule building is provided in **Chapter 7** and for moving data in and out of the spreadsheet in **Chapter 9**.

Select All ()

Selects all atoms in the selected molecule.

Find...(), Find Next ()

Find locates a text string defined in the **Find** dialog if an output window or a spreadsheet is selected, or a structure sequence defined on the clipboard if an on-screen model is selected. **Find Next** locates the next occurrence of a text string or a structure sequence.

Center ()

Centers on screen all molecules in the document for which the selected molecule is a member (only the selected molecule is displayed).

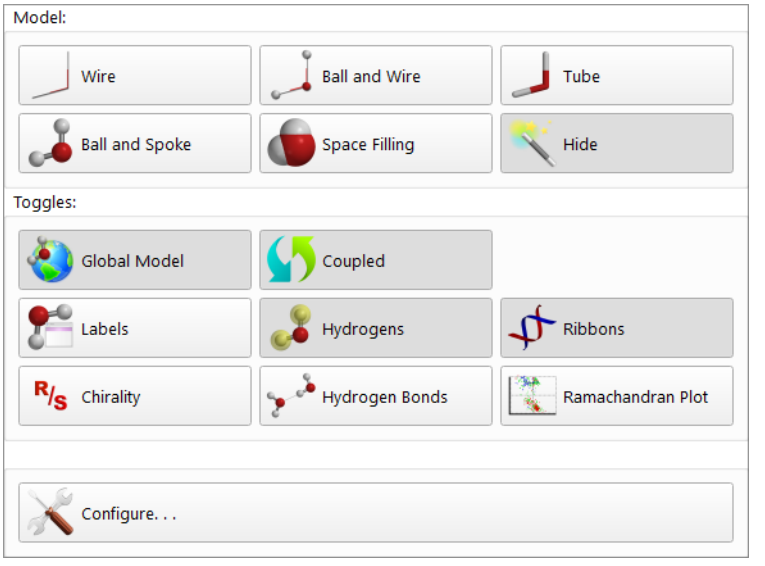
Clear ()

Clears (deletes) the structure and other information for the selected molecule, and brings up a model kit. Information is not removed from the file system until the document is saved.

Chapter 5

The Model Menu

*Structure models available under the **Model** menu include wire, ball-and-wire, tube, ball-and-spoke and space-filling (CPK) models, with or without hydrogens, with or without hydrogen bonds indicated, with or without atom labels, and with or without R/S chirality labels, as well as ribbon displays for polypeptides and polynucleotides, with or without labels and with or without hydrogen bonds indicated. It allows drawing a Ramachandran plot for a protein structure retrieved from the Protein Data Bank (PDB). The menu also provides for configuring atom labels to display element name, mass number, charge or chemical shift, and for specifying color coding and display style for ribbon labels, as well as turning a variety of other labels on and off. Finally, it allows model style to be applied globally (to all molecules in a document) and models to be manipulated in concert.*



Only one model style **Wire**, **Ball and Wire**, **Tube**, **Ball and Spoke**, **Space Filling** or **Hide**) may be selected. The selected model is designated by a check mark ✔ in front of its entry in the drop down menu or by a highlighted button in the case of the button pad menu

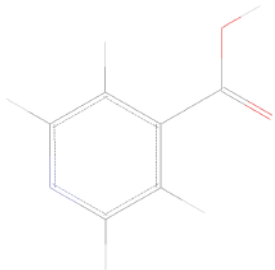
display. **Global Model**, **Coupled**, **Hydrogens**, **Labels**, **Chirality**, **Hydrogen Bonds**, **Ribbons** and **Ramachandran Plot** operate as toggle switches. A ✔ in front of the entry in the menu indicates that it is selected.

All structure models and graphics may be displayed either in orthogonal or perspective projections. The latter may be valuable in helping to visualize large molecules. Selection is done in the **Settings** tab (**Preferences...** under the **Options** menu; **Chapter 10**). Both structure models and graphics may be presented in 3D stereo. This is also controlled from the **Settings** tab. Stereographic displays require perspective projections.

Wire ( )

This represents the molecule as a wire model where the vertices represent the atoms.

Wire Model



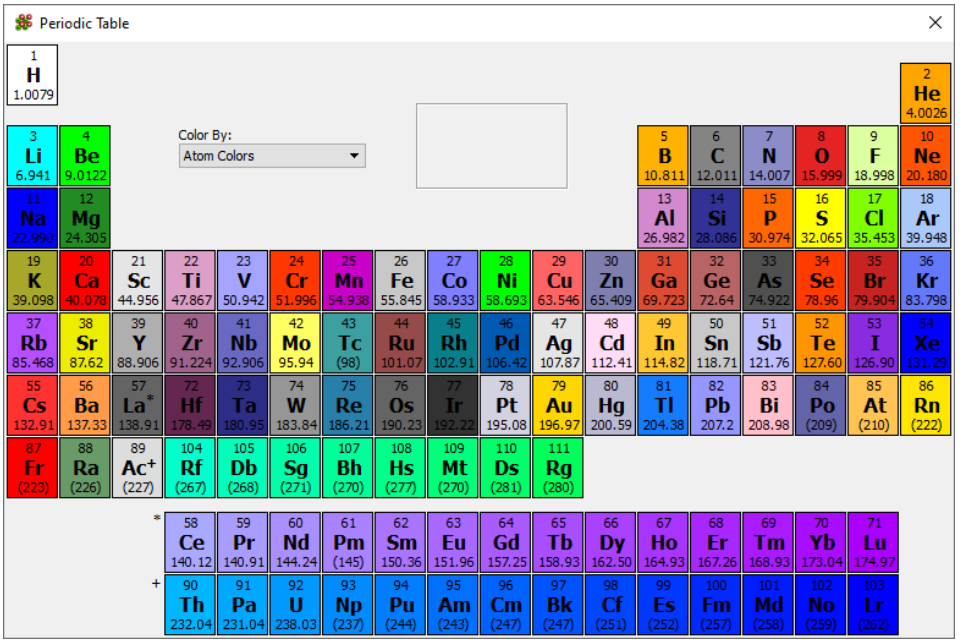
Bonds are drawn in two colors, one for each of the atoms making up the bond. Default atom colors are given in **Figure 5-1**.

Atom colors apply globally (to all atoms of given type), and may be changed using the **Set Colors** dialog (**Colors** under the **Options** menu; **Chapter 10**). All models use the same color scheme for atoms, and provide for the same mechanism of changing colors globally or individually. **Note**: Individual atoms may be custom colored, or may be displayed in a custom model style from the **Atom Style** panel, accessible from the drop down triangle in the lower right of the **Atom Properties** dialog (**Properties** under the **Display** menu, **Chapter 9**).

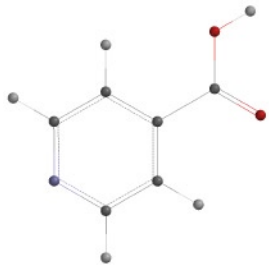
Ball and Wire( )

This represents atoms by small balls and bonds by wires.

Figure 5-1: Default Atom Colors



Ball-and-Wire Model

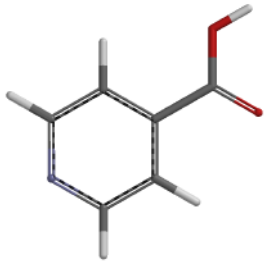


The balls are color coded according to atom type, and the wires representing bonds are drawn in two colors (as in wire models).

Tube ( )

This is similar to the wire model, except that tubes instead of wires are used to represent bonds.

Tube Model

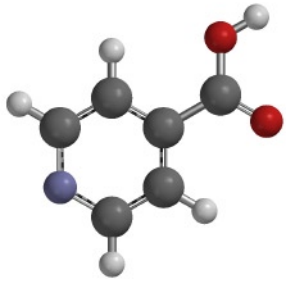


Tubes may either be solid cylinders or be split to represent multiple bonds. As with wire models, bonds are drawn in two colors.

Ball and Spoke ( )

This represents atoms by balls (the color of which depends on atom type), and bonds by spokes.

Ball-and-Spoke Model

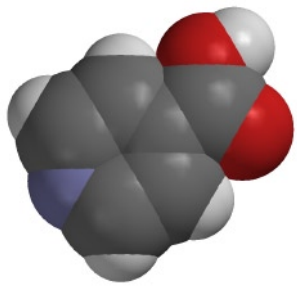


Spokes are either cylinders or are split to represent multiple bonds. Bond (spoke) color is gray by default but it may be changed using the **Color** dialog (**Colors** under the **Options** menu; **Chapter 10**).

Space Filling ( )

This represents the molecule as a composite of spheres, the radii of which have been chosen to approximate van der Waals contact distances.* Also known as CPK models, space-filling models are intended to portray overall molecular size and shape.

Space-Filling Model



Volume, surface area and polar surface area (PSA)** are displayed in the **Molecule Properties** dialog (**Properties** under the **Display** menu; **Chapter 9**) and correspond to a space-filling model.

Hide ( )

This removes the structure model from the screen. This may be desirable where its display leads to unnecessary crowding, for example, in proteins where ribbon displays are more appropriate. A structure model may be restored by selecting it from the **Model** menu.

Global Model ( )

If *checked* (turned on), this signifies that all molecules in a document will share attributes. These include presentation of hydrogens, atom and other labels, hydrogen bonds and ribbon displays. Default model style is controlled from the **Molecule** tab (**Preferences...** under the **Options** menu; **Chapter 10**). **Global Model** acts in a toggle manner, switching between global and individual display. **Global Model** is normally on.

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* Default values for van der Waals radii may be changed from the **VDW Radii** tab accessible from **Preferences** under the **Options** menu (**Chapter 10**). Settings apply to all atoms of given atomic number.

** Polar surface area is defined as the area due to nitrogen and oxygen and any hydrogens attached to nitrogen and oxygen.

Coupled ()

If *checked* (turned on), this signifies that all molecules in a document will be moved together. **Coupled** is turned on following molecule alignment (see **Align** under the **Geometry** menu; **Chapter 6**). **Coupled** acts in a toggle manner, that is, repeated selection couples and decouples the molecules.

Hydrogens ()

If *checked* (turned on), this signifies that hydrogens are to be included in the model display. **Hydrogens** acts in a toggle manner, that is, repeated selection turns the display of hydrogens on and off.

Labels ()

If *checked* (turned on), this signifies that labels associated with atoms, ribbons and bonds as well as with other attributes specified in **Configure...** (see discussion later in this chapter) are to be displayed in conjunction with model display. **Labels** acts in a toggle manner, that is, repeated selection turns display of labels on and off. **Labels** is automatically turned on following selection of **Apply** or **OK** in the **Configure** dialog (if any changes are made).

R/S Chirality ()

If selected, this adds R/S chirality labels to the model. **R/S Chirality** acts in a toggle manner, that is, repeated selection turns R/S labels on and off.

Hydrogen Bonds ()

If *checked*, this signifies that hydrogen bonds are to be drawn as part of the model. **Hydrogen Bonds** acts in a toggle manner, that is, repeated selection turns display of hydrogen bonds on and off.

Ribbons ()

If *checked*, this signifies that ribbons are to be displayed along with the selected model. (If only ribbons are desired, select **Hide** for the model.) **Ribbons** acts in a toggle manner, that is, repeated selection

turns display of ribbons on and off.

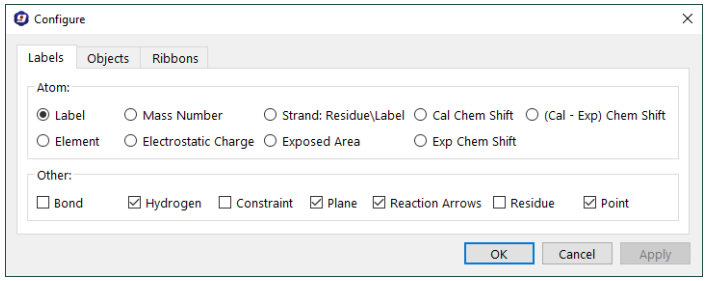
Ramachandran Plot ()

If *checked*, this draws a Ramachandran plot for a protein input from the Protein Data Bank (see **Access PDB Online** under the **File** menu; **Chapter 3**). **Ramachandran Plot** acts in a toggle manner, that is, repeated selection turns the plot on and off. Note that coloring of the points on the plot (red for α-helices, blue for β-sheets, green for "other") is not based on the actual 3D geometry but rather on assignments in the PDB file.

Configure... ()

This selects the types of labels attached to atoms and ribbons, as well as display of other objects such as points, planes, and user annotations.

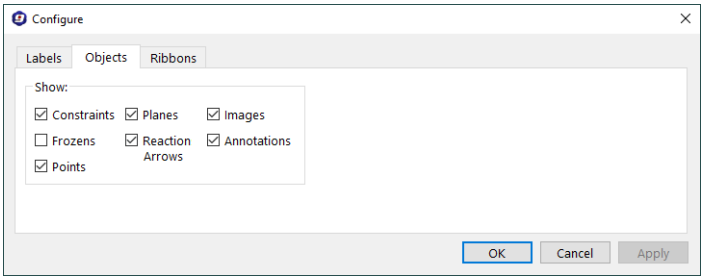
Configure Labels



Atom labels may be selected from among the following: **Labels**, a unique element/number combination that may be changed from the **Atom Properties** dialog (accessible from **Properties** under the **Display** menu; **Chapter 9**), **Element**, **Mass Number**, **Electrostatic Charge**, **Strand: Residue\Label** (polypeptides and polynucleotides), and **Exposed Area** (of an atom in a space-filling model) and **Chem Shift** (Calculated, Experimental, and Calculated-Experimental). In addition, **Bond Labels**, **Point Labels**, **Plane Labels**, **Constraint Labels**, **Residue Labels** and/or **Reaction (Arrow) Labels** may be provided. Default settings (for a new molecule) are made in the **Molecule Preferences** dialog (**Preferences** under the **Options** menu; **Chapter 10**).

Configure Objects

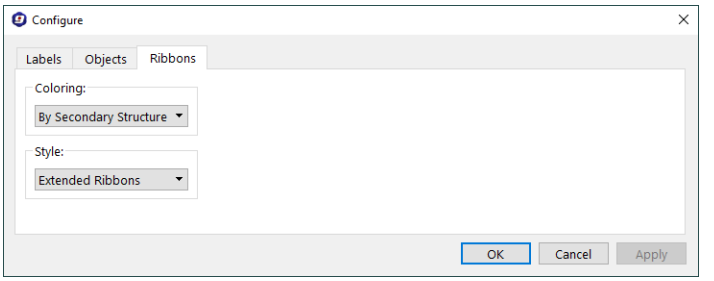
Clicking on the **Objects** tab leads to the **Configure Objects** dialog.



If checked, **Constraint** and **Frozen** markers, **Points** and **Planes** and **Reaction** arrows attach to the model. If not checked, these are shown only in the respective modes, for example, **Frozen** markers are shown only if **Freeze Center** is selected.

Configure Ribbons

Clicking on the **Ribbons** tab leads to the **Configure Ribbons** dialog.



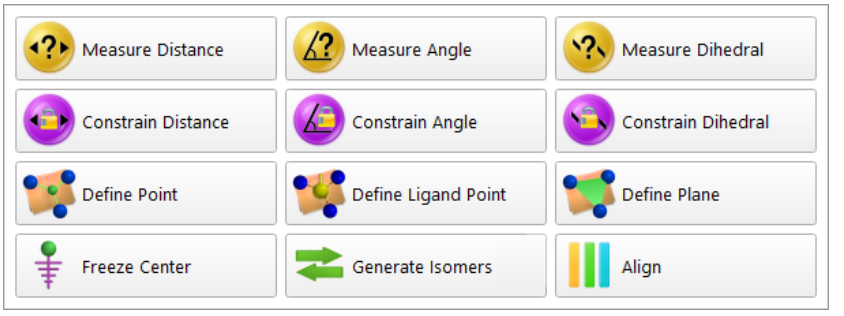
Ribbon coloring may be selected from among the following: **Monochrome**, **By Secondary Structure**, **By Strand** or **By Residue**. Ribbon style may be selected from among the following: **Ribbons**, **Extended Ribbons**, **Beads**, or **Lines**.

The **Configure** dialog is removed from the screen with all selections maintained by *clicking* on **OK**. *Clicking* on **Cancel** or on  removes the dialog but selections are lost. *Clicking* on **Apply** maintains the selections but leaves the **Configure** dialog on screen. Note, that **Labels** (from the **Model** menu) will be turned on following either *clicking* on **OK** or on **Apply**.

Chapter 6

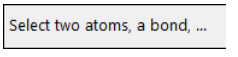
The Geometry Menu

*Functions available under the **Geometry** menu allow querying, changing and constraining bond lengths, angles and dihedral angles, defining points, ligand points and planes, freezing atomic centers and aligning molecules in a document.*



Measure Distance ()
Measure Angle ()
Measure Dihedral ()

Measure Distance displays the distance (in Ångstroms) between two atoms, whether or not they are bonded. Selection results in a message at the bottom left of the screen.



Clicking on two atoms displays the distance at the bottom right of the screen.

Alternatively, *clicking* on a bond displays its length.

Measure Distance may also be used to alter the distance between atoms (as long as both are not incorporated into the same ring), by

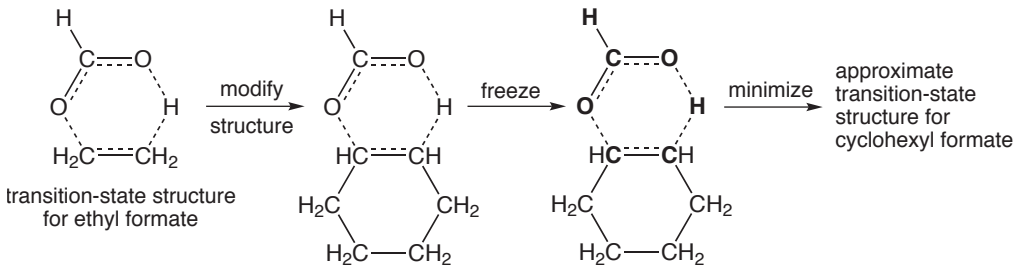
altering the contents of the box to the right of **Distance (A,B)** = or **Length (A)=**, and then *pressing* the **Enter** key (**return** key on Mac). The distance (length) may be entered into the spreadsheet by *clicking* on to the right of its display (see **Spreadsheet** under the **Display** menu; **Chapter 9**). Alternatively, the label "**Distance (A,B)=**" or "**Length (A)=**" may be *dragged* into the spreadsheet.

Angle and dihedral angle queries are handled in a similar manner. Angles require that three atoms or two bonds be identified (in the proper order) while dihedral angles require that four atoms or three bonds be identified (in the proper order).

Freeze Center ( )

This forces atoms to be held in place during minimization (in the 3D builder) or during equilibrium or transition-state geometry optimization, conformational searching, or energy profile generation using methods specified in the **Calculations** dialog (**Calculations...** from the **Setup** menu; **Chapter 8**).

Atom freezing may be useful in a number of situations, among them guessing a transition-state geometry for a reaction that is closely related to one for which a transition state is available. For example, a good guess at the transition state for pyrolysis of cyclohexyl formate will be obtained by modifying the transition state for pyrolysis of ethyl formate, freezing all but the modified sections (designated in bold in the figure below) and then minimizing.



Selection of **Freeze Center** leads to a message at the bottom left of the screen, and **Freeze All**, **Freeze Heavy**, and **Thaw All** options at the bottom right of the screen.

Clicking on an atom or free valence*, freezes it; *clicking* again thaws it. Buttons at the bottom right of the screen allow for freezing all atoms (**Freeze All**), freezing all heavy (non-hydrogen) atoms (**Freeze Heavy**) and for thawing all atoms (**Thaw All**).

Frozen atoms are indicated by magenta colored markers ( ). Whether or not these are included with the model (outside of freeze center mode) is controlled from the **Molecule Preferences** dialog under **Preferences...** in the **Options** menu (**Chapter 10**).

Constrain Distance ( )
Constrain Angle ( )
Constrain Dihedral ( )

These introduce one or more geometrical constraints during structure minimization (in build mode), and during equilibrium or transition-state geometry optimization or conformational searching using methods specified in the **Calculations** dialog (**Calculations...** from the **Setup** menu; **Chapter 8**). They also allow for setting a range of constraints needed for generation of energy profiles. Constraints may be useful in a number of situations, among them:

(i) constructing conformational energy profiles where one or more dihedral angles need to be fixed while other geometrical variables are optimized,

(ii) optimizing molecular structures where the values of certain key parameters are known, for example, optimizing the geometry of a molecule with an intramolecular hydrogen bond or a disulfide linkage, and

(iii) building molecules with unusual geometries, for example, molecules with very long bonds, as might be required in the construction of transition states and intermolecular complexes.

Selecting **Constrain Distance** results in a message at the bottom left of the screen.

* The bond distance in this case is that appropriate for hydrogen being added to the free valence.

Clicking on two atoms, or a bond results in a message at the bottom right of the screen.

Clicking on  changes it to  and shows the current distance.

This (constraint) distance can now be changed by altering the contents of the box and then *pressing* the **Enter** key (**return** key on Mac). Alternatively, the existing distance may be used as the constraint distance. If the selected distance had previously been constrained, the icon  would have been initially displayed. In this case, *clicking* on  turns the constraint off and returns the icon to  . Finally, the value of the constraint (that may be different from the value of the current distance*) may be entered into the spreadsheet by *clicking* on  to its right. Alternatively, the label ***Constraint (A,B)=*** may be *dragged* into the spreadsheet.

This sequence of operations (bond identification followed by turning the constraint on and off) may be repeated as many times as necessary. Any bonds or non-bonded distances on which constraints are to be imposed are indicated by magenta colored markers. Any constraints introduced are automatically enforced.

Angle and dihedral angle constraints are handled in a similar manner. Note that ***points and planes may not be used to define constraints***.

Checking the  leads to additional options at the bottom right of the screen. This allows a sequence of constraints to be defined (from some initial value to some final value in a given number of steps) for the purpose of constructing an energy profile along a predefined set of coordinates (see **Calculations...** under the **Setup** menu; **Chapter 8**).

The leftmost box sets the initial value of the constraint, the middle

* Note, however, that you should not start a constrained geometry optimization from a structure that is very different from that satisfying one or more constraints.

box to the right of **to** sets the final value, and the rightmost box to the right of **Steps:** sets the number of steps. For example, were the initial value set to 0°, the final value to 180° and the number of steps to 10, then a series of ten constraints (0°, 20°, 40°, ... 180°) would be specified. This can also be accomplished using the **Constraint Properties** dialog, (see **Properties** under the **Display** menu; **Chapter 9**) and the value of the constraint posted to the spreadsheet.

Whether or not constraint markers are included as part of the model (outside of constrain distance, constrain angle or constrain dihedral mode) is controlled from the **Molecule Preferences** dialog (**Preferences...** under the **Options** menu; **Chapter 10**).

Define Point ()

This defines a point as the geometric (unweighted) center of selected atoms (or points) previously defined. Selection results in display of a message at the bottom left of the screen.

Clicking on atoms (or points) in any order, and *clicking* a second time on any one of the atoms (or points) defines a point (depicted as a small sphere). As many points as desired can be defined and these are treated in the same way as an atom in defining distances, angles, etc. Points move with the molecule as its geometry is altered.

Whether or not points and ligand points are shown as part of the model is controlled from the **Molecule Preferences** dialog (**Preferences...** under the **Options** menu; **Chapter 10**).

Define Ligand Point ()

This defines a point of attachment directed perpendicular to the geometric center of the plane defined by three atoms (or best plane in the case of four or more atoms). *Clicking* on atoms (or points) in any order, and *clicking* a second time on any one of the atoms (or points) defines a ligand point (depicted as a small sphere). As many ligand points as desired can be defined. A ligand point shares all the characteristics of a normal point, but may also be used to bond to

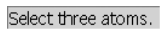
atomic fragments, functional groups, etc. See **Make Bond** under the **Build** menu (**Chapter 7**) for a discussion. Ligand points move with the molecule as geometry is altered.

> **Delete** from the **Build** menu ( ) or the **Delete** key may be used to remove a point or ligand point.

Whether or not points and ligand points are shown as part of the model is controlled from the **Molecule Preferences** dialog (**Preferences...** under the **Options** menu; **Chapter 10**).

Define Plane ( )

This defines and displays a reference plane. Selection results in display of a message at the bottom left of the screen.



Clicking on three atoms or points defines a plane. As many planes as desired may be defined, and these may be used in defining distances, angles, etc. Planes move with the molecule as its geometry changes.

> **Delete** from the **Build** menu ( ) or the **Delete** key may be used to remove a plane.

Whether or not planes are included as part of the model is controlled from the **Molecule Preferences** dialog (**Preferences...** under the **Options** menu; **Chapter 10**).

Align ( )

This aligns all other molecules to the selected molecule in the same document. Note: the **Align** icon or menu entry will only be available if you access it with focus on a multi-molecule document. If your document has a single molecule the icon is grayed out. Selection of **Align** from the **Geometry** menu results in a message at the bottom left of the screen.

Clicking on an atom designates it as an alignment center, and marks it with a red circle. *Clicking* on the circle removes the designation (and the circle). Following selection of alignment centers, *clicking* on the **Align** button at the bottom right of the screen aligns the molecules. If no atoms are selected prior to *clicking* on **Align**, then alignment is based on all (non-hydrogen) atoms.

Following alignment, two or more molecules may be displayed at once using spreadsheet functions (see **Spreadsheet** under the **Display** menu; **Chapter 9**). Their motions (coordinates) will be coupled following alignment, but may be uncoupled allowing the aligned molecules to move independently (see **Coupled** under the **Model** menu; **Chapter 5**). Note that alignment center selections are kept and molecules can be realigned by again selecting **Align** from the **Geometry** menu (or *clicking* on ) followed by *clicking* on the **Align** button.

The alignment score from 0 to 1 (where 1 designates perfect alignment), is available in the spreadsheet. This is accessed by *clicking* on the **Add** button at the bottom of the spreadsheet, and selecting **Alignment Score** from the **Molecule List** tab (see **Spreadsheet** under the **Display** menu; **Chapter 9**). A score of 0 is assigned to molecules that cannot be aligned to the selected molecule.

Chapter 7

The Build Menu

*The **Build** menu provides a sketch palette for drawing molecules in 2D, model kits and associated tools for building and editing organic, inorganic and organometallic molecules as well as polypeptides and polynucleotides in 3D, 2D to 3D conversion and 3D structure refinement using molecular mechanics.*

Spartan Student provides a variety of tools for specification of 3D molecular structure, a necessary first step to any molecular mechanics or quantum chemical calculation. Molecules can either be rendered as 2D sketches and later brought into 3D*, or directly constructed from 3D fragments. Polypeptide and polynucleotide construction is availale from 3D (only).

2D Sketch Palette

The 2D sketch palette contains tools for making and manipulating drawings. There are also tools for specifying charges and radical sites and for designating stereochemistry.

Atom Icons. H, B, C, N, O, F, Si, P, Cl, Br and I only.

* The Windows version of ***Spartan Student*** also allows seamless access to ChemDraw installed and licensed on the same computer. 2D drawings are automatically brought into 3D. Both Windows and Mac versions of ***Spartan Student*** are able to read ChemDraw files. Information is provided in **Appendix E**.

Periodic Table, Groups, Ligands. A **More** icon which appears below the **H** and **B** icons, allows any atom as well as a variety of common functional groups and a selection of common ligands to be specified.

Common Rings. Three icons facilitate the rapid addition of benzene (), cyclohexane () and cyclopropane (), cyclobutane (), cyclopentane () and cycloheptane ().

Common Carbonyl Groups. Three icons facilitate the rapid addition of carbonyl (), carboxylic acid/ester () and amide () groups to drawings.

Stereochemical Markers. Wedges and dashes, represented by  and  , can be used to designate in-out stereochemistry. Once a stereochemical marker has been added to a drawing, it is possible to designate the orientation of hydrogen atoms and/or substituents bonded to six-member rings as **ax(ial)** or **eq(uatorial)** (*ax* and *eq* labels appear only on the drawing, not in the palette).

Charge/Radical Markers. Conventional bonding rules (neutral C makes 4 bonds, neutral N makes 3 bonds, and so on) are enforced when 2D perspective drawings are converted into 3D models. This is accomplished by adding hydrogen atoms to the drawing. For example, a single carbon on screen will give methane, a single line, ethane, and a double line, ethylene. (Hydrogen atoms are added to nitrogen, oxygen, phosphorous and sulfur in the 2D drawings.) When another outcome is desired, for example, for an ion or free radical, charge or radical markers must be added to the drawing.

Two icons,  and  , are used to label atoms that bear formal charges.  is used to label atoms that are neutral, open-shell radicals. Each of these markers affects the number of electrons and the number of hydrogen atoms added to the 3D model. For example, **O** will produce a 3D model of water, H_2O. However, adding the appropriate marker will result in 3D models of H_3O^+ (), HO^- (), or HO radical (), respectively. Only one charge/radical marker can be assigned to an atom.

Only one charge/radical marker is displayed on the palette, but *clicking* on the icon will cause each marker to appear in turn.

Reaction Arrows. designates one ore more curved arrows allowing access to ***Spartan's*** automated search transition state procedure. The tail of the arrow corresponds to the source of the electron pair. If the source is a lone pair, then select the atom that holds the lone pair. If the source is a bond, then select the bond. *Clicking* on an atom or bond highlights (colors gold) the atom or bond. *Clicking* again on the same atom (or same bond) removes the highlighting. The head of the arrow corresponds to the destination of the electron pair. If the destination is an atom (leading to a lone pair), then select the atom that will hold the lone pair by *clicking* on it two times. If the destination is an existing bond (leading to an increase in bond order from single → double or double → triple), then select (*click* on) the bond. If no bond presently exists, select (*click* on) the two atoms that will become bonded upon reaction. These operations result in a curved arrow being drawn on the reactant structure. This extends from an atom, or the center of a bond to an atom, or the center of a bond, or the center of a dotted line that has been drawn between atoms that are to be bonded.

Note that the head and tail do not need to reside on atoms or bonds on the same fragment. Also the tail may involve atoms of two detached fragments.

The process (tail selection followed by head selection) is repeated as necessary to fully define the reaction. Incorrect reaction arrows may be removed by *clicking* on from the palette and *clicking* on the arrow. You then need to select to continue arrow specification.

Once defined, reaction queries can be used to provide a guess at a transition state based on its similarity to an entry in an internal database* of transition states for a variety of common reactions.

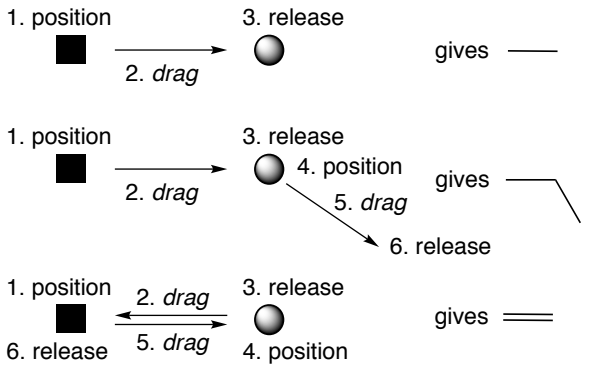
Drawing Tools. Undoes the most recent drawing operation(s). Removes or modifies parts of a drawing. Deletes an entire

* This collection presently consists of more than 2000 named reactions.

drawing (a warning is provided). Improve the readability of a drawing by applying various "clean up" procedures.

Making a Sketch

To start a sketch, first select (*click* on) an atom, group, ring or the **More** icon in the sketch 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, ring or **More** icon in the sketch 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.

Sketch Operations

Add an Atom, Ring, or Carbonyl Group. To add an atom, *click* on that atom's icon. Position the cursor over the atom in the drawing that will connect to the new atom, *drag* it away and release the button. To add a common ring or carbonyl group, *click* on that ring's (group's) icon, position the cursor over the atom in the drawing that will connect to the new ring (group) and *drag* it away and release the button. The carboxylic acid/ester  and amide  icons contain an arrow that shows which atom in these groups will be connected to the existing drawing. To change the location of this connection point (arrow), *click* on the group's icon until the arrow reaches the desired location.

Add Multiple Bonds. To add a multiple bond, first draw a single bond at the location where the multiple bond is needed, then either *double click* to increase the bond order, or redraw the bond once to make a double bond, and redraw it again to make a triple bond (in other words, position the cursor over one end of the bond, drag to the other end, and release the button).

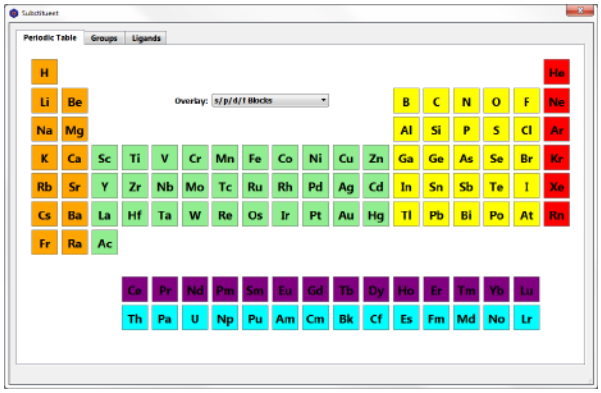
Fuse Rings. *Click* on an icon for the first ring and *double click* on the screen. Next, *click* on the icon for the second ring and *double click* the bond that the rings will share. This will create a drawing with a fused bicyclic ring system. Note that the (*cis* or *trans*) stereochemistry of the ring juncture is ill-defined. This will be addressed later (**Add Stereochemical Markers**).

This technique can also be used to add rings to an existing bond in any drawing. *Click* on the icon for the ring to be added and *double click* on the bond that will become part of the ring.

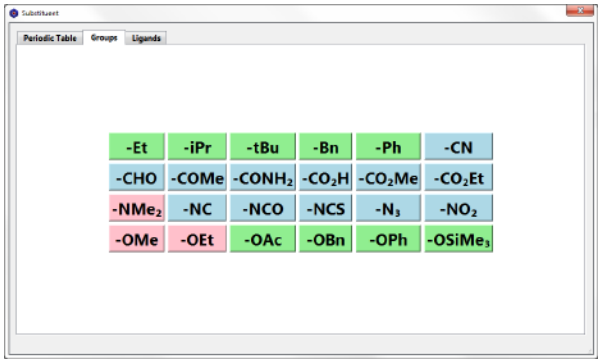
Replace an Atom with Another. If a drawing contains atom A where atom B is needed, *click* on the icon for B, then *double click* on A in the drawing. This allows the drawing of heterocycles. First, draw an all-carbon ring and then replace specific carbons with heteroatoms.

Access an Element, Functional Group, or Ligand. *Click* on the icon underneath **H** and **B** (this icon will initially be labeled

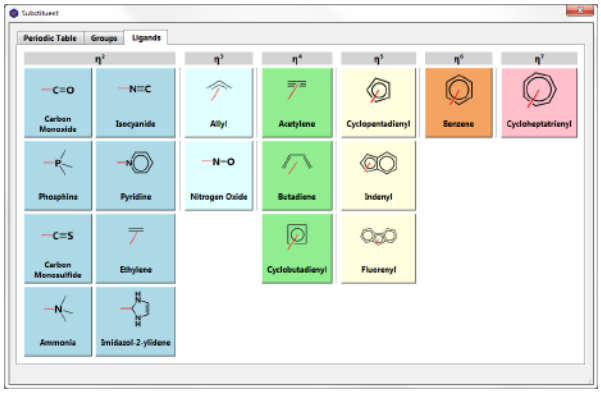
with the name of the group that was previously selected (or with **More** if no previous selection was made) and will change each time you select a new moiety. A tabbed dialog initially displaying a ***Periodic Table*** *results*.



If instead of an element, a functional group is desired, *click* on the **Groups** tab, and then on a group from the dialog that results.



Finally, if a ligand is desired, *click* on the **Ligands** tab, and then a ligand from the dialog that results.



An element, group or ligand defined in this way can be added to a drawing, replaced, or removed using the same drawing techniques used for standard atoms.

Add a Stereochemical Marker (Dash or Wedge). 3D information can be added to a drawing by replacing **single** bonds with stereochemical markers: dashes or wedges.

To use a marker, *click* either  or  , then draw or (re-draw) the single bond. To reverse the orientation of the marker, *re-draw* the bond or marker in the opposite direction. One type of marker can be replaced directly by the other. *Click* on the desired marker and then *re-draw* the existing marker. Markers can also be converted back into single bonds. *Click* on  , then *double click* on the marker.

For best results during 2D-to-3D conversion, all substituent bonds to rings should be drawn with stereochemical markers.

Add an *Axial* or *Equatorial* Marker (6-member rings only). The orientation of a hydrogen/substituent on a 6-member ring can be specified by marking **one** ring substituent as either **ax(ial)** or **eq(uatorial)**. If the molecule contains multiple rings, the conformation of each ring can be specified by marking **one** substituent per ring. *Axial* or *equatorial* markers can only be added to stereochemical markers (dashes, wedge) so the bond connecting the substituent to the ring must be drawn with a stereochemical marker first.

To add an *axial* or *equatorial* marker to a stereochemical marker, *click* on either  or  , then *double click* on the stereochemical marker. ax will appear on top of the stereochemical marker. To replace ax with eq, *double click* on the stereochemical marker again. To remove the marker, *double click* on the marker again.

Although it is possible to produce a drawing in which several bonds are marked as *axial* or *equatorial*, **only one** marker is used when converting a 2D ring drawing into a 3D model.

Assign Charges and Radical Sites. Formal charges and unpaired electrons can be assigned to individual atoms* using charge/unpaired electron markers. To assign a **positive** formal charge to an atom, *click* on  and *double click* on the atom in the drawing. To assign a **negative** formal charge or **unpaired electron**, *click* on the charge/unpaired electron marker until the desired icon appears (tapping the marker rotates it through three possibilities:  ,  , and ) and double tap the atom in the drawing.

To replace a charge/unpaired electron marker on an atom with a different marker, *click* on the desired charge/unpaired electron icon and *double click* the marked atom. To remove a marker, *click* on  and *double click* on the marker.

Charge/unpaired electron markers play an important role during the conversion of 2D drawings into 3D models in that they determine the number of hydrogens that need to be added to the model (it is usually unnecessary to draw hydrogens unless they are needed to mark stereochemistry).

Hydrogens are not shown in 2D perspective drawings unless they have been drawn explicitly (exceptions: hydrogens attached to neutral N, O, P, and S are shown). When a drawing is converted into a 3D model, hydrogens are added to the model according to conventional bonding rules. A neutral carbon atom is assumed to form four bonds, nitrogen three bonds, oxygen two bonds, and so on. Analogous logic is used for atoms that carry a formal charge or unpaired electron marker.

Charge and unpaired electron markers are carried over into specification of quantum chemical calculations (**Calculations...** from the **Setup** menu; **Chapter 8**). The total charge is set equal to the sum of the formal charges in the 2D drawing. A model with one unpaired electron is treated as a free radical (drawings that contain more than one unpaired electron may give unanticipated results).

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* While convenient when sketching in 2D, the radical or charge is not actually located on an atom, rather the quantum chemical calculation will convey delocalization, this is best explored with graphical models. See **Surfaces** in the **Display** menu, **Chapter 9**.

Undo the Last Action. *Click* on  to return to the drawing as it existed before the last action.

Clean Up a Drawing. *Click* on  to clean up a drawing, that is, to equalize bond lengths, bond angles, and so on. Clean up can improve the appearance of a 2D drawing, but not every clean up will produce a desirable result. To undo an unsatisfactory clean up operation, *click* on  .

Remove an Atom or Bond. *Click* on  and then *double click* on the atom or bond. If you *click* an atom, all bonds to that atom will also be removed. Removing a bond, either by *clicking* on an atom or by *clicking* on the bond itself, will also remove terminal atoms, that is, atoms not connected to any other atoms in the drawing will be removed along with the bond.

Remove a Multiple Bond. To remove a multiple bond, *click* on  then *double click* on the multiple bond. This reduces the bond order by one. Repeated *double clicks* on a triple bond will reduce the bond order: triple → double → single → no bond.

Remove a Reaction Arrow. To remove a reaction arrow, *click* on  and *double click* on the reaction arrow.

Remove a Stereochemical Marker. *Click* on  , then *double click* the marker. This replaces the marker with a single bond.

Change or Remove an *Axial* or *Equatorial* Label from a Stereochemical Marker. Tap either  or  , then *double click* on the stereochemical marker where an *axial* or *equatorial* label appears. This cycles the label (in order) among **ax** (*axial*), **eq** (*equatorial*) and nothing. The stereochemical marker itself will not be affected.

Remove a Charge or Radical Marker. *Click* on  and *double click* on the marker.

Clear the Screen. *Click* on  . A warning message will ask you to confirm this operation.

A 3D structure is obtained from the 2D sketch by *clicking* on  .

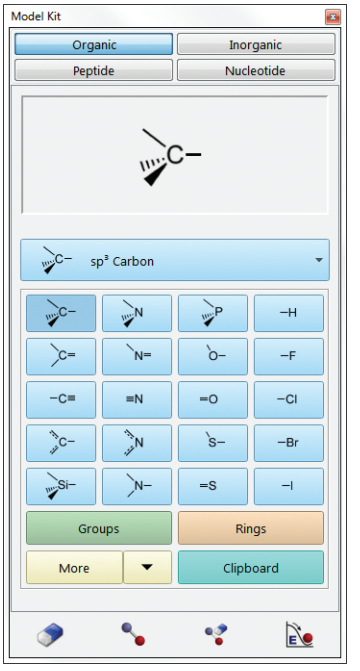
3D Model Kits

Spartan Student provides four different model kits for assembling a variety of molecular systems: an organic model kit for most organic molecules, an inorganic model kit for organic molecules not well represented in terms of an uncharged (non-zwitterionic) valence structure, as well as inorganic and organometallic molecules, and model kits for polypeptides and polynucleotides. The organic and inorganic model kits utilize atomic fragments, functional groups and rings (and ligands in the inorganic model kit), while the peptide model kit uses the set of natural amino acids as building blocks, and the nucleotide model kit the set of nucleotide bases.

3D molecule construction in ***Spartan Student*** proceeds much in the same manner as a chemist would assemble a structure from a plastic model kit, that is, pieces are taken from the kit one at a time and added sequentially to the molecule under construction.

Organic Model Kit

The organic model kit contains a suite of molecule building/editing tools specifically designed to construct organic molecules.



In the center of the model kit are a selection of atomic fragments, which from left to right and then top to bottom, correspond to:

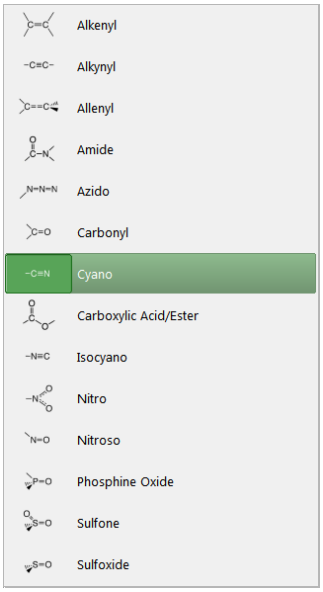
$C(sp^3)$	$N(sp^3)$	$P(sp^3)$	H
$C(sp^2)$	$N(sp^2)$	$O(sp^3)$	F
C(sp)	N(sp)	$O(sp^2)$	Cl
C(aromatic)	N(aromatic)	$S(sp^3)$	Br
$Si(sp^3)$	N(planar)	$S(sp^2)$	I

A fragment is chosen by *clicking* on its icon, which is then displayed 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, hold down the **Insert** key (**option** key on Mac), and then *click* anywhere on screen, or *double click* in a blank area on screen (no **Insert** or **option** key modifier required). 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^2 carbon, depends on the nature of the free valence selected.

While only H, C, N, O, F, Si, P, S, Cl, Br and I are available from the organic model kit, other elements may be substituted using atom replacement feature available in the inorganic model kit (see **General Molecule Building Functionality** later in this chapter). Similarly, bond types may be altered in the inorganic model kit.

Menus inside the model kit provide access to a number of pre-built fragments corresponding to functional groups (**Groups**) and rings (**Rings**), and to additional libraries of rings (as well as any user-defined structures) stored in ***Spartan***'s file system (**More**). The model kit also accesses the clipboard (**Clipboard**).

Groups

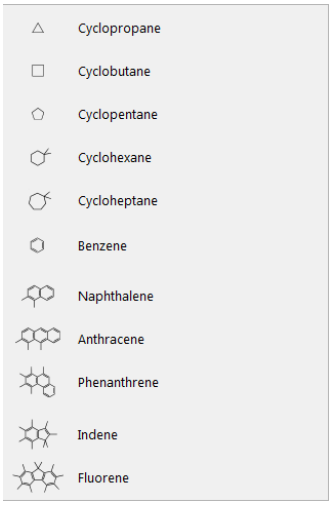


Clicking on **Groups** brings up a menu of groups, and displays an icon of one group in a box at the top of the model kit.

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.

The amide and carboxylic acid/ester groups have more than one different free valence. The free valence that is to be used is marked with a gold • (in the icon at the top of the model kit). The marked position circulates among the possible positions with repeated *clicking* on the icon.

Rings



Clicking on **Rings** brings up a menu of hydrocarbon rings, and displays an icon of one ring in a box at the top of the model kit.

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. A ring may be "fused" by *double clicking* on a bond in an existing ring. Note that the (*cis* or *trans*) stereochemistry of the ring juncture may need to be adjusted by inverting chirality (see discussion later in the chapter).

Cyclohexane, cycloheptane, naphthalene, anthracene, phenanthrene, indene and fluorene have more than one different

free valence. The one that is to be used is marked with a gold • (in the icon). The marked position circulates among the available 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. All rings in this menu are hydrocarbons, but heteroatoms may be substituted (see **General Molecule Building Functionality** later in this chapter).

More

This provides access to a broader selection of rings as well as to access user-defined entities (rings, groups, ligands, etc.). Upon initial entry, the menu to the right of **More** will be empty. It can be populated, by *clicking* on ▾ to the far right. This brings up a file browser that has been set to point toward a **Library** directory containing documents of common rings.

nitrogen heterocycles	saturated nitrogen rings
oxygen heterocycles	saturated oxygen rings
sulfur heterocycles	saturated sulfur rings
mixed heterocycles	saturated mixed rings

Clicking on a document followed by *clicking* on **Open** or *double clicking* on a document populates the menu to just under the 3D space at the top of the **Model Kit**. Menu entries are selected in the usual way. In response, a ball-and-wire model of the selected ring will appear in a box at the top of the model kit. This may be manipulated (rotated, translated, zoomed) using the usual mouse/keyboard commands (you need to position the cursor inside the box) or with the usual one and two-finger touch commands. The ring may be used to initiate building, to add alongside of an existing structure, or to add to an existing structure. In the latter case, the attachment point (on the ring in the window) needs to be identified by *clicking* on the appropriate free valence.

Documents containing ligands, chelates and high-coordination fragments intended for use with the inorganic model kit

(discussed in the next section) are also available. In addition, any ***Spartan Student*** document may also be accessed.

Clipboard

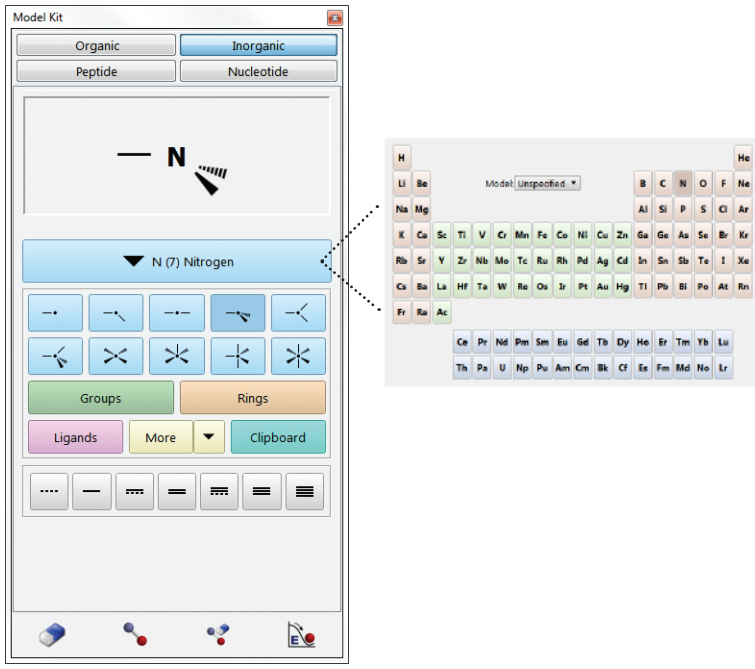
Clicking on **Clipboard** accesses the clipboard. A ball-and-wire model of whatever is on the clipboard is displayed in a box at the top of the model kit. This may be manipulated using the usual mouse/keyboard commands (you need to position the cursor inside the box or with the usual one and two-finger touch commands). Once selected, the contents of the clipboard may be used to initiate building, to add alongside of an existing structure, or to add to an existing structure. In the latter case, the attachment point needs to be identified by *clicking* on the appropriate free valence.

An empty clipboard will be signaled by:

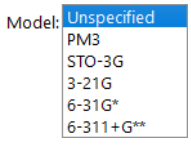
Inorganic Model Kit

Spartan Student's inorganic model kit allows construction of a much wider class of molecules (including inorganic and organometallic species) than possible from the organic model kit. Structures that violate conventional bonding rules may be constructed, as this model kit purposefully provides no bonding rule enforcement. The inorganic model kit is reached by selecting **Inorganic** from among the tabs at the top of the model kit.*

* Tabs may require too much vertical space on computers or tablets with very small screens. Alternative **Builder Selection Methods** are available in the **Miscellaneous** tab (**Preferences** from the **Options** menu; **Chapter 10**).



Atoms may be selected by *clicking* on the selection bar near the center of the model kit. This brings up a full *Periodic Table*. Main-group elements are colored red, transition metals are colored green and lanthanides and actinides are colored blue. The **Model** menu inside the *Periodic Table* highlights elements for which the selected model is available.



Selecting an entry from this menu leads to recoloring of the *Periodic Table*. A light green color is used to indicate elements for which the selected model may be used. Immediately below is a selection of atomic hybrids.

Selection of atom type is accomplished by *clicking* on the appropriate element in the *Periodic Table*. The entry will be highlighted. Selection of an atomic hybrid follows by *clicking* on the appropriate icon which will then be highlighted.* This

* Hybrids for a number of high-coordination centers are available as a library reachable from **More** (see discussion under **Organic Model Kit**).

combination (atom type + atomic hybrid) may be used to initiate building, to add alongside of an existing structure or to append onto an existing molecular fragment. To initiate building, *double click* anywhere on screen. To add alongside of an existing structure, hold down the **Insert** key (**option** key on Mac) and *click* anywhere on screen, or *double click* in a blank area on screen. To bond to an existing fragment, *click* on the appropriate free valence.

Two of the hybrids (trigonal bipyramidal and square-based pyramidal) may bond either *axially* or *equatorially*. Selection of the appropriate bonding point, marked by a •, is effected by repeatedly *clicking* on the icon; the bonding point alternates between the two sites.

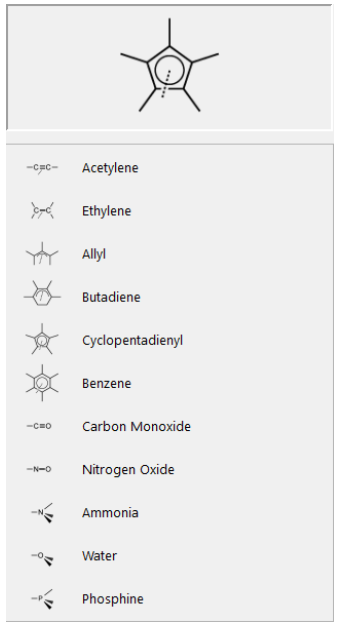
Atoms are connected with whatever bond type (partial single, single, aromatic, double, triple or quadruple) is selected from a menu near the bottom of the model kit. A bond type may be changed by first selecting a type and then *double clicking* on the bond. Bond types have no impact on quantum chemical calculations, but do affect molecular mechanics calculations which reference a Lewis structure (including minimization in the builder; see discussion later in this chapter).

No valence checking is performed in the inorganic model kit, and the user is free to construct any arrangement of atoms.

Menus under **Groups**, **Rings** and **More** are the same as those described for the organic model kit as is **Clipboard**. One additional fragment collection is provided:

Ligands

This provides access to a number of pre-built ligands, useful in the construction of inorganic and organometallic molecules. Its operation is analogous to that of the **Groups** and **Rings** menus. *Clicking* on **Ligands** brings up a menu of available ligands, and results in an icon of one ligand from this menu being displayed in a box at the top of the model kit.

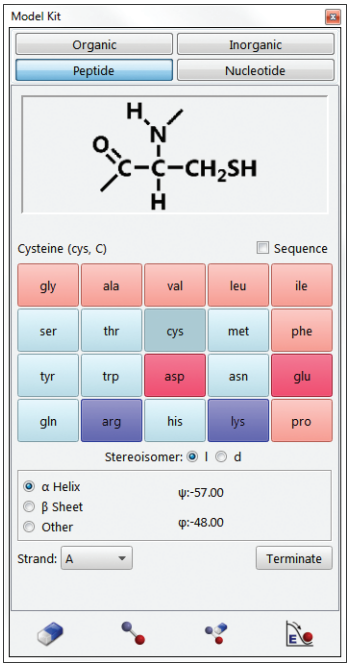


A ligand may be used to initiate building or to add alongside or to an existing structure. Additional ligands are accessible from **More** (see previous discussion). Ligands may also be built with the aid of ligand points (**Define Ligand Point** in the **Geometry** menu; **Chapter 6**).

To toggle the selection bar back to atom selection from the *Periodic Table*, *click* on one of the atomic hybrid icons.

Peptide Model Kit

The peptide model kit available in ***Spartan Student*** is not intended to be used for constructing proteins (although this is actually possible). Rather, it is primarily intended to build idealized helix and sheet structures. Protein structures are best entered from the Protein Data Bank (see **Access PDB Online...** under the **File** menu; **Chapter 3**). A model kit for construction of polypeptides is accessed by selecting **Peptide** from among the tabs at the top of the model kit.



At the middle of the peptide model kit are icons designating the amino acids (specified by their three-letter codes). An amino acid is selected by *clicking* on its three-letter code, the icon of the amino acid is displayed in the box at the top of the model kit. If the **Sequence** check box is selected, the three-letter code for the amino acid is appended to the sequence of codes in the box at the top of the model kit. Amino acids replace atoms, functional groups, rings and ligands as the building blocks in the peptide model kit. Because these other building blocks are missing, modifications of peptides, aside from modifications in sequence and in overall conformation, need to be carried out using the organic or inorganic model kits.

There are two different modes of operation: single amino acid mode and polypeptide mode. The former is used to initiate building with a single amino acid, to add a single amino acid alongside of an existing structure or to add a single amino acid to an existing structure, while the latter is used to construct amino acid sequences (polypeptides). **Sequence** off (unchecked) corresponds to single amino acid mode, and on (checked) corresponds to polypeptide mode.

Peptide construction (**Sequence** on) is accomplished in three steps:

Specify Amino Acid Sequence

This is accomplished by *clicking* in the desired order on the amino acid codes. Building occurs from the N end to the C end of the peptide. In response to each selection, the three-letter code is appended to the sequence of codes in the box at the top of the model kit. The stereochemical configuration of the amino acid is by default the l configuration; this may be changed to the d configuration prior to selection of the amino acid, by *checking* **d** to the right of **stereoisomer** in the model kit. (It may be changed back to l by *checking* **l**). d amino acids are indicated by **.d** following the code in the box.

The sequence may be altered by changing the text in the box. Existing amino acid codes may be deleted or changed or new codes can be added. The entire sequence may be specified in this way if desired. Specification of a non-existent code will result in an error message. The sequence can be cleared by *clicking* on **Clear**.

Specify Macroscopic Structure

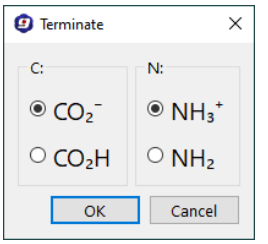
Once sequencing is complete, macroscopic structure (ψ and ϕ angles), is specified by *clicking* on one of α **Helix**, β **Sheet** or **Other**. In the case of the first two, preset angle values are displayed on the right. In the case of specification of **Other**, boxes appear, into which the desired dihedral angles need to be entered.

Terminate

The peptide is not yet terminated, and the two ends are still set up for addition of further amino acids.

C end N end

where the * indicates a free valence. *Clicking* on **Terminate** at the bottom of the model kit leads to the **Terminate** dialog.

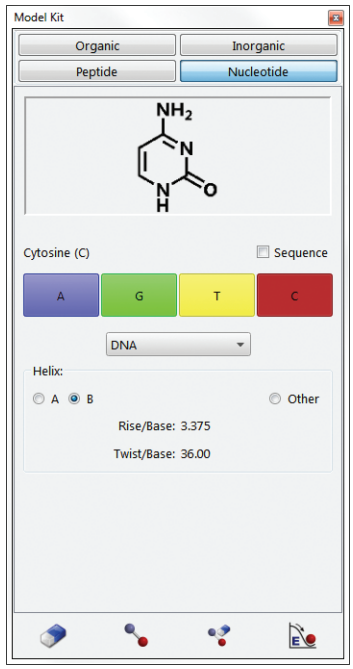


C and N terminating groups may be selected by repeated *clicking* on the C and N icons, respectively. Selection will rotate among the available terminating groups. *Clicking* on **OK** removes the dialog and terminates the polypeptide. *Clicking* on **Cancel** or removes the dialog but does not terminate the polypeptide.

The peptide (or single amino acid) may now be used either to initiate building, by *double-clicking* anywhere on screen or added alongside of an existing structure, by holding down the **Insert** key (**option** key on Mac) and *clicking* anywhere on screen, or by *double clicking* in a blank area on screen. If unterminated, it may also be joined onto an existing structure by *clicking* on a free valence. In the latter case, attachment is made from the N end, unless the free valence corresponds to an unterminated peptide fragment, in which case the appropriate end required to make an amide bond is used.

Nucleotide Model Kit

Finally, ***Spartan Student*** provides a model kit for construction of polynucleotides. It is reached by selecting **Nucleotide** from among the tabs at the top of the model kit.



At the middle of the model kit is a menu designating the type of polynucleotide.

DNA
DNA (single strand)
RNA
RNA (double strand)
DNA-RNA
RNA-DNA

Immediately above this menu are icons, designating the nucleotide bases. Selection of DNA, DNA (single strand) or DNA-RNA from the menu leads to one set of icons.

Selection of RNA, RNA (double strand) or RNA-DNA leads to a second set, the only difference is that uracil (U) has been substituted for thymine (T).

A nucleotide base is selected by *clicking* on its letter, following which either an icon of the base is displayed in the box at the top of

the model kit, or the letter for the base is appended to the sequence of letters in the box. Nucleotide bases replace atomic fragments, functional groups, rings and ligands as the building blocks in the nucleotide model kit. Because these other building blocks are missing, modifications of nucleotides, aside from modifications in sequence and helical structure, need to be carried out using either the organic or inorganic model kits.

There are two different modes of operation: single base mode and polynucleotide mode. The former is used to place a single base or base pair on screen, to add a single base or base pair alongside of an existing structure, or to add a single base or base pair to an existing structure, while the latter is used to construct strands of DNA or RNA (or mixed strands). **Sequence** off (unchecked) corresponds to single base (base pair) mode and on (checked) corresponds to polynucleotide mode.

Polynucleotide construction (**Sequence** on) is accomplished in two steps:

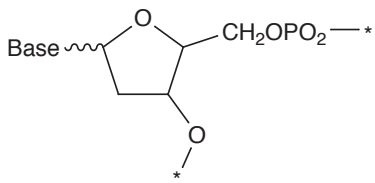
Specify Base Sequence

This is accomplished by *clicking* in order on the base codes. In response to each selection, the letter code is appended to the sequence of codes in the box at the top of the model kit. The sequence may be altered by editing the contents of the box. Existing base codes may be deleted or changed or new codes added. The entire sequence can be specified in this way if desired. The sequence may be cleared by *clicking* on **Clear**.

Specify Helical Structure

Once sequencing is complete, a helical structure may be specified by *clicking* on **A** or **B**. These correspond to A and B helices, respectively. Selecting **Other** allows user modification of the rise (in Å) per base (**Rise/Base**) and twist (in degrees) per base (**Twist/Base**).

Note that the polynucleotide is not yet terminated, and the two ends are still set up for addition of further bases or base pairs.



* indicates a free valence. Hydrogens occupy all free valences (except the *'ed positions at the two ends of the chain).

The polynucleotide (or single base pair) may now be used to either initiate building, by *double-clicking* anywhere on screen, Add alongside an existing structure, by first holding down the **Insert** key (**option** key on Mac) and *clicking* anywhere on screen, or *double clicking* on a blank area on screen. Join onto an existing structure by *clicking* on a free valence. In the latter case, attachment is made from the phosphate end.

General Molecule Building Functionality

Additional capabilities are available with **Edit Build** selected:

Multiple Fragments

Multiple fragments may result either from bond breakage (see **Break Bond** later in this chapter) or from use of the **Insert** key (**option** key on Mac), or *double clicking* in a blank area on screen. A fragment is selected by *clicking* on it, following which the associated free valences are colored yellow (free valences for any non-selected fragments are colored white). Rotation and translation apply to the entire set of fragments, but may be made to apply to the selected fragment (only) by holding down the **Ctrl** key while carrying out these operations.

Fragments may be attached using **Make Bond** (see discussion later in this chapter).

Rotate/Stretch Bonds

In addition to molecule rotation, translation and scaling, the mouse is used to rotate about and stretch bonds not incorporated into rings. This is accomplished via the following sequence of operations:

(i) *Clicking* on the bond, which is then marked by a red cylindrical arrow. (The bond connecting the last atom, group, ring or substituent added to the molecule is automatically selected.)

(ii) Bond rotation (only) follows from moving the cursor up and down inside the demarked area at the left of the screen while holding down the left button. Alternately, simultaneously holding down the **Alt** key (**option** key on Mac) and the left mouse button while *dragging* the mouse up and down, for bond rotation, or the **Alt** (**option**) key and the right mouse button for bond stretching.

Replace Atom/Fragment

Another function of the mouse is atom replacement. This behaves differently in the organic and inorganic model kits. *Double clicking* on an atom (not a free valence) while an atomic fragment in the organic model is highlighted, replaces the atom by selected fragment. Free valences are adjusted to accommodate the replacement, for example, replacement of sp^3 carbon by sp^3 oxygen results in two free valences being removed. Atom replacements that violate valence rules or that would disrupt substituents are not permitted. *Double clicking* on an atom (***not a free valence***) while an element in the *Periodic Table* from the inorganic model kit is selected, replaces the atom by the selected element, that is, changes the atomic number. No changes in the number or arrangement of free valences is made, and no checking is done. Atom replacement is not applicable to the peptide or nucleotide model kits.

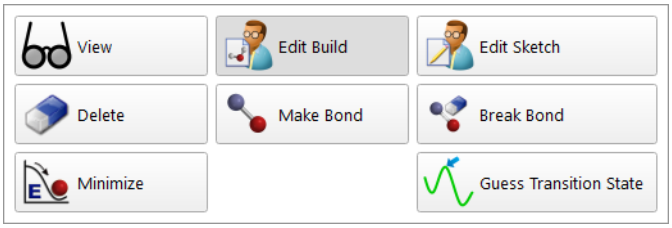
Invert Chirality

In the **Edit Build** mode, *double clicking* on a chiral atom with the **Ctrl** key (**Command** key on Mac) depressed inverts the chirality of the atom (R→S or S→R). *Double clicking* on any atom with both **Ctrl** (**Command** key on Mac) and **Shift** keys depressed inverts the absolute configuration of the molecule.

Replace *click* with *tap* and *double click* with *double tap* for multiple fragment, fragment replacement and chirality inversion. One finger movement up and down the shaded area at the left of the screen results in rotation about the marked bond.

Building/Editing Menu Functions

Molecule building/editing functions are found under the **Build** menu.



Icons for **Delete**, **Make Bond**, **Break Bond** and **Minimize** are also found at the bottom of the model kit. They may also be included in the icon toolbar at the top of the screen.

View ( )

This exits build mode, and removes the model kit from the screen and also adds hydrogens to any open valences (one does ***not*** need to explicitly add hydrogens).

Initial entry into the 3D builder is by way of **New Build** or **Build New Molecule** under the **File** menu (**Chapter 3**). **Edit Build**, **Delete**, **Make Bond**, **Break Bond** and **Minimize** are for modifying existing structures.

Edit Build ( )

In addition to the capabilities discussed under **General Molecule Building Functionality**, this allows access to the libraries of atomic fragments, groups, rings, ligands and substituents, as well as the file system and the clipboard. *Clicking* on any buttons or menus in the organic, inorganic, peptide, nucleotide or substituent model kits, leads to **Edit Build**. (If a model kit is not already on screen, selection brings up the last-accessed model kit.) A

fragment may be used to initiate building by *double-clicking* anywhere on screen, to add alongside an existing structure on screen by holding down the **Insert** key (**option** key on Mac) and by *clicking* anywhere on screen, or by *double clicking* in a blank area on screen, or be added to an existing structure by *clicking* on the appropriate free valence. Fragment addition can be terminated by selection of any other function.

Edit Sketch ()

This allows a 2D sketch to be modified in the 2D sketcher after it has been converted to a 3D structure. **Edit Sketch** is unavailable when the existing 3D molecule contains more than 250 atoms.

Delete ()

This allows atom and free valence removal from a structure. Selection leads to a message at the bottom left of the screen.

Subsequent *clicking* on an atom or free valence results in its deletion. Deletion of an atom results in deletion of all of its associated free valences. Free valences for any atoms to which the deleted atom was previously connected are restored. Note that atom deletion may result in one or more detached fragments. Selection of **Delete** does not bring up a model kit nor does it remove a model kit that is present on screen. **Delete** is (by default) a one-time operation. *Double-clicking* on the **Delete** icon will hold the delete mode open until the user selects another mode (for example  to **View**, or  to return to **Edit Build)**.

> **Delete** is also used to delete points and planes.

Deletion may also be accomplished by holding down on the **Delete** key (on the keyboard) while *clicking* on the item to be deleted. This mode (also) allows multiple deletions.

Make Bond ( )

This allows bonds to be drawn between free valences and/or atoms. Selection leads to a message at the bottom left of the screen.

Select two free valences.

Clicking on two free valences (on different atoms) will cause these atoms to be linked by a single bond. Alternatively, *double clicking* on each of two atoms will bond them, and *clicking* on a free valence on one atom and *double clicking* on a different atom will bond the two atoms. Note that available free valences are consumed as a result of bond formation, irrespective of whether free valences or atoms are selected.* If the selected atoms are already bonded, this will result in the bond order being increased by one, that is, single → double, double → triple. Selection of **Make Bond** does not bring up a model kit nor does it remove a model kit that is already present on screen. **Make Bond** may be terminated by selection of any other function.

Break Bond ( )

This allows breaking an existing bond resulting in free valences. Selection leads to a message at the bottom left of the screen.

Select bond to break.

Clicking on a bond breaks it and restores free valences. Note that bond breaking may result in detached fragments. Selection of **Break Bond** does not bring up a model kit nor does it remove a model kit that is present on screen. **Break Bond** may be terminated by selection of any other function.

Replace *click* with *tap* and *double click* with *double tap* for delete, make bond and break bond operations.

* Free valences can be protected without altering the molecule by adding hydrogens to them (-H from the organic model kit).

Minimize ( )

This uses molecular mechanics to refine the geometry. Selection leads to a message at the bottom left of the screen.

The molecular mechanics energy* in kJ/mol, displayed at the bottom right of the screen, is continually updated during the minimization process. Minimization may be stopped at any time by *clicking* on the icon at the bottom right of the screen. Any geometrical constraints imposed on the structure (see **Constrain Distance**, **Constrain Angle**, **Constrain Dihedral** under the **Geometry** menu; **Chapter 6**) are enforced during minimization. Also, any frozen atoms in the structure (see **Freeze Center** under the **Geometry** menu; **Chapter 6**) remain frozen.

Guess Transition State ( )

Spartan Student provides a facility for automatically guessing the geometries of transition states based on the similarity of the reaction of interest with one or more entries in ***Spartan Student***'s reaction database. Where an exact match is not available, ***Spartan Student*** will attempt to provide as close a match as possible. This will generally involve a less substituted system or one in which substituents differ. Here, the procedure is to use those parts of the structure of the transition state in the database that are common, and to optimize the remaining parts (using molecular mechanics).

> It may be essential for the reactants to be properly oriented to reflect the desired stereochemical outcome of the reaction.

Where a reaction is completely unknown to the database, a fallback technique (the linear synchronous transit method) is automatically invoked.

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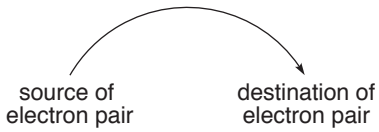
* The mechanics energy is a combination of the strain energy which is either zero or positive and the non-bonded or intramolecular interaction energy which can be either positive or negative. It will most commonly be a positive quantity, although it can be slightly negative.

Input to ***Spartan Student's*** transition-state guessing procedure will be familiar to organic chemistry students (and organic chemists), in that it is based on reaction arrows. The reaction is specified using curved arrows, where each arrow identifies the movement of one electron pair. The direction of electron flow follows customary practice:

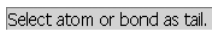


There are two possible sources of an electron pair and three possible destinations, leading to six combinations:

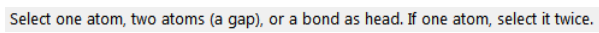
lone pair → lone pair	move lone pair
lone pair → bond	use lone pair to increase bond order
lone pair → space between atoms	use lone pair to make a new (single) bond
bond → lone pair	decrease bond order to make lone pair
bond → bond	decrease bond order of one bond to increase bond order of another bond
bond → space between atoms	decrease bond order to make a new (single) bond

The first of these is a null operation, and its inclusion has no effect.

Selecting **Guess Transition State** results in a message at the bottom left of the screen.



The tail of the arrow corresponds to the source of the electron pair. If the source is a lone pair, then select (*click* on) the atom that holds the lone pair. If the source is a bond, then select (*click* on) the bond. *Clicking* on an atom or bond highlights (colors gold) the atom or bond and leads to a new message at the bottom left of the screen. *Clicking* again on the same atom or bond deselects (de-highlights) it and leads back to the first message.



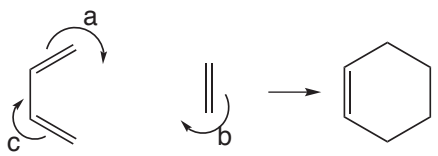
The head of the arrow corresponds to the destination of the electron pair. If the destination is an atom (leading to a lone pair), then select (*click* on) the atom that will hold the lone pair two times. If the destination is an existing bond (leading to an increase in bond order from single → double → or double → triple), then select (*click* on) the bond. If no bond presently exists, then select (*click* on) the two atoms that will become bonded upon reaction. These operations result in a curved arrow being drawn on the reactant structure. This extends from an atom, or the center of a bond to an atom, or the center of a bond, or the center of a dotted line that has been drawn between atoms that are to be bonded. The original message returns to the bottom left of the screen.

The process (tail selection followed by head selection) is repeated as necessary to fully define the reaction. Incorrect reaction arrows may be removed by selecting **Delete** from the **Build** menu ( ) followed by *clicking* on the arrow to be deleted. You can also use the **Undo** feature ( ). Alternatively, *click* on the arrow(s) to be deleted while holding down the **Delete** key on your keyboard.

After all reaction arrows have been properly designated, *click* on the **Search Transition State** icon ( ) at the bottom right of the screen to replace the reactant with a guess at the transition state. In the event that the guess is unreasonable, this operation may be undone with the **Undo** feature ( ). This allows you to review your assignment of arrows and make changes as needed.

Examples

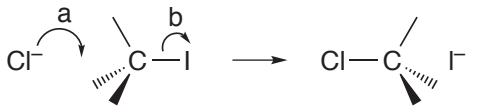
Diels-Alder reaction of 1,3-butadiene and ethylene



a, b. double bond to empty space leading to a single bond and to a new single bond

c. double bond to single bond leading to a single bond and a double bond

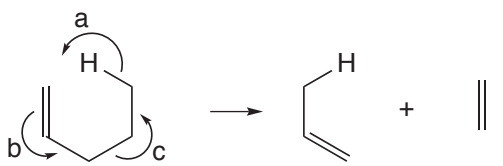
S_N2 reaction of chloride and methyl iodide



a. atom to empty space leading to a new single bond

b. single bond to an atom leading to the loss of the single bond

Ene reaction of 1-pentene

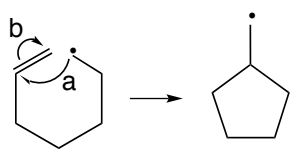


a. single bond to empty space leading to loss of the single bond and to a new single bond

b. double bond to single bond leading to a single bond and a double bond

c. single bond to single bond leading to loss of the single bond and to a double bond

Ring closure of 1-hexenyl radical to methylcyclopentyl radical



a. atom to empty space leading to a new single bond

b. double bond to an atom leading to a single bond

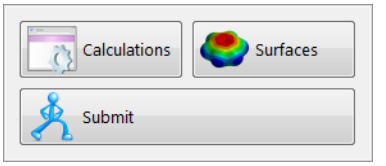
Chapter 8

The Setup Menu

This chapter describes functions available under the ***Setup*** *menu.* ***Calculations...*** *is used to specify MMFF molecular mechanics calculations, PM3 semi-empirical molecular orbital calculations, Hartree-Fock molecular orbital calculations, B3LYP, EDF2, and ωB97X-D density functional calculations, MP2 and T1 thermochemical recipe calculations. Tasks include calculating energy, equilibrium geometry, equilibrium conformation, conformer distribution, and transition-state geometry, enumerating accessible conformers and constructing energy profiles. STO-3G, 3-21G, 6-31G* and 6-311+G** basis sets are provided for Hartree-Fock calculations and 6-31G* and 6-311+G** basis sets for B3LYP, EDF2, ωB97X-D and MP2 calculations. Hartree-Fock and density functional calculations may be carried out in solvent as well as in the gas. Not all methods are applicable to all tasks.* ***Calculations...*** *also optionally requests IR and NMR spectra, QSAR properties.*

Surfaces *is used to designate graphical surfaces, including electron and spin densities, electrostatic potentials, local ionization potentials and molecular orbitals, for later display as surfaces, property maps and contour plots. Inaccessible regions on electron density surfaces and property maps based on these surfaces may be demarked.*

Submit *is used to initiate calculation.*



Calculations... ()

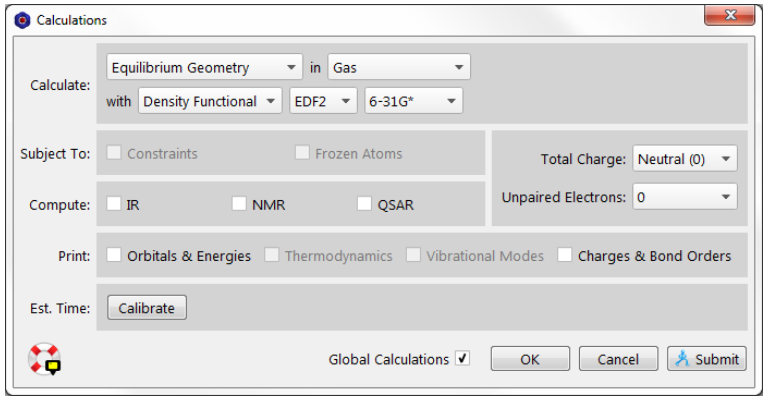
The MMFF molecular mechanics model, the PM3 semi-empirical molecular orbital model, Hartree-Fock molecular orbital models, B3LYP. EDF2 and ωB97X-D density functional models and MP2

Møller-Plesset models are available to calculate energy, equilibrium geometry and make energy profiles. All models except MMFF are available for calculating transition state geometry. The MMFF molecular mechanics model is also available to calculate equilibrium conformation or conformer distribution. STO-3G, 3-21G, 6-31G* and 6-311+G** basis sets are available for Hartree-Fock calculations and 6-31G* and 6-311+G** basis sets for B3LYP, EDF2, ωB97X-D and MP2 calculations. The T1 recipe (although including an equilibrium geometry task) is only available when the task specified is an energy calculation.

Hartree-Fock and density functional calculations, aside from NMR calculations, may be carried out in solvent according to the C-PCM model.

Quantum chemical calculations also provide atomic charges, IR and NMR spectra. IR spectra are available for all models but NMR spectra are only available for Hartree-Fock or density functional models.

Selection of **Calculations...** results in the **Calculations** dialog.

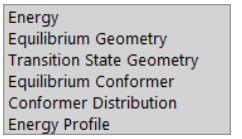


This contains pull-down menus, buttons and check boxes:

Calculate

This section is used to specify the task to be accomplished, theoretical model to be employed and spectra to be supplied.

Specification of a task is by way of a pull-down menu:



Energy specifies calculation of energy (and in the case of quantum chemical methods, a wave function) at a single geometry.

Spartan Student reports energies from molecular mechanics calculations in kJ/mol, from semi-empirical calculations as heats of formation in kJ/mol, and from Hartree-Fock, B3LYP, EDF2, ωB97X-D and MP2 calculations as total energies in atomic units (hartrees).

The molecular mechanics energy comprises two parts: the strain energy and the non-bonded energy. The strain energy is the difference in energy between a molecule and its "strain free" analog. It is nearly always positive and less than a few hundred kJ/mols in magnitude. The non-bonded energy accounts for attraction or repulsion between atomic centers that are not connected due to van der Waals and Coulombic interactions. Because the strain energy of every molecule relates to a different standard, molecular mechanics energies cannot be used to obtain reaction energies (unless there are no changes in bonding between reactants and products).

The heat of formation is to the enthalpy at 298K of a balanced chemical reaction in which a molecule is converted to a set of standard products. For example, the heat of formation of ethylene is given by reaction,

$$C_2H_4 + \rightarrow 2C\ (\text{graphite}) + 2H_2\ (\text{gas})$$

where graphite and hydrogen molecule are the carbon and hydrogen standards, respectively. In practice, the actual measurement is typically carried out for a combustion reaction, for example, for ethylene:

$$C_2H_4 + 3O_2 \rightarrow 2CO_2 + 2H_2O$$

Heats of formation may be either positive or negative quantities and generally span a range of only a few hundred kJ/mol.

Heats of formation are not suitable for presenting energy data from quantum chemical calculations, simply because the standards for several important elements (most notably, carbon) are not well-defined isolated species. In its place is the energy of a reaction that splits a molecule into isolated nuclei and electrons, for example, for ethylene:

$$C_2H_4 \rightarrow 2C^{+6} + 4H^{+} + 16e^{-}$$

Total energies, as the energies of such reactions are termed, are always negative and may be very large (tens of thousands of kJ/mol). They are

most commonly given in atomic units (hartrees).

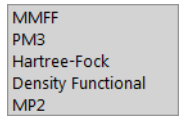
1 atomic unit = 2625 kJ/mol

It is possible to relate total energies to heats of formation by incorporating data on atomic species. Heats of formation reported from T1 calculations (part of the information provided in ***Spartan Student's*** database) relate directly to experimental heats and are given in kJ/mol.

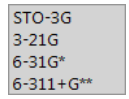
To summarize, the heat of formation differs from the total energy both with regard to the standard reaction and with regard to units. Either provides a suitable basis for thermochemical calculations.

Equilibrium Geometry specifies that the nearest energy minimum will be located, **Equilibrium Conformer** specifies that the lowest energy conformer will be located and **Transition State Geometry** specifies that the nearest transition state (energy maximum in one dimension and energy minima in all other dimensions) will be located. **Energy Profile** steps along user-defined coordinates.

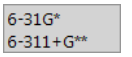
Except for **Equilibrium Conformer** and **Conformer Distribution**, a theoretical model needs to be specified by way of pull-down menus. (**Equilibrium Conformer** and **Conformer Distribution** are limited to MMFF Molecular Mechanics.) The first provides a choice among different classes of models.



Selection of **Molecular Mechanics** leads to a single method, MMFF. Selection of **Semi-Empirical** leads to a single method, PM3. Selection of **Hartree-Fock** leads to a second menu of available basis sets.



Selection of either **B3LYP, EDF2, ωB97X-D** or **MP2** leads to an abbreviated menu of available basis sets.



Transition State Geometry is not available for **Molecular Mechanics**. Use of solvent is available for **Hartree-Fock** and **Density Functional** models.

Spectra

If *checked*, **Infrared Spectra** calculates vibrational frequencies and intensities together with the corresponding vibrational modes. These are available in the output (**Output** under the **Display** menu; **Chapter 9**) along with zero-point energies and thermodynamic properties (enthalpies, entropies, heat capacities and Gibbs energies). Vibrational motions (***normal modes***) may be animated and an IR spectrum displayed from the **IR** dialog accessible from **Spectra** under the **Display** menu (**Chapter 9**). Frequency calculations involving MP2 models are very costly in terms of computation and are not recommended.

Infrared frequencies from B3LYP/6-31G*, EDF2/6-31G*, and ωB97X-D/6-31G* calculations have been uniformly scaled to account for known systematic errors. Calculated frequencies from all other models have not been scaled. The lines in the calculated infrared spectrum obtained from all models have been broadened to account for the fact that the calculations correspond to 0K, whereas experimental measurements are carried out at finite temperature.

If *checked*, **NMR Spectra** specifies that NMR chemical shifts will be calculated. These are then available in the output (**Output** under the **Display** menu; **Chapter 9**) as well as from the **Atom Properties** dialog (**Display** menu) and as atom labels (**Configure...** under the **Model** menu; **Chapter 5**). ^{13}C (proton decoupled) and ^{1}H spectra may be displayed from the **NMR Spectra** pane accessible from **Spectra** under the **Display** menu (**Chapter 9**)*. For density functional calculations with the 6-31G* basis set, ^{13}C, chemical

* Chemical shifts for other nuclei are available in the **Output** dialog (**Output** under the **Display** menu) and may also be attached as labels (**Configure...** under the **Model** menu; **Chapter 5**).

shifts have been empirically corrected for local environment. Line intensities are assumed to be proportional to the number of equivalent carbons or hydrogens. Three-bond HH coupling constants for ^{1}H spectra are estimated empirically and these have been used to simulate splitting patterns.

If *checked*, **UV/vis** specifies that a UV/vis spectrum will be calculated based on the following procedure: energy calculations at the ground state and the first twenty (20) excited states are performed using time dependent density functional theory, specifically B3LYP/6-31+G*. Corresponding wavelength and intensity data are used to generate a calculated UV/visible spectrum.

QSAR

If *checked*, calculates a number of wave function-based properties accessible from the **QSAR** tab in the **Molecular Properties** dialog (**Chapter 9**).

Total Charge

Total charge. The default setting (**Neutral**) may be changed either by *clicking* on , and selecting **Anion**, **Dianion**, **-3**, etc. from the menu, or by typing a number in the. **Total Charge** is ignored for molecular mechanics calculations.

Unpaired Electrons

The number of unpaired electrons. The default setting (**0**) may be changed either by *clicking* on , and selecting **1** or **2** from the menu, or by typing in the menu. **Unpaired Electrons** is ignored for molecular mechanics calculations.

Global Calculations

If *checked*, signifies that settings in the **Calculations** dialog are to be applied to all molecules in the document.

The **Calculations** dialog may be exited by clicking on **Submit**, **Cancel** or **OK** at the bottom right of the dialog, or on at the top. (**Submit** and **OK** are not available if the job is already

executing.) Clicking on **OK** or on **Submit** overwrites any previous information. Additionally, **Submit** enters the job in the execution queue (see discussion later this chapter). Clicking on **Cancel** or on  exits the **Calculations** dialog without saving any changes.

Calibrate/Est. Time

The **Calibrate** feature runs a single back-end calculation that should take no more than 30 seconds. This is compared against a reference calculation and is used to provide an estimate of how long a specified calculation will take. Once calibrated, all future specified calculations will include an **Est. Time**.

Surfaces ()

Spartan Student allows graphical display of the HOMO and LUMO among other molecular orbitals, the electron density, the spin density for molecules with unpaired electrons, the electrostatic potential and the local ionization potential.

The ***electron density*** is the number of electrons found at a point in space. It is the quantity measured in an X-ray diffraction experiment that is then used to locate atomic positions, that is, most electrons are closely associated with atoms. While the electron density is non-zero everywhere, it is possible to define surfaces of constant density. The most important of these contains most of a molecule's electrons and that roughly corresponds to a space-filling model, that is, a van der Waals surface. We will refer to this as the ***electron density***. It is interesting because it reveals overall molecular size and shape and demarks the steric barrier seen by encroaching molecules. Another important surface, that we will refer to as the ***bond density***, contains fewer electrons in total and demarks atomic connectivity.

The ***spin density*** is the difference in the number of electrons of α and β spin at a point in space. It indicates the location of the unpaired electron in a radical or unpaired electrons in a triplet.

The ***electrostatic potential*** is the energy of interaction of a positive charge with a molecule. This assumes a fixed electron distribution for the molecule. It represents a balance between repulsive interactions involving the positively-charged nuclei and attractive interactions involving the negatively-charged electrons. Regions where the balance tips toward

attraction are said to be electron rich (basic) and subject to attack by electrophiles, while regions where the balance tips toward repulsion are said to be electron poor (acidic) and subject to attack by nucleophiles. Electron-rich regions such as lone pairs are typically located outside the van der Waals surface. As such, they may be easily identified by constructing a surface of negative (attractive) electrostatic potential. While interesting electron-poor areas such as acidic hydrogens also lie outside the van der Waals surface, the electrostatic potential is also positive (repulsive) throughout the region inside this surface.

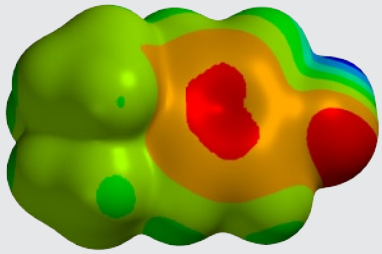
The ***local ionization potential*** indicates the ease or difficulty of electron removal (ionization). Like the negative regions of the electrostatic potential, regions of low local ionization potential are likely to be subject to attack by electrophiles.

Note that neither electrostatic potential nor the local ionization potential are experimental observables, although they relate to quantities that can be given clear chemical interpretation.

Additionally, any one of the quantities listed above (except the electron density) may be mapped onto any surface (except a molecular orbital surface). In practice, the only maps to have received widespread attention are those based on the electron density surface (depicting overall molecular size and shape). Most common are the electrostatic potential map, the local ionization potential map and the LUMO map. Some regions of an electron density surface are inaccessible and are not available for interaction with their environment (or with an incoming reagent). ***Spartan Student*** allows these regions to be identified.*

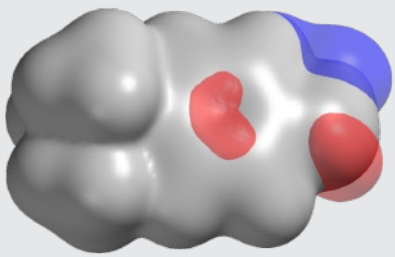
The ***electrostatic potential map*** paints the value of the electrostatic potential onto an electron density surface. By convention, colors toward red depict negative potential, while colors toward blue depict positive potential, and colors in between (orange, yellow, green) depict intermediate values of the potential. Thus, an electrostatic potential map for *p*-*tert*-butylphenol will show oxygen to be red, its attached (acidic) hydrogen to be blue, the π faces of benzene to be orange or yellow and the *tert*-butyl group to be green.

* A region on a density surface is designated as inaccessible if a sphere of radius 1.0 Å centered on a line normal to the surface and touching a point in the middle of the region, impinges on any other regions of the density surface. The sphere radius may be changed in the **Settings** tab (**Preferences** under the **Options** menu; **Chapter 10**).



The main advantages of this presentation relative to separate electron density and electrostatic potential surfaces are its clarity and its compactness. A disadvantage is that it provides information only about the contact surface and does not reveal how far electron-rich and electron-poor areas extend beyond the surface.

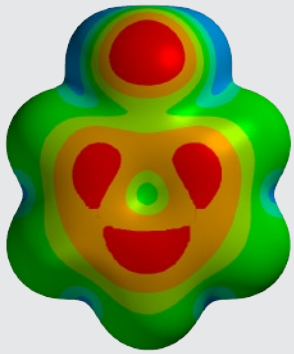
An alternative to an electrostatic potential map, referred to as an ***exposed electrostatic potential surface***, is a composite of three different surfaces: an electron density surface depicting overall molecular size and shape, a negative electrostatic potential surface identifying electron-rich regions and a positive electrostatic potential surface identifying electron-poor regions. These surfaces need to be generated and then displayed simultaneously. The electron density may either be displayed as an opaque solid or as a transparent solid (in order that the molecular skeleton may be seen inside). The two potential surfaces are best represented as transparent solids, the negative surface colored red and the positive surface colored blue. The exposed electrostatic potential surface for *p-tert*-butyl phenol is shown below.



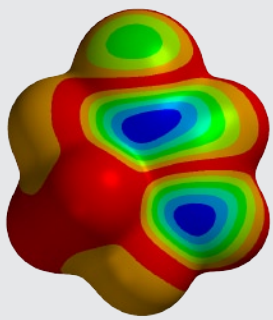
Note that the exposed electrostatic potential surface provides the same information as the electrostatic potential map. Red areas in the map correspond to regions when the negative electrostatic potential surface is likely to protrude from the electron density while blue areas correspond to regions where the positive electrostatic potential surface is likely to stick out.

The ***local ionization potential map*** paints the value of the local ionization potential onto an electron density surface. By convention, colors toward

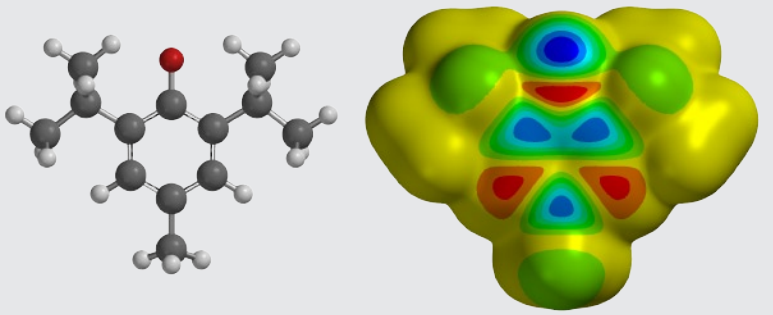
red indicate low ionization potential, while colors toward blue indicate high ionization potential. Thus, the local ionization potential map for aniline shows that the *ortho* and *para* ring positions have a lower ionization potential than the *meta* positions, consistent with the known directing ability of an amino group in electrophilic aromatic substitution.



The ***|LUMO| map*** paints the absolute value of the lowest-unoccupied molecular orbital (the LUMO) onto an electron density surface. By convention, colors near blue indicate high concentration of the LUMO, while colors near red indicate low concentration. Given that the LUMO designates space available for a pair of electrons, a |LUMO| map indicates where nucleophilic attack would likely occur. For example, a |LUMO| map for cyclohexenone shows concentration in two regions, one over the carbonyl carbon and the other over the β carbon, consistent with both carbonyl addition and Michael (conjugate) addition.



The ***spin density map*** paints the value of the spin density onto an electron density surface. By convention, colors near blue indicate high concentration of spin density, while colors near red indicate low concentration. For example, a spin density map for the radical resulting from loss of hydrogen from 3,5-di-*tert*-butylhydroxytoluene (BHT) shows that the spin has delocalized from oxygen onto the *ortho* and *para* ring positions.



This radical would be expected to be particularly stable, which explains why BHT acts as an antioxidant (scavenging less favorable localized radicals).

Surfaces (including those underlying maps) connect points of equal value (they are isosurfaces), and may be displayed as an arrangement of dots, a mesh, or an opaque or translucent solid. Examples of graphical output in orthogonal projection are provided in **Figure 8-1**. Surfaces (and maps) may also be rendered in perspective (see **Chapter 5**) and in stereo (see **Chapter 2**).

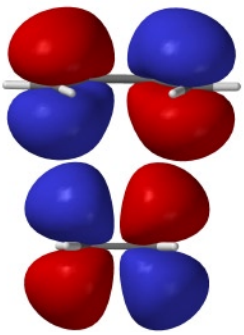
Calculated quantities may also be displayed as two dimensional contour plots (slices). Unlike surfaces and maps, these can be translated, rotated and zoomed independently of the molecular skeleton. An example of a slice display is provided in **Figure 8-1**.

Several different surfaces, maps and slices may be simultaneously displayed. In addition, any of the usual structure models may be displayed along with the graphic. The total display can become very complex, and selective use of meshes and/or translucent solids (as opposed to opaque solids) may facilitate improved visualization.

Selection of **Surfaces** leads to the **Surfaces** dialog.

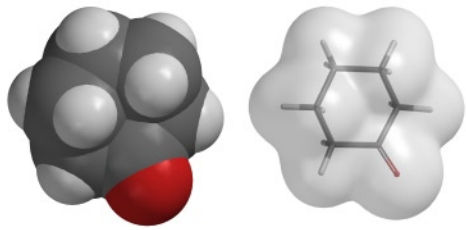
Figure 8-1: Examples of Graphical Displays Available in *Spartan Student*

Frontier orbitals for a symmetry-allowed Diels-Alder reaction,



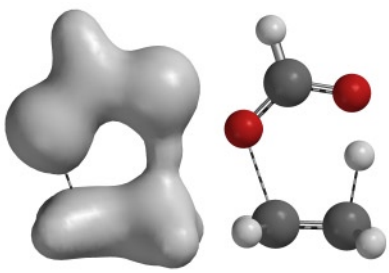
showing interaction of the HOMO of 1,3-butadiene and the LUMO of ethylene.

Space-filling model and electron density surface of cyclohexanone,



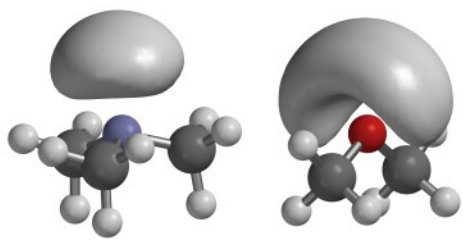
showing overall molecular size and shape.

Electron density surface (0.08 electrons/au^3) of transition structure for pyrolysis of ethyl formate,



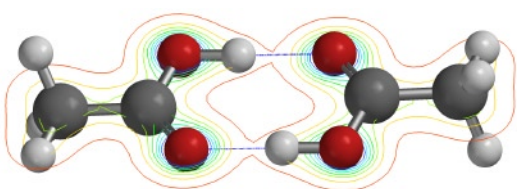
showing bonding in the transition state.

Electrostatic potential surfaces (-40 kJ/mol) of trimethylamine (left) and dimethyl ether (right),



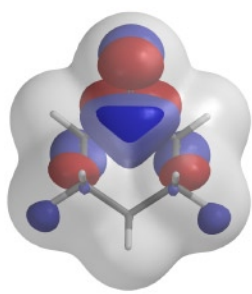
showing the lone pairs on nitrogen and oxygen, respectively.

Electron density slice for acetic acid dimer,

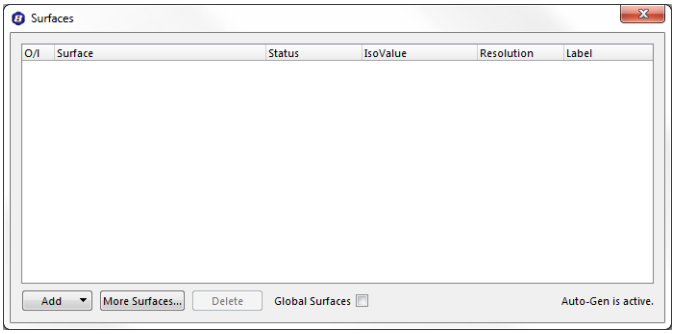


showing hydrogen bonding.

Simultaneous display of the LUMO and the electron density surfaces of cyclohexanone,



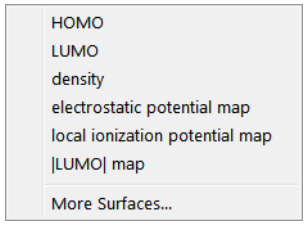
showing accessibility for nucleophilic attack.



This contains a box at the top for listing requested surfaces and property maps.

Common Surfaces and Property Maps

Add at the bottom of the dialog is used to specify a number of commonly-used graphical surfaces and property maps*. *Clicking* on it leads to a menu.

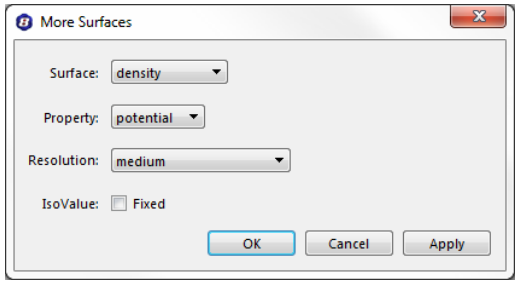


Selection of all but the last entry in the menu leads to a request for the analogous surface or map. A surface and property map specified from this menu will be calculated at medium resolution and will assume a fixed isovalue unless a different resolution has been selected and/or an adjustable isovalue has been requested.

More Surfaces

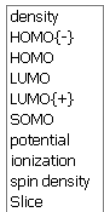
Additional surfaces and maps or the same surfaces or maps at different resolution and with adjustable isosurfaces may be requested by selecting **More Surfaces...** from the menu (or by *clicking* on **More Surfaces...** at the bottom of the **Surfaces** dialog). This leads to the **Add Surfaces** dialog that contains three menus and a check box:

* Additional selections are provided if the molecule has unpaired electrons.



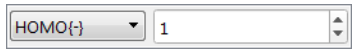
Surface

Available surface types appear under the **Surface** menu.



Density is the total electron density which may be used to reveal bonding as well as overall molecular size and shape, ***HOMO{-}, HOMO, LUMO, LUMO{+}, SOMO**** are molecular orbitals, ***potential*** is the electrostatic potential, ***ionization*** is the local ionization potential and ***spin density**** is the spin density.

Selection of **HOMO{-}** and **LUMO{+}** results in display of a box to decrement the HOMO and increment the LUMO. This allows any molecular orbital to be specified..

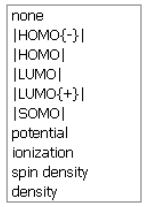


Slice designates that a plane will cut through the graphic defined by **Property**.

Property

Properties for maps appear in the **Property** menu.

* These menu entries appear only for molecules with one or more unpaired electrons.

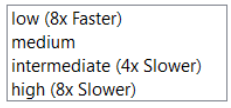


Available properties are the molecular orbitals (**HOMO{-}**, **HOMO**, **LUMO**, **LUMO{+}**, **SOMO**[*]), the electrostatic potential (**potential**), the local ionization potential (**ionization**) and the spin density (**spin density**)[*]. **none** indicates that no property is to be mapped onto the surface). As with **Surface** above, selection of **HOMO{-}** and **LUMO{+}** leads to a decrement (increment) box.

A **Spin** button will be displayed if **Unpaired Electrons** (in the **Calculations** dialog) is set to a value other than **0**, and if **HOMO{-}**, **HOMO**, **LUMO** or **LUMO{+}** has been selected for **Surface** or for **Property**. *Clicking* on **Spin** toggles it between **Alpha** and **Beta**. **Alpha** designates that the molecular orbital either to be displayed as a surface or mapped as a property corresponds to α spin; **Beta** designates that the molecular orbital corresponds to β spin.

Resolution

Selection of surface resolution is from the **Resolution** menu.



High resolution is desirable for surfaces based on percentage enclosure. Both calculation time and disk storage increase significantly in moving from medium to high resolution.

Isovalue

Checking the box to the left of **Fixed** specifies calculation of a surface with fixed isovalue. In the case of a density surface, the default value of 0.002 electrons/bohr^3 corresponds roughly to enclosure of 99% of the total number of electrons and closely resembles a space-filling model. Fixed surfaces take less time to compute and require less storage.

Following **Surface**, **Property**, **Resolution**, **Isovalue** and (optionally) spin selection, *clicking* on **OK** adds the requested surface to the list and removes the (**Add Surfaces**) dialog. *Clicking* on **Apply** adds the requested graphic to the list but leaves the dialog on screen. *Clicking* on **Cancel** does not add a graphic to the list but removes the (**Add Surfaces**) dialog.

The process (*clicking* on **Add...**, followed by selection from the menu or *clicking* on **More Surfaces...** followed by selection of surface, property, resolution and isovalue and *clicking* on **OK** or **Apply**) may be repeated as required.

An existing surface may be deleted from the list by first highlighting (*clicking* on) it and then *clicking* on **Delete**.

Global Surfaces

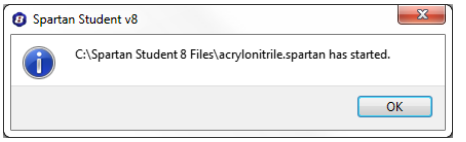
If *checked*, signifies that the requested surfaces will be calculated for all members of the list.

Only one copy of the **Surfaces** dialog may appear on screen, and any actions relate to the currently selected molecule. The dialog may be removed by *clicking* on  .

Submit ()

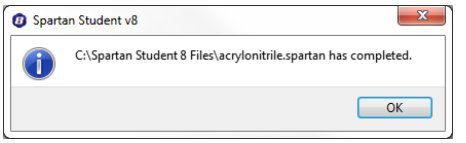
Following setup of a molecular mechanics or quantum chemical calculation, including any requests for spectra and/or graphical displays, the required calculations will begin when **Submit** is selected. If the job has not previously been saved or submitted, selection of **Submit** triggers a request for a name. If the document contains only a single molecule and that molecule exists in the Spartan Spectra and Properties Database, the name in the database will be presented as a default name. Otherwise, the default name presented will be ***spartan*** for the first job and ***spartanx*** (where x is an integer starting with 1) for all successive jobs. After a name has been provided (or the document is saved) a dialog appears indicating that the job has actually been submitted.*

* The job is submitted to a job queue and will begin when released from this queue. See **Monitor** under the **Options** menu (**Chapter 10**) for discussion.



The message will close after 5 seconds, or you may *click* on **OK** to remove it. After a job has started, and until it has completed, all associated files will be designated read only.

Another dialog appears following completion of a calculation.

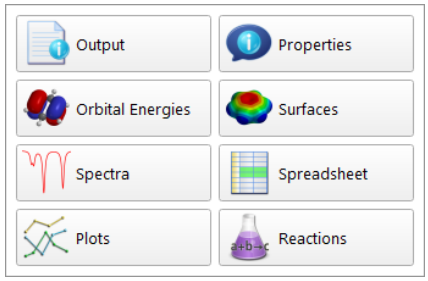


Click on **OK** to remove it.

Upon completion, an energy profile calculation leads to an additional document being created for each molecule in the original document. These new documents are named ***document.Prof.spartan*** where ***document*** is the name given to the original document . A query dialog is provided asking whether the resulting document is to be opened. Similarly, upon completion of a conformer distribution calculation, a new document named ***document.Conf.spartan*** is created, and a prompt to open is provided.

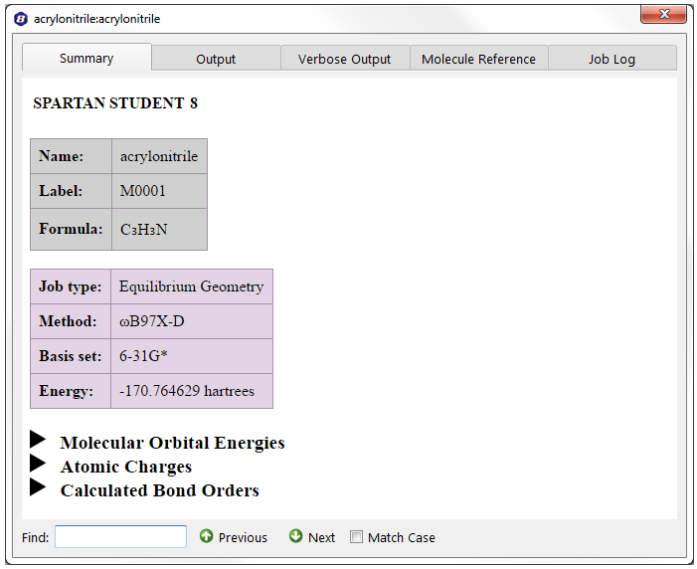
Chapter 9
The Display Menu

*Functions available under the **Display** menu provide for text, dialog, spreadsheet and graphical displays. Functions are also available to query a variety of on-screen objects, display both calculated and (if available) experimental IR and NMR spectra, animate vibrational motions, prepare plots from spreadsheet data and calculate reaction energies.*



Output ( )

Selection of **Output** opens a window:



Tabs at the top left of the window select the type of output.

Summary provides a brief summary of the calculated data, in particular, the energy and any spectral quantities. **Output** provides standard text output. **Verbose Output** contains more detailed output, but is eliminated upon normal completion unless **Keep Verbose** is checked in the **Settings** tab (**Preferences** under the **Options** menu; **Chapter 10**). **Molecule Reference** provides the literature reference for data retrieved from the PDB. **Job Log** contains diagnostic information.

The contents of the output window may be scrolled and may be paged up or down by *clicking* above or below the scroll bar. The contents may be printed or copied by *right clicking* inside the **Output** window and selecting **Print** or **Copy** from the menu that results. Similarly, copying is accomplished by selecting **Copy** from the **Edit** menu when an output is selected. **Find...** and **Find Next** functions from the **Edit** menu are also available.

Only one output window is associated with each document, and changes focus as different molecules from the document are selected. Output windows for different documents may be simultaneously open on screen. An output window may be closed by *clicking* on  .

Output for jobs that are executing may be viewed using the **Monitor** under the **Options** menu (**Chapter 10**).

Properties ()

Spartan Student provides specialized dialogs for reporting (and in some cases changing) the properties of molecules, atoms, bonds, surfaces and constraints. For plots brought into the main ***Spartan Student*** window from the spectra and plot panes, **Properties** may be used to change default plot styles, limits and fitting functions. Only one **Properties** dialog may be open, and this refers either to the selected molecule (**Molecule Properties**), or to the selected component (atom, bond, etc.) or attribute (spectra, graphical surface, constraint, etc.) of the selected molecule (**Atom Properties**, **Bond Properties**, **Surface Properties**, etc.), or to a plot (**Plot Properties**, **Curve Properties**, etc.), or fitting function (**Regression Properties**).

Selection of a different molecule leads to the **Molecule Properties** dialog for that molecule. Dialogs that refer to components/attributes of the (newly selected) molecule follow by *clicking* on the component/attribute.

With the **Molecule Properties** dialog on screen, *clicking* on a component/attribute brings up the appropriate **Properties** dialog. For example, *clicking* on an atom brings up the **Atom Properties** dialog. *Clicking* on a different component/attribute brings up the appropriate **Properties** dialog. *Clicking* a second time on the same component reverts back to the **Molecule Properties** dialog.*

Most **Properties** dialogs have an associated **Utilities** or **Style** toggle. For example, associated with the **Molecule Properties** dialog is a **Molecule Utilities** dialog. These access additional information about the molecule and its components/attributes, or provide style and color controls. This is useful for highlighting (or de-emphasize) a particular molecule, component or attribute. **Utilities**/**Style** dialogs are reached by *clicking* on  at the bottom right of the appropriate **Properties** dialog. Return to the **Properties** dialog follows from *clicking* on at the bottom right of the associated **Utilities**/**Style** dialog.

The **Properties** (or **Utilities**/**Style**) dialog may be removed from the screen by *clicking* on  .

Molecule Properties

The **Molecular Properties** dialog comprises four parts: **Molecule**, **QSAR**, **Thermodynamics** and **2D Drawing**, controlled by tabs at the top. Entries under the **Molecule** tab relate to common molecular properties, only some of which depend on the selected level of calculation.

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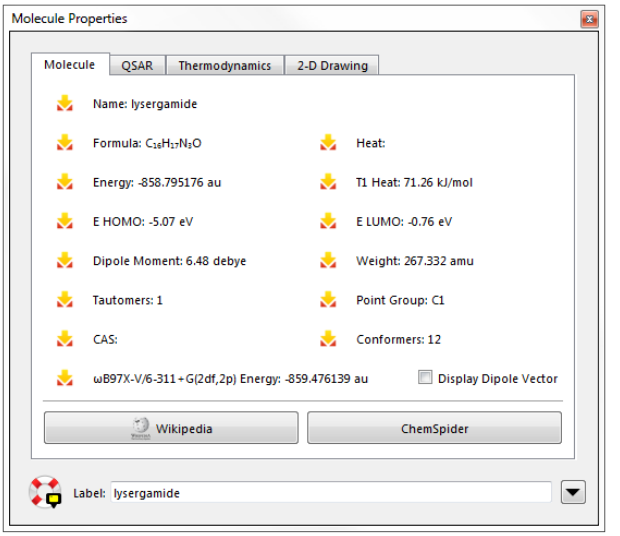
* The only exception involves *clicking* on a graphical surface or property map, for example, *clicking* on a property map to obtain the value of the property at a particular surface location. *Clicking* a second time on the surface or map will report a new value of the property. *Clicking* on the background leads to the **Molecule Properties** dialog.

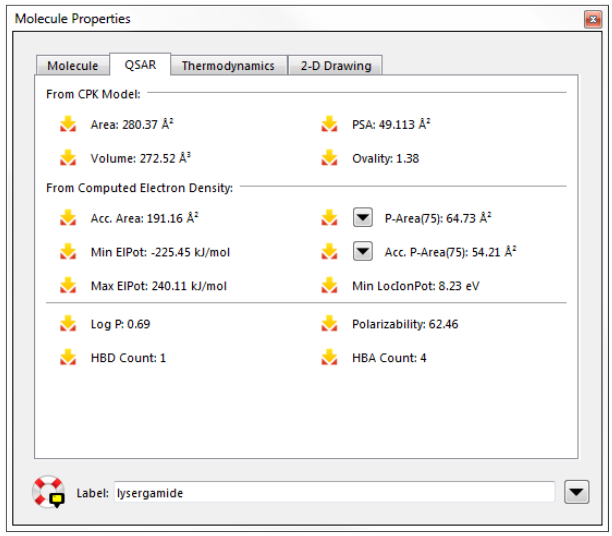
Molecule



Molecule properties include the name and molecular formula, the energy (the specifics of the type of energy and the units it is reported in depend on the theoretical model), the HOMO and LUMO energies (in eV), the dipole moment (in Debye), the molecular weight (in amu), the point group, the predicted number of (non-carbon) tautomers and the predicted number of conformers, and (if available) the experimental heat of formation (in kJ/mol), the heat of formation from the T1 thermochemical recipe (in kJ/mol) and the CAS number. These may be posted to the spreadsheet using the buttons, or *dragged* into the spreadsheet. The dipole moment vector may be added to the model by *checking* the box to the left of **Display Dipole Vector**. Buttons at the bottom right of the dialog access appropriate Wikipedia and ChemSpider pages based on InChi string. **Label** identifies the molecule in a document and appears in the first column of the spreadsheet (see **Spreadsheet**, later in this chapter).

QSAR

Entries under the **QSAR** tab provide additional properties, some of which may be particularly valuable in qualitative structure-activity relationship type analyses.



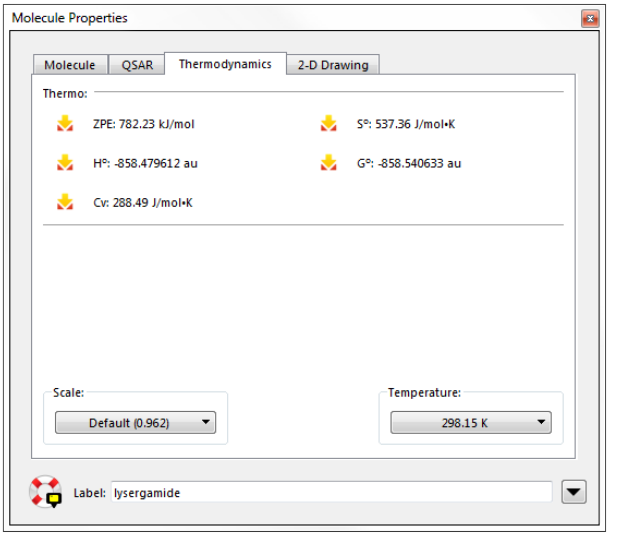
These include: the area, volume, polar surface area (PSA)* and ovality obtained from a space-filling model, and other structure-dependent indicators: LogP, polarizability and the number of hydrogen-bond donor (HBD) and acceptor sites (HBA).** All of these are independent of the level of calculation. Additional quantities which depend on the level of calculation and are based on the electron density surfaces as well as on electrostatic potential maps are also available: the accessible area, the polar area and accessible polar area corresponding to absolute values of the electrostatic potential greater than 75, 100 and 125 kJ/mol (selection is made by repeated *clicking* on ▼), the minimum and maximum values of the electrostatic potential (as mapped onto an electron density surface) and the minimum value of the local ionization potential (as mapped onto an electron density surface). These quantities are not calculated unless explicitly requested by checking **QSAR** inside the **Calculations** dialog (**Calculations...** under the **Setup** menu; **Chapter 8**).

* Polar surface area is defined as the area due to nitrogen and oxygen and any attached hydrogens. Polar surface areas corresponding to arbitrary alternative definitions are available for posting into the spreadsheet using the **PAREA** function. See **Table 22-3**.

** Counts of hydrogen-bond donors and acceptors.

Thermodynamics

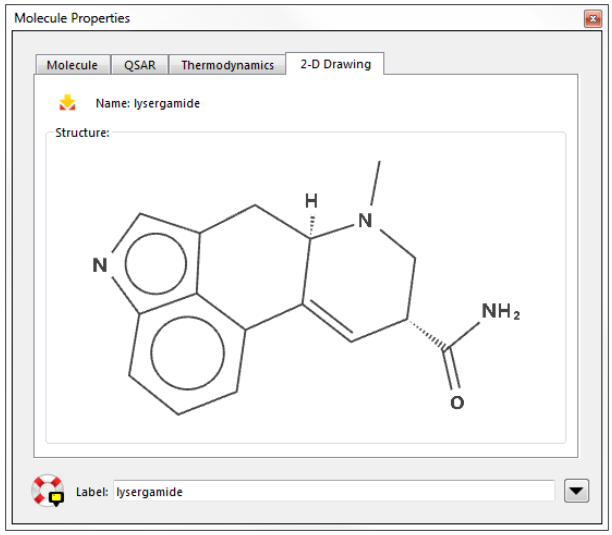
Entries under the **Thermodynamics** tab provide the zero-point energy, the enthalpy, the constant volume heat capacity, the entropy and the Gibbs energy. Except for the zero-point energy, all depend on temperature. The default setting (298.15 K) may be changed. All require vibrational frequencies. Density functional frequency calculations scaled by a number that is slightly smaller than 1 to account for systematic errors.



As discussed under **Properties and Spectra** in **Appendix A**, the entropy and Gibbs energy are subject to considerable uncertainty due to the underlying harmonic approximation.

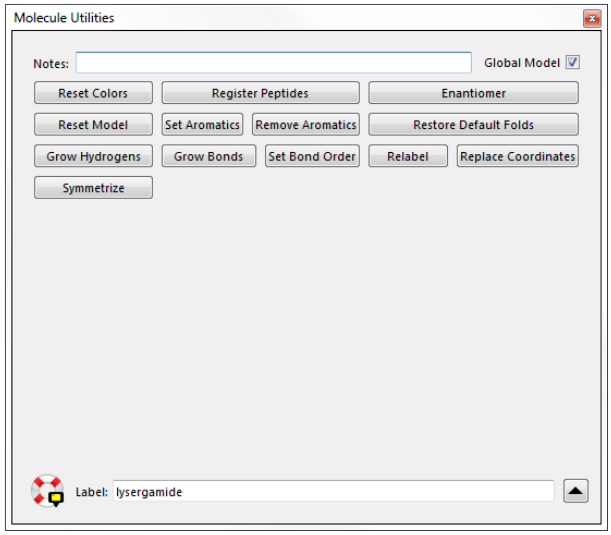
2D Drawing

Displays a 2D drawing for molecules up to 250 atoms.



Molecule Utilities

Clicking on ▼ at the bottom right of the **Molecule Properties** dialog brings up the **Molecule Utilities** dialog (*clicking* on ▲ returns to the **Molecule Properties** dialog).

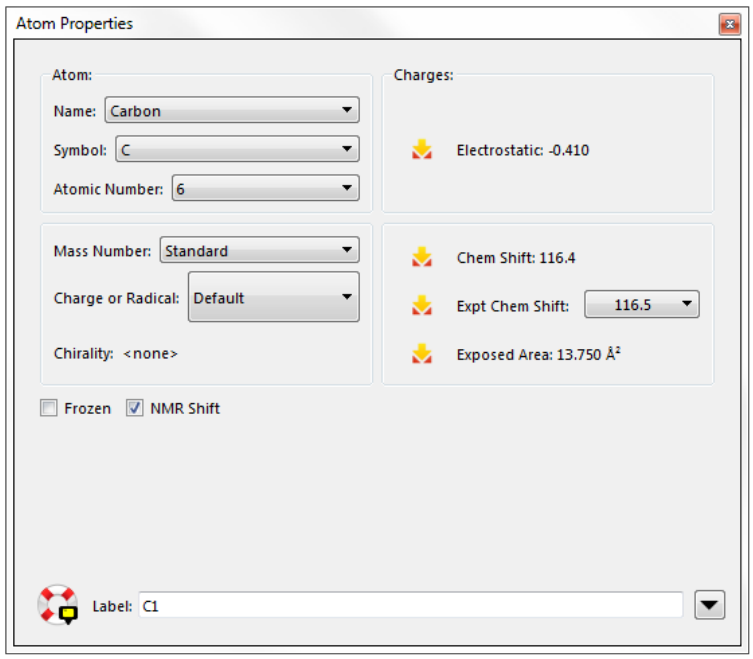


Notes is a user-supplied text string that is reproduced in the output. Controls reset model color and style, add missing hydrogens and

bonds, provide information about amino acids in polypeptides and replace coordinates by standards based only on atomic connectivity, change enantiomers, reset default conformer selections, relabel atoms, and attempt to find local symmetry.

Atom Properties

Selection of an atom with a **Properties** dialog on screen, or selection of **Properties** following selection of an atom, leads to the **Atom Properties** dialog.



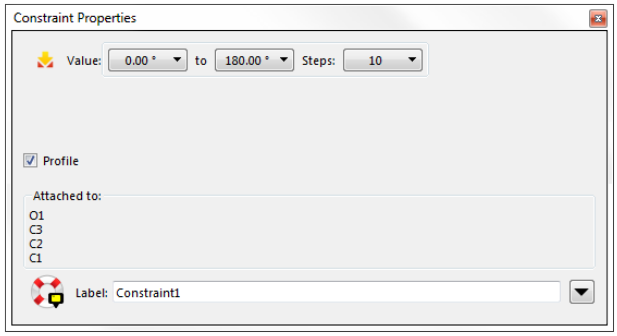
This displays the element name (and allows changing the element), R/S chirality, electrostatic-fit charges (in electrons), calculated NMR chemical shift (in ppm relative to the appropriate standard; tetramethylsilane for both proton and ^{13}C) and exposed surface area of a space-filling model (in $Å^2$). It also allows freezing the atom (see **Freeze Center** in **Chapter 6**), changing its mass number and the default label, setting an atom's charge or number of unpaired electrons, and posting atomic charges, chemical shifts and exposed areas to the spreadsheet.

Bond Properties

Selection of a bond with a **Properties** dialog on screen, or selection of **Properties** following selection of a bond leads to the **Bond Properties** dialog (not shown). This displays the bond length (in Å), Löwdin or Mulliken bond order (in electrons) and bond type (and allows changing the bond type). Note that the results of quantum chemical calculations do not depend on bond types.

Constraint Properties

Selection of a constraint marker with a **Properties** dialog on screen, or selection of **Properties** following selection of a constraint marker, leads to the **Constraint Properties** dialog (expanded form shown).



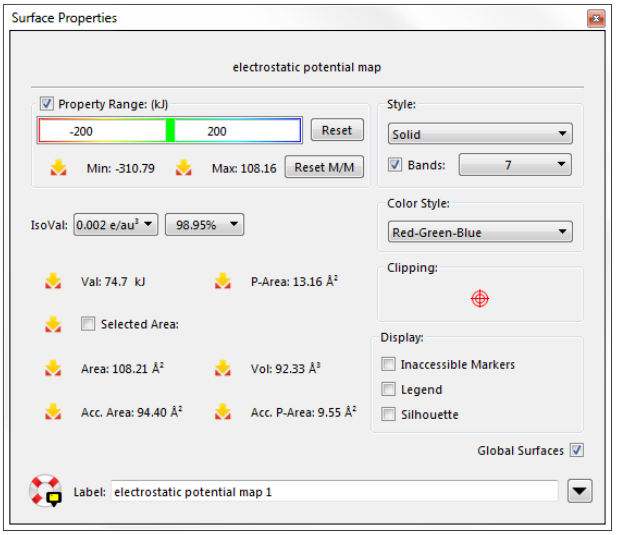
This allows setting the value of a constraint, posting it to the spreadsheet and changing the default constraint label. This also allows specifying a sequence of constraints for an energy profile (see **Calculations...** under the **Setup** menu; **Chapter 8**). The value of the starting constraint is given in the box to the right of **Value**, and the value of the ending constraint is given in the box to the right of **to**. The number of steps in the profile is given in the box to the right of **Steps**. Initially, the numbers in both boxes to the right of **Value** will be the same, and **Steps** will be set to **10**. These may be altered by typing the desired numbers into the appropriate boxes and then *pressing* the **Enter** key (**return** key on Mac). This functionality may also be accessed from **Constrain Distance** (**Angle**, **Dihedral**) under the **Geometry** menu (**Chapter 6**).

Point and Plane Properties

Selection of a user-defined point or plane with a **Properties** dialog on screen, or selection of **Properties** from the **Display** menu following selection of a point or plane, leads to the **Point Properties** or **Plane Properties** dialog (not shown). These allow changing point or plane labels and colors.

Surface Properties

Selection of a graphical display with a **Properties** dialog on screen, or selection of **Properties** following selection of a graphical display, leads to the **Surface Properties** dialog.

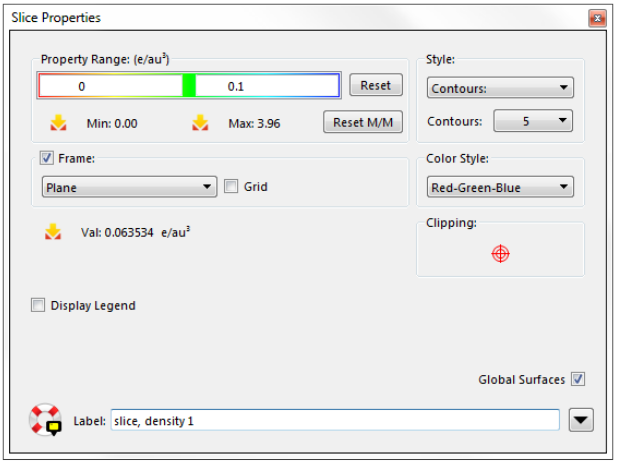


This allows changing display style, isovalue (and in the case of electron density surfaces), percentage of the electrons contained inside the surface, turning on mapped properties, selecting between continuous and banded displays and setting the range of the property, displaying accessible area of surfaces and maps and changing the default labels. A clipping plane may be invoked to allow part of the underlying structural model to be exposed. The dialog also reports (and optionally posts to the spreadsheet) the area and volume of the graphic, the accessible area*, the polar area of an

* A region on a density surface is designated as inaccessible if a sphere of radius 1.0 Å centered on a line normal to the surface and touching a point in the middle of the region, impinges on any other regions of the density surface. The default radius (**Accessible Area Radius**) may be changed

electrostatic potential map*, maximum and minimum value of the mapped property and its value at the cursor position**. If *checked*, **Legend** displays a scale. If *checked*, **Global Surfaces** designates that the settings apply to all molecules in the document.

If the selected graphical surface is a slice, the **Slice Properties** dialog replaces the **Surface Properties** dialog.



This contains similar controls to that found in the previous dialog. Specification of isovalue has been replaced by specification of the number of contours to be displayed. A sphere or a cylinder may be selected instead of a plane, and check boxes allow for a frame around the slice and for a grid.

Regression Properties

Following a linear regression analysis, a new row, labeled **Fit1*****, appears near the bottom of the spreadsheet. This contains information about the fit. *Clicking* on this line with a **Properties** dialog on screen, or selecting **Properties** from the **Display** menu ( ) after *clicking* on the line, leads to the **Regression Properties** dialog.

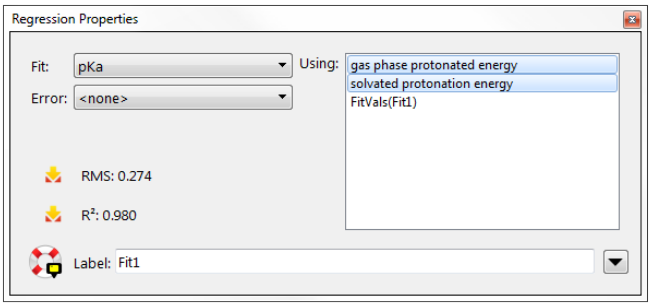
---

in the **Settings Preferences** dialog (**Preferences** under the **Options** menu; **Chapter 10**).

* This is defined as that part of the surface area for which the absolute value of the electrostatic potential is > 100 kJ/mol. The cutoff (**Polar Area Range**) may be changed in the **Settings Preferences** dialog (**Preferences** under the **Options** menu; **Chapter 10**).

** To determine property value at another position *click* on it. To bring up the **Molecule Properties** dialog, *click* on the background.

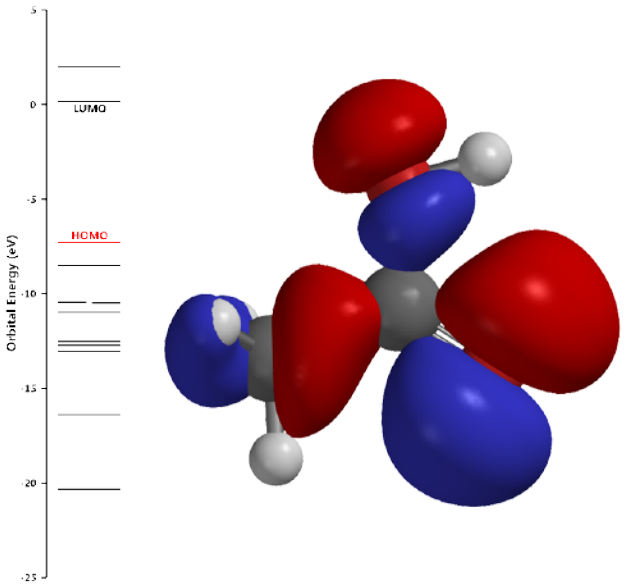
*** More precisely, a row will be written for each fit, and labelled **Fit1**, **Fit2**, ...



This reports RMSD and R^2, as well as allows for changing what is to be fit (**Fit**) and what it is to be fit to (**Using**). The error statistics will immediately update.

Orbital Energies ( )

Selecting **Orbital Energies** leads to the display of an orbital energy diagram (accessible when the wave function is available). This comprises up to ten occupied molecular orbitals and two unoccupied molecular orbitals, the highest-occupied (HOMO) and lowest-unoccupied (LUMO) being explicitly designated.



Clicking on an energy level in the diagram leads to display of the corresponding molecular orbital. This may be manipulated in the usual way; the energy can be posted to the spreadsheet and the display style altered (from the menu at the bottom right of the

screen). After one energy level has been selected and the associated orbital displayed, moving the mouse up or down over the diagram while holding down the left button ("swiping") then releasing the button selects the next higher or lower energy level.

Moving a finger up or down over the diagram then lifting selects the next higher or lower energy level.

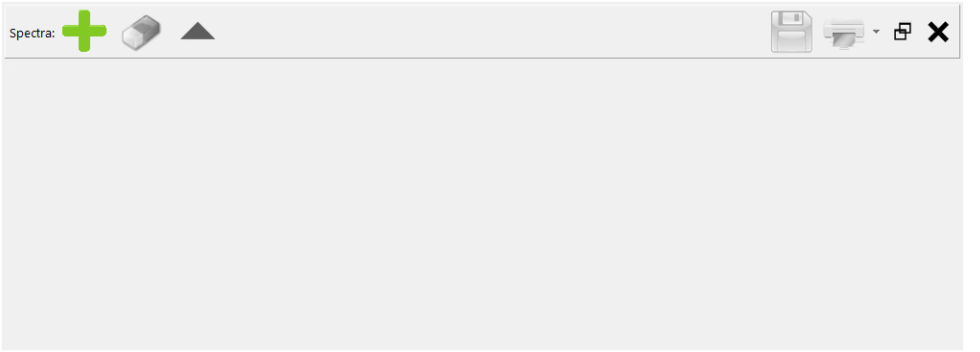
Surfaces ()

This accesses the same dialog described in **Chapter 8**.

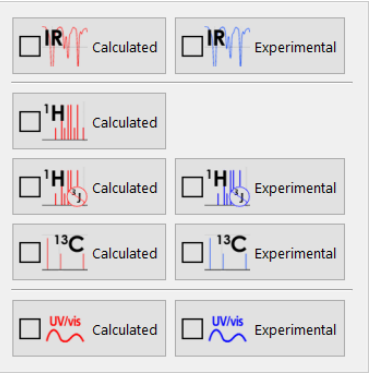
Spectra ()

Spartan Student displays calculated IR and NMR spectra. Spectra need to have been previously requested from the **Calculations** dialog (**Calculations...** under the **Setup** menu; **Chapter 8**). In addition, it provides on-line access and display of experimental IR and NMR spectra from public databases, allowing comparison with calculated spectra.

Selecting **Spectra** from the **Display** menu leads to an empty display pane at the bottom of the screen.

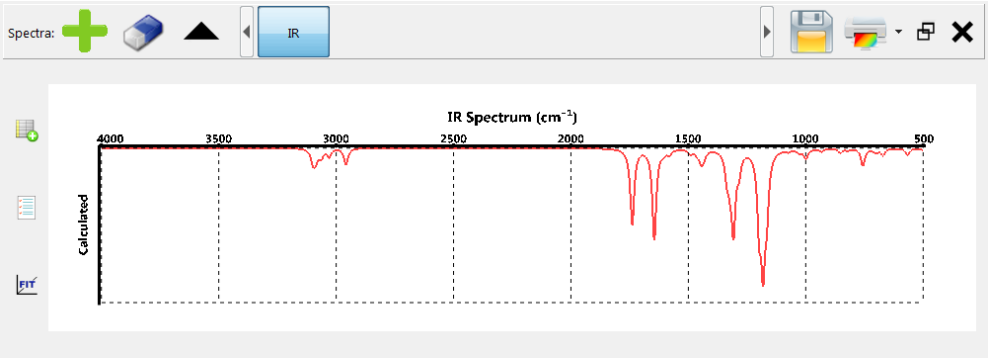


The only accessible control (in a bar at the top of the pane) is  (add a spectrum). *Clicking* on this leads to a palette.



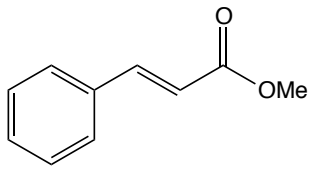
The left hand column lists the types of spectra for which calculations are available: IR, proton NMR with and without three-bond HH coupling, and ^{13}C NMR. The entry is "red" if a calculation has actually been performed and the corresponding spectrum is available. The right hand column lists the types of spectra for which experimental spectra ***may be available*** (from on-line public databases): IR, proton NMR, and ^{13}C NMR. These are shown in blue.

The procedure for displaying either a calculated or experimental spectrum (or both) is independent of the type of spectrum. For the purpose of illustration, we use the IR spectrum of methyl *trans*-cinnamate. A calculated spectrum is displayed by *clicking* on the appropriated (red highlighted) entry, following which the palette is dismissed.



Clicking on IR results in an IR spectrum. Moving the mouse while holding down the left button moves the cursor (unfilled markers at the top and bottom of the spectrum) over the spectrum. When positioned directly over a special line, the markers are darkened and connected by a vertical green line, and a numerical value for the line is provided

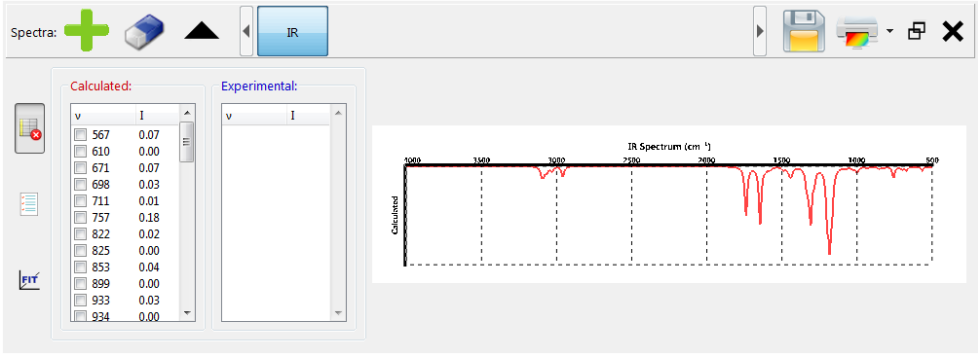
at the bottom of the spectrum. In the case of an IR spectrum, this is a frequency in cm^{-1} and corresponds to a particular vibration of the atoms in the molecule. The molecular model (above the spectrum) vibrates to show this motion. For methyl *trans*-cinnamate, the line at 1645 cm^{-1} corresponds to the C=C stretch while the line at 1739 cm^{-1} corresponds to the C=O stretch.



Moving the mouse while holding down the right button slides the viewable scale from 4000 cm^{-1} to 500 cm^{-1} but does not change the overall range (of 3500 cm^{-1}). The range is changed by using the scroll wheel. The original settings may be restored by *clicking* on  in the bar at the top of the spectra pane.

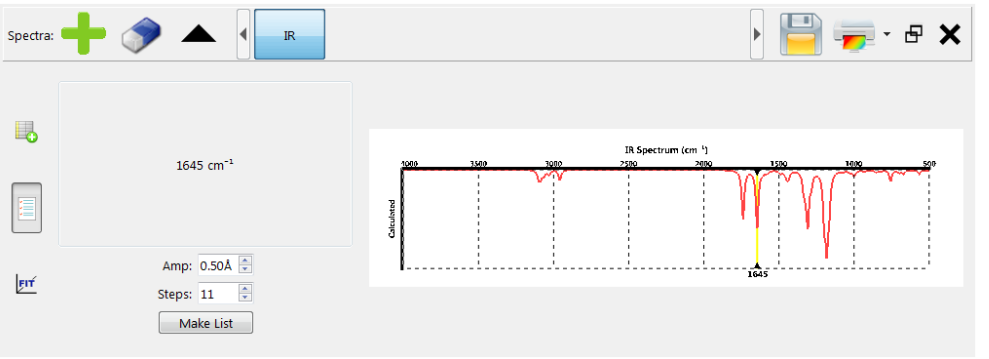

Move one finger over the spectrum to position the cursor, move two fingers to slide the viewable scale and pinch two fingers to change the range.

In the case of IR (only) three buttons appear at the left of the spectrum,  (Tables),  (Make List), and  (Fit). *Clicking* on () leads to a scrollable panel at the left of the spectrum.



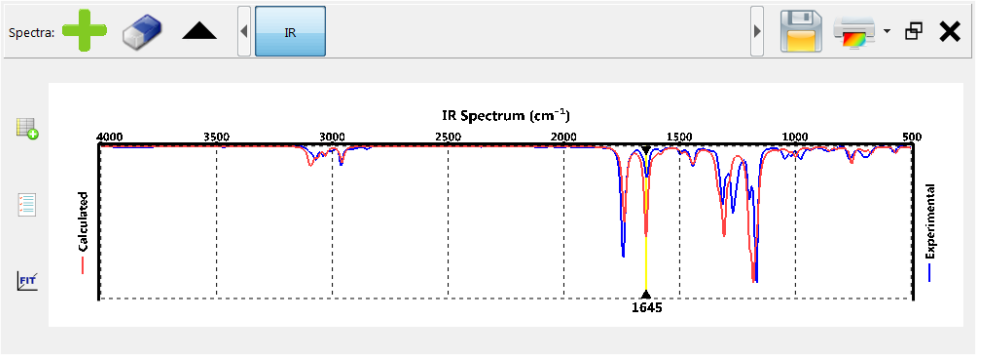
This contains a listing of calculated infrared frequencies and intensities. *Checking* the box to the left of an individual frequency moves the cursor on the spectrum over this line and animates the vibrational motion.

With a frequency selected, clicking on (Make List) leads to a new panel.



This is used to make a list of structures centering around the minimum (or maximum in the case of a transition state) with control over the amplitude of vibration (maximum displacement in Å) and number of steps. *Clicking* on **Make List** leads to a separate document.

If available, an experimental spectrum from one of the public on-line databases may be superimposed on top of the calculated spectrum. The IR spectrum of methyl *trans*-cinnamate is available. *Click* on and select from the palette.



You can if you wish **only** display the experimental spectrum. If a calculated is already displayed, *click* on and re-select (the control operates in toggle mode).

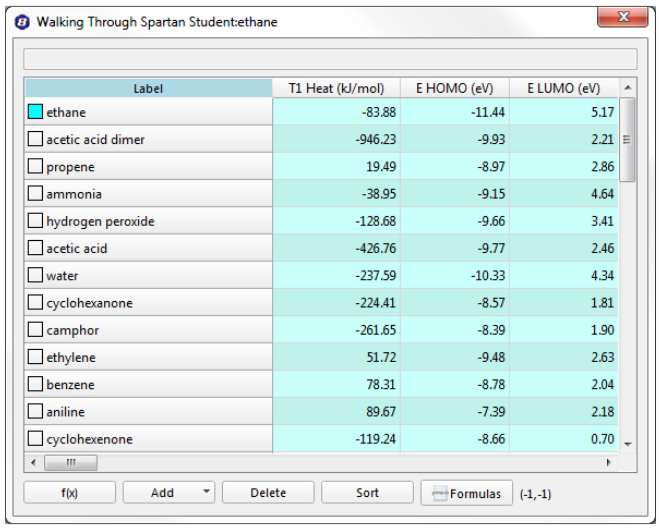
Additional spectra may be requested by *clicking* on in the bar above the spectra pane and then *clicking* on the appropriate entry in the resulting palette. Each new spectrum adds a tab to the bar, although calculated and experimental spectra share the tab. Switching between

tabs changes the display. A spectrum can be deleted by *clicking* on in the bar above the spectra pane. If both calculated and experimental spectra were displayed, both will be deleted.

Controls at the top right of the spectra pane allow saving the spectrum as a PNG, JPEG or Bitmap image file ( ), printing the file ( ), detaching the spectrum pane from the main window ( ) and closing the pane ( ).

Spreadsheet ( )

Associated with each ***Spartan Student*** document (including documents with only a single molecule) is a spreadsheet. This may be displayed by selecting **Spreadsheet** from the **Display** menu.

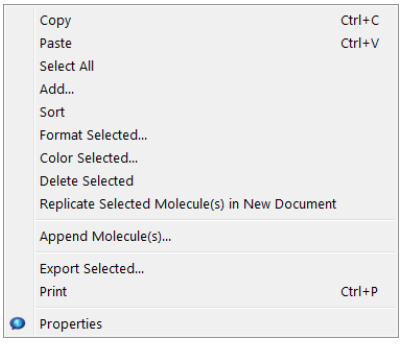


The spreadsheet comprises a series of rows (corresponding to different molecules in the document) and columns (corresponding to different properties). Together, a row and column define a "cell". The spreadsheet may be expanded or contracted by positioning the cursor at one of the corners, *pressing* the left mouse button and *dragging* the mouse.

Only one molecule from one document may be selected (although several molecules may be simultaneously displayed). Molecule selection follows either by *clicking* on the spreadsheet cell containing the molecule label or identifier (leftmost column), or by using the

and buttons or the scroll bar at the bottom left of the screen. Molecules may be ***animated*** (stepped through in succession) using the button at the bottom left of the screen. Animation speed may be adjusted from the **Settings** tab (**Preferences** under the **Options** menu; **Chapter 10**). Selection of a new molecule in the document results in deselection of the previously selected molecule. A molecule may be designated for permanent display by *checking* the box to the left of its identifier (**Label**) in the spreadsheet. The molecules in a document may either be translated and rotated in concert or manipulated independently. This is controlled by **Coupled** under the **Model** menu (**Chapter 5**). By default (**Coupled** checked) molecules move in concert. *Uncheck* **Coupled** to move them independently.

Upon initial entry, all columns of the spreadsheet except the leftmost column, are blank. The leftmost column contains a label that may be changed either by directly typing a new label into the spreadsheet or into the **Label** box in the **Molecule Properties** dialog (see discussion earlier in this chapter). Additionally, default identifiers (***M0001, ...***) can be replaced by chemical names if the molecule has been retrieved from the Spartan Spectra and Properties Database (SSPD).



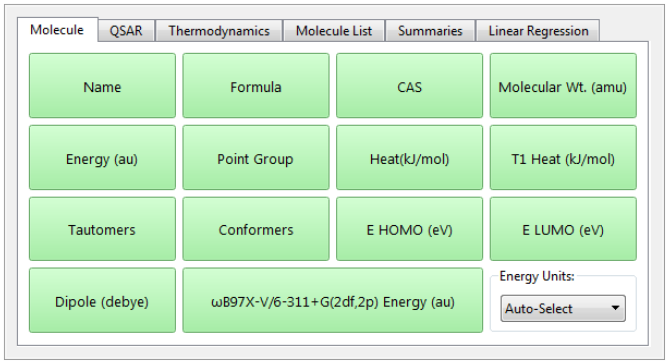
Right-clicking on a column leads to contextual menu with addition spreadsheet controls including copy/paste, selection, sorting, and formatting (to name a few).

Information may be added to the spreadsheet in several ways:

From the Add Dialog

A selection of molecular properties may be entered into the spreadsheet by first *clicking* on the header cell of an empty column, and then *clicking* on **Add...** at the bottom of the spreadsheet. Alternatively, *right click* inside the header cell and then to select **Add...** from the menu that results.

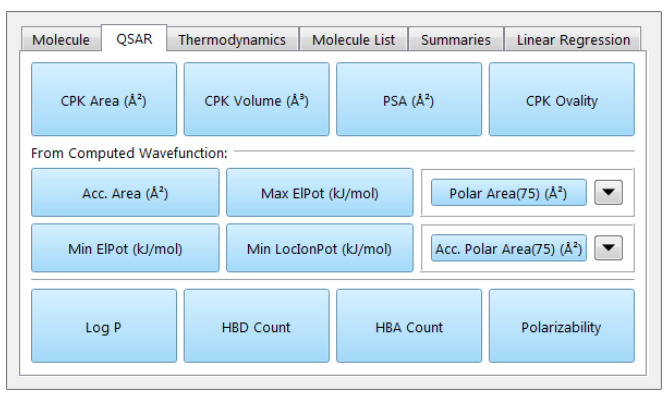
This leads to a multi-tab dialog with **Molecule** selected.



Name	molecule name as it appears in SSPD or SMD
Formula	molecular formula
CAS	Chemical Abstracts designator (if available)
Molecular Weight	molecular weight (in amu)
E	energy (heat of formation, strain energy)
Pt Group	symmetry point group
Heat (kJ/mol)	experimental heat of formation in kJ/mol (if available)
T1 Heat (kJ/mol)	T1 heat of formation in kJ/mol
Tautomers	number of tautomers (proton-transfer isomers)
Conformers	number of conformers
E HOMO	energy of highest-occupied molecular orbital
E LUMO	energy of lowest-occupied molecular orbital
Dipole	dipole moment (in debye)

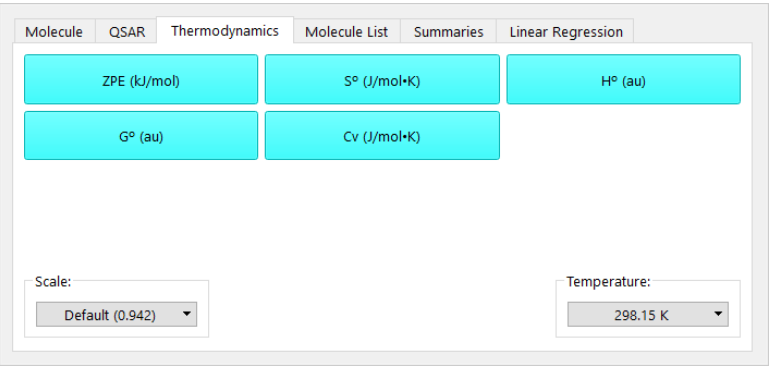
One or more properties may be added to the spreadsheet by *clicking* on their entries.

Clicking on the **QSAR** tab leads to another panel.



CPK Area (Å^2)	surface area of a space-filling (CPK) model (in Å^2)
CPK Volume (Å^3)	volume of a space-filling (CPK) model (in Å^3)
PSA (Å^2)	polar surface area of a space-filling (CPK) model (in Å^2). Defined as the area due to electronegative atoms (N, O) and hydrogens attached to the atoms
CPK Ovality	measure of deviation from a spherical shape, where 1.0 = a sphere and values > 1.0 indicate deviation
Acc. Area (Å^2)	accessible surface area of an electron density surface (in Å^2). Surface is defined by electron density of 0.002 electrons/au^3 and accessible corresponds to a probe with a 1Å radius. Probe radius may be changed in the **Settings** tab of the **Preferences** dialog (**Options** menu)
Max ElPot (kJ/mol)	maximum value of the electrostatic potential on an electron density surface (in kJ/mol)
Min ElPot (kJ/mol)	minimum value of the electrostatic potential on an electron density surface (in kJ/mol)
Min LocIonPot (kJ/mol)	minimum value of the local ionization potential on an electron density surface (kJ/mol)
Polar Area(75) (Å^2)	area of the region on an electrostatic potential map where the absolute value of the electrostatic potential is > 75 kJ/mol (in Å^2). The value of the potential may be changed to 100 and 125 kJ/mol.
Acc. Polar Area(75) (Å^2)	accessible area of the region on an electrostatic potential map where the absolute value of the electrostatic potential is >75 kJ/mol (in Å^2). The value of the potential may be changed to 100 and 125 kJ/mol. Probe radius may be changed from the default of 1Å^2 in the **Settings** tab of the **Preferences** dialog (**Options** menu).
Log P	octanol water partition coefficient
HBD Count	number of hydrogen-bond donor sites
HBA Count	numner of hydrogen-bond acceptor sites
Polarizability	polarizability

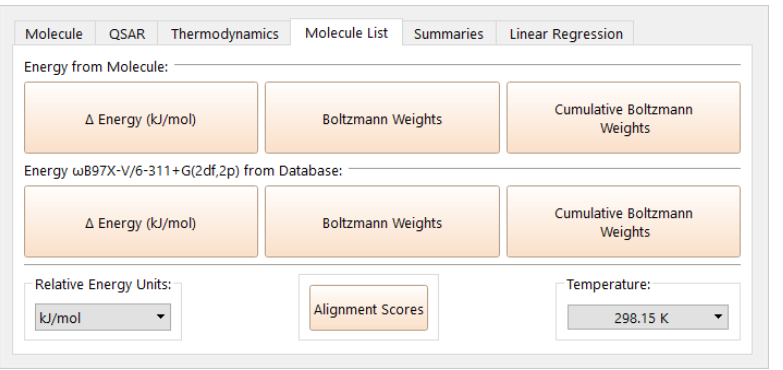
Clicking on the **Thermodynamics** tab leads to another panel:



ZPE (kJ/mol)	zero-point energy (in kJ/mol)
S° (J/mol•K)	entropy (in J/mol•K)
H° (au)	enthalpy (in au). Sum of electronic energy and zero-point energy adjusted for finite temperature
G° (au)	Gibbs energy (in au). Sum of enthalpy and entropy.
Cv (J/mol•K)	heat capacity at constant volume (in J/mol•K)

Scale is used to scale calculated frequencies, where default applies to B3LYP/6-31G* and EDF2/6-31G*, and **Temperature** is used to set temperature. Note that vibrational frequencies need to be available.

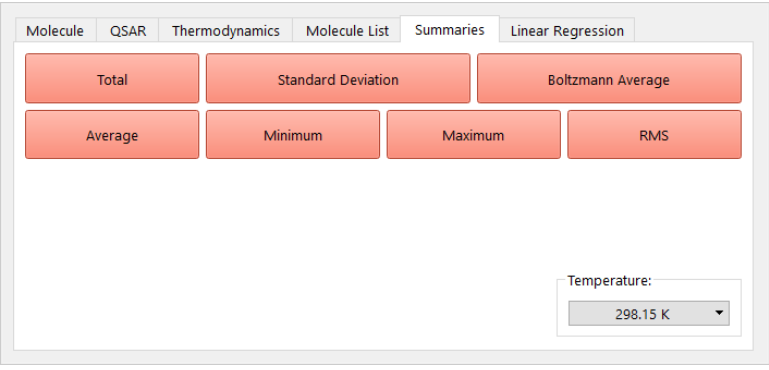
Clicking on the **Molecule List** tab leads to another panel. This allows quantities for different molecules (or different conformers of the same molecule) in a list to be related:



Δ Energy (kJ/mol)	energy (heat of formation, strain energy) relative to selected molecule
Boltzmann Weights	Boltzmann weight
Cumulative Boltzmann Weights	Sum of the Boltzmann weights for the selected molecule and all molecules with lower energy than the selected molecule
Alignment Scores	$1\text{-}R^2/N$, where R^2 is the root mean square distance and N is the number of alignment centers. 1 is a perfect score

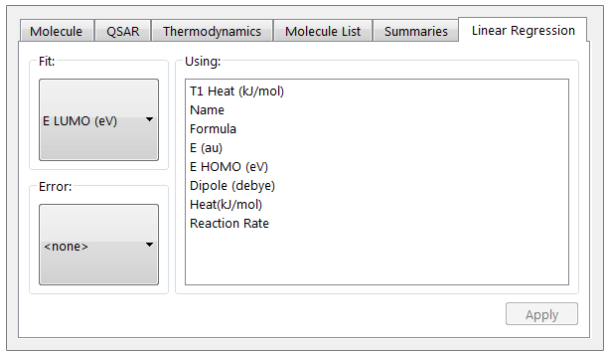
Units for **Δ Energy** and **Temperature** for Boltzmann weights and cumulative Boltzmann weights may be selected from menus at the bottom.

Clicking on the **Summaries** tab leads to another panel:



Total	sum of column values
Minimum	minimum of column values
Stdev	standard deviation of column values
Boltz Avgs	Boltzmann weighted average of column values
Average	average of column values
Maximum	maximum of column values
RMS	rms of column values

Linear regression analysis may be performed on data in the spreadsheet. *Clicking* on the **Linear Regression** tab leads to another panel:



Select one entry from the **Fit** menu and one or more entries from the list under **Using**. *Clicking* on **Apply** performs the linear regression analysis and places the results in a row at the bottom of the spreadsheet identified by **Fit**. As many regression analyses as desired may be performed on the data in the spreadsheet. The individual results will be entered as separate rows in the spreadsheet, with names **Fit1**, **Fit2**, etc. Additional information about the regression analyses is available from the **Regression Properties** dialog (see discussion earlier in this chapter).

From Post ( ) Buttons

Post buttons ( ) found in a number of properties dialogs provide an alternative method to the **Add** dialog for entering calculated properties into the spreadsheet. Note that some properties may require user specification. These include individual bond distances, angles and dihedral angles (available from **Measure Distance**, **Measure Angle** and **Measure Dihedral** under the **Geometry** menu; **Chapter 6**), bond distance, angle and dihedral angle constraints (available from **Constrain Distance**, **Constrain Angle** and **Constrain Dihedral** under the **Geometry** menu; **Chapter 6**), atomic charges, chemical shifts (available from the **Atom Properties** dialog; this chapter), the accessible area of an electron density surface, the polar area and accessible polar area of an electrostatic potential map, the area of a selected region (band) of a banded property map, minimum and maximum property values on a map and the value of the property at a specific location on a property map (available from

the **Surfaces Properties** dialog; this chapter). With the exception of the property value on a map and the area of a selected band, post generates an entire column. Where atom labels are involved, for example, in defining a specific distance, post can be expected to yield consistent results for all molecules in a document only where the molecules are closely related, for example, molecules resulting from a conformational search, or where labels have been explicitly reassigned*. The property value and the area of a selected band on a map is posted only for the selected molecule. Post buttons are also available for CAS numbers, experimental heats of formation and for T1 heats of formation contained in SSPD.

Copy/Paste

Properties of one or more molecules in a document may be copied and then pasted into spreadsheet cells. These include (but are not restricted to) bond distances, angles and dihedral angles (**Measure Distance**, **Measure Angle** and **Measure Dihedral** under the **Geometry** menu), bond distance, angle and dihedral angle constraints (**Constrain Distance**, **Constrain Angle** and **Constrain Dihedral** under the **Geometry** menu), atomic charges and chemical shifts (**Atom Properties** dialog), infrared frequencies and chemical shifts (**IR**, **NMR**, and **UV/vis** data from the **Output Summary** dialog) and the value of a property on a property map (**Surface Properties** dialog). To copy the spreadsheet, first highlight the numerical value of the property in the appropriate screen location (distances, etc.) or dialog (charges, etc.), then select **Copy** from the **Edit** menu, then *click* on the appropriate (destination) cell in the spreadsheet, and finally select **Paste** from the **Edit** menu. Pasting to other programs is achieved in a similar manner.

Numerical Data

Numerical data may be entered by typing directly into the spreadsheet. A column header first needs to be specified. *Double*

* Label reassignment is accomplished using the **Atom Properties** dialog (see discussion earlier in this chapter).

click on an empty column header cell, type in a name and *press* the **Enter** key (**return** key on Mac). Then, type the data into individual cells of the new column (*press* the **Enter** or **return** key following each data entry).

User-Defined Expressions

An expression may be entered either into a header cell (in which case it refers to all entries in a column) or into an individual cell (in which case it refers only to a single entry). Expressions in the column header take the form ***name=formula***, where ***formula*** may involve arithmetic operations, specialty functions, calculated quantities, conversion factors and constants in addition to numerical values. References to specialty functions, molecular mechanics and quantum chemical quantities and conversion factors and constants must be preceded by @. For example, ***mu = @DIPOLE*** typed into a header cell gives the dipole moment. Some functions have arguments, for example, ***c1*** and ***c2*** in the expression ***c12= @DISTANCE (c1,c2)*** refer to atoms c1 and c2, while ***3*** in the expression ***orbitalE=@HOMO (-3)*** designates the energy of the molecular orbital three orbitals below the HOMO. It is necessary to *press* the **Enter** key (**return** key on Mac) following entry of the expression into a cell. The leading ***name=*** is optional for entries in an individual (non-header) cell.

Arithmetic Operations

+	addition
_	subtraction
*	multiplication
/	division
^	raise to a power

Boolean Operations

>	greater than
>=	greater than or equal to
<	less than
<=	less than or equal to
==	equal to
!=	not equal to
|	or
&	and

Mathematical Functions

ABS(x)	absolute value	LN(x)	natural logarithm
ACOS(x)	inverse cosine	LOG(x)	log (base 10)
ASIN(x)	inverse sine	SIN(x)	sine
ATAN(x)	inverse tangent	SQRT(x)	square root
COS(x)	cosine	TAN(x)	tangent
EXP(x)	exponential		

Specialty Functions

AVG (column name)	average of values in column
FITVAL (fit name)	column of fit values from regression analysis
MIN (column name)	minimum of values in column
MAX (column name)	maximum of values in column
NUM (column name)	number of defined entries in column
ROW	the number of the row in the spreadsheet
ROW(molecule name)	the number of the row of molecule
REF(i, x)	the value of the x referenced to row i
STDEV (column name)	standard deviation of values in column
SUM (column name)	sum of values in column

Calculated Quantities

ANGLE(i, j, k)	angle involving atoms i, j, k (degrees)
AREA	area of a user-defined plane ($Å^2$)
DIHEDRAL(i, j, k, l)	dihedral angle involving atoms i, j, k, l (degrees)
DISTANCE(i, j)	distance involving atoms i, j (Å)
ELECTROSTATIC (i)	electrostatic charge on atom i (electrons)
HOMOev(-n)	energy of n^{th} orbital below the HOMO (eV)
HOMOBETAev(-n)	energy of the n^{th} orbital below the β HOMO (eV)
INTERTIA(i)	principle movements of inertia from largest (i=1) to smallest (i=3)
ISOTOPE(i)	mass number of atom i
LENGTH (i)	length of bond i (Å)
LUMOev(+n)	energy of the n^{th} orbital above the LUMO (eV)
LUMOBETAev(+n)	energy of the n^{th} orbital above the β LUMO (eV)
ZPE	zero point energy
HØ	absolute enthalpy at 298K
CV	constant volume heat capacity at 298K
SØ	absolute entropy at 298K
GO	Gibbs energy at 298K

Conversion Factors and Constants

ANGS2AU	Ångstroms to atomic units
AU2ANGS	atomic units to Ångstroms
EV2HART	eV to atomic units (hartrees)

EV2KCAL	eV to kcal/mol
EV2KJ	eV to kJ/mol
HART2KCAL	atomic units (hartrees) to kcal/mol
HART2EV	atomic units (hartrees) to eV
HART2KJ	atomic units (hartrees) to kJ/mol
KCAL2EV	kcal/mol to eV
KCAL2HART	kcal/mol to atomic units (hartrees)
KCAL2KJ	kcal/mol to kJ/mol
KJ2EV	kJ/mol to eV
KJ2HART	kJ/mol to atomic units (hartrees)
KJ2KCAL	kJ/mol to kcal/mol
PI	π

Table 9-5: Examples of User Defined Expressions

E/area = @ENERGY/@AREA	energy divided by surface area
Δ Energy = @ENERGY-@REF (6,@ENERGY)	energy relative to energy of molecule in row 6
Eq = @EXP (-@ENERGY/592.1)	equilibrium constant at room temperature
EnergyFilter = @ENERGY<-99.43	"true" (≠0) for all energies <-99.43
RowFilter = @ROW>10	"true" (≠0) all entries past row 10

Each row in a spreadsheet corresponds to a molecule in a document, and new rows are automatically added in response to adding new molecules to the document. New molecules are added by building (**New Molecule** under the **File** menu; **Chapter 3**), by appending one or more existing documents each containing one or more molecules using either **Append Molecule(s)...** under the **File** menu (**Chapter 3**), or by *right clicking* inside the header cell of the first available row and selecting **Append** from the menu that appears, by pasting from the clipboard, or by *dragging* from the file system. To copy a molecule into the clipboard, first select (*click* on) it, and then select **Copy** from the **Edit** menu, or *click* on its identifier (left most

column) in its spreadsheet, and then select **Copy** from the **Edit** menu. Alternatively *right click* either on the molecule or on its identifier in the spreadsheet and select **Copy** from the menu that appears. Use of the clipboard permits several molecules to be selected (and copied) at once using the **Shift** and **Ctrl** keys in the usual manner. To copy the contents of the clipboard to its destination, *click* on an empty row header in the spreadsheet (for the destination document), and then select **Paste** from the **Edit** menu. An alternative to the two-step **Copy-Paste** procedure is to *drag* the molecule or set of molecules from one spreadsheet to another.

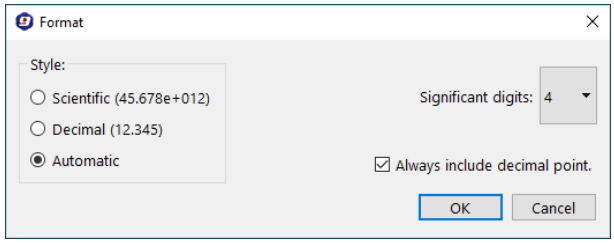
A row (molecule) may be deleted from a spreadsheet, either by first selecting the molecule and then selecting **Delete Molecule** from the **File** menu, or by first *clicking* on its identifier in the spreadsheet (leftmost column) and then either *clicking* on the **Delete** button at the bottom of the spreadsheet, or by *right clicking* on its identifier in the spreadsheet and then selecting **Delete Selected** from the menu that appears. In all cases, a warning is provided prior to deletion. An entire column in the spreadsheet may be deleted by first *clicking* inside its header cell and then *clicking* on the **Delete** button (or **Delete Selected** from the menu).

Rows in the spreadsheet may be sorted according to the numerical values in any column either by first *clicking* inside the header cell and then *clicking* on the **Sort** button at the bottom of the spreadsheet or by *right clicking* inside the header cell and selecting **Sort** from the menu that appears. The rows are placed in ascending order, the smallest (least positive) value of the selected property at the top, largest (most positive) value at the bottom. To sort in descending order, hold down the **Shift** key before *clicking* on the **Sort** button or selecting **Sort** from the menu.

Information in one or more columns of the spreadsheet may be formatted by *right clicking* inside the header cell(s) and selecting **Format Selected** from the menu that appears.

Format as desired and *click* on **OK** to remove the dialog. The full contents of the spreadsheet may be formatted by *right clicking* inside the header cell for the left most column and then selecting **Format**

Selected from the menu.



A button at the bottom right of the spreadsheet toggles between numerical representation of data, **f(x)**, and formula presentation, **=?**.

The spreadsheet may be printed by *right clicking* in the spreadsheet and selecting **Print**.

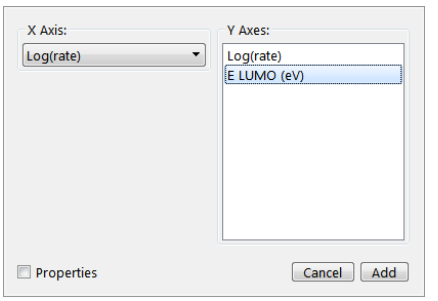
As many spreadsheets as desired (corresponding to the same or to different documents) may be open on screen. A spreadsheet is removed when the associated document is closed and may also be removed by *clicking* on .

> The contents of the spreadsheet may be brought into Excel™ using the clipboard. Select whatever cells are to be copied, select **Copy** from the **Edit** menu. Alternatively, *right click* with the proper cells selected and select **Copy** from the menu that appears. **Paste** into Excel.
>
> The contents of an Excel spreadsheet may be brought into ***Spartan Student***. Copy whatever information is to be transferred from Excel, move into ***Spartan Student***, *click* on the appropriate cell and select **Paste** from the **Edit** menu (or *right click* on the appropriate cell and select **Paste** from the menu that appears). Note, that information on the clipboard that goes beyond the number of rows in ***Spartan Student's*** spreadsheet will be ignored.

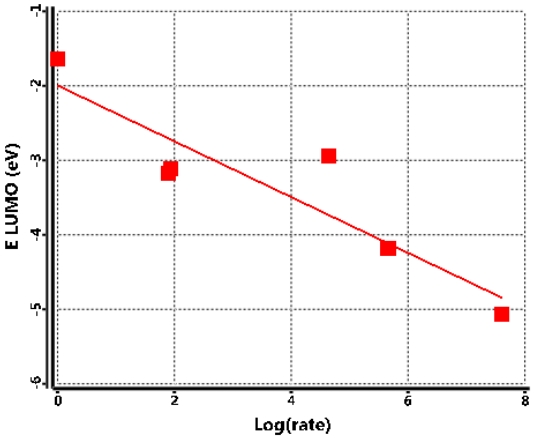
Plots ( )

Plots may be constructed from data in a spreadsheet and a variety of simple curves fit to these data. Selecting **Plots** from the **Display** menu leads to an empty display pane at the right of the screen.

Clicking on (add plot) in the bar at the top of the plots pane leads to a dialog.



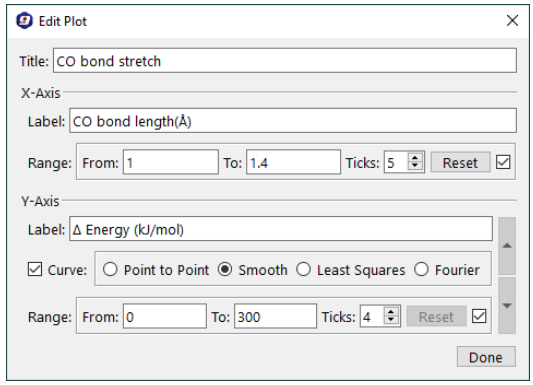
You need to select an item from the **X Axis** menu and one or more items from the **Y Axes** list, and then *click* on the **Create** button at the bottom of the dialog. A plot appears in the plot pane and the **Add Plot** dialog is dismissed.



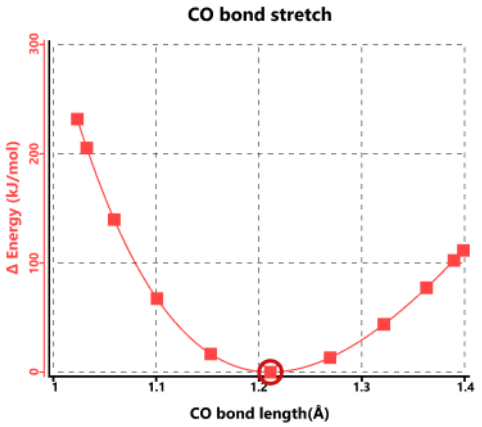
By default, the scales for both horizontal and vertical axes are set to bound the data trying to provide limits and increments that are "rounded". Moving the mouse left and right while holding down the right button slides the horizontal scale but does not change the range. Similarly, moving the mouse up and down while holding down the right button slides the vertical scale. The horizontal range may be changed by moving the mouse left and right while holding down both the right button and shift key, and the vertical range changed by moving the mouse up and down while holding down both the right button and the shift key. The scroll wheel may be used to simultaneously change both horizontal and vertical ranges. The original settings may be restored by *clicking* on  in the bar at the top of the plots pane.

Move two fingers left and right and up and down to slide the viewable horizontal and vertical scales, respectively. Pinch two fingers left and right and up and down to change the horizontal and vertical scales, respectively.

The plot ranges may also be changed by *clicking* on  in the bar at the top of the plots pane.



The resulting dialog also allows axis labels to be altered (from their initial values designated in the spreadsheet) the number of "tics" of horizontal and vertical axes to be changed and a plot title to be added. Finally, the "curve" can be changed, the default is set to display data points only (no curve selected).



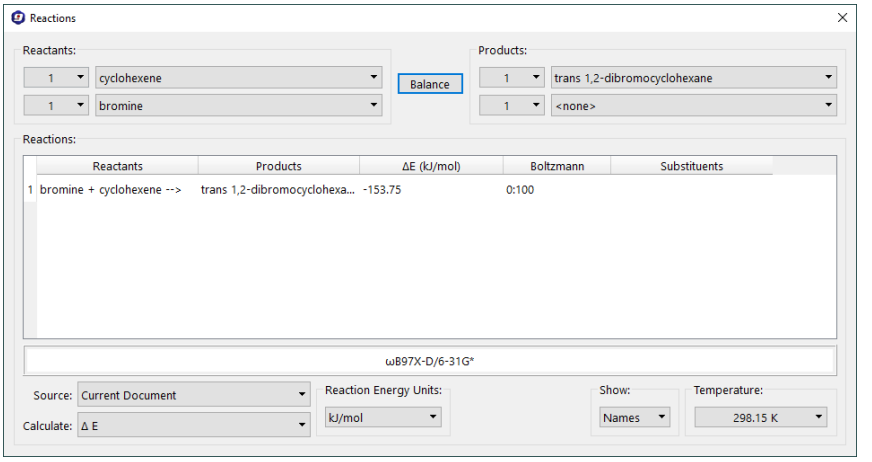
Additional plots may be added by *clicking* on ➕ in the bar at the top of the plots pane. Each plot is given a tab. Only one plot may be displayed at a time as controlled by which tab is selected. The selected (and displayed) plot may be deleted by *clicking* on .

Reactions... ( )

Data in a ***Spartan Student*** document or in SSPD may be used to calculate reaction energies (including activation energies).

$$\Delta E = NP_1\, E_{product1} + NP_2\, E_{product2} - NR_1\, E_{reactant1} + NR_2\, E_{reactant2}$$

NP_1 and NP_2 are the numbers of product molecules 1 and 2 and NR_1 and NR_2 are the numbers of reactant molecules 1 and 2. Selection of **Reactions...** from the **Display** menu leads to the **Reactions...** dialog.



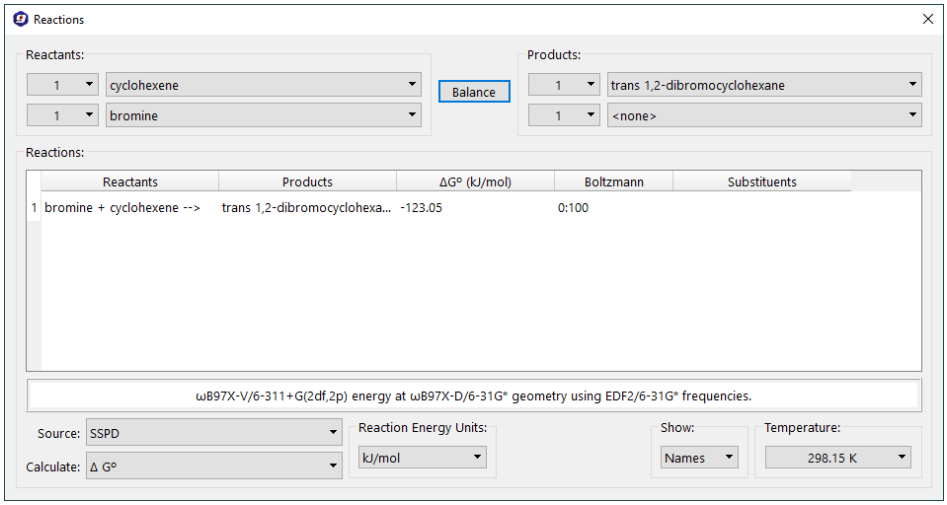
Two sets of menus under **Reactants:** and two sets of menus under **Products:** specify the number of each reactant and product and

identify them. The latter correspond to the labels (identifiers) of the molecules in the document, plus a null entry **<none>**. The overall reaction needs to be mass balanced.

The **Source** menu identifies the source of the energies to be used in the reaction energy calculation. Either the **Current Document** or **SSPD** may be chosen. If the **SSPD** is selected, ΔE will be based on a high quality energy calculation from the ωB97X-V functional with a large (6-311+G(2df,2p)) basis set.

Under **Source** is the **Calculate** drop down menu. This allows for selection of ΔE, ΔH°, or ΔG°. Note that if the **Source** is set to **Current Document**, an IR calculation is required to obtain ΔH° and ΔG° values.

A reaction energy is computed for the selected value: ΔE, ΔH°, or ΔG°.

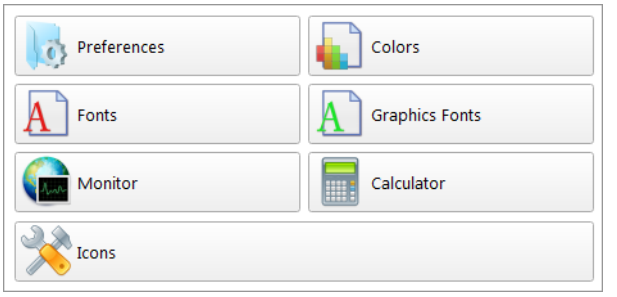


The results of a reaction energy calculation may be printed by *right clicking* inside the display area of the **Reactions** dialog and selecting **Print** from the menu that results.

The **Reactions** dialog is closed by *clicking* on .

Chapter 10
The Options Menu

*Functions under the **Options** menu* access an assortment of preferences. They also allow for changing default colors and fonts, for monitoring executing jobs, access a calculator and turn icon display on or off.*

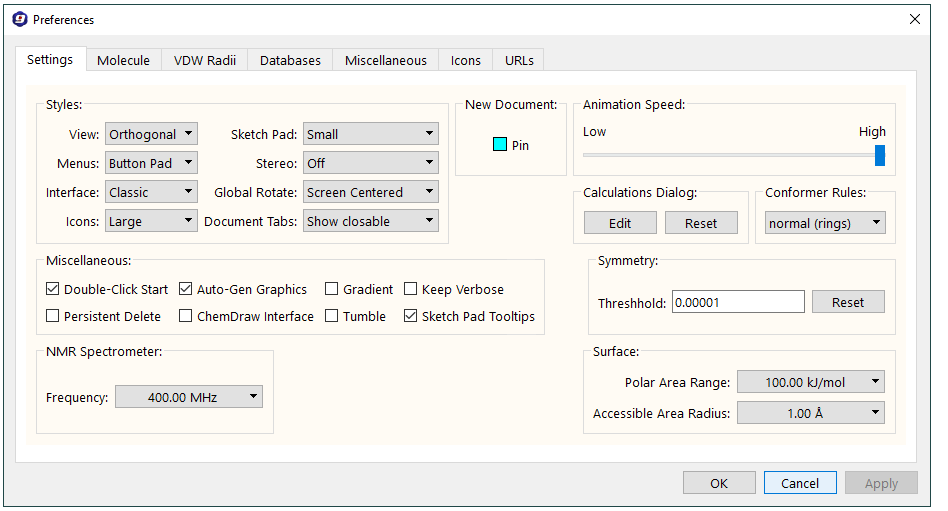


Preferences...(**)**

This sets up preferences relating to the graphical user interface (**Settings**), and to molecule displays (**Molecule**). It permits changes to default van der Waals radii used for space-filling models as well as for calculating molecular surface areas and volumes (**VDW Radii**). It also specifies miscellaneous features (**Miscellaneous**), specifies which icons are to be displayed (**Icons**) and specifies URLs (**URLs**) for on-line connections. Selection results in one of seven tabs. *Clicking* on a tab brings up the associated preference options. To exit a **Preferences** dialog *click* on **OK**. *Clicking* on **Cancel** or exits the dialog without instituting any changes.

* **Preferences** is also found under the ***Spartan Student*** menu in the Macintosh version.

Settings Tab



Style

(i) **View: Orthogonal/Perspective**
Controls the view of structural models and graphics.

(ii) **Menus: Classic List/Button Pad**
Controls presentation of menus either as lists (Classic List) or as icon palettes (Button Pad). The latter is likely to be better suited to touch screen computers and tablets.

(iii) **Interface: Classic/Touch**
Under the **Touch** setting, some menu/dialog items (including up/down arrows) are displayed in a larger size to better support touch screen computers and tablets.

(iv) **Icons: Small/Medium/Large/Extra Large/Jumbo**
Controls size of program icons in the tool bar.

(v) **Sketch Pad: Small/Medium/Large**
Controls the size of the sketch pad (palette of sketch tools) for ***Spartan***'s 2D builder.

(vi) **Stereo: Off/Red-Cyan**
Turns stereographic display on and off. This can also be controlled by toggling the "**3**" key on the keyboard.

(vii) **Global Rotate: Screen Centered/Molecule Centered**
Screen Centered rotates all molecules about a common center. **Molecule Centered** rotates each molecule about its own center.

(viii) **Document Tabs**
Hide will revert display style to that of versions of ***Spartan*** prior to ***Spartan'14***, that is, all open documents will be visible when in **View** mode. If **Show** is *checked*, this displays a tab at the bottom of the screen for each open document. This allows for displaying molecules from documents other than the currently selected document by *checking* the box to the left of the tab. **Show closable** is the same as **Show** but includes the ability to close the document by *clicking* on the  button at the right of the tab

(ix) **New Document: Pin**
If *checked*, defaults to display of any new documents (from building or brought in from the **File** menu) irrespective of whether or no they have been explicitly selected. Does not affect the status of existing open documents. **Pin** setting is only applicable if either **Show** or **Show closable** is selected (see **Documents Tabs** above).

(x) **Animation Speed**
Slider bar controls the speed for animations.

(xi) **Calculations Dialog**
Controls the default task that is displayed upon entering **Calculations...** () from the **Setup** menu. The default is Equilibrium Geometry with the ωB97X-D/6-31G* model, this can be modified by clicking the **Edit** button, which leads to a sample **Calculations** dialog. *Clicking* on **Reset** restores the default task.

(xii) **Conformer Rules: Normal/Skeletal/Thorough**
Chooses between rule sets for conformational searching. **Normal** is the default and should be used for **Equilibrium Conformer** and **Conformer Distribution** calculations

where the Monte Carlo approach is involved. **Skeletal** (in prior versions this was called **Trimmed**) eliminates degrees of freedom and should be used for **Similarity Library** calculations where a systematic approach is carried out. **Thorough** considers twist-boat conformers of six-membered rings (in addition to chair conformers).

Miscellaneous

(xiii) **Double-Click Start**
If *checked*, *double-click* as opposed to *single-click* is required to place the initial atom, group, ring, ligand, etc. on screen when using the 3D builder (consistent with the 2D Sketch builder behavior).

(xiv) **Persistent Delete**
If *checked*, delete function is persistent. If not *checked*, delete will revert to the previously selected function after a single delete operation.

(xv) **Auto-Gen Graphics**
If *checked*, graphics calculations will be performed by the graphical interface (without having to submit a calculation) as long as the information necessary to generate the surface is available (a previous calculation has been run, or the molecule has been retrieved from the SSPD). Note, however, that graphics calculations will not be auto-generated on documents containing more than 25 molecules. These will need to be submitted as a calculation.

(xvi) **ChemDraw Interface** (Windows only)
If *checked*, adds **ChemDraw** as a tab at the top of the model kit. This allows for use of the ChemDraw program (version 10 or newer) as an alternative for sketching molecules

(xvii) **Gradient**
If *checked*, this replaces the single color background by a color gradient background.

(xviii) **Tumble**

If *checked*, allows automatic tumbling of molecules. To tumble a molecule, select it, *press* the left mouse button, move the mouse and release the button. To stop tumbling, *left click*.

To start tumbling, swipe one finger over the screen. To stop, tap anywhere on screen.

(xix) **Keep Verbose**

If *checked*, keeps extended Q-Chem output. Normally discarded upon successful completion of submitted calculations, this may be useful for identifying the source of problems for calculations that have not successfully completed or have led to suspicious results. (The last 100 lines of the verbose output is automatically kept for a job that has abnormally terminated). Verbose output significantly increases the size of the ***Spartan*** document.

(xx) **Sketch Pad Tooltips**

If *checked*, hovering over icons in the sketch pad palette will also display a description of the icon.

NMR Spectrometer

(xxi) **Frequency**

The frequency of the spectrometer, used in coupling constant calculations.

Surface

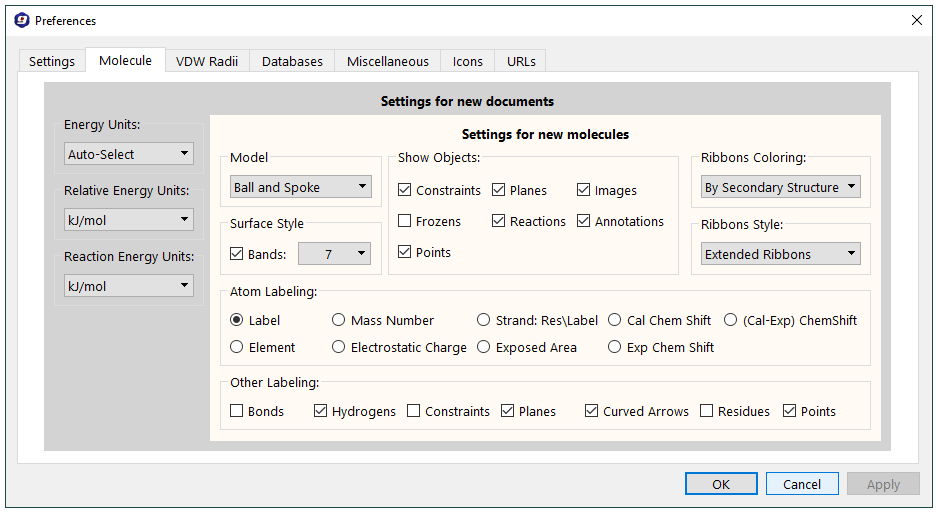
(xxii) **Polar Area Range (kJ/mol)**

Sets the potential (in kJ/mol) for calculating polar area from the electrostatic potential map. The range is given as a single number but represents the range between –value to +value, for example, the default range of 100 kJ/mol means a range from -100 to +100 kJ/mol. Values above and below the range are considered when determining polar area. *Click* inside the box and use the number pad that appears.

(xxiii) **Accessible Area Radius (Å)**

Sets sphere radius (in Å) for determining accessible area, the default is 1.0Å. *Click* inside the box and use the number pad that appears.

Molecule Tab



This specifies default settings for model appearance. These settings may be overridden for individual molecules in a document using entries under the **Model** menu and for specific portions of a molecule using **Utilities/Style** dialogs associated with **Properties** dialogs (**Properties** under the **Display** menu; **Chapter 9**).

(i) **Energy Units**

Auto Select, where units depend on the computational model and on whether they refer to absolute or relative quantities, ***au*** (atomic units), ***kJ/mol*** and ***kcal/mol***

(ii) **Δ Energy Units**

au (atomic units), ***kJ/mol*** and ***kcal/mol***

(iii) **Reaction Energy Units**

au (atomic units), ***kJ/mol*** and ***kcal/mol***

(iv) **Model: Wire/Ball and Wire/Tube/Ball/Spoke/Space Filling/Line**

Controls default model style.

(v) **Surface Style**
If **Bands** is *checked*, this specifies that graphical surfaces, for example electrostatic potential maps, are to be displayed in terms of a series of color bands, rather than as a continuous spectrum. The number of bands is selected from the menu to the right. This setting can be changed at the document level and individual surface level as well (**Surface Properties** under the **Display** menu; **Chapter 9**).

(vi) **Show Objects: Constraints/Frozens/Points/Planes/Reactions/CFD's/Images/Annotations**
If *checked*, constraints and frozen markers, points and planes, reaction arrows, and attached images and text will always be shown as part of the model. Otherwise, they will be shown only in the appropriate mode.

(vii) **Atom Labeling: Label/Element/Mass Number/Mulliken Charge/Electrostatic Charge/Natural Charge/Strand: Residue/Label/R/S/Exposed Area/Cal Chem Shift/Exp Chem Shift/Cal-Exp Chem Shift**
Controls default label type.

Other Labeling:

(viii) **Bonds**
If *checked*, bond labels will be shown.

(ix) **Hydrogens**
If *checked*, displays labels on hydrogen atoms.

(x) **Constraints**
If *checked*, constraint labels will be shown.

(xi) **Planes**
If *checked*, plane labels will be shown.

(xii) **Reactions**
If *checked*, reaction arrow labels will be shown.

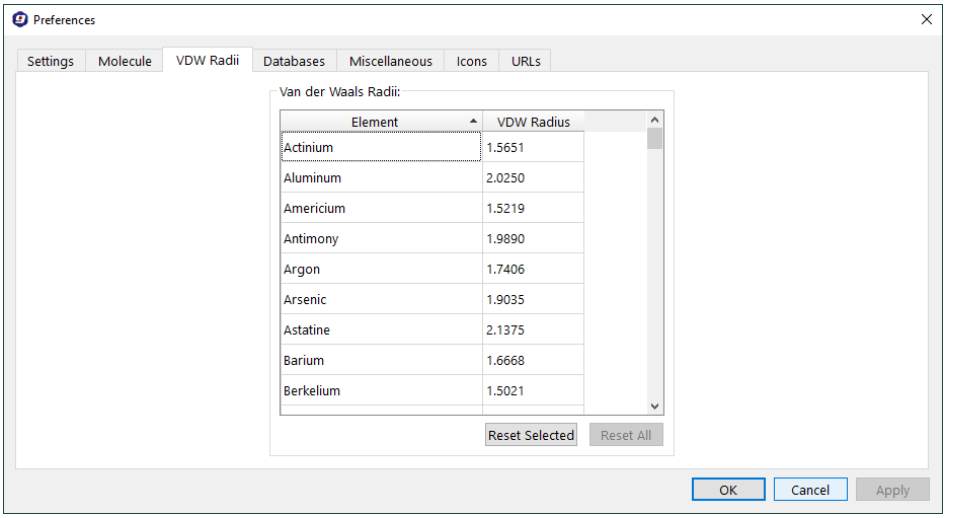
(xiii) **Residues**
If *checked*, residue labels will be shown.

(xiv) **Points**

If *checked*, point labels will be shown.

vdW Radii Tab

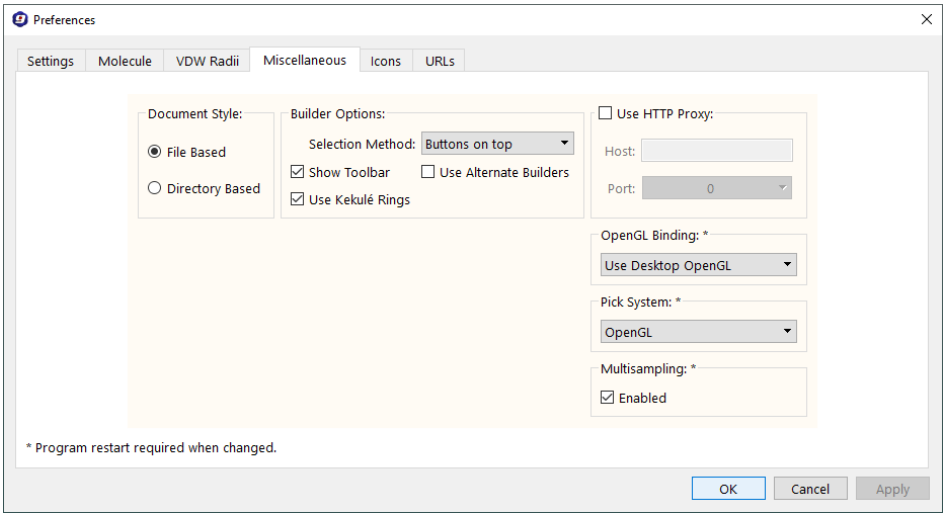
This provides a list of van der Waals radii



To order the list by element name *click* on **Element**, and by atomic radius *click* on **vdW Radius**. Individual entries may be changed from default values by first *clicking* on the entry and then entering a new value. The currently selected entry may be returned to its default radius by *clicking* on **Reset Selected** at the bottom of the dialog, and the full set of radii may be returned to their default values by *clicking* on **Reset All** at the bottom of the dialog.

Miscellaneous

A number of miscellaneous preferences are accessible from this tab.



(i) **Document Style**
Toggles between **File Based** and **Directory Based**. The former is the default and the latter is for compatibility with older ***Spartan*** Linux and Macintosh versions.

(ii) **Builder Selection Method**
Toggles among **Buttons on top**, **Tabs on side** and **Menu** to control selection of the model kits in the 3D builder. The second and third choices conserve vertical space on small screen laptops and tablets.

(iii) **Show Toolbar**
Turns on/off the delete, make bond, break bond, and minimize icons at the bottom of the 3D model kit.

(iv) **Use Kekulé Rings**
Displays aromatic rings with the alternating single and double bonds or an aromatic (1.5) bond style.

(v) **Use Alternate Builders**
Provides a different presentation of the model kits in the 3D builder. Try both and see which one you like.

(vi) **Use HTTP Proxy**
Allows setting up of an alternative path for access to external websites, for example, experimental spectra databases. Rarely needed.

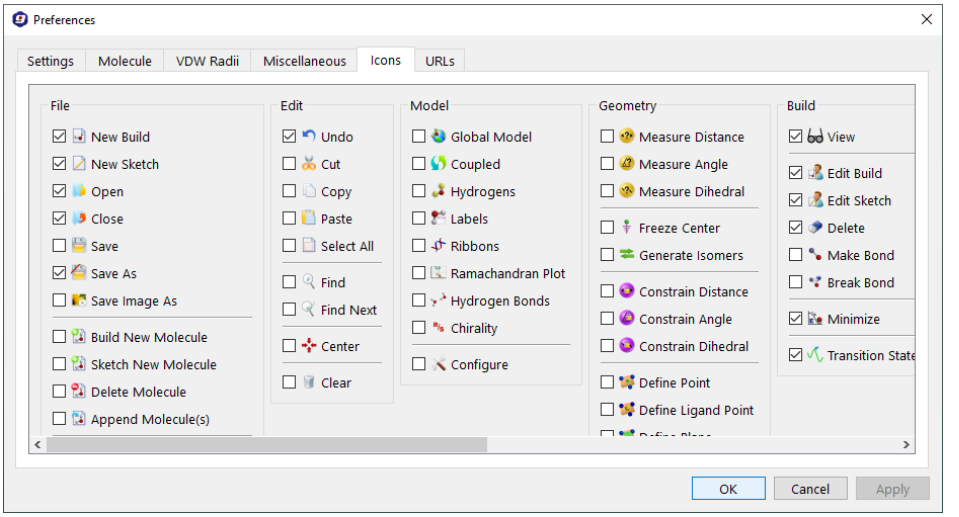
(vii) **Open GL Binding**
Allows for use of the OpenGL (3D visualization) libraries associated with your video card (**Use Desktop OpenGL**) or the option of using software-based libraries (**Use Software OpenGL**), or the three-dimensional viewing libraries developed to support web-based visualization (**Use OpenGL ES**).

(viii)**Pick System**
Toggles between **OpenGL**, **Color** and **Color + Geometric** picking models. **OpenGL** is the standard but causes problems for Intel HD4000 and HD5000 series graphics (very common), where either **Color** or **Color + Geometric** should be used. Graphics chip is automatically detected at installation and this control should be properly set.

(ix) **Multisampling**
Improves visualization using anti-aliasing.

Icons

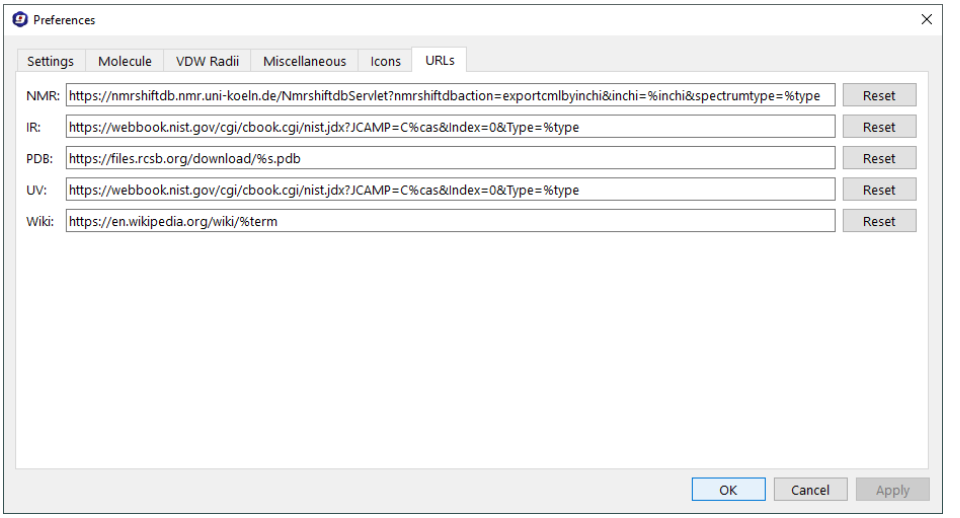
Icons for all menu entries are listed (you will need to use the horizontal slider bar to see them all). If *checked*, the icon will appear above the menu bar at the top of the ***Spartan Student*** screen.



Icon display is limited to one "permanent" row. Approximately 20 medium size icons will fit on screen. All icon choices may be accessed via menu, irrespective of their selection preferences for permanent display.

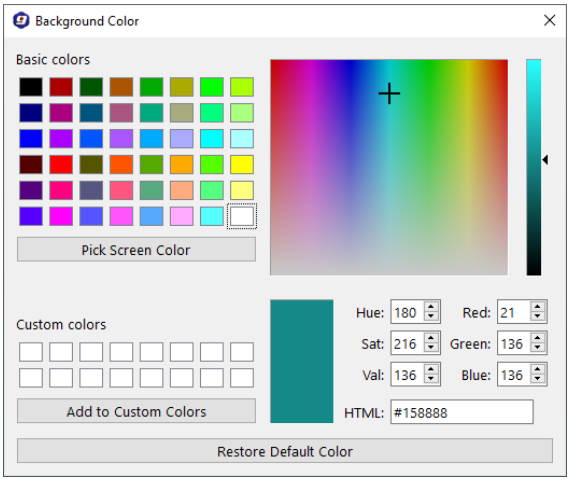
URLs

Lists URLs for access to experimental structural and spectral databases and to Wikipedia.



Colors ()

This alters default colors. Selection leads to the **Colors** dialog.

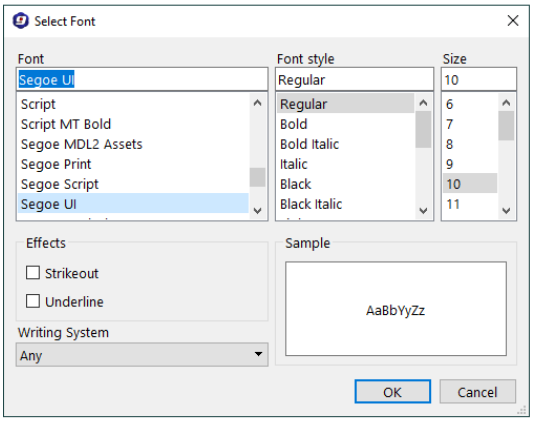


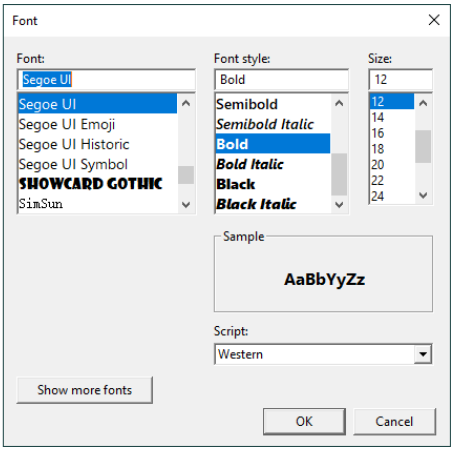
After selecting an object, its color may be set by choosing from the palette, moving the cursor inside the window of colors, or by selecting either a set of hue, saturation and values, or red, green and blue settings. The default color may be reset by *clicking* on **Restore Default Color**. Color selection applies to all objects of the same type, for example, all carbon atoms, and not just to the selected carbon.

To change the default Label Color, hold the shift key down and *click* on the **Colors** entry in the **Options** menu. Further control of colors is available from **Utilities/Style** dialogs associated with **Properties** dialogs (**Properties** under the **Display** menu; **Chapter 9**). *Clicking* on  removes the dialog.

Fonts/Graphics Fonts ( / )

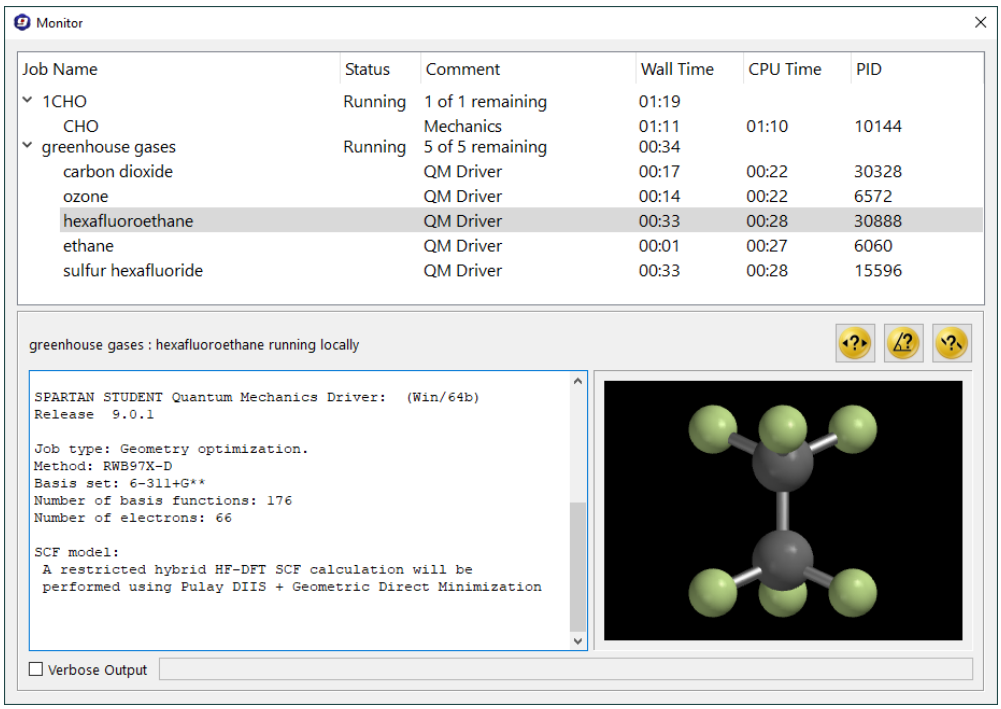
This selects fonts, style and size of ***Spartan's*** menus and dialogs (Fonts) and of labels attached to molecules, plots, and other objects (Graphic Fonts). Selection leads to the **Appropriate** dialog.





Clicking on **OK** dismisses the dialog with selections kept. *Clicking* on **Cancel** or on  dismisses the dialog and does not apply new selections.

Monitor ( )



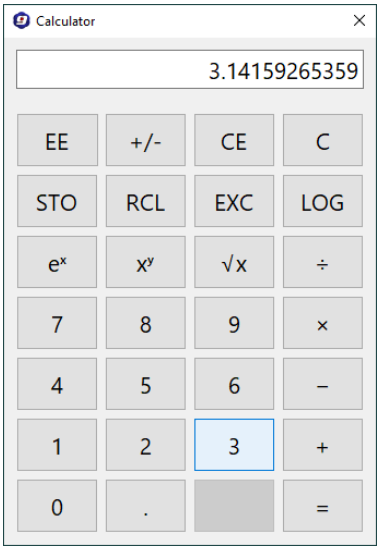
This provides a listing of all executing/queued jobs and their status. To see accumulated output for an executing job, *click* on its name. A ball-and-spoke model of the selected (executing) job will be displayed in a window to the right of the dialog. It can be manipulated using the usual mouse commands (you need to position the cursor inside the window). Touch-screen commands are presently limited to rotation (move one finger). Model style cannot be changed. Note that (except for molecular mechanics and semi-empirical calculations) the structure is updated throughout an equilibrium geometry or transition state optimization. Bond lengths, angles and dihedral angles can be queried.

To terminate a job, *right click* on its name, and then select **Terminate**. To start a queued job, *right click* on its name and select **Start**.

The **Monitor** may be removed by *clicking* on at the top of the dialog.

Calculator ( )

Selection brings up a **Calculator**.



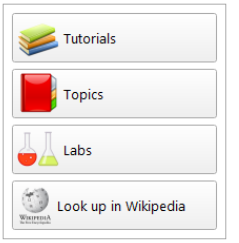
This functions the same way as a normal pocket calculator. The **Calculator** is removed by *clicking* on .

Icons ( )

Toggles the display of icons above the menu bar on and off.

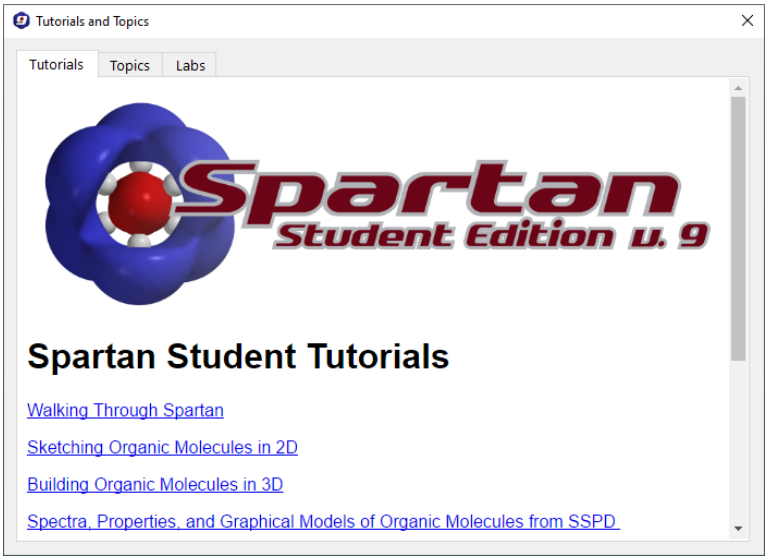
Chapter 11
The Activities Menu

*The **Activities** menu permits on-screen display of the full set of **Spartan Student** tutorials and a series of topics of practical relevance to molecular modeling. A series of lab activities, organized by subject, is available for assignment or self-study. It also allows a Wikipedia page to be brought up (external to **Spartan Student**).*



Tutorials, Topics, and Labs

Selection brings up an HTML page (**Tutorials** shown).

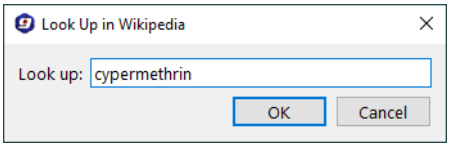


Clicking on an entry (link) brings up the computer's PDF reader alongside of ***Spartan Student***. This allows you to access the materials while working with the program.

Note that the full Manual is available as a PDF under the **Help** menu (see next chapter).

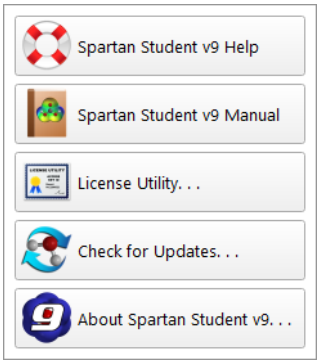
Look Up in Wikipedia...

Selection results in a dialog.



Entering a query followed by *clicking* on **OK** leads to a Wikipedia page. This occupies a window that is external to ***Spartan Student***.

Chapter 12
The Help Menu



Spartan Student v9 Help

This provides information relating to application of computational methods available in ***Spartan Student***, as well as technical details regarding the program's operation, and also provides a link to Wavefunction's website. Help files are HTML documents.

Spartan Student v9 Manual

Opens a PDF file providing documentation on ***Spartan Student Edition*** menus and features (this document).

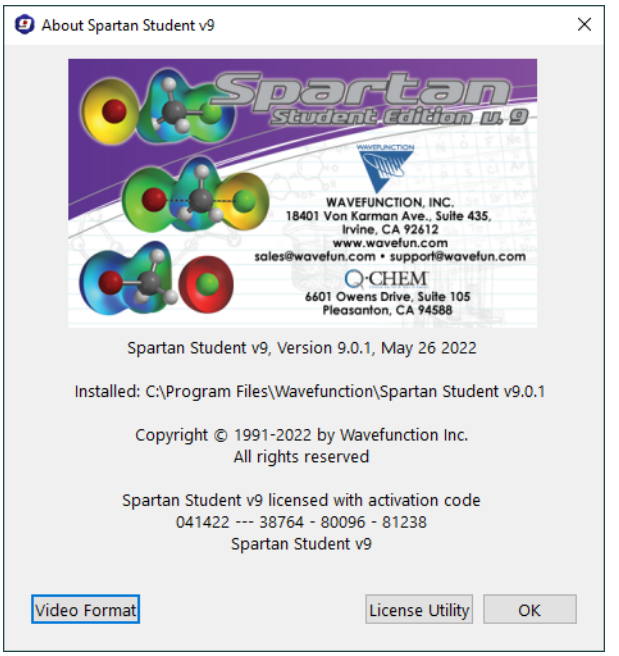
License Utility . . .

Provides access to the **License Utility** dialog. From here you can access your license **activation code** or **KeyID**, **Maintenance Status** and academic licenses can request a **Transfer**.*

* Transfers are not available for student-purchased licenses that utilize an activation code.

About *Spartan Student* v9. . .*

Provides information about the user's release of ***Spartan Student***, and their license type. It also contains information on the machines video format and a button to access the license utility dialog.



* About is located under the **Spartan Student** menu in the Macintosh version.

Section IV
Appendices and Glossary

This section is comprised of a set of six appendices. The first of these (**Topics**) is also available in PDF form (by topic) from the **Activities** menu. The included appendices provide further details on ***Spartan Student* version 9's Capabilities and Limitations**, an abridged guide to all menu entries **Menus**), a **Units** and an energy conversion table, details on proper **Citation** (if citing in publication), and instructions for **Accessing ChemDraw**. Both the Windows and Macintosh version can open native ChemDraw files, additionally (Windows version only) includes the ability to open ChemDraw (must be installed and licensed) from within ***Spartan Student***. This seamless access allows Windows users to build in 2D in ChemDraw, and auto-convert the ChemDraw structure into 3D. This can also be done without ChemDraw access via ***Spartan Student's 2D Sketch builder***.

The final section includes a glossary of terms used throughout the documentation, and more generally in the "molecular modeling" or "computational chemistry" community.

Appendix A

Topics

Essays address topics that are important to molecular modeling in general and to modeling applications of ***Spartan*** in particular. Most of these essays are at an elementary level and provide only fundamentals.

The first two essays are foundational. **Potential Energy Surfaces** relates two of the quantities that directly result from a quantum chemical calculation, geometry and energy. **Theoretical Models** outlines the steps taken in moving from the Schrödinger equation to practical techniques and broadly outlines the scope of these techniques.

Finding and Verifying Equilibrium and Transition-State Geometries and **Total Energies and Thermodynamic and Kinetic Data** provide specifics about the relationship between geometry and energy in the context of practical quantum chemical models. **Calculating Accurate Heats of Formation** details procedures that are available in ***Spartan*** to reliably reproduce the experimental heats of formation.

Interpreting Conformational Preferences shows how information resulting from a calculated energy profile for single-bond rotation may be related to familiar chemical notions.

Calculating Infrared Spectra shows how the raw data resulting from a quantum chemical calculation may be combined with two empirical parameters to produce accurate infrared spectra. **Calculating NMR Spectra** describes a multi-parameter scheme to obtain ^{13}C chemical shifts into close agreement with experiment.

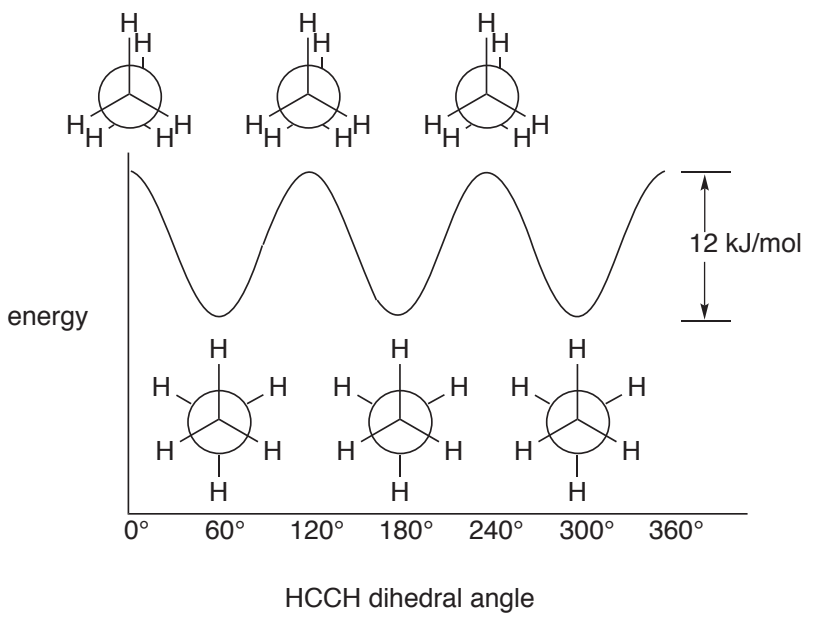
Atomic and Molecular Orbitals describes how molecular orbitals arise from atomic orbitals in the context of the practical quantum chemical models introduced previously, and illustrates the

information that can be drawn from them. **Electron Densities: Sizes and Shapes of Molecules** describes molecular size and shape from the perspective of quantum mechanics and in so doing provides a "platform" from which to evaluate how a molecule interacts with its environment. **Electrostatic Potential Maps: Charge Distributions** describes a model that uses color to "map" the electrostatic potential (the energy of a positive point charge with the nuclei and electrons of a molecule) in order to distinguish neutral, positive and negative regions on an accessible surface. **Local Ionization Potential Maps and LUMO Maps: Electrophilic and Nucleophilic Reactivities** show how maps colored using the energy of ionization and the absolute value of the lowest-unoccupied molecular orbital, respectively, may be used to account for electrophilic and nucleophilic reactivity.

POTENTIAL ENERGY SURFACES

One Dimensional Energy Surfaces

Every chemist has encountered a plot depicting the change in energy of ethane as a function of the angle of torsion (dihedral angle) around the carbon-carbon bond.

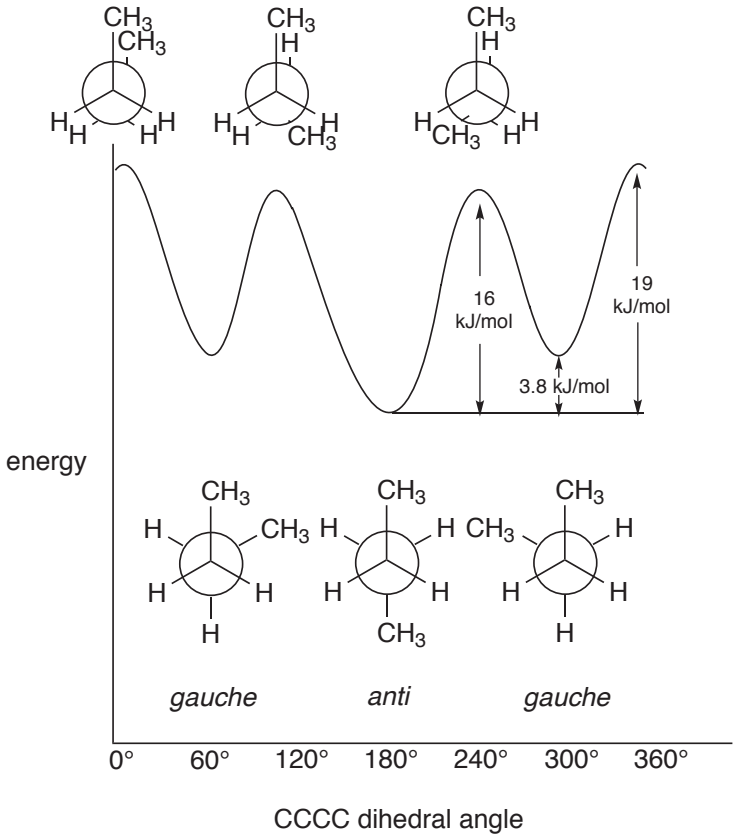


Full 360° rotation leads to three identical energy minima in which the hydrogens are staggered, and three identical energy maxima in which the hydrogens are eclipsed. The difference in energy between eclipsed and staggered structures of ethane, termed the barrier to rotation, is known experimentally to be approximately 12 kJ/mol. Note that any physical measurements on ethane pertain only to its staggered structure, or more precisely the set of three identical staggered structures. Eclipsed ethane ***does not exist*** in the sense that it cannot be isolated and characterized. Rather, it can only be imagined as a structure in between equivalent staggered forms.

Open ***ethane rotation*** in the ***topics*** directory*. The image which appears is one frame in a sequence depicting rotation about the carbon-carbon bond in ethane. *Click* on the  and  keys at the bottom left of the screen to look at other frames. Verify that the staggered structures correspond to minima on the energy plot and that the eclipsed structures correspond to maxima. *Click* on the  key to animate the sequence. Close ***ethane rotation*** when you are finished.

Somewhat more complicated but also familiar is a plot of energy vs. the dihedral angle involving the central carbon-carbon bond in *n*-butane.

* For Windows, the ***Topics*** directory is found in ***Program Files/Wavefunction/Spartan Student***. It needs to be copied to another location available to the user prior to opening it in ***Spartan***. For Macintosh, this is located at the top level of the ***Spartan Student*** disc image. Copy the ***Topics*** directory to a location that allows write permission, typically the user's home directory.



This plot also reveals three energy minima, corresponding to staggered structures, and three energy maxima, corresponding to eclipsed structures. In the case of *n*-butane, however, the three structures in each set are not identical. Rather, one of the minima, corresponding to a dihedral angle of 180° (the *anti* structure), is lower in energy and distinct from the other two *gauche* minima (dihedral angles around 60° and 300°), which are identical. Similarly, one of the energy maxima corresponding to a dihedral angle of 0°, is distinct from the other two maxima (with dihedral angles around 120° and 240°), which are identical. As with eclipsed ethane, eclipsed forms of *n*-butane do not exist, and correspond only to hypothetical structures in between *anti* and *gauche* minima. Unlike ethane, which is a single compound, any sample of *n*-butane is made up of two distinct compounds, *anti n*-butane and *gauche n*-butane. The relative abundance of the two compounds as a function of temperature is given by the Boltzmann equation (see the topic ***Total Energies and Thermodynamic and Kinetic Data***).

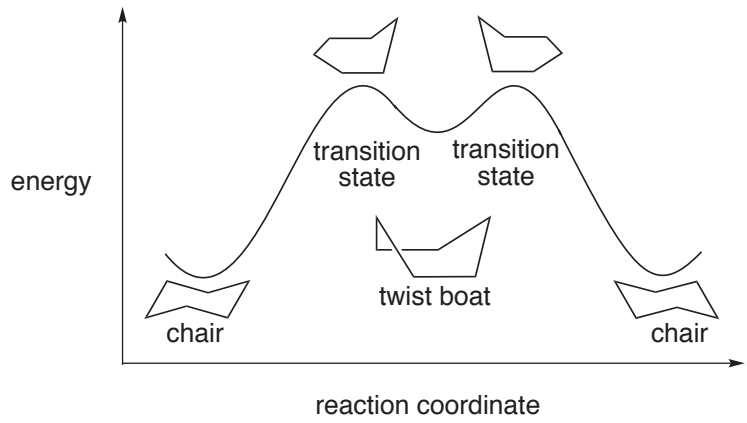
Open ***n-butane rotation*** in the ***topics*** directory. The image which appears is one frame of a sequence depicting rotation about the central carbon-carbon bond in *n*-butane. *Click* on the  and  keys at the bottom left of the screen to look at other frames. Verify that the staggered structures correspond to minima on the energy plot and that the eclipsed structures correspond to maxima. Also, verify that the *anti* structure is lower in energy than the *gauche* structure. *Click* on  to animate the sequence. Close ***n-butane rotation*** when you are finished.

The important geometrical coordinate in *n*-butane may clearly be identified as a torsion about the central carbon-carbon bond. This is an oversimplification, as bond lengths and angles no doubt change during rotation around the carbon-carbon bond.

Quantum chemical models available in ***Spartan*** are able to account for the subtle changes in bond lengths and angles which result from changes in conformation. Open ***n-butane geometry changes*** in the ***topics*** directory. The two plots depict the variation in central CC bond distance and in CCC bond angle as a function of the CCCC torsional angle. The variation in energy is superimposed on each plot. Note how closely the bond distance and energy changes parallel each other. Note also that the bond angle is insensitive to conformation except in the region of the *syn* (0° torsional angle) structure where it has opened up by several degrees. Close ***n-butane geometry changes*** when you are finished.

Many Dimensional Energy Surfaces

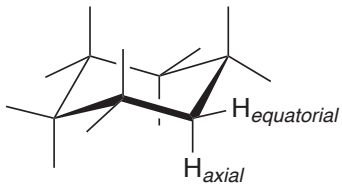
It will usually not be possible to identify a simple geometrical coordinate to designate a chemical transformation. A good example of this is provided by the potential energy surface for ring inversion in cyclohexane.



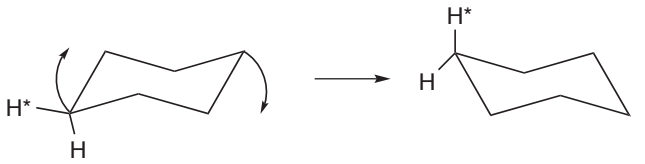
In this case, the geometrical coordinate connecting stable forms is not specified in detail (as it was in the previous two examples), but is referred to simply as the ***reaction coordinate***. The two energy maxima on the ***reaction coordinate diagram*** have been designated as ***transition states*** to indicate that their structures may not be simply described (as are the energy maxima for rotation in ethane and *n*-butane).

The energy surface for ring inversion in cyclohexane, like that for *n*-butane, contains three distinct energy minima, two of lower energy referred to as chair forms, and one of higher energy referred to as a twist boat form. In fact, the energy difference between the chair and twist boat structures is around 23 kJ/mol and, only the former can be observed at normal temperatures. For a discussion, see the topic ***Total Energies and Thermodynamic and Kinetic Data***.

All six carbons are equivalent in the chair form of cyclohexane, but the hydrogens divide into two sets of six equivalent *equatorial* hydrogens and six equivalent *axial* hydrogens.



However, only one kind of hydrogen can normally be observed, meaning that *equatorial* and *axial* positions interconvert via some low-energy process. This is the ring inversion process just described, in which one side of the ring is bent upward while the other side is bent downward.



As shown in the potential energy diagram on the previous page, the overall ring inversion process appears to occur in two steps, with a twist boat structure as a midway point (an intermediate). The two (equivalent) transition states leading to this intermediate adopt structures in which five of the ring carbons lie (approximately) in one plane.

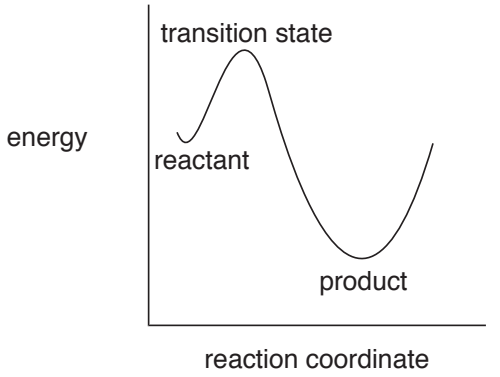
The energy profile for ring inversion in cyclohexane may be rationalized given what we have already said about single-bond rotation in *n*-butane. Basically, the interconversion of the reactant into the twist-boat intermediate via the transition state can be viewed as a restricted rotation about one of the ring bonds.

Correspondingly, the interconversion of the twist boat intermediate into the product can be viewed as rotation about the opposite ring bond. Overall, two independent bond rotations, pausing at the high-energy (but stable) twist-boat intermediate effect conversion of one chair structure into another equivalent chair, and at the same time switch *axial* and *equatorial* hydrogens.

Open ***cyclohexane ring inversion*** in the ***topics*** directory. The image which appears is one frame in a sequence depicting ring inversion in cyclohexane. *Click* on the ◀| and |▶ keys at the bottom left of the screen to look at other frames. Verify that the three minima on the energy plot correspond to staggered structures and that the two maxima correspond to eclipsed structures. Also, verify that the twist boat structure is higher in energy than the chair structures. *Click* on ▶ to animate the sequence. Note that the overall ring inversion appears to occur in two steps, one step leading up to the twist boat and the other step leading away from it. Close ***cyclohexane ring inversion*** when you are finished.

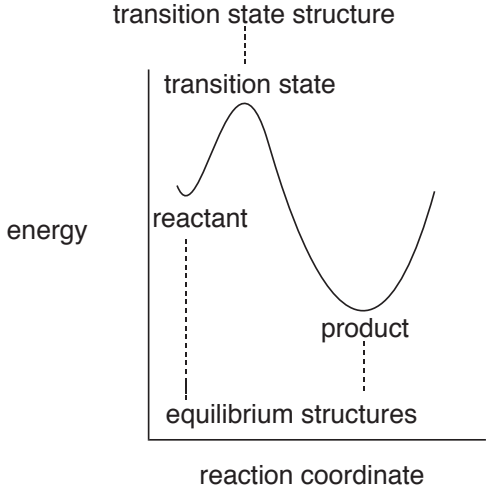
Ethane, *n*-butane and cyclohexane are all examples of the types of motions which molecules may undergo. Their potential energy

surfaces are special cases of a general type of plot in which the variation in energy is given as a function of reaction coordinate.

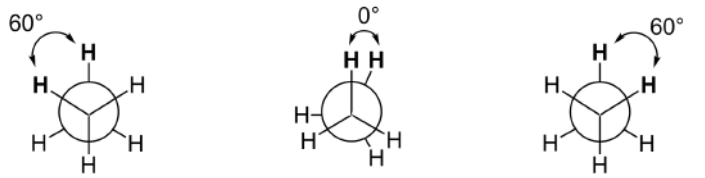


Diagrams like this provide essential connections between important chemical observables - structure, stability, reactivity and selectivity - and energy.

The positions of the energy minima along the reaction coordinate give the equilibrium structures of the reactant and product. Similarly, the position of the energy maximum gives the structure of the transition state. Both energy minima (which correspond to stable molecules) and the energy maximum (which may correspond to a transition state) are well defined. However, the path connecting them (reaction coordinate) is not well defined, in the sense that there are many possible paths. Liken this to climbing a mountain. The starting and ending points are well defined as is the summit, but there can be many possible routes.

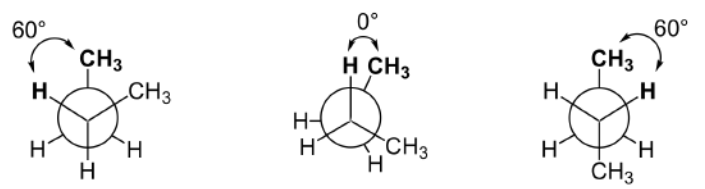


The reaction coordinate for some processes may be quite simple. For example, where the "reaction" is rotation about the carbon-carbon bond in ethane, the reaction coordinate may be thought of as the HCCH torsion angle, and the structure may be thought of in terms of this angle alone. Thus, staggered ethane (both the reactant and the product) is a molecule for which this angle is 60° and eclipsed ethane is a molecule for which this angle is 0°.



staggered ethane "reactant" | eclipsed ethane "transition state" | staggered ethane "product"

A similar description applies to "reaction" of *gauche n*-butane leading to the more stable *anti* conformer. Again, the reaction coordinate may be thought of as a torsion about the central carbon-carbon bond, and the individual reactant, transition state and product structures in terms of this coordinate.



gauche n-butane "reactant" | "transition state" | *anti n*-butane "product"

Equilibrium structure (geometry) may be determined from experiment, given that the molecule can be prepared and is sufficiently long-lived to be subject to measurement. On the other hand, the geometry of a transition state may not be experimentally established. This is simply because a transition state is not an energy well which can trap molecules. Therefore, it is impossible to establish a population of molecules on which measurements may be performed.

Both equilibrium and transition-state structures may be determined from quantum chemical calculations. The fact that a molecule may not be stable enough to be detected and characterized (or even exist) is not important. It would seem from our discussion that equilibrium

and transition-state structures can be distinguished from one another simply by inspecting the shape of the potential energy surface in the vicinity of the structure. Of course, such a surface cannot actually be visualized for a system with more than one or at most two degrees of freedom. However, the set of frequencies associated with the vibrational motions around the structure, the same quantities measured by infrared spectroscopy, will all be real numbers for stable molecules (energy minima), whereas there will be one (and only one) vibrational frequency which is an imaginary number for a transition state. This does not guarantee that this is the transition state "of interest", but if it is, the coordinate (vibrational motion) associated with it is the reaction coordinate. Further discussion is provided in the topic ***Calculating Infrared Spectra***.

THEORETICAL MODELS

A variety of different procedures based on quantum mechanics (so-called quantum chemical models) have been developed to calculate molecular structure and properties as well as infrared, NMR and UV/visible spectra. All follow from a deceptively simple looking ***Schrödinger equation*** first written down in 1927.

$$\hat{H}\Psi = \varepsilon\Psi$$

$\hat{H}$ (the ***Hamiltonian*** or more precisely ***Hamiltonian operator***) is the only known. It describes the kinetic energies of the particles that make up a molecule and the Coulombic interactions between the individual particles. Positively-charged nuclei repel other nuclei, and negatively-charged electrons repel other electrons, but nuclei attract electrons. Ψ (the ***wave function***) is a function of the Cartesian coordinates, and ε (the ***energy***) is a number. The goal in solving the Schrödinger equation is to find a function that when operated on by the Hamiltonian yields the same function multiplied by a number. Note that there are many (actually an infinite number of) solutions to the Schrödinger equation. These correspond to the ground and numerous excited states of an atomic or molecular system.

The energy of a molecule can be measured. On the other hand, the wave function has no physical meaning, and is not subject to experimental

measurement, although the square of the wave function times a small volume element gives the probability of finding an electron inside that volume. This exactly corresponds to what is actually measured in an X-ray diffraction experiment.

The Schrödinger equation has been solved exactly for the hydrogen atom (a one-electron system), where the wave functions are familiar to chemists as the s, p, d, ... atomic orbitals. The lowest-energy s orbital corresponds to the ground state of the hydrogen atom, whereas the higher-energy solutions correspond to excited states.

s orbital *p orbital* *d orbital*

The Schrödinger equation may easily be written down for many-electron atoms as well as for molecules, although it cannot be solved. Even something as seemingly simple as the helium atom with only two-electrons presents an insurmountable problem. Approximations must be made.

Hartree-Fock Molecular Orbital Models

Hartree-Fock molecular orbital models or ***molecular orbital models***, as they are commonly referred to, were the first practical quantum chemical models to be formulated. They result from making three approximations to the Schrödinger equation:

1. Separate nuclear and electron motions. The ***Born-Oppenheimer approximation*** says that "from the point of view of the electrons", the nuclei are stationary. This eliminates nuclear motion and leads to an ***electronic Schrödinger equation*** which can be solved for the H_2^+ molecule, but cannot be solved for molecules with more than one-electron. The Born-Oppenheimer approximation is of little consequence for the description of molecular properties, for example, equilibrium geometries and reaction energies, and may be used without concern.

2. Separate electron motions. The ***Hartree-Fock approximation*** eliminates the need of having to simultaneously account for the motions of several electrons. It leads to a much simpler set of equations in which the motion of each electron in an environment made up of the nuclei and all the other electrons is sought.

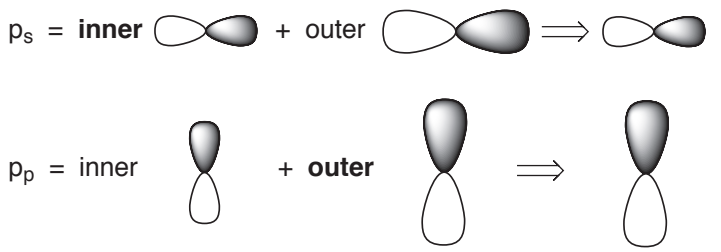
3. Represent each one-electron solution or ***molecular orbital*** by a linear combination of atom-centered functions or ***atomic orbitals***. The ***LCAO*** (***L***inear ***C***ombinations of ***A***tomic ***O***rbitals) ***approximation*** reduces the problem of finding the best functional form for the molecular orbitals to the much simpler problem of finding the best set of linear coefficients. As the number and complexity of the atomic orbitals increases, the energy and other properties approach limiting values. However, computational cost also increases. The goal is to provide as few functions as possible to yield a value for the property of interest that adequately reflects its limit. Note, that the limiting values of properties are not expected to be the same as experimental values, but rather reflect the behavior of the Hartree-Fock model. ***Spartan Student*** includes Hartree-Fock for molecules with up to 30 atoms.

Basis Sets

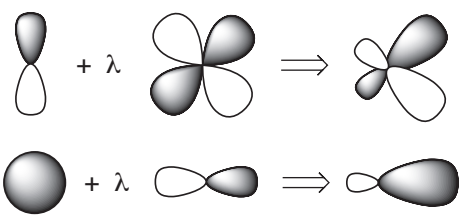
Gaussian functions are polynomials in the Cartesian coordinates times an exponential in the ***square*** of the distance from the origin. They are distinct although very closely related to the exact solutions of the hydrogen atom (exponential functions in the distance), and are labeled 1s, 2s, 2p, ... , the same nomenclature used to describe hydrogen atom solutions.

A ***minimal basis set*** includes only sufficient functions to hold all the electrons on an atom and to maintain its spherical shape. This involves a single 1s orbital for each hydrogen atom, and a set of five orbitals (1s, 2s, $2p_x$, $2p_y$ and $2p_z$) for each carbon atom. Because a minimal basis set incorporates only one set valence p functions, the components of which are the same size, atoms in nearly spherical environments will be better described than atoms in aspherical environments. A ***split-valence basis set*** addresses this problem by

providing two different sets of valence p functions, one compact set and one loose set. This allows different linear combinations for different directions. For example, the compact p orbital can be emphasized to construct a σ bond while the loose p orbital can be emphasized to construct a π bond.



Because the functions in a minimal or split valence basis set are centered on the atoms, they may have difficulty describing electron distributions that fall in between atoms (that is, bonds). ***Polarization basis sets*** address this problem by providing a set of d-type functions (***polarization functions***) on main-group elements, and (optionally) a set of p-type functions on hydrogen. The resulting combinations can be thought of as hybrid orbitals, for example, the pd and sp hybrids shown below.



The so-called 6-31G* basis set will be used for the infrared and NMR calculations described in future topics. The number "6" to the left of the "-" in the name indicates that 6 functions are used to describe each inner-shell (core) atomic orbital. The numbers, "31" to the right of the "-" indicate that groups of 3 and 1 functions are used to describe each valence-shell atomic orbital. "*" designates that polarization functions are supplied for non-hydrogen atoms. Were two stars to be present (as in 6-31G**) this would indicate that p-type polarization functions would also be placed on hydrogen atoms.

The valence basis functions can be further split and additional polarization functions can be added including f-type functions. A commonly used basis set is designated 6-311+G(2df,2p). "311" indicates a triply-split valence, "2df" indicates that two sets of d-type functions and a set of f-type functions are added to the valence of heavy atoms, and "2p" indicates that two sets of p-type functions are added to the valence of hydrogen atoms.

Taken together, these three approximations lead to a set of equations known as the ***Roothaan-Hall equations***. They increase in computational cost as the cube of the size (number of basis functions), and can easily be applied to molecules incorporating up to 100 heavy (non- hydrogen) atoms.

Beyond Hartree-Fock Models

Of the three approximations we have made to reach Hartree-Fock models, the second is to be taken most seriously. According to the Hartree-Fock approximation, electrons "move independently", which means that both the electron-electron repulsion energy and the total energy will be too large. The limiting Hartree-Fock energy is, therefore, necessarily higher (less negative) than the experimental energy. ***Electron correlation*** is the term give to describe the coupling or correlation of electron motions. The ***correlation energy*** is defined as the difference between the Hartree-Fock energy and the experimental energy and is necessarily a negative quantity.

There are two conceptually different approaches for calculating the correlation energy, and numerous specific models arising from each of these approaches. Wave function based models start from the Hartree-Fock wave function combining it with wave functions resulting from electron excitations from filled to empty molecular orbitals. Density functional models supplement the Hartree-Fock Hamiltonian.

Configuration Interaction Models

Configuration interaction models are archetypal of wave function based correlated models. In the unachievable limit, so-called ***full configuration interaction***, all possible single and multiple electron

promotions from occupied to unoccupied Hartree-Fock molecular orbitals and assuming a complete basis set, the energy is same as would be achieved by solution of the electronic Schrödinger equation. More practical ***limited configuration interaction*** schemes have been formulated by limiting the number of electron simultaneously promoted (1-electron, 2-electron, ...) and the number of filled and unfilled molecular orbitals involved in the promotions. **CI** models are not included in the ***Spartan Student*** edition.

Møller Plesset Models

An alternative and more commonly used wave function based model is ***Møller-Plesset theory***. This assumes that the Hartree-Fock energy E_0 and wave function Ψ_0 are solutions to an equation involving a Hamiltonian, $\hat{H}_0$, that is very close to the exact Schrödinger Hamiltonian, $\hat{H}$. This being the case, $\hat{H}$ can be written as a sum of $\hat{H}_0$ and a small correction, V. λ is a dimensionless parameter.

$$\hat{H} = \hat{H}_0 + \lambda\hat{V}$$

Expanding the exact energy in terms of a power series of the Hartree-Fock energy yields:

$$E = E^{(0)} + \lambda E^{(1)} + \lambda^2 E^{(2)} + \lambda^3 E^{(3)} + ...$$

Substituting this expansion into the Schrödinger equation and collecting terms in powers of λ leads to an explicit expression for the energy correction. The sum of $E^{(0)}$ and $E^{(1)}$ is the Hartree-Fock energy. Including the next term gives rise to the so-called ***MP2*** (second-order Møller-Plesset) ***model***.

Both the simplest configuration interaction (limited to single and double electron excitations only) and the MP2 models increase in computational cost as the power of the total number of basis 5th functions. ***Spartan Student*** includes the MP2 model for molecules with up to 20 atoms.

Density functional theory or simply **DFT**, is based on two theorems elaborated by Hohenberg and Kohn, which taken together, prove that the energy and other properties of a many-electron system in its ground state may be correctly and uniquely described in terms of a

function of the electron density. The term "functional" or a function of a function arises because the electron density is itself a function of the three spatial coordinates. What the two Hohenberg-Kohn theorems imply is that the Schrödinger equation can actually be solved; that is, the completely "intractable" problem involving the coupled motions of n electrons in a static field due to the nuclei (a "molecule") may be replaced by an eminently "solvable" problem that treats the electrons as independent (that is, non-interacting) particles. Because the electron density is a function of only three coordinates, in effect a 3 dimensional problem is substituted for a 3n dimensional problem. Unfortunately, the Hohenberg-Kohn theorems do not tell us anything about the functional itself.

In the density functional formalism, the electronic energy, E^{el}, is written as a sum of the kinetic energy, E_T, the electron-nuclear interaction energy, E_V, the Coulomb energy, E_J, and a term combining the exchange and correlation energies, E_{XC}.

$$E^{el} = E_T + E_V + E_J + E_{XC}$$

What is "the" exchange/correlation functional? The quest has gone on for several decades and hundreds of functionals have actually been proposed and divided into several distinct classes. ***Spartan Student*** includes 3 functionals: B3LYP, EDF2, and ωB97X-D for molecules with up to 30 atoms.

Local Density Approximation (LDA)

The functional first proposed stems from a purely hypothetical problem in which a uniform gas of non-interacting electrons moves in a positively charged field. An analytical solution for the exchange energy is available and takes the form of the density raised to the 4/3's power. The correlation energy may be arrived at through numerical simulation, and is also only dependent on only the local density at each point.

$$E_{XC} = E(\rho)$$

Functionals that depend only on the electron density (ρ) are referred to as LDA functionals. They are not very successful in describing the properties of molecules and have largely been replaced.

Generalized Gradient Approximation (GGA)

GGA functionals depend on the gradient of the electron density, $\nabla\rho$, in addition to the density itself.

$$E_{xc} = E\ (\rho,\ \nabla\rho)$$

They have been around since the mid 1980's and were the first to provide a reasonable account of molecular properties and in particular the energies of chemical reactions. In this sense, they were instrumental in drawing attention to density functional theory as a viable "low-cost" alternative to wave function based correlation techniques, something that LDA functionals had failed to do. The BLYP functional is representative.

Global Hybrid Generalized Gradient Approximation (GH-GGA)

GH-GGA functionals often referred to as hybrid functionals) replace a fixed fraction of the exchange by the "exact" Hartree-Fock exchange, the fraction being an adjustable parameter. It is likely that it was the introduction of hybrid functionals that caused the community to recognize that density functional theory was "semi-empirical" in nature. Adding the Hartree-Fock exchange is "costly", but led to significant improvements in the description of reaction energies. While GH-GGA functionals were introduced in the early 1990's, they remain a mainstay in the application of density functional theory to chemistry. The B3LYP functional, in particular, is perhaps still more widely used than any other functional, even though there are now much better choices. B3LYP and EDF2 are representative GH-GGA functionals in ***Spartan Student***.

Range Separated Hybrid Generalized Gradient Approximation (RSH-GGA)

The idea behind range separated GGA hybrid functionals is that the "optimum" amount of Hartree-Fock exchange varies with electron-electron distance, from a small percentage in the long range limit to a large percentage in the short range limit, in the extreme from 0% to100%. Both ωB97X-D and ωB97X-V functionals are range-

separated GGA hybrids. Both incorporate so-called local corrections to account for dispersive interactions (see discussion following), the former is included in ***Spartan Student***.

meta Generalized Gradient Approximation (mGGA)

A *meta* GGA functional not only depends on the electron density and its gradient (as does a GGA functional) but also on the Laplacian of the electron density. As such, it can be construed as the next logical step beyond GGA in constructing a Taylor series expansion of the electron density.

$$E = E(\rho, \nabla\rho, \nabla^2\rho)$$

More commonly, *meta* GGA functionals are viewed as adding the so-called kinetic energy density to GGA.

$$E = E(\rho, \nabla\rho, \nabla^2\psi)$$

In either case, the addition can be construed as second-order term in a Taylor series expansion of the electron density. The B97M-V functional is an example of a "pure" *meta* functional.

Global Hybrid *meta* Generalized Gradient Approximation (GH-mGGA)

These are strictly akin to global hybrid GGA (GH-GGA) functionals in that a fixed percentage of the Hartree-Fock exchange is introduced. The "only" difference is that a *meta* GGA functional including a second-order term replaces a GGA functional. The M06-2X functional, widely accepted as an excellent choice for thermochemical comparisons, is an example of a GH-*meta* GGA functional.

Range Separated Hybrid meta Generalized Gradient Approximation (RSH-mGGA)

A range-separated *meta* GGA (RSH-mGGA) functional is identical to a range-separated GGA (RSH-GGA) functional except that a *meta* GGA functional has replaced the underlying GGA functional. M11 and ωB97M-V are examples of range-separated *meta* GGA functionals.

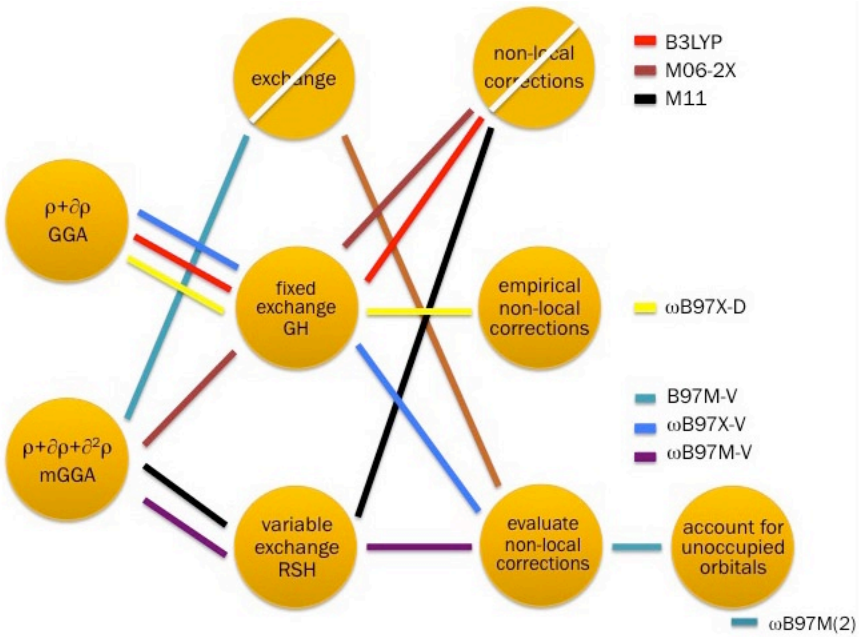
Double Hybrid *meta* Generalized Gradient Approximation (DH-RSH-mGGA)

A double hybrid *meta* GGA (DH-RSH-mGGA) functional accounts for contributions of unoccupied molecular orbitals as well as occupied orbitals, by way of a MP2 like approach. The ωB97M(2) functional is now supported for energy calculations only.

Non Local Corrections

The previous functional classes are all considered "local" in that they are described in terms of a single integral over the three spatial coordinates. In order to capture dispersive van der Waals interactions, so-called non local correlation functionals are needed. These involve a double integral over two sets of coordinates, these may add significant cost to the calculations. For example, the range-separated GGA hybrid ωB97X-V functional used throughout this text, incorporates theVV10 non-local correlation functional and is 3-5 times more costly than the parent ωB97X functional. An alternative and less costly way to account for dispersive interactions is to add an empirical correction to the functional. So-called Grimme corrections are designated by appending "-D" as in ωB97X-D, or "D3" as in B3LYP-D3, to the end of the functional.

A graphical summary of a number of commonly-used functionals stemming from different classes is provided in the figure below.



Which classes of functionals are "best" and which functionals within each class are "best"? A broad base of experience allows some general remarks to be made.

Numerical Integration

Unlike both Hartree-Fock and wave function based correlated models, density functional models cannot be evaluated wholly analytically. Some components require numerical integration, which introduces another variable into the mix, specifically the form and size of the integration grid. An oversimplified description places the grid points along a set number of angular directions and at a set number of distances from the origin. This is referred to as a ***Lebedev grid***.

"Cost" of Density Functional Models

The computation "cost" of density functional models depends on the class, the number of basis functions, η, and the number of points in the numerical integration grid, κ, where $\kappa >> \eta$. GGA and pure meta-GGA functionals such as B97M-V that do not require the Hartree-Fock exchange formally scale as $O(\eta 2\kappa)$. The other functionals combine this dependence with the cost of the Hartree-Fock exchange, which formally scales as $O(\eta 4)$ but in practice is $O(\eta 3)$ or lower. Finally,

functionals such as ωB97X-V that directly account for dispersion have a step that scales as O(η2κ2). This typically dominates the calculation. Times (in minutes) for calculation of the energy together with its gradient ("one step" in the optimization of molecular geometry) for morphine (C17H19NO3) with the B3LYP (GH-GGA), ωB97X-D (RSH-GGA), ωB97X-V (RSH-GGA+dispersion), B97M-V (mGGA), M06-2X (GH-mGGA) and M11 and ωB97M-V (RSH-mGGA) functionals, as well as with RI-MP2, which formally scales as O(η5), with the 6-31G* basis set are provided in **Table A-1**. These have been obtained using a single core of a 3.3 GHz Intel i7 5820K processor. **Table A-2**provides times for 6-311+G(2df,2p) calculation, a dual basis set 6-311+G(2df,2p) calculation and a dual basis set cc-pVQZ-g (cc-pVQZ minus the set of g functions) energy calculation, relative to the corresponding 6-31G* energy/gradient calculations. For example, the value of 26 for the dual basis set cc-pVQZ–g ωB97X-D energy calculation given in **Table A-2**, means that this calculation is 26 times more costly than the ωB97X-D energy/gradient calculation. Put another way, a structure optimization requiring 26 cycles would cost the same as an energy obtained using the larger basis set.

The manner of reporting is deliberate. The 6-31G* basis set is usually deemed satisfactory for calculation of equilibrium geometry, whereas larger basis sets (for example, 6-311+G(2df,2p) and cc-pVQZ-g) are known to be required for accurate descriptions of the energies of most chemical reactions. Determination of geometry for molecules of the complexity of morphine typically requires upwards of 10-20 energy/gradient cycles, that is, an order of magnitude or more greater than the time reported in the first column of the table. Both parts must be considered in order to correctly access cost and practicality.

Table A-1: Times for energy and gradient calculations on morphine with B3LYP, ωB97X-D, ωB97X-V, B97M-V, M06-2X, M11 and ωB97M-V density functional models and RI-MP2 model with the 6-31G* basis set (need ωB97M-V times)

	6-31G* + gradient
B3LYP	7
ωB97X-D	15
ωB97X-V	41
B97M-V	50
M06-2X	19
M11	22
RI-MP2	10

Table A-2: Times for B3LYP, ωB97X-D, ωB97X-V, B97M-V, M06-2X, M11 and ωB97M-V density functional and RI-MP2 energy calculations with 6-311+G(2df,2p), dual 6-311+G(2df,2p) and dual cc-pVQZ-g basis sets relative to the corresponding times for energy and gradient calculations with the 6-31G* basis set give in Table A-1 (need ωB97M-V times)

	6-311G(2df,2p)	6-311+G(2df,2p) [6-311G*]	cc-pVQZ-g [rcc-pVQZ]
B3LYP	26	5	48
ωB97X-D	14	3	26
ωB97X-V	6	2	10
B97M-V	5	2	6
M06-2X	13	3	21
M11	11	3	20
RI-MP2	18	3	33

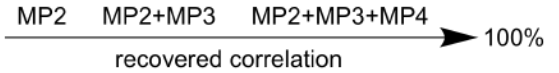
Several conclusions may be drawn:

1. Times for calculation of the energy together with its gradient vary by close to an order of magnitude among the seven models. The B3LYP model is the least costly and the ωB97X-V, B97M-V and ωB97M-V models most costly. The latter result suggests that calculation of the gradient of dispersion functional common to both models is to blame. In terms of cost, the ωB97X-D model is closest to B3LYP. The surprising result is perhaps the good performance of the RI-MP2 model, surpassed only by B3LYP.

2. 6-311+G(2df,2p) energy calculations are roughly an order of magnitude more costly than the corresponding energy/gradient calculations. At the high end and low ends is the factor of 26 for the B3LYP model and a factor of 5 for the B97M-V model. Structure optimization typically requires upwards of 20 steps (energy/gradient), and will likely dominate the overall task.
3. The dual basis set approximation applied to 6-311+G(2df,2p) basis set leads to significant cost savings. If this is the chosen energy method, the costly step will most certainly be determination of geometry.
4. Except for the ωB97X-V and B97M-V functionals, dual basis set cc-pVQZ-g calculations are roughly an order of magnitude more costly than the corresponding 6-311+G(2df,2p) calculations. This means that geometry and energy steps are likely to contribute equally to overall cost. The much smaller increase in cost for B97M-V is presumably due to its lack of the Hartree-Fock exchange.
5. The RI-MP2 model is clearly competitive, greater in overall cost only to the B3LYP models. Because of its inherent O(η5) scaling, RI-MP2 will eventually fall significantly behind density functional models in performance as molecular size is increased.

Disadvantages of Density Functional Models

Low computation cost relative to wave function based electron correlation models is the principal attraction of density functional models. Aside from the RI-MP2 model, density functional models are the only procedures that are both reliable and routinely applicable to molecules of moderate size. However, density functional models come with some disadvantages not shared by wave function based procedures. By far the most serious of these is that they do not offer a clear pathway to improvement. Whereas wave function based procedures return a higher and higher percentage of the correlation energy with increasing degree of complexity, for example, in successively adding orders in the Møller-Plesset models,

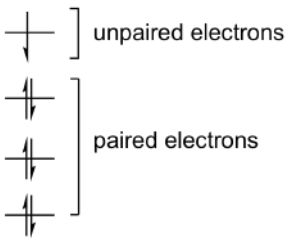


there is no guarantee that increasing the flexibility (and complexity) of a particular functional will actually lead to improvement. It is clear that present generation functionals are "better" than those of previous generations, for example, ωB97X-D and M06-2X are significantly better than B3LYP, in particular for calculation of reaction energies. What is less clear is whether the improvement is to large extent due to careful parameterization to high quality reference data (and to an increased number of parameters) rather than from insight into the "proper" functional form. Functional selection, even while guided by clear physical models, certainly has an uncertain component, and at least at present it is not possible to say from first principles which of several functionals is likely to provide the "best" results. This can only be done by way of thorough comparisons with "known" data.

In practice, density functional models increase in computational cost as the cube of the total number of basis functions (the same dependence seen for Hartree-Fock models). Because most functionals require calculation of the Hartree-Fock exchange energy, they are necessarily more costly than Hartree-Fock models, but can easily be applied to molecules incorporating up to 100 heavy (non-hydrogen) atoms.

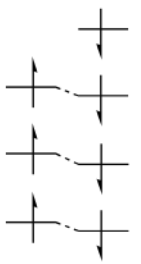
Models for Open-Shell Molecules

Thus far, discussion has been limited to molecules with closed-shell electron configurations, that is, with all electrons being paired. This covers the vast majority of organic molecules as well as most organometallic molecules. There are two ways to think about molecules with unpaired electrons. The obvious way is to insist that electrons are either paired or are unpaired.



This is referred to as ***restricted*** and the individual models as restricted models, for example, the restricted Hartree-Fock (or RHF) model.

The restricted procedure does not necessarily yield the lowest possible energy, simply because it forces the "paired" electron into the same spatial orbitals. Removing this constrains provides greater flexibility and generally lead to a lower energy. This is termed ***unrestricted*** and the resulting models are termed unrestricted models, for example, the unrestricted Hartree-Fock (or UHF) model.



Aside from yielding lower energy, unrestricted models are generally less costly than restricted models, and are much more widely used and is the default procedure in ***Spartan***.

Semi-Empirical Molecular Orbital Models

The principal disadvantage of Hartree-Fock, density functional and MP2 models is their computational cost. It is possible to introduce further approximations together with empirical parameters in order to significantly reduce cost while still retaining the underlying quantum mechanical formalism. So-called ***semi-empirical molecular orbital models*** follow in a straightforward way from Hartree-Fock models:

1. Insist that basis functions on different atoms do not overlap ("see each other"). The so-called ***NDDO approximation*** is rather drastic but reduces the computation effort by more than an order of magnitude over Hartree-Fock models.
2. Restrict to a ***minimal valence basis set*** of atomic functions. This means that there are no inner-shell (core) functions in the basis set. As a consequence, the cost of doing a calculation involving a second-row element such as silicon, is no more than that incurred for the corresponding first-row element such as carbon.

3. Introduce adjustable parameters to reproduce specific experimental data. This is what distinguishes the various semi-empirical models currently available. Choice of parameters, more than anything else, appears to be the key to formulating successful semi-empirical models.

Spartan Student includes the PM3 semi-empirical model for systems with up to 75 atoms.

Molecular Mechanics Models

The alternative to quantum chemical models are molecular mechanics models. These do not start from the Schrödinger equation, but rather from a simple but chemically reasonable picture of molecular structure, a so-called ***force field***. In this picture, just as with a Lewis structure, molecules are made up of atoms (as opposed to nuclei and electrons), some of which are connected (bonded). Both crowding (van der Waals) and charge-charge (Coulombic) interactions between atoms are then considered, and atom positions are adjusted to best match known structural data (bond lengths and angles).

Molecular mechanics is much simpler than attempts at solving an "approximate" Schrödinger equation, but requires an explicit description of chemical bonding, as well as a large amount of information about the structures of molecules. This biases results and seriously limits the predictive value of molecular mechanics models. Nevertheless, molecular mechanics has found an important role in molecular modeling as a tool to establish equilibrium geometries of proteins and other large molecules. It has also been widely used to establish the preferred conformation of molecules with multiple degrees of conformational freedom and hundreds or even thousands of accessible conformers. With regard to the latter, comparisons with results of high-level quantum chemical calculations have, however, clearly shown that present-generation molecular mechanics models are often not satisfactory in identifying the "best" (lowest-energy) conformer and are not to be trusted for obtaining Boltzmann weighed averages. However, they have proven to be useful for identifying highly unfavorable conformers allowing some shortening of the initial

list of possible structures. ***Spartan Student*** includes the MMFF94 model with no restrictions on atom counts.

Choosing a Theoretical Model

No single method of calculation is likely to be ideal for all applications. A great deal of effort has been expended to define the limits of different molecular mechanics and quantum chemical models, and to judge the degree of success of different models. The latter follows from the ability of a model to consistently reproduce known (experimental) data. Molecular mechanics models are restricted to determination of geometries and conformations of stable molecules. Quantum chemical models also provide energy data, which may in turn be directly compared with experimental thermochemical data, as well as infrared, Raman, UV/visible and NMR spectra and properties such as dipole moments, which may be compared directly with the corresponding experimental quantities. Quantum chemical models may also be applied to transition states. While there are no experimental structures with which to compare (see the topic ***Potential Energy Surfaces***), experimental kinetic data may be interpreted to provide information about activation energies (see the topic ***Total Energies and Thermodynamic and Kinetic Data***).

Success is not an absolute. Different properties, and certainly different problems may require different levels of confidence to be placed in the calculation to actually be of value. Neither is success sufficient. A model also needs to be practical for the task at hand. Were this not the case, there would be no reason to look further than the Schrödinger equation itself. Models that may be practical for small to medium size organic molecules cannot be expected to be applied to proteins. Models that are successful and practical for organic molecules may not necessarily meet either criterion for inorganic molecules or transition-metal organometallics. Not only does the nature and size of the system needs to be taken into account, with due attention to the available computational resources and the experience (and patience) of the practitioner. Specifics aside, practical models usually share one common feature in that they are not likely to be the best possible treatments which have been formulated. Compromise is almost always

an essential component of model selection. Continued advances in both digital computers and computer software will continue to raise the bar, but it will be some time before fully reliable models will be routinely applicable to all chemical systems of interest.

The MMFF model generally provides a satisfactory description of equilibrium geometry for organic molecules. It has also proven to be suitable for removing high-energy conformers for molecules with multiple degrees of freedom in preface to quantum chemical calculations of conformer energy differences.

Semi-empirical model are appropriate for:

i) Equilibrium geometry determinations for large molecules.

ii) Transition-state geometry determinations.

iii) Equilibrium and transition-state geometry determinations involving transition metals.

Semi-empirical models are unsuitable for:

i) Calculation of reaction energies.

ii) Calculation of conformer energy differences.

Small basis set Hartree-Fock models such as HF/3-21G and HF/6-31G* are appropriate for:

i) Equilibrium and transition-state structure determinations of organic molecules.

ii) Calculation of energies of *isodesmic* reactions, including comparisons of regio and stereoisomers.

They are unsuitable for:

i) Calculation of reaction energies that involve bond making or breaking and calculation of absolute activation energies.

ii) Comparison of isomer energies of molecules with different bond types.

iii) Equilibrium and transition-state structure determinations for transition-metal organometallic molecules.

iv) Calculation of conformer energy differences.

Small basis set density functional models such as B3LYP/6-31G* and ωB97X-D/6-31G* are appropriate for:

i) Equilibrium and transition-state structure determinations for organic molecules as well as molecules incorporating transition metals.

ii) Calculation of all types of reaction energies, although some caution is needed.

iii) Calculation of conformer energy differences, although caution is needed.

The RI-MP2/6-31G* model is appropriate for:

i) Equilibrium and transition-state structure determinations except for molecules including transition metals.

ii) Calculation of all types of reaction energies, although some caution is needed.

It is unsuitable for:

i) Equilibrium and transition-state structure determinations for transition-metal organometallic molecules.

ii) Calculation of reaction and activation energies where transition-metals are involved.

The ωB97X-V/6-311+G(2df,2p) model is appropriate for calculating all types of reaction energies. Implemented together with a dual basis set, it provides a practical and reliable means to establish conformer energy differences.

FINDING AND VERIFYING EQUILIBRIUM AND TRANSITION-STATE GEOMETRIES

The energy of a molecule depends on its geometry. Even small changes in structure can lead to quite large changes in total energy. What is the "best" choice of geometry for use in a molecular modeling study? While experimental structures, where available, would at first glance seem to be ideal, there are multiple problems with this. First, while upwards of one million structures have been established experimentally, many, many more have not been. Second, the vast majority of experimental structures follow from X-ray crystallography on solid samples and may differ significantly from those of isolated molecules to which the calculations pertain. An additional problem with X-ray structures is that bonds to hydrogen are too short (by as much as 0.1 - 0.2Å). Finally, experimental data for reactive or otherwise short-lived molecules are scarce, and data for transition states are completely lacking. In the final analysis, there is no alternative to obtaining geometries from calculation. Fortunately, this is not difficult, although it may be demanding in terms of computer time.

Determination of geometry (geometry optimization) is an iterative process. The energy and energy gradient (first derivative of the energy with respect to all geometrical coordinates) are calculated for the initial geometry, and this information is then used to project a new geometry. This process continues until three criteria are satisfied. First, the gradient must closely approach zero. This ensures that the optimization is terminating in a flat region of the potential surface (either the bottom of an energy well in the case of equilibrium geometry or the top of an energy hill in the case of transition-state geometry). Second, successive iterations must not change any geometrical parameter by more than specified (small) value. Third, successive iterations must not change the total energy by more than a specified (small) value.

Equilibrium Geometries

In order for a geometry to correspond to an energy minimum, the curvature of the energy surface must be positive, that is, the structure must lie at the bottom of an energy well. The surface's curvature is defined by the ***Hessian*** (the matrix of second derivatives of the energy

with respect to geometrical coordinates).

> What is actually done is to transform from the original coordinates to a new set of geometrical coordinates (***normal coordinates***) for which the Hessian will be diagonal, that is, all off-diagonal elements will be zero. In this representation, all (diagonal) elements must be positive for the geometry to correspond to an energy minimum. Normal coordinate analysis, as it is termed, is required for the calculation of vibrational frequencies, which relate directly to the square root of the elements of the (diagonal) Hessian. Positive Hessian elements yield real frequencies; negative Hessian elements yield imaginary frequencies.

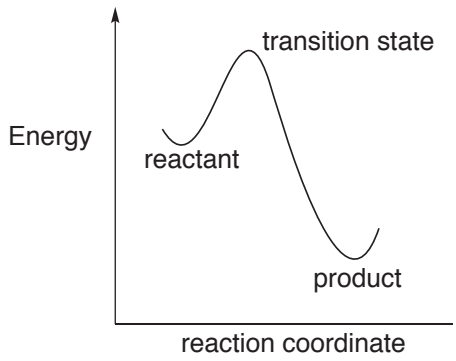
Geometry optimization does not guarantee that the final structure has a lower energy than any other structure of the same molecular formula. All that it guarantees is a ***local minimum***, that is, a geometry with a lower energy than that of any similar geometry, although not necessarily the lowest energy geometry possible for the molecule. The number and types of chemical bonds are maintained in the optimization process as are single bond and flexible-ring conformers. Altering bond types would lead to isomers (stable molecules of the same molecular formula) which under normal conditions could not be reached, whereas altering conformation would lead to different "shapes" of the same molecule, which would be in equilibrium under the same conditions. Finding the best conformer or ***global minimum*** requires repeated optimization starting with different initial geometries corresponding to different initial conformers. Only when all local minima have been located is it possible to say with certainty that the lowest energy geometry has been identified. This process is termed ***conformational analysis***.

In principle, geometry optimization carried out in the absence of symmetry, that is, with C_1 symmetry, must result in a local minimum. On the other hand, imposition of symmetry may result in a geometry that is not a local minimum. For example, optimization of ammonia constrained to a planar trigonal geometry (D_{3h} symmetry) will result in a structure that corresponds to an energy maximum in the direction of motion toward a puckered trigonal geometry (C_{3v} symmetry). This is the transition state for inversion at nitrogen in ammonia.

The most conservative tactic is always to optimize geometry in the absence of symmetry. If this is not done, it is always possible to verify that the structure located indeed corresponds to a local minimum by calculating the vibrational frequencies on the final (optimized) structure. If one or more frequencies are imaginary, then the geometry does not correspond to an energy minimum.

Transition-State Geometries

Chemists recognize a transition state as the structure that lies at the top of a potential energy surface connecting reactant and product (see the topic ***Potential Energy Surfaces***).



More precisely, a transition state is a point on the potential energy surface for which the gradient is zero (just as it is for an equilibrium geometry), but for which the diagonal representation of the Hessian has one and only one negative element, corresponding to the reaction coordinate (see diagram above). All the other elements are positive. In other words, a transition state is a structure that is an energy minimum in all dimensions except one, for which it is an energy maximum. Mathematically, such a structure is referred to as a first-order saddle point.

The geometries of transition states on the pathway between reactants and products are not as easily anticipated as the equilibrium geometries of the reactants and products themselves. This is not to say that transition-state geometries do not exhibit the same systematic behavior as equilibrium geometries, but rather that there is not sufficient experience to identify what systematics do exist, and more

importantly how to capitalize on structural similarities. It needs to be recognized that transition states cannot even be detected let alone characterized experimentally, at least not directly. While measured activation energies relate to the energies of transition states above reactants, and while activation entropies and activation volumes as well as kinetic isotope effects may be interpreted in terms of transition-state structure, no experiment can actually provide direct information about the detailed geometries and/or other physical properties of transition states. Quite simply, transition states do not exist in terms of a stable population of molecules on which experimental measurements may be made. Experimental activation parameters may act as a guide, although here too it needs to be pointed out that their interpretation is in terms of ***transition state theory***. This assumes that all molecules proceed over a single transition state (the high point along the reaction coordinate) on their way to products. Even then, experiments tell little about what actually transpires in going from reactants to products.

Lack of experience about "what transition states look like" is one reason why their detailed geometries are more difficult to obtain than equilibrium geometries. Other reasons include:

i) Algorithms for locating transition states are less well developed than procedures for finding equilibrium structures. After all, minimization is an important task in many diverse fields of science and technology, whereas saddle point location has few if any important applications outside of chemistry.

ii) It is likely that the potential energy surface in the vicinity of a transition state is more "flat" than the surface in the vicinity of a local minimum. After all, transition states represent a delicate balance of bond breaking and bond making, whereas overall bonding is maximized in equilibrium structures. As a consequence, the potential energy surface in the vicinity of a transition state is likely to be less well described in terms of a simple quadratic function (assumed in all common optimization procedures) than the surface in the vicinity of a local minimum.

iii) To the extent that transition states incorporate partially (or completely) broken bonds, it might be anticipated that very

simple theoretical models lacking adequate treatment of electron correlation will not be able to provide entirely satisfactory descriptions.

In time, all of these problems will be overcome, and finding transition states will be as routine as finding equilibrium geometries is today. Chemists can look forward to the day when reliable tools become available for the elucidation of reaction mechanisms.

While the same iterative procedure previously described for optimization of equilibrium geometry applies as well to transition states, the number of steps required for satisfactory completion is likely to be somewhat larger. This is due to the factors discussed earlier. Note, however, that the task of transition state determination may be completely automated and needs no more human intervention than that involved in locating equilibrium geometries.

Having found a transition-state geometry, two tests need to be performed in order to verify that it actually corresponds to a proper transition state, and further that it actually corresponds to the transition state for the process of interest, that is, it smoothly connects energy minima corresponding to reactant and product:

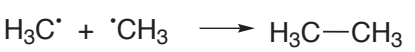
i) Verify that the Hessian (matrix of second energy derivatives) yields one and only one imaginary frequency. This requires that a normal mode analysis be carried out on the proposed transition-state geometry. The imaginary frequency will typically be in the range of 400-2000 cm^{-1}, quite similar to real vibrational frequencies. In the case of flexible rotors, for example, methyl groups or floppy rings, the analysis may yield one or more additional imaginary frequencies with very small (<100 cm^{-1}) values. These can be difficult to "get rid of" simply because energy changes are likely to be very small and inside the precision settings of the optimization procedure. Small imaginary frequencies can almost always be ignored, but make certain to verify what motions these small imaginary frequencies actually correspond to (see discussion following) before doing so. Most important, be wary of structures that yield only very small imaginary frequencies. This suggests a very low energy

transition state, which quite likely will not correspond to the particular reaction of interest.

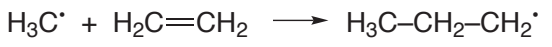
ii) Verify that the normal coordinate corresponding to the imaginary frequency smoothly connects reactants and products. A simple way to do this which requires no additional calculations, is to animate the normal coordinate corresponding to the imaginary frequency, that is, to walk along this coordinate without any additional optimization. This does not necessarily require any additional calculations beyond the normal mode analysis already performed. "Incorrect" transition states located by calculation, that is, transition states that do not link the reactant to the expected product, may indicate new chemistry, so don't discard them too quickly! There are more costly procedures that actually involve "walking" the geometry down from the transition state to both reactants and products. In our view these are rarely worth the effort.

Reactions Without Transition States

Not all chemical reactions have transition states, and that the rates of some reactions depend only on the speed with which reactants diffuse into one another (so-called, ***diffusion controlled reactions***). In fact, reactions without energy barriers are quite common. Two radicals will typically (but not always*) combine without activation, for example, two methyl radicals to form ethane.



Radicals will often add to paired-electron species with no (or very small) activation, for example, methyl radical and ethylene forming 1-propyl radical.



Exothermic ion-molecule reactions that have activation energies in solution, do not necessarily have activation energies in the gas phase. Any complex of an ion and a neutral molecule is likely to be lower in energy than the separated species and the entire reaction coordinate for

* Exceptions may occur where both radicals are delocalized, for example, combing two benzyl radicals.

an ion-molecule reaction might lie below the energy of the separated reactants for example, nucleophilic attack by OH^- on CH_3Cl to give CH_3OH and Cl^-.

Failure to find a transition state, and location instead of what appears to be a stable intermediate or even the final product, does not necessarily mean failure of the theoretical model (nor does it rule this out). It may simply mean that there is no transition state!

Calculations Using Approximate Geometries

Given that small-basis set Hartree-Fock models, semi-empirical models and even molecular mechanics models generally provide geometries for organic molecules that are quite close to those obtained from Hartree-Fock, density functional and MP2 models, it is legitimate to ask whether or not structures from these techniques may be used as the basis for energy and property calculations.* It would be of great help were this the case as geometry optimization is a major cost in any modeling investigation.

"Exact" geometries must be used for frequency (infrared and Raman spectra) calculations. The reason for this is that frequencies are related to the first finite term in a Taylor series expansion of the energy (as a function of geometry). This is (assumed to be) the second-derivative term, which will not be true if the first-derivative term (the gradient) is not precisely zero. (Cubic and higher order terms are assumed to be small and are ignored.) Frequencies evaluated at non-equilibrium (or non-transition-state) geometries are meaningless.

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* Molecular mechanics models are not applicable to transition states as they have been parameterized to account for the structures of stable molecules. This is not to say that molecular mechanics parameterizations could not be developed for transition states, simply that they have not been.

TOTAL ENERGIES AND THERMODYNAMIC AND KINETIC DATA

In addition to molecular geometry, energy is certainly the most important quantity to come out of molecular modeling. Energy can be used to reveal which of several isomers is most stable, to determine whether a particular chemical reaction will have a thermodynamic driving force (an *exothermic* reaction) or be thermodynamically uphill (an *endothermic* reaction), and to ascertain how fast a reaction is likely to proceed. Other molecular properties, such as dipole moment, and infrared, Raman, UV/visible and most importantly NMR spectra are also of great interest, but energy plays a special role.

There is more than one way to express the energy of a molecule. Most common to chemists is the heat of formation, ΔH_f. This is the heat of a hypothetical chemical reaction that creates a molecule from well defined (but arbitrary) standard states of each of its constituent elements. Note that the heat of formation, which most commonly assumes a value between -1,000 and +500 kJ/mol, cannot be directly measured, but must be obtained indirectly.

An alternative, total energy, is the heat of a hypothetical reaction that creates a molecule from a collection of separated nuclei and electrons. Like the heat of formation, total energy cannot be measured directly, and is used solely to provide a standard method for expressing and comparing energies. Total energies are always negative numbers and are much larger than the sum of the bond energies By convention, they are expressed in so-called atomic units* or au, but may be converted to other units as desired:

$$1 \text{ au} = 2625 \text{ kJ/mol}$$

It makes no difference which reference reaction (heat of formation or total energy) is used to calculate the thermochemistry of a balanced chemical reaction (reactant 1 + reactant 2 + . . . → product 1 + product 2 + . . .):

$$\Delta E(\text{reaction}) = E_{\text{product 1}} + E_{\text{product 2}} + \ldots - E_{\text{reactant 1}} - E_{\text{reactant 2}} - \ldots$$

* The exact energy of hydrogen atom is -0.5 atomic units.

Total energies will be used in the discussion that follows. A negative ΔE indicates an *exothermic* (thermodynamically favorable) reaction, while a positive ΔE an *endothermic* (thermodynamically unfavorable) reaction.

A special case involves energy differences among isomers. Each comparison may be viewed as a chemical reaction involving only two molecules:

$$\Delta E(\text{isomer}) = E_{\text{isomer 2}} - E_{\text{isomer 1}}$$

A negative ΔE means that isomer 2 is more stable than isomer 1.

Total energies may also be used to calculate activation energies, $\Delta E^{\ddagger}$:

$$\Delta E^{\ddagger} = E_{\text{transition state}} - E_{\text{reactant 1}} - E_{\text{reactant 2}} - \ldots$$

Here, $E_{\text{transition state}}$ is the total energy of the transition state, and $E_{\text{reactant1}}$, $E_{\text{reactant2}}$, ... are the total energies of the reactants. Activation energies are expected to be positive numbers*, meaning that the transition state is less stable that reactants.

Reaction and activation energies are sufficient to know whether a reaction is *exothermic* or *endothermic* and whether it proceeds with small or large activation barrier. There are, however, situations where energies need to be replaced by Gibbs energies in order to take proper account contributions due to entropy.** For example, a proper account of the equilibrium concentrations of reactants and products requires calculation of the equilibrium constant, K_{eq}, which according to the Boltzmann equation, is related to the Gibbs energy of reaction, ΔG_{rxn}:

$$K_{eq} = \exp(-\Delta G_{rxn}/RT)$$

Here R is the gas constant and T is the temperature (in K). At room temperature (298K) and for ΔG_{rxn} in au, this is given by:

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* Referred to separated reactants, "negative activation energies" are possible. This is due to the formation of a complex, the total energy of which is lower than the sum of the total energies of the reactants. Also note that some reactions proceed with zero activation energy, meaning that there is no transition state.

** Entropy contributions will be largest where the numbers of reactants and products differ. On the other hand, entropy might be expected to largely cancel where reactants and products are very similar.

$$K_{eq} = \exp(-1060\ \Delta G_{rxn})$$

ΔG_{rxn} has two components, the enthalpy of reaction, ΔH_{rxn}, and the entropy of reaction, ΔS_{rxn}. These are defined as follows:

$$\Delta G_{rxn} = \Delta H_{rxn} - T\Delta S_{rxn}$$

$$\Delta H_{rxn} \approx \Delta E_{rxn} = E_{product\ 1} + E_{product\ 2} + \ldots - E_{reactant\ 1} - E_{reactant\ 2} - \ldots$$

$$\Delta S_{rxn} = S_{product\ 1} + S_{product\ 2} + \ldots - S_{reactant\ 1} - S_{reactant\ 2} - \ldots$$

Although ΔG_{rxn} depends on both enthalpy and entropy, it is often assumed that the entropy contribution will be small, and can be neglected. Further assuming that $\Delta H_{rxn} \approx \Delta E_{rxn}$, equilibrium constants can then be estimated according to the "Boltzmann" equation:

$$K_{eq} \approx \exp(-\Delta E_{rxn}/RT) \approx \exp(-1060\ \Delta E_{rxn})$$

This equation may also be used to establish the equilibrium composition of a mixture of isomers:

$$\text{Isomer 1} \rightleftharpoons \text{Isomer 2} \rightleftharpoons \text{Isomer 3} \rightleftharpoons \ldots$$

$$\%\ \text{Isomer i} = \frac{100 \exp(-1060\ E_{\text{Isomer i}})}{\sum_{k} \exp(-1060\ E_{\text{Isomer k}})}$$

Isomer energies, E_{isomer}, are given in atomic units relative to the energy of the lowest-energy isomer. An important special case involves an equilibrium between two isomers:

$$\text{Isomer 1} \rightleftharpoons \text{Isomer 2}$$

$$\frac{[\ \text{Isomer 1}\ ]}{[\ \text{Isomer 2}\ ]} = \exp\left[-1060\ (E_{isomer1} - E_{isomer2})\right]$$

Reaction rate constants, k_{rxn}, are also related to Gibbs energies. As before, if entropy contributions can be neglected, the rate constant can be obtained directly from the activation energy, $\Delta E^{\ddagger}$, according to the Arrhenius equation:

$$k_{rxn} \approx (k_B T/h)[\exp(-\Delta E^{\ddagger}/RT)]$$

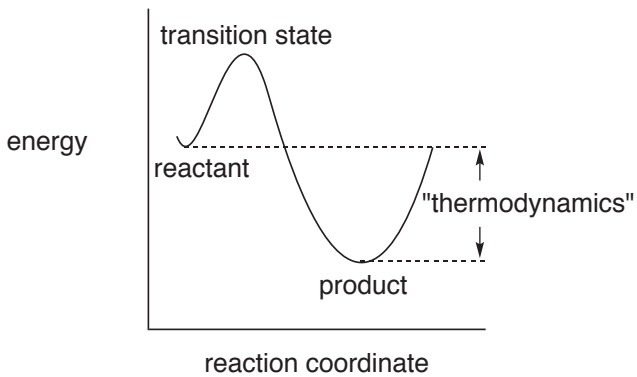
Here k_B and h are the Boltzmann and Planck constants, respectively. At room temperature and for $\Delta E^{\ddagger}$ in au, k_{rxn} is given by:

$$k_{rxn} = 6.2x10^{12} \exp(-1060\ \Delta E^{\ddagger})$$

Another way to describe reaction rates is by half-life, $t_{1/2}$, the amount of time it takes for the reactant concentration to drop to one half of its original value. When the reaction follows a first-order rate law, rate = $-k_{rxn}$[reactant], $t_{1/2}$ is given by:

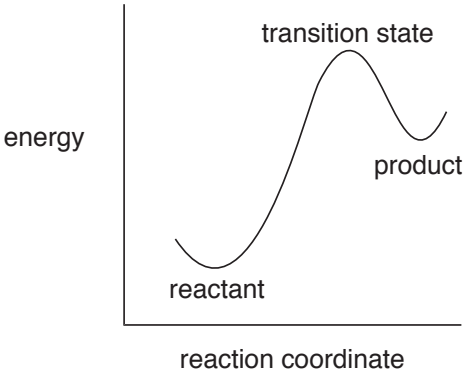
$$t_{1/2} = \ln 2/k_{rxn} = 0.69/k_{rxn}$$

It is useful to associate reaction energies and reaction rates with potential energy diagrams introduced earlier. The thermodynamics of reaction is given by the Δ Energy of the reactant and product on the potential surface.

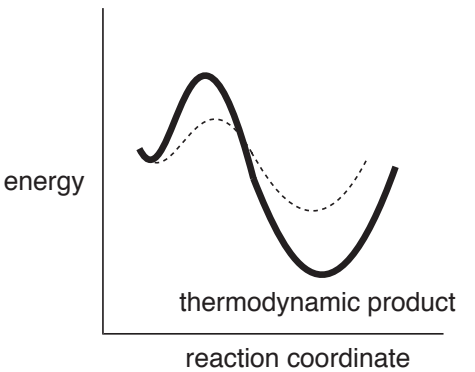


For situations such as bond rotation in ethane and ring inversion in cyclohexane, the reactant and product are the same and the reaction is said to be ***thermoneutral***. The most common case, as depicted in the above diagram, is where the energy of the products is lower than that of the reactants. The reaction is said to be *exothermic*, and the difference in stabilities of reactant and product is simply the difference in their energies. For example, the "reaction" of *gauche n*-butane to *anti n*-butane is *exothermic*, and the difference in stabilities of the two conformers is simply the difference in the energies (~3.8 kJ/mol).

Chemical reactions can also be *endothermic*, which give rise to a reaction profile.

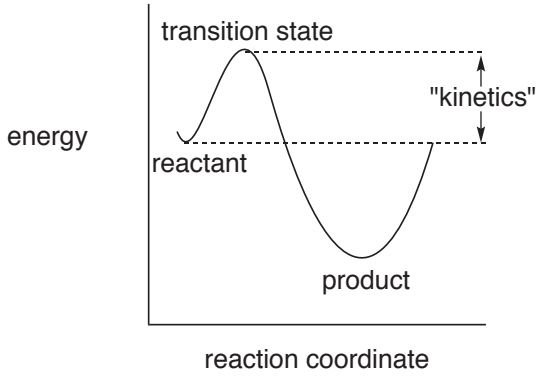


Where two or more different products may form in a reaction, thermodynamics tells us that if we wait long enough, the product formed in greatest abundance will be that with the lowest energy irrespective of pathway.



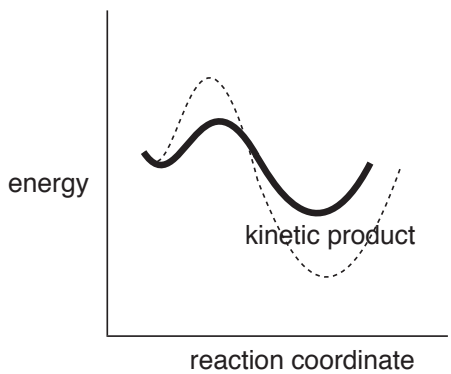
In this case, the product is referred to as the ***thermodynamic product*** and the reaction is said to be ***thermodynamically controlled***.

The energy of the transition state above the reactants (the activation energy) provides the connection with reaction rate (kinetics). Of course, such an interpretation is based on the notion that all reactions actually pass through a single transition state.



Aside from the obvious dependence on the concentration of reactants, absolute reaction rates also depend on the percentage that encounters between molecules will actually lead to reaction (the so-called pre-exponential or A factor). The hope is that pre-exponential factors for closely-related reactions will be very similar and therefore can be ignored. Thus, it is not at all evident that activation energies for disparate reactions will parallel measured reaction rates.

The product formed in greatest amount in a kinetically controlled reaction (the kinetic product) is that proceeding via the lowest energy transition state, irrespective of whether or not this is lowest energy product (the thermodynamic product).



Kinetic product ratios show dependence with activation energy differences which are identical to thermodynamic product ratios with difference in reactant and product energies.

THERMOCHEMICAL RECIPES AND CALCULATING ACCURATE HEATS OF FORMATION

The "energy" of a molecule is most commonly reported as a heat of formation. As noted in the previous topic, this is defined as the enthalpy at 298.15K of a hypothetical chemical reaction in which the molecule is transformed into a set of products that correspond to the most stable forms of its constituent pure elements at room temperature. For example, the heat of formation of ethylene corresponds to the enthalpy of a reaction to yield graphite and molecular hydrogen.

$$C_2H_4 \rightarrow 2C\ (graphite) + 2H_2$$

Differences in heats of formation between the products and reactants (reaction enthalpies) indicate the extent to which the reaction will be favorable (*exothermic*) or unfavorable (*endothermic*), and allow thermodynamic product distributions to be established.*

In almost all cases, the heat of formation is obtained from a heat of combustion. For example, the heat of formation of ethylene would likely have been established from its reaction with oxygen to produce carbon dioxide and water.

$$C_2H_4 + 3O_2 \rightarrow 2CO_2 + 2H_2O$$

Experimental heats of formation are available for ~2000 compounds. While much of the data is accurate to within 4-8 kJ/mol, a significant portion is subject to greater uncertainty. The most egregious source of error is that the reported heat actually does not correspond to the reported structure. More common sources of error include impure samples, incomplete combustion and most importantly, poorly characterized combustion products. Hydrocarbons and oxycarbons present fewest problems as combustion leads only to carbon dioxide and water. However, combustion of molecules with other elements may give rise to a complex mixture of products and greater uncertainty, with nitrogen compounds being particularly problematic.

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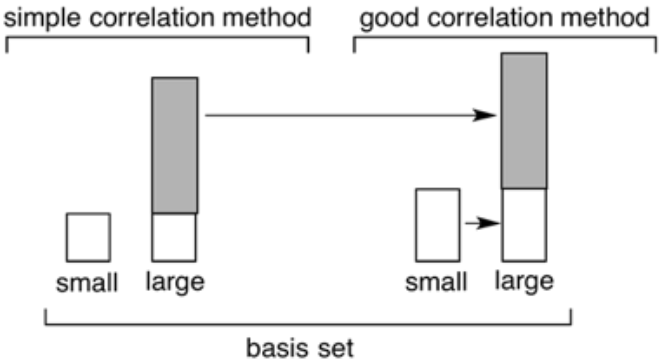
* Of course, other references are equally suitable for examining mass balanced reactions. For example, total energies from quantum chemical calculations are referenced to separated nuclei and electrons, in the case of ethylene.

$$C_2H_4 \rightarrow 2C^{6+} + 4H^{+} + 16C^{-}$$

Despite their fundamental importance, heats of formation are not routinely determined for new compounds. While the combustion experiment is straightforward and does not require particularly expensive instrumentation, accurate measurements may require (and will likely destroy) significant quantities of compound. Very few chemists are willing to part with hundreds of mg of a compound that they have just spent days, weeks or months preparing.

Because of the lack of experimental data and serious concerns over the accuracy of part of the data that do exist, considerable attention has been directed at the use of quantum chemical calculations to obtain heats of formation. One avenue that has been pursued relies on the knowledge that CCSD (T) calculations (coupled cluster singles and doubles with triples corrections introduced perturbatively) reliably reproduce the energetics of a wide variety of organic reactions. The problem is that the singles and doubles contribution scale as $O(\eta^6)$, where η is the number of basis functions, and the triples correction scales as $O(\eta^7)$. This limits practical applications of the method to very small molecules (<15 non-hydrogen atoms).

A simplified account of the "solution" first proposed by John Pople is depicted in the next page. The essential idea is that the energy obtained using a "good" electron correlation method and a large basis set may be closely approximated by combining the energy calculated using the good correlation method with a small basis set with difference in calculated energies for a "simple" correlation method with small and large basis sets. In principle, only three calculations are required: small and large basis set calculations with the simple correlation method and a small basis set calculation with the good correlation method. In practice, some of the schemes that have been formulated do exactly this while others employ a combination of simple correlation methods.



The original Pople implementation and subsequent developments primarily by Larry Curtiss are now collectively known as Gx methods. G1 relied on MP4 as the "good" correlation method with a gradual shift to the more costly and more accurate CCSD(T) method. To some extent, the overall objective has also broadened, from a means to approximate correlation energy to a stand-alone source of thermochemical data (298° heats of formation). Our focus is on the former, as possible low-cost replacements of the CCSD(T) correlation method.

The two most widely-used methods are G3(MP2) and G3, and the two most recent additions to the series are G4(MP2) and G4. A summary of the procedures involved in calculating electronic energy using these four methods is provided on the next page. The full recipes lead to heat of formation in addition to electronic energy, and require specifying an equilibrium geometry and a procedure for obtaining vibrational frequencies in addition to "empirical" corrections to account for the standard states of each of the elements. While each the four procedures involves several steps, these can be carried out in proper sequence without user intervention.

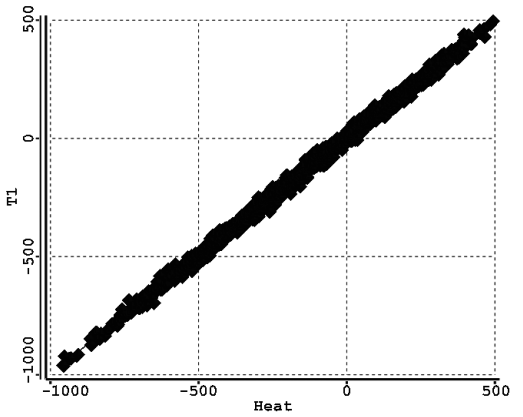
	simple correlation method	good correlation method	limiting steps
G3(MP2)	MP2	QCISD(T)/6-31G*	T in QCISD(T)
G3	MP2 & MP4	QCISD(T)/6-31G*	MP4 and T in QCISD(T)
G4(MP2)	MP2	CCSD(T)/6-31G*	T in CCSD(T)
G4	MP2 & MP4	CCSD(T)/6-31G*	MP4 and T in CCSD(T)

The T1 Thermochemical Recipe

The simplest of the GX recipes, termed G3(MP2), involves several costly steps, most significantly an MP2/6-31G* geometry calculation, a HF/6-31G* frequency calculation and a QCISD(T)/6-31G* energy calculation. In practice, G3(MP2) scales as the 7^{th} power of size and is applicable only to molecules with molecular weights less than 150 amu. Clearly, even simpler procedures are required for routine application to larger molecules.

The goal behind the T1 recipe was to maintain the accuracy of G3(MP2) but at significantly reduced computation cost. It is limited to uncharged, closed-shell molecules comprising H, C, N, O, F, Si, P, S, Cl and Br. T1 substitutes the MP2/6-31G* geometry used in G3(MP2) by a HF/6-31G* geometry, eliminates both the HF/6-31G* frequency and the QCISD(T)/6-31G* energy calculations and approximates the MP2 energy calculation with the G3MP2 large basis set by an analogous calculation using a dual basis set RI-MP2 model. Taken together, these changes reduce computation time by 2-3 orders of magnitude, and T1 calculations on molecules in the molecular weight range of 400-500 amu are practical.

The T1 recipe, unlike G3(MP2), involves parameters, specifically atom counts, Mulliken bond orders and HF/6-31G* and RI-MP2 energies. These have been determined using linear regression as a best fit to G3(MP2) (not experimental) heats of formation for >1100 small molecules. It reproduces these values with mean absolute and RMS errors of 1.8 and 2.5 kJ/mol, respectively. More important, the T1 recipe reproduces experimental heats of formation for a set of >1800 diverse organic molecules from the NIST thermochemical database with mean absolute and RMS errors of 8.5 and 11.5 kJ/mol, respectively. The plot provided below covers the data from -1000 to +500 kJ/mol.



Heats of formation from the T1 recipe are included as a property in the Spartan Spectra and Properties Database (SSPD), a database that presently comprises more than a 300,000 entries.

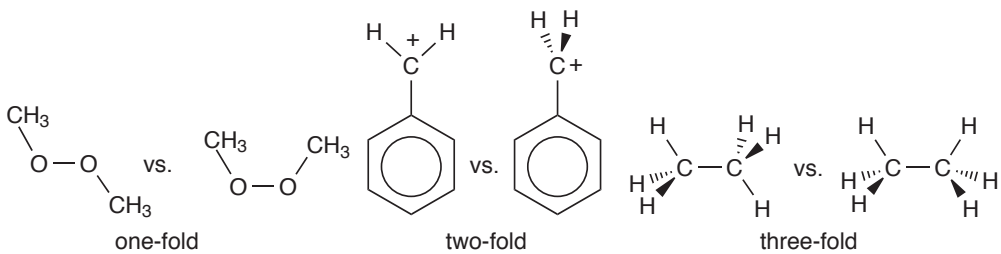
INTERPRETING CONFORMATIONAL PREFERENCES

Rotation about single bonds is periodic, retracing itself every 360°, and any function that seeks to describe the energy of internal rotation must also repeat itself every 360°. In practice, the energy function, $E^{torsion}$, is written as a combination of simpler functions, V_n, in the torsion angle ω, each of which repeats n times in a 360° interval.

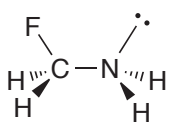
$$E^{torsion}(\omega) = V_1(\omega) + V_2(\omega) + V_3(\omega)...$$

The first three terms, V_1, V_2, and V_3 repeat every 360°, 180°, and 120°, respectively, and are referred to as one-fold, two-fold, and three-fold potentials.*

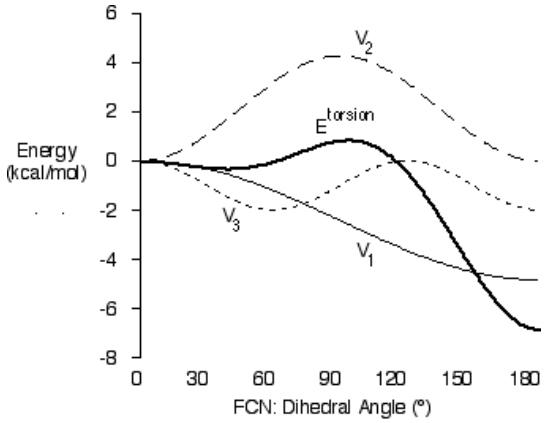
Separation into distinct n-fold potentials is a useful concept because each can be associated with a particular chemical phenomenon. For example, a one-fold potential describes the different energies of *anti* (COOC=180°) and *syn* (COOC=0°) conformers of dimethylperoxide, while a two-fold potential describes the different energies of planar and perpendicular conformers of benzyl cation. Three-fold potentials, which are more familiar to chemists, describe the difference between staggered and eclipsed conformers in molecules like ethane.



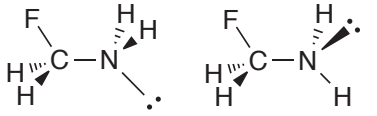
While rotation in some molecules might be adequately described using only one of the components or a combination of two components, other molecules require more complex combination. This is illustrated by fluoromethylamine.



* The torsional potential in most organic molecules will be adequately described in terms of one, two and three-fold components, and only rarely will higher-order terms be needed.

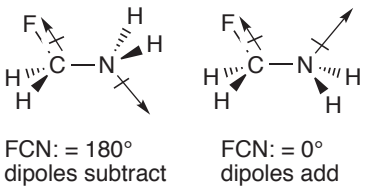


The heavy solid line describes $E^{torsion}$ for rotation about the CN bond, while the light solid line, the dashed line and the dotted line correspond to the one-fold, two-fold and three-fold components, respectively. There are two distinct minima.



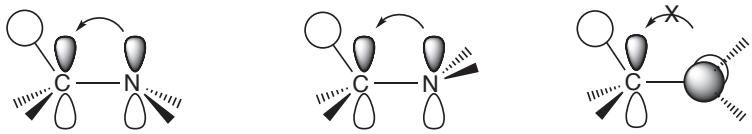
The lower (global) minimum arises when the CF bond and the nitrogen lone pair are *anti*, while the higher and much more shallow minimum is close to a *gauche* structure, FCN: dihedral angle of ~45°. Also, note that one of the two energy maxima is close to an eclipsed structure, with the FCCN: dihedral angle of ~115°.

The behavior of $E^{torsion}$ becomes clear when it is resolved into its components. The one-fold term reflects a clear and very strong preference for the CF bond and the nitrogen lone pair to be *anti* and not *syn*. This preference might be electrostatic since the *anti* structure arranges the dipoles associated with the CF bond and nitrogen lone pair in opposite directions.



The three-fold term reflects the preference for staggered over eclipsed structures, and contributes less to the variation in $E^{torsion}$ than either of the one-fold or two-fold terms.

What is most interesting, and perhaps not have been easily anticipated without this type of analysis, is the large contribution made by the two-fold potential, which reflects a strong preference for a planar arrangement of FCN:. This can be attributed to stabilization resulting from donation of the lone pair orbital on nitrogen into low-energy unfilled molecular orbital associated with the CF bond, requiring that the molecule adopts either a *syn* planar or *anti* planar conformation and not a perpendicular conformation.



syn planar *anti* planar *perpendicular*

Note that the terms that contribute to $E^{torsion}$ are completely independent of each other, and each may be treated as one part of a larger picture. Thus, the observation that electron donation from the nitrogen lone pair into the empty orbital associated with the CF bond is optimal when the two groups are planar is independent of the observation that *cis* coplanar structure is destabilized, relative to the *anti* structure, by dipole-dipole interactions.

CALCULATING INFRARED SPECTRA

The infrared spectrum of a molecule arises because of transitions between vibrational energy levels. Each line in an infrared spectrum is characterized by a frequency (energy) and an intensity. In one dimension (a diatomic molecule), it is common practice to assume that the frequency is proportional to the square root of the ratio of the second-derivative of the energy with respect to the internuclear distance, r, and the reduced mass (the product of the masses of the two atoms divided by their sum).

$$\text{vibrational frequency} \propto \sqrt{[(d^2E(r)/dr^2/)\text{reduced mass}]}$$

This is referred to as the ***harmonic approximation***, the origin of which can be seen by expanding the energy in a Taylor series.

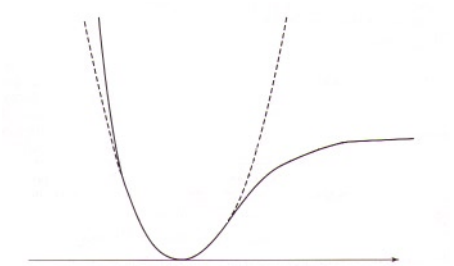
$$E(r) = E(r_0) + (dE(r)/dr)\, r + (d^2E(r)/dr^2)\, r^2 + \text{higher-order terms}$$

$E(r_0)$ is a constant and dE(r)/dr (the gradient) is assumed to be zero. The latter implies that the underlying structure corresponds precisely to a minimum (or a maximum) on the potential energy curve. Were this not the case, the first derivative would be non zero and the calculated frequency would be meaningless. Nearly all practical calculations ignore cubic and higher-order terms (***anharmonic*** terms), leaving only the second derivative term (the ***force constant***). This said, the frequency may be interpreted as the relative ease or difficulty of stretching the bond away from its equilibrium position, that is, the curvature of the energy surface at the minimum. Where distortion away from the equilibrium position is easy, the result is a low frequency; where it is difficult the result is a high frequency. High (reduced) mass leads to a low frequency while low mass leads to high frequency.

The expression for vibrational frequency qualitatively accounts for mass effects on reaction energies (***equilibrium isotope effects***). Even at 0K molecules vibrate, giving rise to the so-called zero-point vibrational energy (or simply ***zero-point energy***). Zero-point energy is directly proportional to the sum of the vibrational frequencies and decreases with increasing mass. For example, the zero-point energy of HCl is lowered upon replacement of hydrogen by deuterium. Thus, the measured energy

(enthalpy) decreases with increasing mass and the energy of DCl is smaller (more negative) than that for HCl.

Because the potential energy has been approximated by a quadratic function, calculated frequencies will almost always be larger than measured frequencies. This is because a quadratic function goes to infinity with increase in distance rather than going asymptotically to a constant (separated atoms), meaning that the potential curve will be too steep.



It is possible to extract the harmonic frequency from an experimental spectrum by measuring the spacing of the energy levels associated with the ground and excited states of a particular vibration. (The lines would be evenly spaced were the potential quadratic.) However, such an analysis is impractical for any but diatomic and very simple polyatomic molecules.

Generalization from a diatomic to a polyatomic molecule is straightforward. The energy of displacement away from the equilibrium position is expanded in the same way as before, the only difference being that a vector quantity, **x**, replaces a scalar quantity, x.

$$E(\mathbf{x}) = E(\mathbf{x_0}) + \Sigma_i(\partial E(\mathbf{x})/\partial x_i)x_i + \tfrac{1}{2}\Sigma_{ij}(\partial^2 E(\mathbf{x})/\partial x_i \partial x_j)x_i x_j + \text{higher-order terms}$$

As with the expression for a diatomic molecule, the leading term is a constant, the first derivative term is zero and cubic and higher-order terms are ignored. For a molecule with N atoms, the dimension of **x** is 3N (x,y,z Cartesian coordinates for each atom), although there

are only 3N-6 (3N-5 for a linear molecule) vibrational frequencies. Six dimensions (five for a linear molecule) correspond to translation away from and rotation around the center of mass.

The first (and only computationally expensive) step involved in calculating the vibrational spectrum of a polyatomic molecule is evaluation of the full set of second energy derivatives in Cartesian coordinates. These then need to be mass weighted. Diagonal terms ($\partial^2 E(\mathbf{x})/\partial x_i^2$) are divided by the mass of the atom associated with x_i, and off-diagonal terms ($\partial^2 E(\mathbf{x})/\partial x_i \partial x_j$) are divided by the product of the square root of the masses of the atoms associated with x_i and x_j. These expressions reduce to that already provided for the one-dimensional case.

The second step involves replacing the Cartesian coordinates by a new set of coordinates $\boldsymbol{\zeta}$, such that the matrix of mass-weighted second derivatives is diagonal. δ_{ij} is the so-called Kronecker delta function which is 1 if i=j and 0 otherwise.

$$[\partial^2 E(\zeta)/\partial \zeta_i \partial \zeta_j]/(\sqrt{M_i}\sqrt{M_j}) = \delta_{ij}\,[\partial^2 E(\zeta)/\partial \zeta_i^2]/M_i$$

These new coordinates are referred to as ***normal coordinates***. While the normal coordinates for some vibrations may be described in terms of stretching of one bond or bending of one angle, more commonly they will be made up of mixtures of several bond stretches, angle bends and other motions.

The third step involves removing the six coordinates corresponding to the three translations and three rotations, leaving 3N-6 vibrational coordinates.

The intensity of a line in the infrared spectrum is proportional to the change in the dipole moment along the vibrational coordinate. It follows that where there is no change in dipole moment, for example, in a homonuclear diatomic molecule, the infrared intensity is zero.

The two major components of the earth's atmosphere, N_2 and O_2, are homonuclear diatomics and do not absorb in the infrared, that is, the intensity is zero. However, two of the four vibrational motions of CO_2, the third most common but very minor molecular component in

the atmosphere, have non-zero infrared intensities. As a result, carbon dioxide absorbs radiation reflected from the earth's surface thereby trapping heat and leading to an increase in temperature (the so-called ***greenhouse effect***).

Lack of a line in the infrared spectrum does not mean that the molecule does not vibrate or that the vibrational energy for this line does not contribute to the zero-point energy. Rather, it means that absorption of radiation does not occur leading to a change in vibrational energy state. It should also be noted that a particular line that is infrared inactive might be visible in the Raman spectrum (an alternative form of vibrational spectroscopy based on reflectance rather than absorption). Here the intensity is related to the change in the polarizability rather than the change in dipole moment.

The application of quantum chemical models to infrared spectroscopy requires calculation of the second energy derivatives and first dipole moment derivatives with regard to changes in geometrical coordinate. The former completely dominates and scales as the fifth power of the size (number of basis functions). Infrared spectra may be calculated using semi-empirical molecular orbital models, for example, the PM3 models available in ***Spartan***, Hartree-Fock molecular orbital models, density functional models and MP2 models. Of the theoretical models available in ***Spartan***, semi-empirical models provide a poor account, Hartree-Fock models provide a reasonable account but density functional and MP2 models with polarization or larger basis sets perform best. Density functional models are the obvious choice for infrared spectra calculations, offering better results than Hartree-Fock models at comparable cost, and comparable results at much lower cost than MP2 models.

For two reasons, we recommend EDF2/6-31G* over the ωB97X-D/6-31G* model for infrared spectra calculations. First, EDF2/6-31G* was specifically formulated to reproduce measured infrared frequencies. Second, it is significantly (factor of two) less costly than ωB97X-D for frequency calculation and is easily applicable to the calculation of infrared spectra of organic molecules of moderate size (up to 400-500 amu). There are two major deficiencies with infrared

spectra obtained directly from the EDF2/6-31G* model. The first is that calculated frequencies are almost always too large, typically by 3-5%. This can be directly traced to the harmonic approximation and to a potential energy curve that is too steep.

> Other density functional models and the MP2 model show similar behavior. Vibrational frequencies obtained from Hartree-Fock models show an even larger systematic error in the same direction (frequencies too large), typically by 12-14%. Here two factors contribute. The first is the insistence on a quadratic potential, the same problem associated with density functional and MP2 models. The second is due to the fact that bond dissociation is improperly described by Hartree-Fock models, as evidenced by the fact that Hartree-Fock bond lengths are uniformly shorter than experimental distances. This suggests that the potential energy surface will be too steep and the frequency will be too large.

The second and more conspicuous deficiency is due to the fact that the lines in an infrared spectrum measured at finite temperature are broadened due primarily to rotational structure, whereas the lines in a calculated spectrum correspond to an isolated molecule at 0K and are sharp. There may be other differences, such as the absence of overtones, that is, vibrational transitions originating from excited vibrational states and, more importantly, lack of solvent. Although these are more difficult to quantify.

It is straightforward to correct the calculated spectrum to account for both deficiencies. First the spectrum may be uniformly scaled (multiplied by a parameter in the range of 0.95-0.97 for density functional models). Second, the calculated frequencies and intensities may be fit to a Lorentzian function with peak width and half peak height being treated as a second parameter.

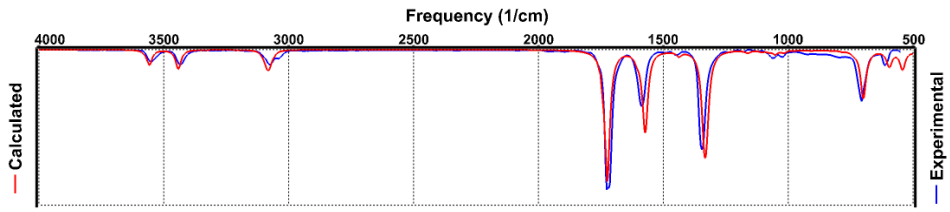
Quality of Calculated Infrared Spectra

An infrared spectrometer records frequencies in the range 500-4500 cm^{-1}. Frequencies below this range (which may require special instrumentation to measure) typically correspond to torsional motions and may depend strongly on conformation. It should be noted that the spectral region beyond ~2800 cm^{-1} is dominated by

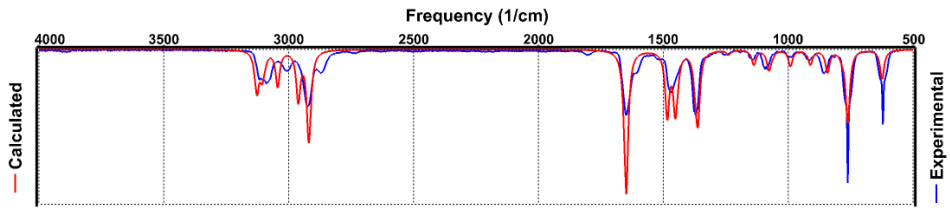
CH stretching vibrations and may be too crowded to be of value.

Calculated infrared spectra from the EDF2/6-31G* model that have been scaled to account for the systematic error in frequency and broadened to account for finite temperature are visually quite similar to the corresponding experimental spectra (taken from the NIST database). The four examples that follow, benzamide, (dimethylmethylidene) cyclopentadiene, 1,2-epoxy-*cis*-4-vinylcyclohexane and camphor are typical of the ~1000 comparisons that have been made.

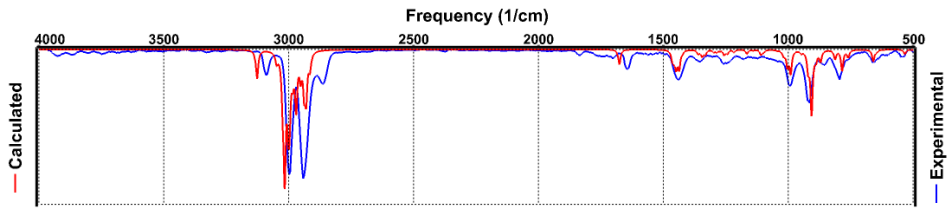
benzamide



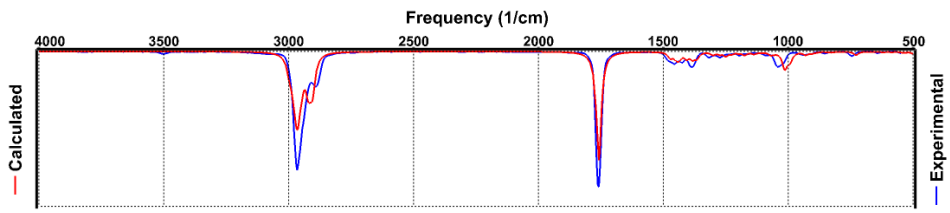
(dimethylmethylidene)cyclopentadiene



1,2-epoxy-cis-4-vinylcyclohexane



camphor



Even though scale and line-broadening parameters have been individually adjusted for these four examples, the values of the parameters are quite similar. Default parameters could have been substituted with little change.

CALCULATING NMR SPECTRA

There are several reasons why NMR spectroscopy, in particular proton and ^{13}C NMR, is the most important analytical technique for characterizing organic molecules. The experiment is straightforward and can be carried out rapidly. It requires relatively small samples and is non destructive. The so-called proton-decoupled ^{13}C NMR is particularly simple, comprising a single line (resonance) for each and every unique carbon. Despite its simplicity (or perhaps because of it), associating an ^{13}C spectra to a particular molecular structure can be problematic and prone to error, in particular, where alternative structures might be very similar. 2D spectra, in particular, COSY and HMBC spectra that combine chemical shifts and HH and CH coupling constants are more and more commonly employed to assist in assignment.

A routine and reliable method to predict ^{13}C chemical shifts as a function of three-dimensional structure would clearly be of value in helping to assign experimental NMR spectra of complex molecules, at the very least, either providing supporting evidence or casting doubt on a proposed assignment. One might argue that such a method already exists in the form of extensive NMR spectral databases. An exact match to an existing spectrum provides a definitive structure, while one or more close matches to entries in a database suggest what types of structures are reasonable. Of course, entirely new compounds will never give exact matches, simply because the spectrum is not in the database. Closely related are empirical relationships based primarily on connectivity and obtained from fitting previously assigned (and presumed correctly assigned) spectra. While these can achieve some degree of success, the fact that NMR chemical shifts (and of course three-bond HH and CH coupling constants) are sensitive to conformation means that molecules that appear to be very similar may give rise to entirely different spectra. Closely

related to this is the fact that most organic molecules are not rigid and described by a single 3D structure. Rather, they comprise a connection of different 3D structures (conformers) and the resulting spectrum is a weighted average of energy weighted spectra of the individual conformer.

One alternative to databases and purely empirical schemes would be to calculate chemical shifts *a priori* using quantum mechanics.* In so doing, differences in structure and conformation are directly taken into account. The underlying methodology has been available for several decades for both Hartree-Fock and density functional models. However, calculations have only rarely been used to actually assist in the interpretation of spectra, and few practicing chemists seem to be aware that quantum chemical calculations are now possible (and practical) for real molecules, and how well calculations perform in accounting for chemical shifts. Those who are aware, are confronted and all too often stymied, with what must seem to be an endless list of calculation methods. We believe that the full potential of quantum chemical calculations as assists to assigning NMR spectra will only be realized after a small number of alternatives or standard models are elaborated and their limits and reliability clearly defined. Stated differently, chemists need to approach quantum chemical calculations much in the same way that they now approach a spectrometer.

Underlying Theory

Application of an external magnetic field causes the nuclear spins to align either parallel or antiparallel to the field. The difference in energy (ΔE) between nuclear spin states is given by.

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

γ is the gyromagnetic ratio, a constant that depends on the magnetic moment of the nucleus, $\hbar$ is Planck's constant/2π and B_0 is the strength of the magnetic field ***at the nucleus***. What makes nuclear magnetic resonance (NMR) spectroscopy useful to chemists is that

* Neural nets offer another alternative, the downside being that their construction requires very large datasets. We are in the process of exploring this replacing experimental chemical shifts as reference data by values calculated from quantum chemical models.

the magnetic field felt at the nucleus is different for each chemically distinct nucleus in a molecule. This is because the applied magnetic field is slightly weakened by electrons around the nucleus and the extent of this weakening depends on the detailed chemical environment. Nuclei that are well shielded by the electron cloud experience a lesser field than those that are poorly shielded and, as a result, show a smaller energy splitting. The splitting, relative to a standard, is termed a ***chemical shift***.

Two additional comments need to be made. First, not all nuclei possess non-zero magnetic moments and, therefore, give rise to an NMR signal. The magnetic moment for the proton is non-zero, although that of the dominant isotope of carbon (^{12}C) is not. Fortunately, the minor (1%) isotope ^{13}C possesses a finite magnetic moment. The fact that the dominant isotope of carbon has a zero magnetic moment is both a "curse" and a "blessing". A curse because it certainly slowed the application of carbon NMR to organic chemistry by several decades (waiting for magnet and spectrometer technology to catch up). A blessing because it results in a ^{13}C spectrum being much simpler (and easier to interpret) than a proton NMR spectrum.

The second comment is that proximate nuclei with finite magnetic moments will contribute to the magnetic field felt by the nuclei under investigation. Whereas nearby protons interact (couple) leading to splitting of the individual lines in the proton NMR spectrum, the very low probability (1% x 1%) that two ^{13}C nuclei will be adjacent all but eliminates carbon-carbon coupling. Proton-^{13}C coupling does occur but can be (and nearly almost always is) removed. The result is that the ^{13}C NMR spectrum contains only one line per unique carbon.

From the perspective of the experiment, the fact that the difference in energy between nuclear spin states (and ultimately the ability of an NMR spectrometer to distinguish chemically-different nuclei) is directly proportional to the magnetic field strength is disheartening. Magnets used in NMR spectrometers are now approaching practical and perhaps theoretical limits, and a mere 10-20% increase in field strength (translating to an equivalent increase in resolution) can mean more than doubling the cost of the spectrometer. Without a

major breakthrough in magnet technology, the prognosis for greatly improved resolution over what is now possible (practical) is bleak. On the other hand, computer performance continues to double every few years (anticipated by Moore's law), and NMR spectra calculations on larger and ever more complex molecules continue to become more routine.

Correcting ^{13}C Chemical Shifts from B3LYP/6-31G*, ωB97X-D/6-31G* and ωB97X-V/6-31G* Density Functional Models

Spartan can calculate NMR chemical shifts using Hartree-Fock models as well as a range of density functional models. We have focused on and carefully examined three density functional models, specifically B3LYP, ωB97X-D and ωB97X-V models with the 6-31G* basis set. Used directly, all three models lead to rms errors in ^{13}C chemical shifts on the order of 5-6 ppm (over a range from 0-250 ppm), and are not reduced by replacing 6-31G* by a larger more complete basis set. Errors of this magnitude are likely to be too large for reliably assigning the lines in an experimental ^{13}C spectrum, for supporting a proposed structure assignment or perhaps most important for casting doubt on one.

Empirically Corrected ^{13}C Chemical Shifts

Empirical schemes have been developed to dramatically reduce errors in ^{13}C chemical shifts, specifically for B3LYP/6-31G*, ωB97X-D/6-31G* and ωB97X-V/6-31G* models. These utilize the same dataset for the linear regression comprising ~8000 sp^3 carbons, ~6200 sp^2 carbons (including aromatic carbons) and ~450 sp carbons.* The functional form is as follows:

$$^{13}\mathbf{C}_i = {}^{13}C_i \cdot \mathrm{Scale} + \Sigma_k \left[X^{(0)}_k + X^{(1)}_k (R_{i,k} - 1) + X^{(2)}_k (R_{i,k} - 1)^2\right]$$

$^{13}\boldsymbol{C}$ is the corrected chemical shift and ^{13}C is the uncorrected chemical shift and *Scale* is a scaling factor. Summation is carried out over all bonds (1 or 2 for sp carbons, 3 for sp^2 carbons and 4 for sp^3 carbons). $X^{(0)}_k$, $X^{(1)}_k$ and $X^{(2)}_k$ are parameters that depend on the atom bonded

* Care has been taken to select either rigid molecules or molecules where a single conformer dominates the equilibrium (Boltzmann) distribution.

to carbon (H, C, N, O, F, Si, P, S, Cl or Br) and $R_{i,k}$ are bond lengths to carbon. Different expressions apply to sp, sp^2 and sp^3 carbons. The equation for sp carbon involves four $X^{(0)}$parameters, four $X^{(1)}$ parameters and one $X^{(2)}$ parameter (11 parameters in total), that for sp^2 carbon involves all ten $X^{(0)}$ parameters, six $X^{(1)}$ parameters and four $X^{(2)}$ parameters (21 parameters in total), and that for sp^3 carbon involves all ten $X^{(0)}$ parameters but no $X^{(0)}$or $X^{(1)}$ parameters (11 parameters in total).*

Resulting rms errors are 2.4, 2.1 and 2.1 ppm for B3LYP, ωB97X-D, and ωB97X-V models, all significantly (factor of 2-3) smaller than the uncorrected shifts. In our view, these are close to experimental deviations in ^{13}C shifts commonly noted due to changes in solvent.

ATOMIC AND MOLECULAR ORBITALS

Chemists have developed a variety of methods for describing electrons in molecules. Lewis structures are the most familiar. These drawings assign pairs of electrons either to single atoms (lone pairs) or pairs of atoms (bonds)**. The quantum mechanical equivalents are atomic and molecular orbitals which arise from solution of (approximate) Schrödinger equations for atoms and molecules, respectively. Molecular orbitals are spread throughout the entire molecule, that is, they are delocalized.*** Because of this, they are typically more difficult to interpret than Lewis structures.

Orbital Surfaces

Molecular orbitals may be able to provide important clues about chemical reactivity, but before we can use this information we first need to understand the fundamentals for very simple molecules. The following figure shows two representations, a hand drawing and

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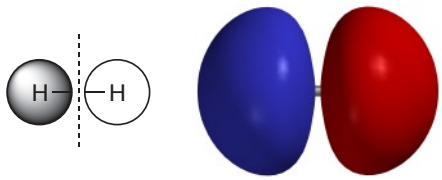
* Parameter files are available for review from: https://downloads.wavefun.com/NMR_Correction_Parameters.zip.

** The present discussion is limited to molecules in which all electrons are paired. Molecules with one or more unpaired electrons (radicals, triplet states, etc.) may also be treated.

*** Is it possible to localize molecular orbitals such that they correspond more closely to conventional Lewis structures. Because this is costly in terms of computation and to some extent "ill defined" (the need to specify what conditions are to be met) localization is only rarely performed.

a ***Spartan***-generated image of an unoccupied molecular orbital of hydrogen molecule, H_2.



unoccupied molecular orbital in hydrogen

Open ***hydrogen empty*** in the ***topics*** directory. Note that except for the colors (sign of the orbital) the two sides of the graphic are identical. The junction between red and blue regions is where the value of the orbital is zero. Close ***hydrogen empty*** when you are finished.

The familiar hand drawing shows the orbital as two circles and a dashed line. The circles identify regions where the orbital takes on a significant value, either positive (*shaded*) or negative (*unshaded*). The dashed line identifies locations where the orbital's value is exactly zero (a ***node***). The drawing is useful, but it is also limited. We only obtain information about the orbital in two dimensions, and we only learn the location of significant regions and not how the orbital builds and decays inside and outside of these regions.

The ***Spartan***-generated image depicts the same orbital as a surface of constant value. The surface is accurate in that it is derived from an authentic (but approximate) calculated solution to the quantum mechanical equations of electron motion (the Schrödinger equation). Equally important, the image is three-dimensional, and can be manipulated and looked at from a variety of different perspectives. It is not unexpected that the orbital consists of two distinct surfaces represented by different colors. The two surfaces have the same meaning as the two circles in the orbital drawing. They identify regions where the orbital takes on a significant value, either positive (blue) or negative (red). The orbital node is not shown, but we can guess that it lies midway between the two surfaces (this follows from the fact that the orbital's value can only change from positive to negative by passing through zero).

Atomic Orbitals

Atomic orbitals (descriptions of atoms) are the fundamental building blocks from which molecular orbitals (descriptions of molecules) are assembled. The familiar atomic orbitals for the hydrogen atom are in fact exact solutions of the Schrödinger equation which can actually be solved exactly for this one electron system. They form an infinite collection (a complete set), the lowest-energy member representing the best location for the electron, and higher-energy members representing alternative locations. Orbitals for real many-electron atoms are normally (and necessarily) assumed to be similar in form to those of hydrogen atom, the only difference being that, unlike hydrogen, more than the lowest-energy atomic orbital is utilized. In practical quantum chemical calculations, atomic orbitals for many-electron atoms are made up of sums and differences of a finite collection of hydrogen-like orbitals (see the topic ***Theoretical Models***).

It is common practice to divide the full set of atomic orbitals into core and valence orbitals, and further to ignore the former. Valence orbitals for an element in the first long row of the *Periodic Table* are 2s, $2p_x$, $2p_y$ and $2p_z$, and for the second long row are 3s, $3p_x$, $3p_y$ and $3p_z$. In the case of first-row elements, a single orbital, 1s, lies underneath (is a core orbital) while in the case of second-row elements, a set of five orbitals, 1s, 2s, $2p_x$, $2p_y$ and $2p_z$, lie underneath.

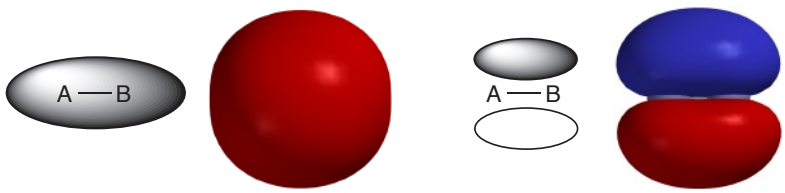
Open ***fluoride and chloride*** in the ***topics*** directory. On the top row are the four valence orbitals of fluoride anion and on the bottom row the four valence orbitals of chloride anion. You can select among them by *clicking* (left mouse button) on each in turn. First note that the three 2p orbitals in fluoride are identical except for the direction in which they point. The same is true for the three 3p orbitals in chloride. Next, note that the valence orbitals in chloride are larger than those in fluoride. Atoms further down in the *Periodic Table* are generally larger than analogous atoms further up. Close ***fluoride and chloride*** when you are finished.

Orbitals and Chemical Bonds

Although molecular orbitals and Lewis structures are both used to describe electron distributions in molecules, they are used for

different purposes. Lewis structures are used to count the number of bonding and non-bonding electrons around each atom. Molecular orbitals are not useful as counting tools, but orbitals and associated orbital energies are useful tools for describing chemical bonding and reactivity. This section describes a few common orbital shapes and illustrates their use.

Molecular orbital surfaces can extend over varying numbers of atoms. If the orbital surface (or surfaces) is confined to a single atom or to atoms which are not close together, the orbital is regarded as non-bonding. If the orbital contains a surface that extends continuously over two neighboring atoms, the orbital is regarded as bonding with respect to these atoms. Adding electrons to such an orbital will strengthen the bond between these atoms and cause them to draw closer together, while removing electrons will have the opposite effect. Two different kinds of bonding orbitals are depicted below. The drawing and surface on the left correspond to a σ bond while the drawing and surface on the right correspond to a π bond.

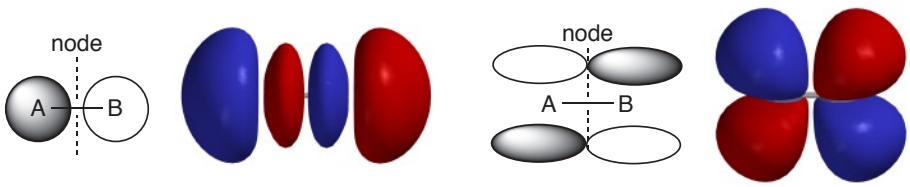


σ bonding π bonding

Open ***nitrogen bonding*** in the ***topics*** directory. The image on the left corresponds to the σ bonding orbital of N_2, while that on the right corresponds to one of two equivalent π bonding orbitals. Switch to a transparent or mesh model to see the underlying molecular skeleton. Note that the σ orbitals is drawn in a single color (insofar as NN bonding is concerned) while the π orbital is made up of red and blue parts. This indicates a node or a break in the latter, although not involving the NN bond. Close ***nitrogen bonding*** when you are finished.

It is also possible for an orbital to contain a node that divides the region between two neighboring atoms into separate atomic regions. Such an orbital is regarded as antibonding with respect to these atoms. Adding electrons to an antibonding orbital weakens the bond

and pushes the atoms apart, while removing electrons from such an orbital has the opposite effect. The following pictures show drawings and orbital surfaces for two different kinds of antibonding orbitals. As above, the left and right-hand sides correspond to σ and π type arrangements, respectively.



σ antibonding π antibonding

Open ***nitrogen antibonding*** in the ***topics*** directory. The image on the left corresponds to the σ antibonding (so-called σ*) orbital of N_2 while that on the right corresponds to one of the two equivalent π antibonding (so-called π*) orbitals. Switch to a mesh or transparent surface to see the underlying molecular skeleton. Note that the σ* orbital has a single node (change in color from red to blue) in the middle of the NN bond, while the π* orbital has two nodes (one in the middle of the NN bond and to the other along the bond). Close ***nitrogen antibonding*** when you are finished.

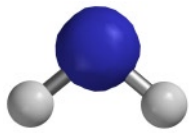
To summarize, bonds can be strengthened in two different ways, by adding electrons to bonding orbitals, or by removing electrons from antibonding orbitals. The converse also holds. Bonds can be weakened either by removing electrons from bonding orbitals or by adding electrons to antibonding orbitals.

Singlet Methylene

Molecular orbitals in molecules which contain many atoms are typically spread throughout the molecule (they are delocalized). Delocalized orbitals have complicated shapes and contain multiple interactions that may be bonding, non-bonding, antibonding, or any mixture of all three. Nevertheless, these shapes can usually be broken down into two-atom interactions and analyzed using the principles outlined earlier. This process is illustrated for a triatomic molecule, singlet methylene, CH_2. (Singlet refers to the fact that the eight electrons in this highly reactive molecule are organized into four

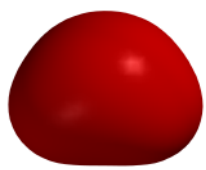
pairs, and that each pair of electrons occupies a different molecular orbital. The lowest-energy state of methylene is actually a triplet with three electron pairs and two unpaired electrons.)

The lowest energy molecular orbital of singlet methylene is not very interesting in that it looks like a 1s atomic orbital on carbon. The electrons occupying this orbital restrict their motion to the immediate region of the carbon nucleus and do not significantly affect bonding. Because of this restriction, and because the orbital's energy is very low, this orbital is referred to as a ***core orbital*** and its electrons are referred to as ***core electrons***.



core orbital for methylene

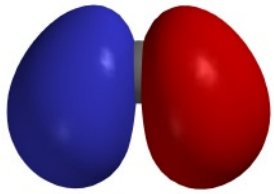
The next orbital is much higher in energy. It consists of a single surface that is delocalized over all three atoms. This means that it is simultaneously (σ) bonding with respect to each CH atom pair.



core orbital for methylene

The next higher energy orbital is described by two surfaces, a positive (blue) surface that encloses one CH bonding region and a negative (red) surface that encloses the other CH bonding region*. Since each surface encloses a bonding region, this orbital is also (σ) bonding with respect to each CH atom pair. This reinforces the bonding character of the previous orbital. The node that separates the two surfaces passes through the carbon nucleus, but not through either of the CH bonding regions, so it does not affect bonding.

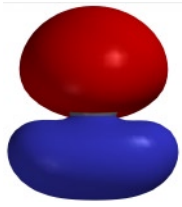
* While the absolute signs (colors) of a molecular orbital are arbitrary, the relative signs (colors) indicate bonding and antibonding character.



core orbital for methylene

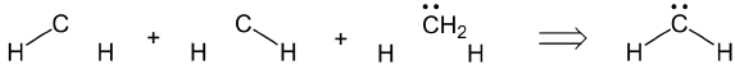
Thus, the two CH bonds in the Lewis structure for singlet methylene are replaced by two bonding molecular orbitals.*

The highest-occupied molecular orbital (the HOMO) is also described by two orbital surfaces. One surface extends into carbon's non-bonding region opposite the two hydrogens. The other surface encompasses the two CH bonding regions. Although it is hard to track the exact path of the orbital node in this picture, it happens to pass almost exactly through the carbon. This means that this particular orbital possesses only weak CH bonding character (it is H---H bonding). It turns out that the non-bonding character of the orbital is much more important than the bonding character, in that it leads to the fact that singlet methylene is able to behave as an electron-pair donor (a nucleophile).



core orbital for methylene

In addition to two CH bonds, the Lewis structure for singlet methylene shows a lone pair on carbon.



The above analysis shows that while the occupied orbitals of singlet methylene are spread over all three atoms, they are comprehensible.

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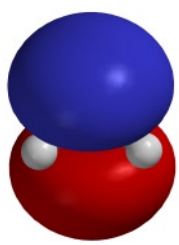
* Unlike the two Lewis structures, the two CH bonding molecular orbitals reflect the fact that the two CH bonds in methylene are identical. Specifically, the square of each of the orbitals, corresponding to the electron distribution or electron density, has the same 2-fold symmetry as the molecule. The square of either the molecular orbitals themselves or a combination of so-called degenerate (same energy) molecular orbitals must have the same symmetry as the underlying nuclear skeleton.

The orbitals divide into two groups, a single low-energy core orbital and three higher-energy valence orbitals. The latter consist of two CH bonding orbitals and a non-bonding orbital on carbon. There is no one-to-one correspondence between these orbitals and the Lewis structure. The bonding orbitals are not associated with particular bonds, and the non-bonding orbital contains bonding interactions as well.

> Open ***methylene bonding*** in the ***topics*** directory. Four images appear corresponding to the core and three valence orbitals of singlet methylene. Switch to a mesh or transparent surface to see the underlying molecular skeleton. Close ***methylene bonding*** when you are finished.

Singlet methylene also possesses unoccupied molecular orbitals. The unoccupied orbitals have higher (more positive) energies than the occupied orbitals, and these orbitals, because they are unoccupied, do not describe the electron distribution in singlet methylene.* Nevertheless, the shapes of unoccupied orbitals, in particular, the lowest-unoccupied orbital (LUMO), is worth considering because it provides valuable insight into the methylene's chemical reactivity.

The LUMO in methylene has non-bonding character, and looks like a 2p atomic orbital on carbon. This suggests that singlet methylene should be able to behave as an electron-pair acceptor (an electrophile). Note, however, that were the molecule to accept electrons, these would go into non-bonding orbital; carbon would become more electron-rich, but the CH bonds would not be much affected.



LUMO of methylene

* Because Lewis structures describe electron pair bonds and non-bonding electron pairs, they may not be related to unoccupied molecular orbitals.

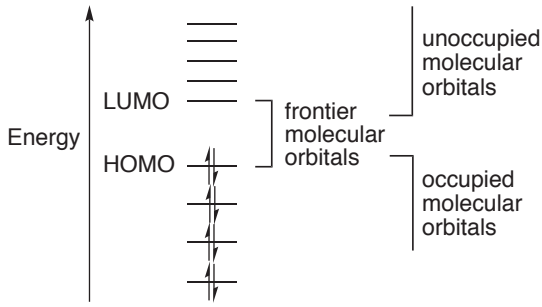
Open ***methylene LUMO*** in the ***topics*** directory and switch to a mesh or transparent surface to see the underlying skeleton. Close ***methylene LUMO*** when you are finished.

Frontier Molecular Orbitals and Chemical Reactivity

Chemical reactions often involve movement of electrons from an electron donor (base, nucleophile, reducing agent) to an electron acceptor (acid, electrophile, oxidizing agent). This electron movement between molecules can also be thought of as electron movement between molecular orbitals, and the shapes and energies of orbitals that act as electron donors or electron acceptors may provide considerable insight into chemical reactivity.

The first step in constructing a molecular orbital picture of a chemical reaction is to decide which orbitals are most likely to act as electron donors and acceptors. It is obvious that an electron-donor orbital must be drawn from the set of occupied orbitals, and an electron-acceptor orbital must be an unoccupied orbital, but there are many orbitals in each set to choose from.

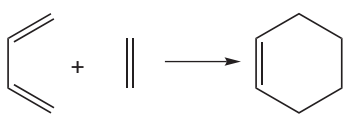
Orbital energy is usually the deciding factor. The highest-energy occupied orbital (the HOMO) is most commonly assumed to be the relevant electron-donor orbital and the lowest-energy unoccupied orbital (the LUMO) is most commonly assumed to be the relevant electron-acceptor orbital. For example, the HOMO and LUMO of singlet methylene (σ and π non-bonding orbitals, respectively) would serve as the donor and acceptor orbitals. The HOMO and LUMO are collectively referred to as the ***frontier molecular orbitals***, and most chemical reactions involve electron movement between them. In this way, the energy input required for electron movement is kept to a minimum.



Closely related to chemical reactivity (reaction rate) is chemical selectivity. The relevant question is, where more than one combination of reagents can react, which combination will react more quickly? The answer can often be found by examining the energies of the frontier orbitals. Consider ranking the rates of a series of reagents, where chemical reaction requires electron donation from the donor's HOMO. It is reasonable to expect that the donor with the highest energy HOMO will give up its electrons most easily and be the most reactive. Electron-acceptor reagents should follow the opposite pattern. The reagent with the lowest energy LUMO should be able to accept electrons most easily and be the most reactive. For a mixture of several donor and acceptor reagents, the fastest chemical reaction would be expected to involve the reagent combination that yields the smallest HOMO-LUMO energy gap.

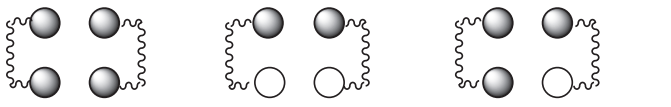
The Fukui-Woodward-Hoffmann Rules

In certain cases, multiple frontier orbital interactions must be considered. A good example is provided by so-called cycloaddition reactions, such as the Diels-Alder reaction between 1,3-butadiene and ethylene.



The key feature of this reaction is that the reactants combine in a way that allows two bonds to form simultaneously. This implies two different sites of satisfactory frontier orbital interaction (the two new bonds that form are sufficiently far apart that they do not interact with each other during the reaction). If we focus exclusively on the

interactions of the terminal carbons in each molecule, then three different frontier orbital combinations made up of upper and lower components can be imagined.

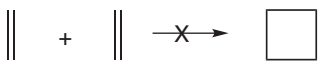


The upper orbital components are the same sign in all three combinations, meaning that their overlap is positive. In the two cases on the left, the lower orbital components also lead to positive overlap. Thus, the two interactions reinforce, and the total frontier orbital interaction is non zero. Electron movement (leading to chemical reaction) can occur. The right-most case is different. Here the lower orbital components lead to negative overlap (the orbitals have opposite signs at the interacting sites), and the total overlap is zero. No electron movement and no chemical reaction can occur in this case.

As it happens, the frontier orbital interactions in the Diels-Alder cycloaddition shown above correspond to those found in the middle drawing, that is, the upper and lower interactions reinforce and the reaction proceeds.

Open ***1,3-butadiene+ethylene*** in the ***topics*** directory. The image on top is the LUMO of ethylene while that on the bottom is the HOMO of 1,3-butadiene. They are properly poised to interact, but you can manipulate them independently. Close ***1,3-butadiene+ethylene*** when you are finished.

The same arguments suggest that cycloaddition of two ethylene molecules is unlikely to occur. This is because it involves a frontier orbital interaction like that found in the right drawing.



Open ***ethylene+ethylene*** in the ***topics*** directory. The image on top corresponds to the LUMO of one ethylene while that on the bottom corresponds to the HOMO of the other ethylene. You can manipulate them

independently or in concert (hold down on the **Ctrl** key while you carry out rotation and translation). Note, that in this case, the two individual atom-atom interactions cancel. Close ***ethylene+ethylene*** when you are finished.

The importance of orbital overlap in determining why certain chemical reactions proceed easily while other seemingly similar reactions are sluggish or do not go at all was first advanced by Fukui and then beautifully elaborated by Woodward and Hoffmann, and collectively their ideas are now known as the Fukui-Woodward-Hoffmann rules.

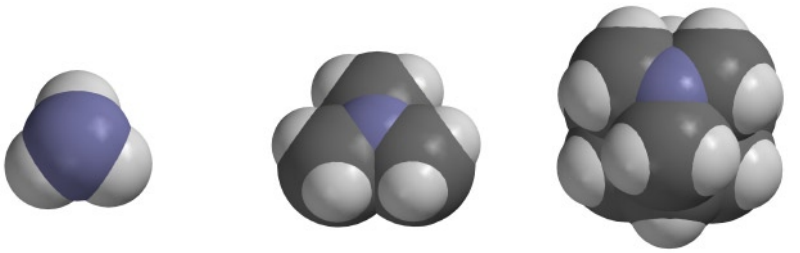
ELECTRON DENSITIES: SIZES AND SHAPES OF MOLECULES

How big is an atom or a molecule? Atoms and molecules require a certain amount of space, but how much? We know that gases can be compressed into a smaller volume but only so far, and that liquids and solids are very difficult is not nearly impossible to compress. While the individual atoms or molecules in a gas are widely separated and can be pushed into a much smaller volume, the atoms or molecules in a liquid or a solid are already close together and cannot be squeezed much further. Atoms can be talked about as having well-defined size. What is it?

Space-Filling Models

Chemists have long tried to answer the size question by using a special set of molecular models known as space-filling or CPK models. The space-filling model for an atom is simply a sphere of fixed radius. A different radius is chosen for each element in order to reproduce certain experimental observations, such as the compressibility of a gas, or the spacing between atoms in a crystal. Space-filling models for molecules consist of a set of interpenetrating atomic spheres. This reflects the idea that the chemical bonds that hold the molecule together cause the atoms to move closer together than the sum of the radii for the individual space-filling models. Interpenetration can be used as a criterion for chemical bonding. If two atomic spheres in a space-filling model strongly interpenetrate then the atoms must be

bonded. Space-filling models not only show how big molecules are, but also show which parts of the molecule are shielded and which are exposed.

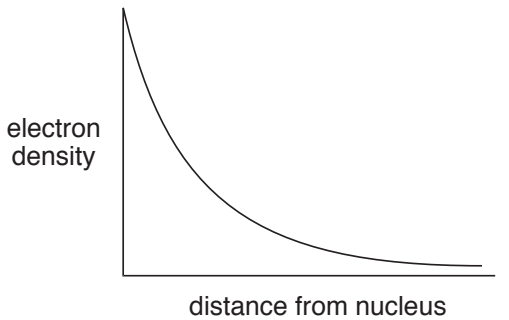


space-filling models for ammonia (left), trimethylamine (center) and 1-azaadamantane (right)

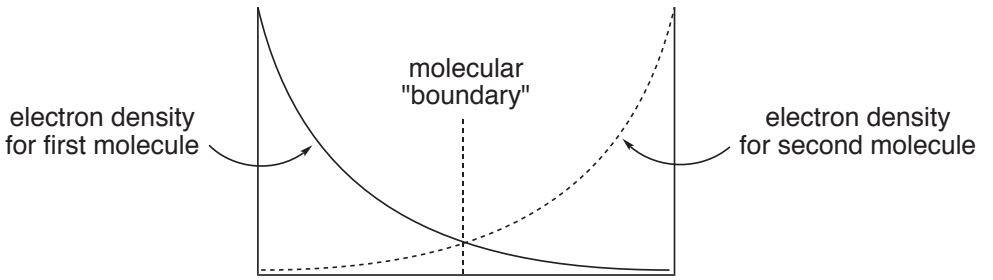
Open ***amines space filling*** in the ***topics*** directory. Space-filling models for ammonia, trimethylamine and 1-azaadamantane all appear on screen. Carbon atoms are colored dark grey, hydrogen atoms white and nitrogen blue. Note that the models clearly reveal the extent to which the nitrogen is exposed. Close ***amines space filling*** when you are finished.

Electron Density Surfaces

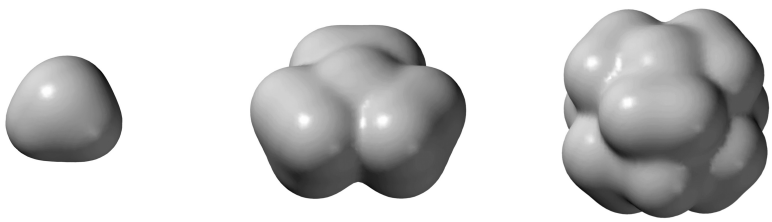
An alternative technique for portraying molecular size and shape relies on the molecule's own electron cloud. Atoms and molecules are made up of positively-charged nuclei surrounded by a negatively-charged electron cloud, and it is the size and shape of the electron cloud and not that of the nuclear skeleton that defines the size and shape of an atom or molecule. The size and shape of an electron cloud is described by the electron density (the number of electrons per unit volume). Consider a graph of electron density in the hydrogen atom as a function of distance from the nucleus.



The graph brings up a problem for chemists seeking to define atomic and molecular size, in that the electron cloud lacks a clear boundary. While electron density decays rapidly with distance from the nucleus, nowhere does it fall to zero. Therefore, when atoms and molecules rub up against each other, their electron clouds overlap and merge to a small extent.



This suggests that molecular size and shape is ill defined and that the best that can be done is to pick a value of the electron density, and to connect together all the points that have this value. The criteria for selecting this value is exactly the same as that for selecting atomic radii in space-filling models, the only difference being that only a single parameter (the value of the electron density) is involved (rather than a different radius for each element). The result is an electron density surface which, just like a space-filling model, is intended to depict overall molecular size and shape.



electron density surfaces for ammonia (left), trimethylamine (center) and 1-azaadamantane (right)

Open ***amines electron density*** in the ***topics*** directory. Electron density surfaces for ammonia, trimethylamine and 1-azaadamantane all appear on screen. Switch to a mesh or transparent surface in order to see the underlying skeletal model. *Click* on one of the surfaces, and select **Mesh** or **Transparent** from the menu which appears at the bottom right of the screen. With mesh selected, change the model to **Space Filling** (**Model** menu). This allows you to see how similar the electron density

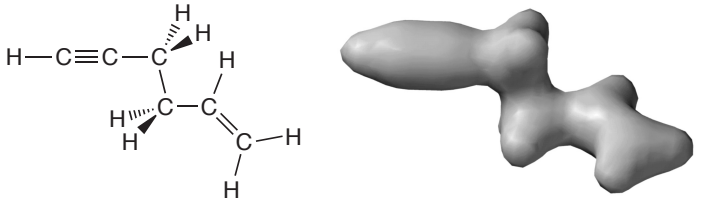
representation is to that offered by a simple space-filling model. Close ***amines electron density*** when you are finished.

Both space-filling models (atomic radii) and electron density models can be chosen to yield similar molecular volumes, and both show differences in overall size among molecules. Because the electron density surfaces provide no discernible boundaries between atoms, the surfaces may appear to be less informative than space-filling models in helping to decide to what extent a particular atom is exposed. This raises an important point. Electrons are associated with a molecule as a whole and not with individual atoms. The space-filling representation of a molecule with its discernible atomic boundaries does not reflect reality.

Bond Density Surfaces

More closely representing a conventional Lewis structure is a so-called ***bond density surface***, where the boundary corresponds to a much higher value of the electron density*. As such a surface is located much closer to the atomic nuclei, it encloses a relatively small volume, and does not give a correct impression of molecular size.

The bond density surface for hex-5-ene-1-yne clearly shows which atoms are connected, although it does not clearly distinguish single, double and triple carbon-carbon bonds.

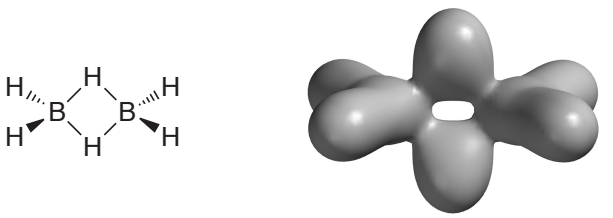


bond density surface for hex-5-ene-1-yne

Open ***hex-5-ene-1-yne bond density*** in the ***topics*** directory, and switch to a mesh or transparent surface to see the connection between the chemical bonds in a conventional model and the electron density. Close ***hex-5-ene-1-yne bond density*** when you are finished.

* An even higher value of the electron density leads to a surface in which only nearly spherical regions of electron density around the non-hydrogen atoms are portrayed. This serves to locate the positions of these atoms and is the basis of the X-ray diffraction experiment.

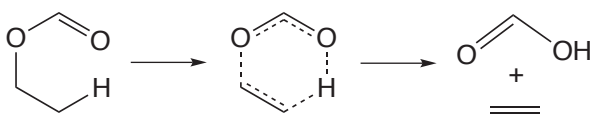
The usefulness of the bond density surface is more apparent in the following model of diborane. The surface clearly shows that there is relatively little electron density between the two borons, suggesting the absence of a boron-boron bond. This is information extracted from the bond density surface model, and has been obtained without reference to any preconceived ideas about the bonding in diborane.



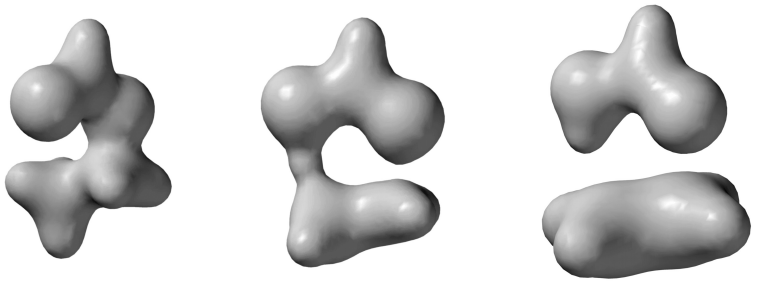
bond density surface for diborane

Open ***diborane bond density*** in the ***topics*** directory, and switch to a mesh or transparent surface to see how few electrons actually accumulate in the region between the two borons. Close ***diborane bond density*** when you are finished.

Bond density surfaces can also be informative in describing changes in bonding in moving from reactants to products through a transition state in a chemical reaction. For example, heating ethyl formate causes the molecule to fragment into two new molecules, formic acid and ethylene. A line drawing can show which bonds are affected by the overall reaction, but it cannot tell us if these changes occur all at once, sequentially, or in some other fashion.



On the other hand, the bond density surface is able to provide quantitative information.



bond density surfaces for the reactant, ethyl formate (left), pyrolysis transition state (center) and for the products, formic acid and ethylene (right)

Comparison of the bond density surface in the pyrolysis transition state with those of the reactant and the products suggests that the CO single bond of the reactant is clearly broken in the transition state and that the migrating hydrogen seems more tightly bound to oxygen (as in the product) than to carbon (as in the reactant). It can be concluded that the transition state more closely resembles the products than the reactants, and this provides an example of what chemists refer to as a late (product-like) transition state.

To see the smooth change in electron density throughout the course of the ethyl formate pyrolysis reaction, open ***pyrolysis bond density*** in the ***topics*** directory. *Click* on ▶| at the bottom left of the screen to animate the graphic (*click* on ⏸ to stop the animation). Switch to a mesh or transparent surface to follow the change in bonding. Close ***pyrolysis bond density*** when you are finished.

ELECTROSTATIC POTENTIAL MAPS: CHARGE DISTRIBUTIONS

The charge distribution in a molecule can provide critical insight into its physical and chemical properties. For example, molecules that are charged, or highly polar, tend to be water-soluble, and polar molecules may stick together in specific geometries, such as the double helix in DNA. Chemical reactions are also associated with charged sites, and the most highly-charged molecule, or the most highly-charged site in a molecule, is often the most reactive. The sign of the charge is also important. Positively-charged sites in a molecule invite attack by bases and nucleophiles, while negatively-charged sites are usually

targeted by acids and electrophiles.

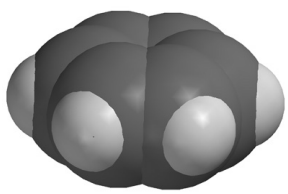
One way to describe a molecule's charge distribution is to give a numerical atomic charge for each atom. A particularly simple and familiar recipe yields so-called formal charges directly from Lewis structures. Unfortunately, formal charges are arbitrary. In fact, all methods for assigning charge are arbitrary and necessarily bias the calculated charges in one way or another. This includes methods based on quantum mechanics. The reason may be traced back to the notion that atomic boundaries are themselves ill-defined and it is impossible to decide which electrons are associated with which nuclei.

An attractive alternative for describing molecular charge distributions makes use of a quantity termed the electrostatic potential. This is the energy of interaction of a point positive charge with the nuclei and electrons of a molecule. The value of the electrostatic potential depends on the location of the point positive charge. If the point charge is placed in a region of excess positive charge (an electron-poor region), the point charge-molecule interaction is repulsive and the electrostatic potential will be positive. Conversely, if the point charge is placed in a region of excess negative charge (an electron-rich region), the interaction is attractive and the electrostatic potential will be negative. Thus, by moving the point charge around the molecule, the molecular charge distribution can be surveyed.

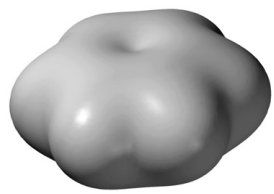
Electrostatic potentials can be depicted in various ways. For example, it is possible to make an electrostatic potential surface by finding all of the points in space where the electrostatic potential matches some particular value. This is precisely what was previously done for both molecular orbitals and electron densities. A much more useful way to show molecular charge distribution is to construct a so-called electrostatic potential map. This is done first by constructing an electron density surface corresponding to a space-filling model (see the topic ***Electron Densities: Sizes and Shapes of Molecules***). The electrostatic potential is then mapped onto this surface using different colors to represent the different values of the electrostatic potential. Mapping requires an arbitrary choice for a color scale. ***Spartan*** uses the rainbow. Red, the low energy end of the spectrum, depicts

regions of most negative (least positive) electrostatic potential, and blue depicts the regions of most positive (least negative) electrostatic potential. Intermediate colors represent intermediate values of the electrostatic potential, so that potential increases in the order: red < orange < yellow < green < blue.

The connection between a molecule's electron density surface, its electrostatic potential surface, and an electrostatic potential map is illustrated below for benzene. The electron density surface defines molecular shape and size, and performs the same function as a conventional space-filling model by indicating how close two benzenes can get in a liquid or in a crystal.



space-filling model
for benzene

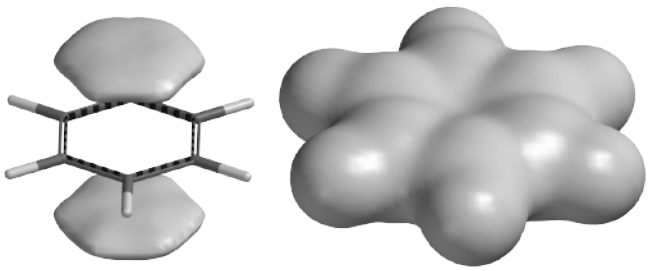


electron density surface
for benzene

Open ***benzene electron density*** in the ***topics*** directory. Two different images, a space-filling model and an electron density surface, appear side by side. You can switch between the two models (in order to manipulate them) by *clicking* on each in turn. Notice how similar they are. To get an even clearer impression, switch to a mesh surface. *Click* on the graphic and select **Mesh** from the menu which appears at the bottom right of the screen. Switch to a space-filling model (**Space Filling** from the **Model** menu). The two are now superimposed. Close ***benzene electron density*** when you are finished.

The electrostatic potential corresponding to points where the potential is negative shows two different surfaces, one above the face of the ring and the other below. Since the molecule's π electrons lie closest to these surfaces, we conclude that these electrons are responsible for the attraction of a point positive charge (or an electrophile) to the molecule. An electrostatic potential surface corresponding to points where the potential is positive has a completely different shape. It is disk-shaped and wrapped fairly tightly around the nuclei. The shape

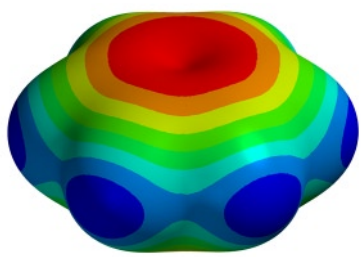
and location of this surface indicates that a point positive charge is repelled by this region, or that a point negative charge (a nucleophile) would be attracted here.



negative (left) and positive (right) electrostatic potential surfaces for benzene

Open ***benzene electrostatic potential*** in the ***topics*** directory. Two different images appear side by side. The one on the left depicts a surface of constant negative potential, while the one on the right depicts a surface of equal positive potential. You can switch between the two models (in order to manipulate them) by *clicking* on each in turn. Close ***benzene electrostatic potential*** when you are finished.

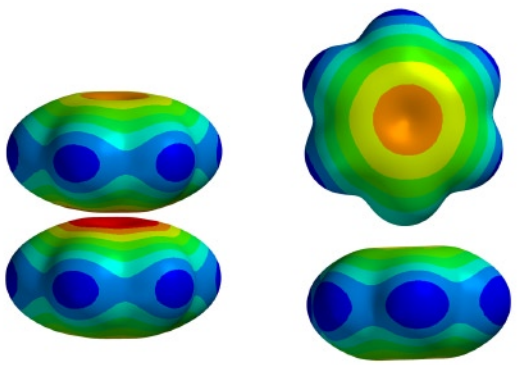
Next, combine the electron density and electrostatic potential surfaces to produce an electrostatic potential map. This simultaneously conveys both the molecule's size and shape as well as its charge distribution in a compact and easily interpretable manner. The size and shape of the map are, of course, identical to that of the electron density surface, and indicates what parts of the molecule are easily accessible to other molecules (the outside world). The colors reveal the overall charge distribution. The faces of the ring, the π system, are red (electron rich), while the plane of the molecule and especially the hydrogens are blue (electron poor).



electrostatic potential map for benzene

Open ***benzene electrostatic potential map*** in the ***topics*** directory. Manipulate the image to convince yourself that the red regions are on the π faces and the blue regions are around the edges. Close ***benzene electrostatic potential map*** when you are finished.

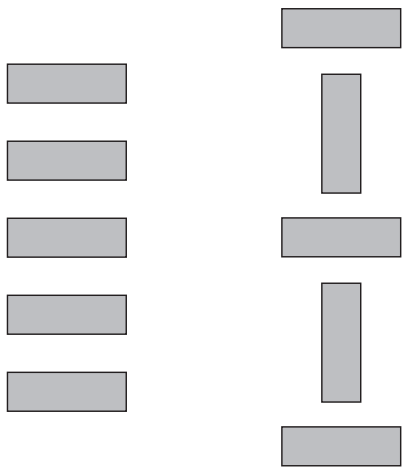
Electrostatic potential maps have made their way into mainstream general and (especially) organic chemistry textbooks as a means of displaying charge distributions in molecules. In addition, they have found application as a natural step beyond steric models for interpreting and predicting the way in which molecules fit together. A good example of this follows from the electrostatic potential map for benzene, which recall is negative on the π faces and positive around the periphery. The benzene dimer would, therefore, be expected to exhibit a perpendicular geometry, to best accommodate Coulombic interactions, instead of a parallel arrangement.



electrostatic potential maps for parallel (left) and perpendicular (right) benzene dimers

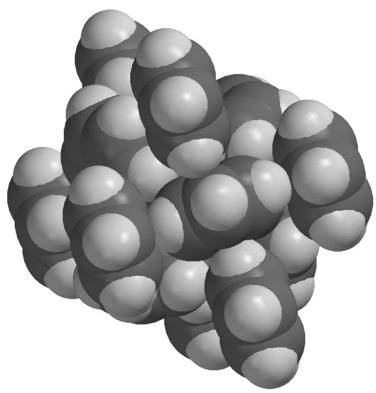
Open ***benzene dimer electrostatic potential map*** in the ***topics*** directory. Note that the parallel arrangement forces the negative region of one benzene onto the negative region of the other, while the perpendicular structure associates the negative region of one benzene with a positive region of the other. Close ***benzene dimer electrostatic potential map*** when you are finished.

Of greater interest is the structure of benzene in solid state. Intuition suggests a parallel stack. After all, benzene is flat and flat things (plates, pancakes, hamburgers) make stacks. However, Coulombs law clearly favors a perpendicular arrangement.



parallel perpendicular

The experimental X-ray crystal structure indeed shows a perpendicular arrangement, albeit in three dimensions. There are two lessons here. Intermolecular interactions go beyond steric interactions and sometimes our simple one and two-dimensional views of the world will lead us astray.



X-ray crystal structure of benzene

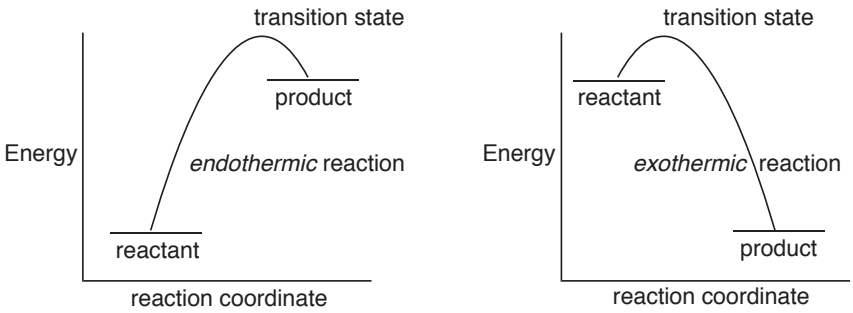
Open ***benzene crystal*** in the ***topics*** directory. Manipulate in order to see the packing of benzene molecules. Close ***benzene crystal*** when you are finished.

Electrostatic potential maps may also be used to describe in great detail the workings of chemical reactions. For example, a map may be used to show the transfer of negative charge during the S_n2 reaction of cyanide with methyl iodide.

Open ***Sn2 cyanide+methyl iodide*** in the ***topics*** directory. One frame of a sequence of electrostatic potential maps for the S_n2 reaction will appear. Animate by *clicking* on ▶ at the bottom left of the screen (stop the animation by *clicking* on ⏸). Note that the negative charge (red color) flows smoothly from cyanide to iodide during the reaction. Note also, that cyanide (as the reactant) is more red than iodide (as the product). Iodide is better able to carry negative charge, that is, it is the better leaving group. Switch to mesh or transparent map to see the making and breaking of bonds. Close ***Sn2 cyanide+methyl iodide*** when you are finished.

LOCAL IONIZATION POTENTIAL MAPS AND LUMO MAPS: ELECTROPHILIC AND NUCLEOPHILIC REACTIVITIES

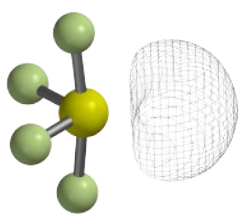
The Hammond Postulate states that the transition state in a (one-step) reaction will more closely resemble the side of the reaction that is higher in energy. Thus, the transition state of an *endothermic* reaction will more closely resemble the products, and the transition state of an *exothermic* reaction will resemble the reactants. One way to rationalize the Hammond postulate is to suggest that similarity in energy implies similarity in structure. That is, the transition state will resemble whichever reactants or products to which it is closer in energy. As seen in the reaction coordinate diagrams below this is the product in an *endothermic* reaction and the reactants in an *exothermic* reaction.



The Hammond Postulate provides a conceptual basis both for the Fukui-Woodward-Hoffmann rules (see the topic ***Atomic and Molecular Orbitals***) and for the use of graphical models. Both consider the properties of reactants as an alternative to direct calculations of transition states and reaction pathways as a way to assess chemical reactivity and selectivity. In this context, two models stand out as being particularly useful: the local ionization potential map for electrophilic reactions and (with some caveats) the LUMO map for nucleophilic reactions.

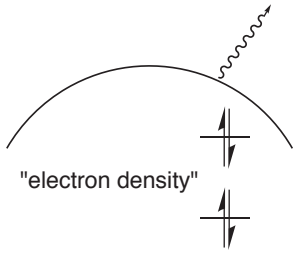
Local Ionization Potential Maps and Electrophilic Reactivity

The local ionization potential provides a measure of the relative ease of electron removal (ionization) at any location around a molecule. For example, a surface of low local ionization potential for sulfur tetrafluoride demarks the areas which are most easily ionized, and is clearly recognizable as a lone pair on sulfur.

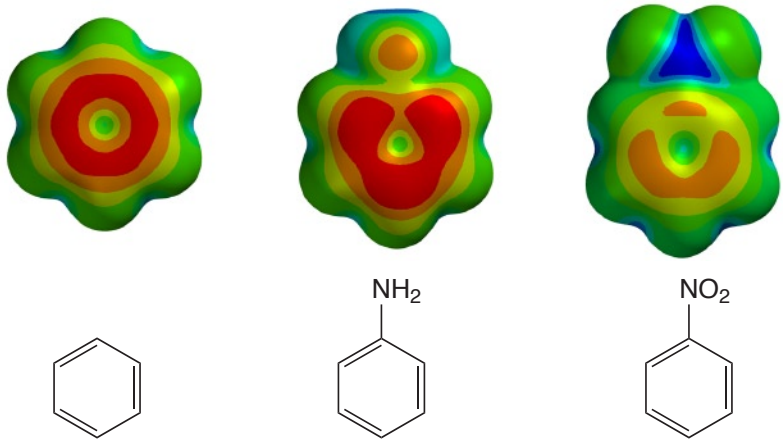


local ionization potential for sulfur tetrafluoride

While the local ionization potential by itself is not a particularly useful model, a map of the local ionization potential onto an electron density surface (a local ionization potential map) has proven to be of value in revealing regions from which electrons are most easily ionized and susceptible to electrophilic attack.



For example, they show both the positional selectivity in electrophilic aromatic substitution (NH_2 directs *ortho*/*para*, and NO_2 directs *meta*), and the fact that π-donor groups (NH_2) activate benzene while electron-withdrawing groups (NO_2) deactivate benzene.

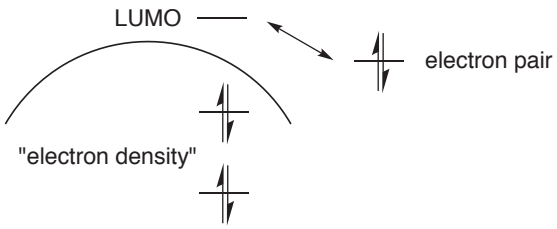


local ionization potential maps for benzene (left), aniline (center) and nitrobenzene (right)

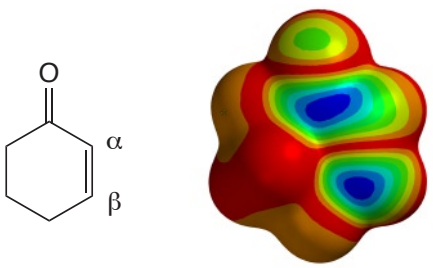
Open ***benzene, aniline, nitrobenzene local ionization potential maps*** in the ***topics*** directory. Here, the color red corresponds to regions of lowest ionization potential (most accessible to electrophiles). Note, that the π system in aniline is more accessible than the π system in benzene (the standard) and that the *ortho* and *para* positions are more accessible than *meta* positions. Note also, that the π system in nitrobenzene is less accessible than the π system in benzene and that here the *meta* positions are more accessible than the *ortho* and *para* positions, in accord with observation. Close ***benzene, aniline, nitrobenzene local ionization potential maps*** when you are finished.

LUMO Maps and Nucleophilic Reactivity

As elaborated in the topic ***Atomic and Molecular Orbitals***, the energies and shapes of the frontier molecular orbitals may anticipate chemistry of a molecule. Molecular orbital maps may also lead to informative models. The most common of these is the so-called LUMO map, in which the (absolute value) of the LUMO is mapped onto an electron density surface. This anticipates where an electron pair (a nucleophile) might attack.

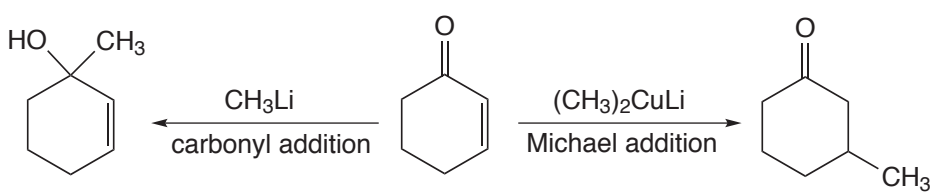


A good example is provided by the LUMO map for cyclohexenone.



LUMO map for cyclohexenone showing positions for nucleophilic attack in blue

The LUMO shows which regions of a molecule are most electron deficient, and hence most subject to nucleophilic attack. In this case, one such region is over the carbonyl carbon, consistent with the observation that carbonyl compounds undergo nucleophilic addition at the carbonyl carbon. Another region is over the β carbon, again consistent with the known chemistry of α,β-unsaturated carbonyl compounds, in this case conjugate or Michael addition.



The buildup of positive charge on the β carbon leading to possibility of Michael addition could have been anticipated from resonance arguments, although the LUMO map, like an experiment, has the advantage of showing the result ("you don't have to ask").

Open ***cyclohexenone LUMO map*** in the ***topics*** directory and *click* on the resulting surface. Switch to a mesh or transparent surface in order to see the underlying skeletal model. On Windows, *click* on the graphic and select **Mesh** or **Transparent** from the menu which appears at the bottom right of the screen. On the Mac, position the cursor over the graphic, hold down on either the left or right button and select from the menu which appears alongside. Orient the molecule such that the two "blue regions" are positioned over the appropriate carbons and then switch back to a solid surface. Close ***cyclohexenone LUMO map*** when you are finished.

Some caution needs to be exercised. Specifically the LUMO may not be the important molecular orbital for the chemical reaction of interest, and it may be necessary to base the map on a higher-energy unoccupied molecular orbital (LUMO+1, LUMO+2, ...).

Appendix B
Capabilities and Limitations

Molecular Mechanics Models[1]

The MMFF molecular mechanics model is available for the calculation of energy (a combination of strain energy and intramolecular interaction energy), equilibrium geometries, equilibrium conformers, conformer energy distributions and vibrational frequencies. There are no atom limits for molecular mechanics calculations.

Semi-Empirical Models[1]

The PM3 semi-empirical model is available for calculation of heats of formation, wave functions, equilibrium and transition-state geometries and vibrational frequencies. The elements H, Li-F, Mg-Cl, Ca, Ti-Br, Zr, Mo-Pd, Cd-I, Hf-Pt and Hg-Bi and Gd are supported. PM3 calculations are limited to 75 atoms.

Hartree-Fock Models[1-3]

Hartree-Fock models are available for calculation of energies and wave functions, equilibrium and transition-state geometries and vibrational frequencies with STO-3G, 3-21G, 6-31G* and 6-311+G** basis sets. Hartree-Fock calculations are limited to 30 atoms.

Density Functional Models[1,]

B3LYP, EDF2, and ωB97X-D density functional models are available for calculation of energies and wave functions, equilibrium and transition-state geometries and vibrational frequencies with both 6-31G* and 6-311+G** basis sets. Density functional calculations are limited to 30 atoms.

MP2 Møller-Plesset Models[1]

The MP2 Møller-Plesset model is available for calculation of energies and wave functions and equilibrium and transition-state geometries with 6-31G* and 6-311+G** basis sets. Vibrational frequencies are also available, but are very costly in terms of computation time. MP2 calculations are limited to 20 atoms.

T1[4] Thermochemical Recipe

The T1 recipe has been developed to closely reproduce G3(MP2) heats of formation. It makes use of an HF/6-31G* geometry, instead of the MP2/6-31G* geometry, replaces the large basis set MP2 calculation in G3(MP2) by a dual-basis set RI-MP2 calculation, eliminates both the QCISD(T) calculation and the vibrational frequency calculation (needed to obtain zero-point energy and to correct the energy for finite temperature) and introduces an empirical correction based on the atom counts and Mulliken bond orders. The result is that T1 requires 2-3 orders of magnitude less computation time than G3(MP2).

T1 is limited to closed-shell, uncharged molecules comprising H, C, N, O, F, Si, P, S, Cl and Br only and, because it incorporates parameters which depend explicitly on molecular geometry, is in practice limited to molecules that can be properly described in terms of a conventional valence structure. T1 is likely to be unsatisfactory for transition states. T1 calculations are limited to 20 atoms.

Solvent Models

Spartan Student supports SM5.0R[5] for molecular mechanics calculations this estimates the aqueous solvation energy. For systems with H, C–F, S–Cl, Br and I. Hartree-Fock and density functional models support the C-PCM[6,7] solvent model, allowing for calculations in water and both polar and non-polar solvents.

Properties and Spectra

The properties module (that is automatically called from the molecular mechanics module or one of the quantum chemical modules) provides for text output printing, population analyses based on fits

to electrostatic potentials), evaluation of thermodynamic quantities (enthalpy, entropy, free energy and heat capacity), and calculation of the dipole moment.

IR spectra calculations may be carried out with molecular mechanics models, semi-empirical models, Hartree-Fock models, B3LYP, EDF2, ωB97X-D and MP2 models. NMR spectra calculations may be carried out with Hartree-Fock, B3LYP, EDF2, and ωB97X-D models. UV/vis spectra calculations are only available from B3LYP/6-31+G* as a property following a density functional energy or optimization.

Graphical Models

The graphics module provides for data preparation associated with the display as surfaces, property maps and slices of molecular orbitals, electron densities, spin densities, electrostatic potentials and local ionization potentials. The sizes of electron density surfaces (and of property maps based on electron density surfaces) may be chosen either using a specific value of the density or a value that encloses a specific percentage of the total number of electrons. Accessible and inaccessible regions may be distinguished for electron density surfaces and all property maps based on electron density surfaces.

Database

The database supported with ***Spartan Student*** is a subset of the Spartan Spectra and Properties Database (SSPD). It contains structures, energies, T1 heats of formation, IR and NMR spectra and diverse molecular properties for ≈6,000 molecules obtained from EDF2/6-31G* and ωB97X-D/6-31G* calculations. In addition, it contains the wave function, allowing for function on-the-fly calculation and display of the full variety of graphical surfaces and property maps. The full version of SSPD (currently >300,000 molecules) may be licensed separately with the ***Spartan Parallel Suite*** (the research version of ***Spartan***).

1. For a general discussion and assessment of the techniques and methods available in ***Spartan Student***, see: W.J. Hehre, ***A Guide to Molecular Mechanics and Quantum Chemical Calculations***, Wavefunction, Inc., Irvine, CA 2003. This is available from Wavefunction's website (www.wavefun.com).
2. For a review of the quantum chemical methods utilized in ***Spartan Student*** (except for the PM3 semi-empirical method) with emphasis on recent developments, see: Yihan Shao, Zhengting Gan, Evgeny Epifanovsky, Andrew T.B. Gilbert, Michael Wormit, Joerg Kussmann, Adrian W. Lange, Andrew Behn, Jia Deng, Xintian Feng, Debashree Ghosh, Matthew Goldey, Paul R. Horn, Leif D. Jacobson, Ilya Kaliman, Rustam Z. Khaliullin, Tomasz Kuś, Arie Landau, Jie Liu, Emil I. Proynov, Young Min Rhee, Ryan M. Richard, Mary A. Rohrdanz, Ryan P. Steele, Eric J. Sundstrom, H. Lee Woodcock III, Paul M. Zimmerman, Dmitry Zuev, Ben Albrecht, Ethan Alguire, Brian Austin, Gregory J. O. Beran, Yves A. Bernard, Eric Berquist, Kai Brandhorst, Ksenia B. Bravaya, Shawn T. Brown, David Casanova, Chun-Min Chang, Yunqing Chen, Siu Hung Chien, Kristina D. Closser, Deborah L. Crittenden, Michael Diedenhofen, Robert A. DiStasio Jr., Hainam Do, Anthony D. Dutoi, Richard G. Edgar, Shervin Fatehi, Laszlo Fusti-Molnar, An Ghysels, Anna Golubeva-Zadorozhnaya, Joseph Gomes, Magnus W.D. Hanson-Heine, Philipp H.P. Harbach, Andreas W. Hauser, Edward G. Hohenstein, Zachary C. Holden, Thomas-C. Jagau, Hyunjun Ji, Benjamin Kaduk, Kirill Khistyaev, Jaehoon Kim, Jihan Kim, Rollin A. King, Phil Klunzinger, Dmytro Kosenkov, Tim Kowalczyk, Caroline M. Krauter, Ka Un Lao, Adèle D. Laurent, Keith V. Lawler, Sergey V. Levchenko, Ching Yeh Lin, Fenglai Liu, Ester Livshits, Rohini C. Lochan, Arne Luenser, Prashant Manohar, Samuel F. Manzer, Shan-Ping Mao, Narbe Mardirossian, Aleksandr V. Marenich, Simon A. Maurer, Nicholas J. Mayhall, Eric Neuscamman, C. Melania Oana, Roberto Olivares-Amaya, Darragh P. O'Neill, John A. Parkhill, Trilisa M. Perrine, Roberto Peverati, Alexander Prociuk, Dirk R. Rehn, Edina Rosta, Nicholas J. Russ, Shaama M. Sharada, Sandeep Sharma, David W. Small, Alexander Sodt, Tamar Stein, David Stück, Yu-Chuan Su, Alex J.W. Thom, Takashi Tsuchimochi, Vitalii Vanovschi, Leslie Vogt, Oleg Vydrov, Tao Wang, Mark A. Watson, Jan Wenzel, Alec White, Christopher F. Williams, Jun Yang, Sina Yeganeh, Shane R. Yost, Zhi-Qiang You, Igor Ying Zhang, Xing Zhang, Yan Zhao, Bernard R. Brooks, Garnet K.L. Chan, Daniel M. Chipman, Christopher J. Cramer, William A. Goddard III, Mark S. Gordon, Warren J. Hehre, Andreas Klamt, Henry F. Schaefer III, Michael W. Schmidt, C. David Sherrill, Donald G. Truhlar, Arieh Warshel, Xin Xu, Alán Aspuru-Guzik, Roi Baer, Alexis T. Bell, Nicholas A. Besley, Jeng-Da Chai, Andreas Dreuw, Barry D. Dunietz, Thomas R. Furlani, Steven R. Gwaltney, Chao-Ping Hsu, Yousung Jung, Jing Kong, Daniel S. Lambrecht, WanZhen Liang, Christian Ochsenfeld, Vitaly A. Rassolov, Lyudmila V. Slipchenko, Joseph E. Subotnik, Troy Van Voorhis, John M. Herbert, Anna I. Krylov, Peter M.W. Gill and Martin Head-Gordon. Mol.Phys. 113, 184-215 (2015).
3. For an older account see: W.J. Hehre, L. Radom, P.v.R. Schleyer and J.A. Pople, ***Ab Initio* Molecular Orbital Theory**, Wiley, New York, 1986.
4. W.S. Ohlinger, P.E. Klunzinger, B.J. Deppmeier, W.J. Hehre; *J. Phys. Chem. A*., **113**, 10, 2165 (2009).
5. G.D. Hawkins, C.J. Cramer and D.G. Truhlar, *J. Phys. Chem. B*., **101**, 7147 (1997).
6. A.W. Lange, J.M. Herbert, *Chem. Phys. Lett.,* **509**, 77 (2011).
7. V. Barone and M. Cossi, *J. Phys. Chem. A*., **102**, 11,1995 (1998).

Appendix C

Menus

Spartan Student Screen

File

New Build	Brings up a model kit for 3D molecule building or substitution
New Sketch	Brings up the sketch pad for molecule sketching in 2D
Build New Molecule	Adds a molecule to an existing document; brings up a model kit for molecule building
Sketch New Molecule	Adds a molecule to an existing document; brings up the sketch pad for molecule sketching in 2D
Delete Molecule	Deletes a molecule (or molecules) from a document
Append Molecule(s)...	Appends molecules to an existing document
Open...	Opens (imports) a molecule or multi-molecule document
Close	Closes a molecule or multi-molecule document
Open Recent Documents	Brings up a list of recent documents, allowing one of which to be opened
Save	Saves (exports) a molecule or multi-molecule document
Save As...	Saves a document as one of a number of file formats under a user-specified name

Save Image As 	Saves molecule or graphical model as a high-resolution PNG file
Print... 	Prints on-screen display; also prints contents of output window and the **Spreadsheet**
Access PDB Online... 	Accesses the online Protein Data Bank (PDB)
Access Database by Name 	Searches the ***Spartan Student*** database by name or partial name
Start/Stop QuickTime Recording 	Starts and stops QuickTime recording of contents of main ***Spartan Student*** screen (Macintosh only)
Exit 	Exits ***Spartan Student***

Edit

Undo 	Undoes previous operations
Cut 	Moves the current molecule or contents of the selection box to the clipboard
Copy 	Copies the current molecule or contents of the selection box to the clipboard
Paste 	Pastes contents of the clipboard to the screen
Select All 	Selects all atoms in the selected molecule
Find... 	Locates a text string in the output dialog or an on-screen molecular fragment
Find Next 	Locates next occurrence of a text string or molecular fragment
Center 	Centers the molecule on screen; applies to all molecules in a document
Clear 	Clears the selected molecule

Model

Wire	Displays structure as wire-frame model
Ball and Wire	Displays structure as ball-and-wire model
Tube	Displays structure as tube model
Ball and Spoke	Displays structure as ball-and-spoke model
Space Filling	Displays structure as space-filling model
Hide	Hides structure model from view
Global Model	Applies model type and labels of current molecule to all molecules in the document
Coupled	Couples motions of all molecules in the document
Labels	Toggles labels on and off
Hydrogens	Toggles hydrogens on and off
Ribbons	Toggles ribbons on and off
R/S Chirality	Toggles R/S chirality labels on and off
Hydrogen Bonds	Toggles hydrogen bonds on and off
Ramachandran Plot	Display a Ramachandran plot for a protein that has been brought in from the Protein Data Bank (PDB)
Configure...	Labels atoms, bonds, etc., provides information about polypeptides/ polynucleotides residues and designates ribbon displays

Geometry

Measure Distance	Displays and/or sets bond distance
Measure Angle	Displays and/or sets bond angle

Measure Dihedral	Displays and/or sets dihedral angle
Constrain Distance	Constrains bond distance
Constrain Angle	Constrains bond angle
Constrain Dihedral	Constrains dihedral angle
Define Point	Defines a point as a geometric mean of a set of atoms
Define Ligand Point	Defines a ligand point as a position that is perpendicular to the centroid of a plane made by three or more atoms
Define Plane	Defines a plane made by three or more atoms
Freeze Center	Freezes selected atomic positions
Generate Isomer	Generates a list of stereo and/or regioisomers based on user specification.
Align	Aligns molecules in a document

Build

View	Removes the model kit
Edit Build	Brings up a 3D model kit (organic, inorganic, peptide, nucleotide, or ChemDraw) with the presently selected molecule
Edit Sketch	Brings up the sketch pad with the presently selected molecule. This function is only available if the sketch has not been altered using any of the 3D model kits or has not been replaced by an entry in SSPD.
Delete	Deletes atoms, bonds, points, planes, etc. Also available at the bottom of the 3D model kits
Make Bond	Makes bonds between free valences or atoms. Also available at the bottom of the 3D model kits

Break Bond	Breaks a bond. Also available at the bottom of the 3D model kits
Minimize	Performs energy minimization using MMFF molecular mechanics. Also available at the bottom of the 3D model kits
Guess Transition State	Provides transition-state guess based on reaction database or, lacking a database entry, based on a linear synchronous transit procedure

Setup

Calculations...	Sets up molecular mechanics and quantum chemical calculations; specifies calculation of IR and NMR spectra and QSAR properties
Surfaces	Sets up generation of and displays graphical surfaces
Submit	Submits job to the execution queue

Display

Output	Displays text output
Properties	Displays molecule, bond and atom properties as well as information about geometrical constraints, graphical surfaces and statistical analyses
Orbital Energies	Displays an orbital energy diagram and allows on-the-fly generation and display of molecular orbitals
Surfaces	Sets up generation of and displays graphical surfaces (same as entry in **Setup** menu)

Spectra	Displays IR and NMR spectra, animates vibrational modes (IR), and accesses on-line experimental spectral databases
Spreadsheet	Displays spreadsheet
Plots...	Creates 2D plots from the data in the spreadsheet
Reactions	Calculates reaction (and activation) energies using data either from current document or from the Spartan Spectra and Properties Database (SSPD)

Options

Preferences...	Sets various run-time and labeling preferences, icon displays, establishes URL's for on-line access
Colors	Sets screen and model colors
Fonts...	Sets fonts for menus and dialogs
Graphics Fonts...	Sets fonts for graphical displays and labels
Monitor	Monitors and allows for killing jobs
Calculator	Pocket calculator
Icons	Toggles display of icons on and off

Activities

Tutorials	Brings up ***Spartan Student*** tutorials as PDF documents
Topics	Brings up selection of topics relevant to calculations performed in ***Spartan Student*** as PDF documents
Labs	Brings up a sample set of student lab activities
Look up in Wikipedia	Brings up a Wikipedia page

Help

Spartan Student v9 Help 	Provides information about the performance and timing of computational methods in ***Spartan Student***; provides information about using graphical models in ***Spartan Student***; bulletin board for FAQs about ***Spartan Student***
Spartan Student v9 Manual 	Opens a PDF file providing a guided tour through ***Spartan Student Edition*** menus
License Utility . . . 	Accesses information about your ***Spartan Student*** license
Check for Updates . . . 	Provides information on availability of newer versions.
About Spartan Student v9. . . 	Provides program version information for citation and support

Contextual

Main Screen

Copy	Copies selected molecule to the clipboard
Paste	Pastes the contents of the clipboard into the selected document
Delete Selected	Deletes selected molecule from document
Properties	Brings up the **Molecular Properties** dialog

Spreadsheet

Copy	Copies text of selected cell or cells to the clipboard. If leftmost cell (or cells) selected, copies molecule(s) to the clipboard

Paste	Pastes the contents of the clipboard into selected cells. If leftmost cell (or cells) selected, either pastes text or molecule(s) depending on menu choice
Add	Brings up a wide selection of calculated quantities for adding to the spreadsheet
Sort	Sorts the column from low to high. *Pressing* the **Shift** key prior to menu selection sorts from high to low
Format Selected	Formats selected cell(s), selected column(s) if selection is in a header cell, or entire spreadsheet if selection is header cell of leftmost column
Delete Selected	Deletes selected molecule or group of molecules
Append	Appends the contents of ***Spartan Student*** document(s) to the spreadsheet (corresponding to the selected document)
Rename Selected Using SSPD	Renames selected molecule(s) with names in the Spartan Spectra and Properties Database (SSPD)
Properties	Brings up the **Molecular Properties** dialog

Reactions

Copy	Copies selected text to the clipboard
Print	Prints selected text

Output Window

Copy	Copies selected text to the clipboard
Find/Find Next	Performs text search of Output
Print	Prints selected text
Save As PDF	Saves output as .pdf file

Appendix D

Units

Geometries

Cartesian coordinates are given in Ångstroms (Å), and in atomic units (au).

Bond distances are given in Å and in au. Bond angles and dihedral angles are given in degrees (°).

Surface areas, accessible surface areas and polar surface areas are available in $Å^2$ and volumes in $Å^3$, and in au^2 (au^3).

1 Å = 0.1 nm=1.889762 au

Energies, Heats of Formation and Strain Energies, Zero-Point Energies, Enthalpies and Gibbs Energies and Entropies

Total energies from Hartree-Fock calculations are available in au, kcal/mol, kJ/mol and electron volts (eV).

Experimental heats of formation as well as those from semi-empirical calculations and from thermochemical recipes are available in kJ/mol, au, kcal/mol and eV.

Strain energies from molecular mechanics calculations are available in kJ/mol, au, kcal/mol and eV.

Zero-point energies, enthalpies and Gibbs energies available in kJ/mol, kcal/mol and au/mol. Entropies are available in kJ/mol•degree, kcal/mol•degree and au/mol•degree.

Orbital Energies

Orbital energies are available in eV, kcal/mol, kJ/mol and au.

Energy Conversions

	au	kcal/mol	kJ/mol	eV
1 au	-	627.5	2625	27.21
1 kcal/mol	1.593 (-3)	-	4.184	4.337 (-2)
1 kJ/mol	3.809 (-4)	2.390 (-1)	-	1.036 (-2)
1 eV	3.675 (-2)	23.06	96.49	-

a) exponent follows in parenthesis, e.g., 1.593 (-3) = 1.593×10^{-3}

Electron Densities, Spin Densities, Dipole Moments, Charges, Electrostatic Potentials and Local Ionization Potentials

Electron densities and spin densities are given in electrons/au^3.

Dipole moments are given in debye.

Atomic charges are given in electrons.

Electrostatic potentials are given in kJ/mol.

Local ionization potentials are given in eV.

Vibrational Frequencies

Vibrational frequencies are given in wavenumbers (cm^{-1}).

Chemical Shifts, Coupling Constants

Chemical shifts are given in parts-per-million (ppm) relative to the following standards: hydrogen, tetramethylsilane; carbon, tetramethylsilane; nitrogen, nitromethane; fluorine, fluorotrichloromethane; silicon, tetramethylsilane, phosphorous, phosphoric acid.

Coupling constants are in ppm.

Appendix E

Citation

The proper citation for ***Spartan Student*** is as follows:

Spartan Student
Wavefunction, Inc.
Irvine, CA

Except for molecular mechanics, semi-empirical models and the T1 thermochemical recipe, the calculation methods used in ***Spartan Student*** have been documented in: Yihan Shao, Zhengting Gan, Evgeny Epifanovsky, Andrew T.B. Gilbert, Michael Wormit, Joerg Kussmann, Adrian W. Lange, Andrew Behn, Jia Deng, Xintian Feng, Debashree Ghosh, Matthew Goldey, Paul R. Horn, Leif D. Jacobson, Ilya Kaliman, Rustam Z. Khaliullin, Tomasz Kuś, Arie Landau, Jie Liu, Emil I. Proynov, Young Min Rhee, Ryan M. Richard, Mary A. Rohrdanz, Ryan P. Steele, Eric J. Sundstrom, H. Lee Woodcock III, Paul M. Zimmerman, Dmitry Zuev, Ben Albrecht, Ethan Alguire, Brian Austin, Gregory J. O. Beran, Yves A. Bernard, Eric Berquist, Kai Brandhorst, Ksenia B. Bravaya, Shawn T. Brown, David Casanova, Chun-Min Chang, Yunqing Chen, Siu Hung Chien, Kristina D. Closser, Deborah L. Crittenden, Michael Diedenhofen, Robert A. DiStasio Jr., Hainam Do, Anthony D. Dutoi, Richard G. Edgar, Shervin Fatehi, Laszlo Fusti-Molnar, An Ghysels, Anna Golubeva-Zadorozhnaya, Joseph Gomes, Magnus W.D. Hanson-Heine, Philipp H.P. Harbach, Andreas W. Hauser, Edward G. Hohenstein, Zachary C. Holden, Thomas-C. Jagau, Hyunjun Ji, Benjamin Kaduk, Kirill Khistyaev, Jaehoon Kim, Jihan Kim, Rollin A. King, Phil Klunzinger, Dmytro Kosenkov, Tim Kowalczyk, Caroline M. Krauter, Ka Un Lao, Adèle D. Laurent, Keith V. Lawler, Sergey V. Levchenko, Ching Yeh Lin, Fenglai Liu, Ester Livshits, Rohini C. Lochan, Arne Luenser, Prashant Manohar, Samuel F. Manzer, Shan-Ping Mao, Narbe Mardirossian, Aleksandr V. Marenich, Simon A. Maurer, Nicholas J. Mayhall,

Eric Neuscamman, C. Melania Oana, Roberto Olivares-Amaya, Darragh P. O'Neill, John A. Parkhill, Trilisa M. Perrine, Roberto Peverati, Alexander Prociuk, Dirk R. Rehn, Edina Rosta, Nicholas J. Russ, Shaama M. Sharada, Sandeep Sharma, David W. Small, Alexander Sodt, Tamar Stein, David Stück, Yu-Chuan Su, Alex J.W. Thom, Takashi Tsuchimochi, Vitalii Vanovschi, Leslie Vogt, Oleg Vydrov, Tao Wang, Mark A. Watson, Jan Wenzel, Alec White, Christopher F. Williams, Jun Yang, Sina Yeganeh, Shane R. Yost, Zhi-Qiang You, Igor Ying Zhang, Xing Zhang, Yan Zhao, Bernard R. Brooks, Garnet K.L. Chan, Daniel M. Chipman, Christopher J. Cramer, William A. Goddard III, Mark S. Gordon, Warren J. Hehre, Andreas Klamt, Henry F. Schaefer III, Michael W. Schmidt, C. David Sherrill, Donald G. Truhlar, Arieh Warshel, Xin Xu, Alán Aspuru-Guzik, Roi Baer, Alexis T. Bell, Nicholas A. Besley, Jeng-Da Chai, Andreas Dreuw, Barry D. Dunietz, Thomas R. Furlani, Steven R. Gwaltney, Chao-Ping Hsu, Yousung Jung, Jing Kong, Daniel S. Lambrecht, WanZhen Liang, Christian Ochsenfeld, Vitaly A. Rassolov, Lyudmila V. Slipchenko, Joseph E. Subotnik, Troy Van Voorhis, John M. Herbert, Anna I. Krylov, Peter M.W. Gill and Martin Head-Gordon. Mol.Phys. 113, 184-215 (2015).

Appendix F
Accessing ChemDraw (Windows Only)*

The ChemDraw program may be seamlessly accessed inside of ***Spartan Student***** allowing chemical drawings to be produced in a familiar environment and then brought over as 3D structures***. The conversion is unambiguous as long as all stereochemical cues are in place in the 2D drawing. Note that the conformation implied by the 2D drawing may be ambiguous and need to be altered.

You need to check the box next to **ChemDraw Interface** in the Settings Preferences dialog under the **Options** menu (**Chapter 10**). This will add a **ChemDraw** button, tab or menu entry to the 3D builder.

To access ChemDraw, select **ChemDraw** from the buttons or menu at the top of the model kit, and *click* on **Edit** at the bottom of the panel that results. ChemDraw will appear. To return to ***Spartan Student***, close ChemDraw. The 2D drawing will appear at the center of the panel and manipulable 3D structure will appear at the top of the panel. *Clicking* on screen will move the 3D structure into ***Spartan Student***'s main window.

* ChemDraw files (.cdx) may be read with all versions of ***Spartan***.

** ChemDraw is not provided with ***Spartan*** but must be obtained from Perkin Elmer.

*** Transfer is one directional only. 3D structures that have been altered may not be transferred back to ChemDraw, however, ***Spartan's*** sketch builder and molecule properties dialog will provide a modified 2D structure for molecules with up to 100 atoms.

Glossary

This glossary addresses nomenclature ("jargon") used throughout the manual, and more generally, in applications of molecular modeling. Some of the terms, such as **Basis Set**, will be familiar to the modeling community but foreign to the broader community, while other terms, such as **Kinetic Product**, may be foreign to the modeling community and familiar to the broader community. Terms such as **Entropy** should be familiar to all and are generally avoided. A number of terms from both categories have been defined "in the context" of their use in molecular modeling rather than more generally.

3-21G. A **Split-Valence Basis Set** in which each **Core Basis Function** is written in terms of three **Gaussians**, and each **Valence Basis Function** is split into two parts, written in terms of two and one **Gaussians**, respectively. 3-21G basis sets have been determined to yield the lowest total **Hartree-Fock Energies** for atoms. The nomenclature 3-21G implies use of the **3-21G(*)** basis set on molecules incorporating second-row (and heavier) main-group elements.

3-21G$^{(*)}$. The **3-21G Basis Set** supplemented by d-type **Gaussians** for each second-row and heavier main-group elements only. This is required in order to get good equilibrium geometries. Without the added functions, the 3-21G basis set is not recommended for use for molecules incorporating second-row (and heavier) main-group elements.

6-31G. A **Split-Valence Basis Set** in which each **Core Basis Function** is written in terms of six **Gaussians**, and each **Valence Basis Function** is split into two parts, written in terms of three and one **Gaussians**, respectively. 6-31G basis sets have been determined to yield the lowest total **Hartree-Fock Energies** for atoms. The 6-31G basis set is rarely used alone but rather is supplemented by one or more sets of **Polarization Functions** and/or **Diffuse Functions**.

6-31G*, **6-31G****. The **6-31G Basis Set** in which non-hydrogen atoms are supplemented by d-type **Gaussians** and (for 6-31G**) hydrogen atoms are supplemented by p-type **Gaussians** (**Polarization Functions**). 6-31G* and 6-31G** are **Polarization Basis Sets**.

6-31+G*, **6-31+G****. **Basis Sets** that are identical to **6-31G*** and **6-31G**** except that all non-hydrogen atoms are supplemented by diffuse s and p-type **Gaussians** (**Diffuse Functions**). 6-31+G* and 6-31+G** are supplemented **Polarization Basis Sets**.

6-311G. A **Split-Valence Basis Set** in which each **Core Basis Function** is written in terms of six **Gaussians**, and each **Valence Basis Function** is split into three parts, written in terms of three, one and one **Gaussians**, respectively. 6-311G basis sets have been determined to yield the lowest total **MP2 Energies** for atoms. The 6-311G basis set is rarely used alone but rather is supplemented by one or more sets of **Polarization Functions** and/or **Diffuse Functions**.

6-311G*, **6-311G****. The **6-311G Basis Set** in which non-hydrogen atoms are supplemented by d-type **Gaussians** and (for 6-311G**) hydrogen atoms are supplemented by p-type **Gaussians** (**Polarization Functions**). 6-311G* and 6-311G** are **Polarization Basis Sets**.

6-311+G*, **6-311+G****. **Basis Sets** that are identical to **6-311G*** and **6-311G**** except that non-hydrogen atoms are supplemented by diffuse s and p-type **Gaussians** (**Diffuse Functions**). 6-311+G* and 6-311+G** are supplemented **Polarization Basis Sets**.

***Ab Initio* Models**. The general term used to describe methods seeking approximate solutions to the many-electron **Schrödinger Equation**, but which do not involve empirical parameters. *Ab initio* models include **Hartree-Fock Models**, **Møller-Plesset Models** and **Density Functional Models**.

Acidity. The energy required to break an XH bond into X^- and H^+, that is, to undergo **Heterolytic Bond Dissociation**. Acidities in the gas phase are very large positive numbers (producing isolated ions is highly unfavorable); they are much smaller (and of either sign) in solution.

Activation Energy. The energy of a **Transition State** above that of reactants. Activation energy is related to reaction rate by way of the **Arrhenius Equation**.

Anharmonic Frequency Correction. Non-quadratic contributions to a **Vibrational Frequency**. Because calculated frequencies are harmonic, that is, assume that the potential is quadratic, they are typically ~5% larger than measured frequencies, which include anharmonic corrections. Frequencies can be corrected for anharmonicity but, due to high computational cost, this is seldom done for any but very small molecules.

Anion. An atom or molecule with a **Total Charge** of -1.

Antibonding Molecular Orbital. A **Molecular Orbital** which is antibonding between particular atomic centers. The opposite is a **Bonding Molecular Orbital**.

Arrhenius Equation. An equation governing the rate of a chemical reaction as a function of the **Activation Energy** and the temperature.

Atomic Orbital. A **Basis Function** centered on an atom. Atomic orbitals typically take on the form of the solutions to the hydrogen atom (s, p, d, f... type orbitals).

Atomic Units. The set of units which remove all of the constants from inside the **Schrödinger Equation**. The **Bohr** is the atomic unit of length and the **Hartree** is the atomic unit of energy.

Atomization Energy. The energy of dissociation of an atom or molecule into separated nuclei and electrons. This is another term for **Total Energy**.

B3LYP Model. A **Global Hybrid Generalized Gradient Approximation (GH-GGA)** functional which improves on the **Local Density Model** by accounting explicitly for non-uniformity in electron distributions. It incorporates the **Exchange Energy** from the **Hartree-Fock Model** and involves three adjustable parameters. The B3LYP model is perhaps the most widely used density functional model and provides a solid account of equilibrium geometries (including the geometries of molecules incorporating transition metals), vibrational frequencies and reaction energies.

Basicity. The energy gained from adding a proton to an atom or molecule. Basiscities in the gas phase are very large negative numbers; they are much smaller (and of either sign) in solution.

Basis Functions. Functions usually centered on atoms which are linearly combined to make up the set of **Molecular Orbitals**. Except for **Semi-Empirical Models** where basis functions are **Slater** type, basis functions are **Gaussian** type.

Basis Set. The entire collection of **Basis Functions**.

Bohr. The **Atomic Unit** of length. 1 bohr = 0.529167Å.

Boltzmann Distribution. The equilibrium distribution of products in a **Thermodynamically-Controlled Reaction**. A special (and very important) case involves the equilibrium distribution of **Conformers** of a flexible molecule.

Boltzmann Equation. The equation governing the distribution of products in **Thermodynamically-Controlled Reaction**.

Bonding Molecular Orbital. A **Molecular Orbital** which is bonding between particular atom centers. The opposite is an **Antibonding Molecular Orbital**.

Bond Order. A measure of the number of electrons shared between "bonded" atoms.

Bond Separation Reaction. An ***Isodesmic*** **Reaction** in which a molecule described in terms of a conventional valence structure is broken down into the simplest (two-heavy-atom) molecules containing the same component bonds.

Bond Density Surface. A **Density Surface** used to elucidate the bonding in molecules. The value of the density is typically taken as 0.1 electrons/**bohr**.^{3}

Born-Oppenheimer Approximation. An approximation based on the assumption that nuclei are stationary. Applied to the **Schrödinger Equation**, it leads to the **Electronic Schrödinger Equation**.

C-PCM. The **Conductor** like **Polarizable Continuum Model** is a solvent model that depends on the shape and charge distribution of

the molecule (solute) and the dielectric constant of the solvent. This is the solvent model used in the ***Spartan Student*** version.

Cambridge Structural Database (CSD). A collection of >1,000,000 experimental structures for organic and organometallic compounds almost entirely from X-ray crystallography. Structures lacking carbon are excluded as are biopolymers (the latter are available from the Protein Data Bank).

Cartesian Coordinates. x, y, z spatial coordinates.

CAS Number. Chemical Abstract Service registry number; a unique substance identifier used to a large degree in the chemistry literature, see www.cas.org for more information.

Cation. An atom or molecule with a **Total Charge** of +1.

Chemical Shift. The difference in the energies of nuclear spin states for a nucleus in a molecule caused by an external magnetic field. This is the fundamental quantity measured in **NMR** spectroscopy.

Chiral Molecule. A molecule with a non-superimposible mirror image. Most commonly (but not necessarily) a chiral molecule will incorporate one or more **R/S** centers.

Closed Shell. An atom or molecule in which all electrons are paired.

Conformation. The arrangement about single bonds and of flexible rings.

Conformational Analysis. One of several different procedures to deal with molecules that are not properly described in terms of a single **Conformer**. Determination of **Equilibrium Conformer** or establishing a **Conformer Distribution** or a **Similarity Library** are examples of conformational analysis.

Conformer. One of a number of possible shapes a flexible molecule can assume.

Core. Electrons which are primarily associated with individual atoms and do not participate significantly in chemical bonding (1s electrons for first-row elements, 1s, 2s, $2p_x$, $2p_y$, $2p_z$ electrons for second-row elements, etc.).

Core Orbital. A **Molecular Orbital** that is primarily involved with the **Core** rather than with the **Valence.**

Correlated Models. Models which take implicit or explicit account of the **Correlation** of electron motions. **Møller-Plesset Models**, **Configuration Interaction Models** and **Density Functional Models** are correlated models.

Correlation. The coupling of electron motions not explicitly taken into account in **Hartree-Fock Models**.

Correlation Energy. The difference in energy between the **Hartree-Fock Energy** and the experimental energy.

Correlation Functional. A function of the **Electron Density** and perhaps as well the gradient of the **Electron Density**. The functional form derives from "exact" solution of the **Schrödinger Equation** for an idealized many-electron problem. Used in **Density Functional Models**.

Coulomb Energy. The electron-electron repulsion energy according to Coulomb's law.

Coulombic Interactions. Charge-charge interactions which follow Coulomb's law. Stabilizing when charges are of opposite sign and destabilizing when they are of the same sign.

Coupling Constant. A measure of the extent to which nuclear spins on neighboring atoms interact (couple) with each other, causing splitting of the lines in an NMR spectrum.

CPK Model. A molecular model in which atoms are represented by spheres, the radii of which correspond to **van der Waals Radii**. Intended to portray molecular size and shape. Also known as a space-filling model.

CSD; *See* **Cambridge Structural Database**.

Curtin-Hammett Principle. The idea that the reactive conformer in a **Kinetically-Controlled Reaction** is not necessarily the lowest-energy conformer. The rationale is that the energy barriers separating

conformers are typically much smaller than barriers to chemical reaction, and that any reactive conformers will be replenished.

Density; *See* **Electron Density**.

Density Functional Models. Methods in which the energy is evaluated as a function of the **Electron Density**. **Electron Correlation** is taken into account explicitly by incorporating into the **Hamiltonian** terms which derive from exact solutions of idealized many-electron systems.

Diffuse Functions. Functions added to a **Basis Set** to allow description of electron distributions far away from atomic positions. Important for descriptions of anions.

Diffusion-Controlled Reactions. Chemical reactions without **Transition States** (or energy barriers), the rates of which are determined by the speed in which molecules encounter each other and how likely these encounters are to lead to reaction.

Dipole Moment. A vector indicating the magnitude, sign and direction of the overall distribution of charge in a molecule based on the combination of nuclear and electron charges. Most commonly only the magnitude of the dipole moment is known experimentally.

Double Hybrid Functional. A class of functionals that take account of unoccupied molecular orbitals in addition to occupied molecular orbitals (the density) usually by way of an MP2-like procedure.

Doublet. A molecule with one unpaired electron**,** also known as a radical.

Dual Basis Set. A technique whereby the converged wavefunction resulting from a calculation using a small basis set is passed on for a single **SCF** cycle using a large basis set. This closely approximates the energy and wavefunction that would have resulted from a full calculation using the large basis set but with 5-10 times less computation.

EDF2 Model. **A Global Hybrid Generalized Gradient Approximation (GH-GGA)** functional which improves on the **Local Density Model** by accounting explicitly for non-uniformity in

electron distributions. EDF2 was explicitly formulated to reproduce experimental vibrational frequencies (infrared spectra), and it was for this reason (together with practical concerns) that the EDF2/6-31G* model was chosen for use in the **Spartan Spectra and Properties Database (SSPD)**.

Electron Affinity. The energy gained as a result of adding an electron to an atom or molecule. May be calculated as the (negative of) the difference in energies between the atom/molecule and it corresponding radical anion. Note that not all atoms/molecules have positive electron affinities, that is, bind an electron.

Electron Correlation. *See* **Correlation**.

Electron Density. The number of electrons per unit volume at a point in space. This is the quantity which is measured in an X-ray diffraction experiment.

Electron Density Surface. A surface of constant **Electron Density**. May be used to elucidate bonding (**Bond Density Surface**) or to characterize overall moelcular size and shape.

Electronic Schrödinger Equation. The equation which results from incorporation of the **Born-Oppenheimer Approximation** to the **Schrödinger Equation**.

Electrostatic Charges. Atomic charges chosen to best match the **Electrostatic Potential** at points surrounding a molecule, subject to overall charge balance.

Electrostatic Potential. A function describing the energy of interaction of a positive point charge with the nuclei and fixed electron distribution of a molecule.

Electrostatic Potential Map. A graph that shows the value of **Electrostatic Potential** on an **Electron Density Isosurface** corresponding to a **van der Waals Surface**.

Electrostatic Potential Surface. It may be used to elucidate regions in a molecule which are particularly electron rich and subject to electrophilic attack and those which are particularly electron poor, subject to nucleophilic attack.

Energy Profile. A plot of energy vs. change in geometrical coordinate, for example, change in bond length or in dihedral angle.

Enthalpy. The heat of a chemical reaction. Related to energy by a pressure-volume that is insignificant at normal pressures.

Equilibrium Conformer. The lowest-energy **Conformer**.

Equilibrium Geometry. A **Local Minimum** on a **Potential Energy Surface**.

Equilibrium Isotope Effect. The effect on the heat of reaction due to a change in nuclear mass of one or more atoms. The most common (and largest) isotope effects arise from substitution of deuterium for hydrogen.

Exchange Functional. A function of the **Electron Density** and perhaps as well the gradient of the **Electron Density**. The functional form derives from "exact" solution of the **Schrödinger Equation** for an idealized many-electron problem. Used in **Density Functional Models**.

Exchange Energy. An "attractive" (negative) component of the electron-electron interaction energy. Arises due to an overestimation of the "repulsive" (positive) component or **Coulomb energy**.

Excited State. An electronic state for an atom or molecule which is not the lowest-energy or **Ground State**.

Force Constant. For a diatomic molecule, the second derivative of the energy with respect to change in bond length. For a polyatomic molecule, the second derivative of the energy with regard to a change in **Normal Coordinate.**

Force Field. The set of rules underlying **Molecular Mechanics Models**. Comprises terms which account for distortions from ideal bond distances and angles and for **Non-Bonded van der Waals** and **Coulombic Interactions**.

Fourier Series. An expansion of a periodic (in 360^{o} rotation) in terms of powers of the cosine of the torsion angle.

Frontier Molecular Orbitals. The **HOMO** and **LUMO**.

Gx Models. "Recipes" which combine a series of **Hartree-Fock** and **Correlated Models** to properly account for **Atomization Energies** of atoms and molecules. Useful for providing accurate thermochemical data.

G3(MP2). A "simplified" version of the **G3 Model**. Reproduces experimental **Heats of Formation** with an RMS errors of ~8 kJ/mol, practical for molecules comprising less than 20 atoms.

Gaussian. A function of the form $x^l y^m z^n \exp(\alpha r^2)$ where l, m, n are integers (0, 1, 2 . . .) and α is a constant. Used in the construction of **Basis Sets** for **Hartree-Fock**, **Density Functional**, **MP2** and other **Correlated Models**.

Gaussian Basis Set. A **Basis Set** made up of **Gaussian Basis Functions**.

Global Minimum. The lowest energy **Local Minimum** on a **Potential Energy Surface**.

Ground State. The lowest energy electronic state for an atom or molecule.

Hamiltonian. An operator which accounts for the kinetic and potential energy of an atom or a molecule.

Hammond Postulate. The idea that the **Transition State** for an *exothermic* reaction will more closely resemble reactants than products. This provides the basis for "modeling" properties of **Transition States** in terms of the properties of reactants.

Harmonic Frequency. A **Vibrational Frequency** which has been corrected to remove all non-quadratic (anharmonic) components. Calculated **Vibrational Frequencies** correspond to harmonic frequencies. The corrections require data on isotopically-substituted systems and are typically available only for small molecules.

Hartree. The **Atomic Unit** of energy. 1 hartree = 627.47 kcal/mol.

Hartree-Fock Approximation. Separation of electron motions in many-electron systems into a product form of the motions of the individual electrons.

Hartree-Fock Energy. The energy resulting from **Hartree-Fock Models**.

Hartree-Fock Equations. The set of differential equations resulting from application of the **Born-Oppenheimer** and **Hartree-Fock Approximations** to the many-electron **Schrödinger Equation**.

Hartree-Fock Models. Methods in which the many-electron wavefunction in written terms of a product of one-electron wavefunctions. Electrons are assigned in pairs to functions called **Molecular Orbitals**.

Hartree-Fock Wavefunction. The simplest quantum-mechanically correct representation of the many-electron wavefunction. Electrons are treated as independent particles and are assigned in pairs to functions termed **Molecular Orbitals**. Also known as **Single-Determinant Wavefunction**.

Heat of Formation. The **Enthalpy** at 298 K of a balanced chemical reaction in which a molecule is converted into the most stable form of the each element, for example, hydrogen molecule for hydrogen and graphite for carbon.

Hessian. The matrix of second energy derivatives with respect to geometrical coordinates. The Hessian together with the atomic masses lead to the **Vibrational Frequencies** of molecular systems.

Heterolytic Bond Dissociation. A process in which a bond is broken and a cation and anion result. The number of electron pairs is conserved, but a non-bonding electron pair has been substituted for a bond.

HOMO. **H**ighest **O**ccupied **M**olecular **O**rbital.

Homolytic Bond Dissociation. A process in which a bond is broken and two radicals result. The number of electron pairs is not conserved.

HOMO-LUMO Gap. The difference in energies between the **HOMO** and **LUMO**.

HOMO Map. A graph of the absolute value of the **HOMO** on an **Isodensity Surface** corresponding to a **van der Waals Surface**.

Hydrogen-Bond Acceptor. An electronegative element (typically, nitrogen, oxygen or halogen) with one or more lone pairs able to "accept" a hydrogen from a **Hydrogen-Bond Donor**.

Hydrogen-Bond Donor. A hydrogen bonded to an electronegative element (typically nitrogen or oxygen) that can be donated to a **Hydrogen-Bond Acceptor**.

Hydrophobe. A non polar region of a molecule.

Hypervalent Molecule. A molecule containing one or more main-group elements in which the normal valence of eight electrons has been exceeded. Hypervalent molecules are common for second-row and heavier main-group elements but are uncommon for first-row elements.

Imaginary Frequency. A frequency which results from a negative element in the diagonal form of the **Hessian**. **Equilibrium Geometries** are characterized by all real frequencies while **Transition States** are characterized by one imaginary frequency.

Infrared Spectrum. Spectrum resulting from transitions between vibrational energy levels. Infrared intensities depend on the change in dipole moment associated with the vibration.

Internal Coordinates. A set of bond lengths, bond angles and dihedral angles (among other possible variables) describing molecular geometry. The **Z Matrix** is a set of internal coordinates.

Ionization Potential. The energy required to completely eject an electron from an atom or molecule. May be calculated as the difference in energies between the atom/molecule and its corresponding radical cation. May be approximated from **Koopman's Theorem** as the negative of the **HOMO Energy**.

***Isodesmic* Reaction**. A chemical reaction in which the number of formal chemical bonds of each type is conserved.

Isosurface. A three-dimensional surface defined by the set of points in space where the value (isovalue) of the function is constant.

Kinetically-Controlled Reaction. Refers to a chemical reaction which has not gone all the way to completion, and the ratio of products is not related to their thermochemical stabilities, but rather inversely to the heights of the energy barriers separating reactants to products.

Kinetic Isotope Effect. The effect on the rate of reaction due to a change in nuclear mass of one or more atoms. The most common (and largest) isotope effects arise from substitution of deuterium for hydrogen.

Kinetic Product. The product of a **Kinetically-Controlled Reaction**.

kJ/mol. The unit commonly used to express chemical energy differences, replacing kcal/mol. 1 kJ/mol = 0.239 kcal/mol = 0.000381 au.

LCAO Approximation. **L**inear **C**ombination of **A**tomic **O**rbitals approximation. Approximates the unknown **Hartree-Fock Wavefunctions** (**Molecular Orbitals**) by linear combinations of atom-centered functions (**Atomic Orbitals**) and leads to the **Roothaan-Hall Equations**.

Ligand. This term has two meanings in the context of molecular modeling. It denotes a molecular fragment that is (viewed as) non-covalently bonded to a transition metal in an inorganic or organometallic compound. For example, both carbon monoxide and benzene are said to be ligands in benzene chromium tricarbonyl. It also denotes a molecule that is "associated" (non-covalently bonded) to a protein.

Linear Synchronous Transit. The name given to procedures which estimate the geometries of transition states based on "averages" of the geometries of reactants and products, sometimes weighted by the overall thermodynamics of reaction.

Local Ionization Potential. A function of the relative ease of electron removal (ionization) from a molecule.

Local Ionization Potential Map. A graph of the **Local Ionization Potential** on an **Isodensity Surface** corresponding to a **van der Waals Surface**.

Local Minimum. Any **Stationary Point** on a **Potential Energy Surface** for which all elements in the diagonal representation of the **Hessian** are positive.

LogP. An empirical measure of the extent to which a molecule partitions between water and octanol.

Lone Pair. A **Non-Bonded Molecular Orbital** which is typically associated with a single atom.

LUMO. **L**owest **U**noccupied **M**olecular **O**rbital.

LUMO Map. A graph of the absolute value of the **LUMO** on an **Isodensity Surface** corresponding to a **van der Waals Surface**.

Mechanism. The sequence of steps connecting reactants and products in an overall chemical reaction. Each step starts from an equilibrium form (reactant or intermediate) and ends in an equilibrium form (intermediate or product).

Minimal Basis Set. A **Basis Set** which contains the fewest functions needed to hold all the electrons on an atom and still maintain spherical symmetry. **STO-3G** is a minimal basis set.

Minimal Valence Basis Set. A **Minimal Basis Set** from which **Core Orbitals** have been removed. **Semi-Empirical Models** make use of a minimal valence basis set.

MMFF94. **M**erck **M**olecular **F**orce **F**ield. A **Molecular Mechanics Force Field** for organic molecules and biopolymers developed by Merck Pharmaceuticals.

Molecular Mechanics Models. Methods for structure, conformation and strain energy calculation based on bond stretching, angle bending and torsional distortions, together with **Non-Bonded Interactions**, and parameterized to fit experimental data.

Molecular Orbital. A one-electron function made of contributions of **Basis Functions** on individual atoms (**Atomic Orbitals**) and delocalized throughout the entire molecule.

Molecular Orbital Models. Methods based on writing the many-electron solution of the **Electronic Schrödinger Equation** in terms of a product of one-electron solutions (**Molecular Orbitals**).

Møller-Plesset Energy. The energy resulting from **Møller-Plesset Models** terminated to a given order, e.g., the **MP2** energy is the energy of the second-order **Møller-Plesset Model** (or **MP2**).

Møller-Plesset Models. Methods which partially account for **Electron Correlation** by way of the perturbation theory of Møller and Plesset.

Monte-Carlo Conformation Search. A limited search of **Conformers** resulting from a random sampling of all torsional angles (including constrained torsions associated with flexible rings) while satisfying the requirements imposed by the **Boltzmann Equation**.

MP2 Energy. The energy resulting from **MP2 Models**.

MP2 Model. A **Møller-Plesset Model** terminated to be second order in the energy.

Multiplicity. The number of unpaired electrons (number of electrons with "down" spin) +1. 1=singlet; 2=doublet; 3=triplet, etc.

NIST Chemistry Web Book (National Institutes of Standards and Technology). On-line source of experimental **Infrared** and **UV/visible spectra**.

NMR Spectrum. Spectrum resulting from transitions between nuclear spin states under the influence of an external magnetic field. Both 1D spectra (most important, proton and ^{13}C) and 2D spectra (most important COSY, HMBC and HSQC) are available.

Non-Bonded Interactions. Interactions between atoms which are not directly bonded. **van der Waals Interactions** and **Coulombic Interactions** are non-bonded interactions.

Non-Bonded Molecular Orbital. A molecular orbital which does not show any significant **Bonding** or **Antibonding** characteristics. A **Lone Pair** is a non-bonded molecular orbital.

Normal Coordinates. Coordinates that lead to a diagonal **Hessian**, and which correspond to vibrational motions in molecules.

Normal Mode Analysis. The process for calculating **Normal Coordinates** leading to **Vibrational Frequencies**. This involves diagonalizing the **Hessian** and accounting for atomic masses.

Octet Rule. The notion that main-group elements prefer to be "surrounded" by eight electrons (going into s, p_x, p_y, p_z orbitals).

Orbital Energy. The energy of a **Molecular Orbital.**

Orbital Energy Diagram. A diagram listing **Orbital Energies** from most negative at the bottom. Usually restricted to occupied **Valence Orbitals** and the few lowest unoccupied orbitals.

Orbital Symmetry Rules; *See* **Woodward-Hoffmann Rules**.

Open Shell. An atom or molecule in which one or more electrons are unpaired.

PM3. **P**arameterization **M**ethod **3**. A **Semi-Empirical Model**.

Polar Area. The area of an **Electrostatic Potential Map** that is either more positive or more negative than some preset value (typically between 80-120 kJ/mol).

Polarization Basis Set. A **Basis Set** which contains functions of higher angular quantum number (**Polarization Functions**) than required for the **Ground State** of the atom, e.g., d-type functions for main-group elements and p-type functions for hydrogen. **6-31G***, **6-31G****, **6-311G***, **6-311G****, **cc-pVDZ**, **cc-pVTZ** and **cc-pVQZ** are polarization basis sets.

Polarization Functions. Functions of higher angular quantum than required for the **Ground State** atomic description. Added to a **Basis Set** to allow displacement of **Valence Basis Functions** away from atomic positions.

Polar Surface Area. The area of a space-filling (**CPK**) model due to electronegative elements (typically, nitrogen and oxygen) and any hydrogens that are bonded to these elements.

Pople-Nesbet Equations. The set of equations describing the best **Unrestricted Single Determinant Wavefunction** within the **LCAO Approximation**. These reduce the **Roothaan-Hall Equations** for **Closed Shell** (paired electron) systems.

Potential Energy Surface. A function of the energy of a molecule in terms of the geometrical coordinates of the atoms.

Property Map. A representation or "map" of a "property" on top of an **Isosurface**, typically an **Isodensity Surface**. **Electrostatic Potential Maps**, and **HOMO** and **LUMO Maps** and **Spin Density Maps** are useful property maps.

Proton Affinity; *See* **Basicity.**

Pseudopotential. A **Basis Set** which treats only **Valence** electrons in an explicit manner, all other electrons being considered as a part of a "**Core**". **LAVCP** (and extensions including **Polarization** and/or **Diffuse Functions**) are pseudopotentials.

Pseudorotation. A mechanism for interconversion of *equatorial* and *axial* sites around trigonal bipyramidal centers, e.g., fluorines in phosphorous pentafluoride.

QSAR. **Q**uantitative **S**tructure **A**ctivity **R**elationships. The name given to attempts to relate measured or calculated properties to molecular structure.

Quantum Mechanics. Methods based on approximate solution of the **Schrödinger Equation**.

Ramachandran Plot. A plot for each α carbon in a polypeptide of the two dihedral angles that define the conformation of the backbone. The points will typically cluster in two regions denoting helices and sheets.

Rate Limiting Step. The step in an overall chemical reaction (**Mechanism**) which proceeds via the highest-energy **Transition State**.

Reaction Coordinate. The coordinate that connects the **Local Minima** corresponding to the reactant and product, and which passes through a **Transition State**.

Reaction Coordinate Diagram. A plot of energy vs. **Reaction Coordinate**.

Restricted SCF. An **SCF** procedure which restricts electrons to be paired in orbitals or permits orbitals to be singly occupied.

Roothaan-Hall Equations. The set of equations describing the best **Hartree-Fock** or **Single-Determinant Wavefunction** within the **LCAO Approximation**.

R/S. Atomic chirality markers.

SCF. **S**elf **C**onsistent **F**ield. An iterative procedure whereby a one-electron orbital is determined under the influence of a potential made up of all the other electrons. Iteration continues until self consistency. **Hartree-Fock**, **Density Functional** and **MP2 Models** all employ SCF procedures.

Schrödinger Equation. The quantum mechanical equation which accounts for the motions of nuclei and electrons in atomic and molecular systems.

Self Consistent Field; *See* **SCF**.

Semi-Empirical Models. **Quantum Mechanics** methods that seek approximate solutions to the many electron **Schrödinger Equation**, but which involve empirical parameters.

Size Consistent. Methods for which the total error in the calculated energy is more or less proportional to the (molecular) size. **Hartree-Fock** and **Møller-Plesset** models are size consistent, while **Density Functional Models**, (limited) **Configuration Interaction Models** and **Semi-Empirical Models** are not size consistent.

Size Surface. A **Density Surface** used to establish overall molecular size and shape. The value of the density is typically taken as 0.002 electrons/**bohr**^{3}.

Slater. A function of the form $x^l y^m z^n \exp(-\zeta r)$ where l, m, n are integers (0, 1, 2 . . .) and ζ is a constant. Related to the exact solutions to the **Schrödinger Equation** for the hydrogen atom. Used as **Basis Functions** in **Semi-Empirical Models**.

Space-Filling Model; *See* **CPK Model**.

Spartan Reaction Database (SRD). A collection of ~2,500 transition-state structures for a wide variety of simple organic and organometallic reactions obtained from up to five different quantum chemical models. Searchable by structure.

Spartan Spectra and Properties Database (SSPD). A collection of molecular structures, infrared and NMR spectra, molecular and atomic properties and QSAR descriptors for >300,000 organic molecules obtained from the ωB97X-D/6-31G* and EDF2/6-31G* density functional models based on the lowest-energy conformer assigned from the **T1** model. The wavefunction is available, as such, surfaces and property maps may be generated "on-the-fly". Searchable by structure, name, formula, molecular weight and isomer.

Spin Density. The difference in the number of electrons per unit volume of "up" spin and "down" spin at a point in space.

Spin Density Map. A graph that shows the value of the **Spin Density** on an **Isodensity Surface** corresponding to a **van der Waals Surface**.

Spin Orbital. The form of **Wavefunction** resulting from application of the **Hartree-Fock Approximation** to the **Electronic Schrödinger Equation**. Comprises a space part (**Molecular Orbital**) and one of two possible spin parts ("spin-up" and "spin-down").

Split-Valence Basis Set. A **Basis Set** in which the **Core** is represented by a single set of **Basis Functions** (a **Minimal Basis Set**) and the **Valence** is represented by two or more sets of **Basis Functions**. This allows for description of aspherical atomic environments in molecules. **3-21G**, **6-31G** and **6-311G** are split-valence basis sets.

SSPD; *see* Spartan Spectra and Properties Database.

Stationary Point. A point on a **Potential Energy Surface** for which all energy first derivatives with respect to the coordinates are zero. **Local Minima** and **Transition States** are stationary points.

STO-3G. A **Minimal Basis Set**. Each atomic orbital is written in terms of a sum of three **Gaussian** functions taken as best fits to **Slater**-type (exponential) functions.

Systematic Conformation Search. An exhaustive search of **Conformers** resulting from stepping through all torsional angles (including constrained torsions associated with flexible rings). This is the only procedure that guarantees identification of the **Global Minimum**.

T1. A combination of quantum chemical models and empirical parameters formulated to reproduce **Heats of Formation** obtained from the **G3(MP2) Model** using 2-3 orders of magnitude less computation. T1 reproduces experimental heats with an RMS error of ~8 kJ/mol (the same error as obtained from the **G3(MP2) Model**).

Tautomer. An isomer related by rearrangement of hydrogen atoms, for example vinyl alcohol is a tautomer of acetaldehyde. All tautomers are isomers but not all isomers are tautomers.

TDDFT (Time Dependent Density Functional Theory).

Theoretical Model. A "recipe" leading from the **Schrödinger Equation** to a general computational scheme. A theoretical models needs to be unique and well defined and, to the maximum extent possible, be unbiased by preconceived ideas. It should lead to **Potential Energy Surfaces** which are continuous. It is also desirable (but not required) that a theoretical model be **Size Consistent** and **Variational**. Finally, a theoretical model will be applicable for the problems of interest.

Theoretical Model Chemistry. The set of results following from application of a particular **Theoretical Model**.

Thermochemical Recipes. Combinations of quantum chemical models and (in the case of **T1**) empirical parameters to reproduce

experimental (or in the case of **T1**) **G3(MP2) Heats of Formation. G3(MP2)** and **T1** are thermochemical recipes.

Thermodynamically-Controlled Reaction. A chemical reaction which has gone all the way to completion, and the ratio of different possible products is related to their thermochemical stabilities according to the **Boltzmann Equation**.

Thermodynamic Product. The product of a reaction which is under **Thermodynamic Control**.

Total Charge. The sum of the nuclear charges minus the total number of electrons.

Total Energy. The energy of a balanced chemical reaction in which a molecule is split into single particle fragments, that is, nuclei and electrons. Total energy is the standard way to report energy data derived from quantum chemical models (except **Semi-Empirical Models** and **Thermochemical Recipes**).

Transition State. A **Stationary Point** on a **Potential Energy Surface** in which all but one of the elements in the diagonal representation of the **Hessian** are positive, and one element is negative. Corresponds to the highest-energy point on the **Reaction Coordinate**.

Transition-State Geometry. The geometry (bond lengths and angles) of a **Transition State**.

Transition State Theory. The notion that all molecules react through a single well-defined **Transition State**.

Triplet. A molecule with two unpaired electrons.

Unrestricted SCF. An **SCF** procedure which does not restrict electrons to be paired on orbitals.

UV/visible Spectrum. The spectrum resulting between ground and excited electronic states.

Valence. Electrons which are delocalized throughout the molecule and participate in chemical bonding (2s, $2p_x$, $2p_y$, $2p_z$ for first-row elements, 3s, $3p_x$, $3p_y$, $3p_z$ for second-row elements, etc.).

Valence Orbital. A **Molecular Orbital** that is primarily involved with the **Valence** rather than the **Core**.

van der Waals Interactions. Interactions which account for short-range repulsion of non-bonded atoms as well as for weak long-range attraction.

van der Waals Radius. The radius of an atom (in a molecule), which is intended to reflect its overall size. van der Waals radii are used to define space-filling models.

van der Waals Surface. A surface formed by a set of interpreting spheres (atoms) with specific **van der Waals radii**, and which is intended to represent overall molecular size and shape.

Variational. Methods for which the calculated energy represents an upper bound to the exact (experimental) energy. **Hartree-Fock** and **Configuration Interaction Models** are variational while **Møller-Plesset Models**, **Density Functional Models** and **Semi-Empirical Models** are not variational.

Vibrational Frequencies. The energies at which molecules vibrate. Vibrational frequencies correspond to the peaks in an infrared and Raman spectrum.

Wave function. The solution of the **Schrödinger Equation**. In the case of the hydrogen atom, a function of the coordinates which describes the motion of the electron as fully as possible. In the case of a many-electron system a function which describes the motion of the individual electrons.

Zero-Point Energy. The energy of molecular vibration at 0K, given as half the sum of the **Vibrational Frequencies** times Planck's constant.

Z Matrix. A set of internal coordinates (bond lengths, bond angles and dihedral angles only) describing molecular geometry. Of historical interest only. Not supported in ***Spartan***.

Zwitterion. A neutral valence structure which incorporates both a formal positive charge and a formal negative charge.